Canadian Digestive Diseases Week™ 2018

TORONTO, ON
FAIRMONT ROYAL YORK
FEBRUARY 9 - 12

# EXHIBIT & ABSTRACT GUIDE



Canadian Association of Gastroenterology
L'Association Canadienne de Gastroentérologie

**A world free from immune and inflammatory diseases. That's our vision.**

Janssen is committed to improving patients' lives through a growing **product portfolio**, an innovative product **pipeline**, and **patient care** programs

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RGBM170696E | Janssen Inc. 19 Green Belt Drive | Toronto, ON | M3C 1L9 | www.janssen.com/canada

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SAVE THE DATE

**Come experience CDDW™ in Banff, showcasing the best of Canadian gastroenterology and hepatology.**

Canadian Digestive Diseases Week 2019

CDDW™ 2019
BANFF, AB
FAIRMONT BANFF SPRINGS
FEBRUARY 24 - MARCH 6

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The Gastro Expo allows sponsors and exhibitors to showcase their latest products and innovations in live, 30-minute presentations. The Gastro Expo rooms are located in Network Hall - lunch and nutrition break refreshments will also be available. Gastro Expo sessions are the responsibility of the company and are neither endorsed nor accredited by the CAG.

## GASTRO EXPO A

**FRIDAY, FEBRUARY 9, 2018**

11h45-12h15
Intercept Pharma Canada Inc.
Long-term data for obeticholic acid in PBC
*Vlad Popovic, MD*

14h30-15h00
Janssen Inc.
EXITING HELL BAR: A Real Life Patient Story *Dr. Remo Panaccione*

**SATURDAY, FEBRUARY 10, 2018**

10h30-11h00
Janssen Inc.
LOST AND FOUND: A Real Life Crohn's Story
*Dr. Gabor Kandel & Crohn's and Colitis Canada*

12h45-13h15
AbbVie
IBD Research in Canada: Past, Present and Future,
*AbbVie Medical Affairs*

15h00-15h30
Allergan (visit booth #108 for more details)

**SUNDAY, FEBRUARY 11, 2018**

12h45-13h15
AbbVie
IBD Research in Canada: Past, Present and Future,
*AbbVie Medical Affairs*

## GASTRO EXPO B

11h45-12h15
Allergan (visit booth #108 for more details)

14h30-15h00
Olympus Canada Inc.
Advanced Polyp Detection
*Dr. Seth A. Gross, NYU Langone Medical Centre*

10h30-11h00
PENTAX Medical (visit booth #116 for more details)

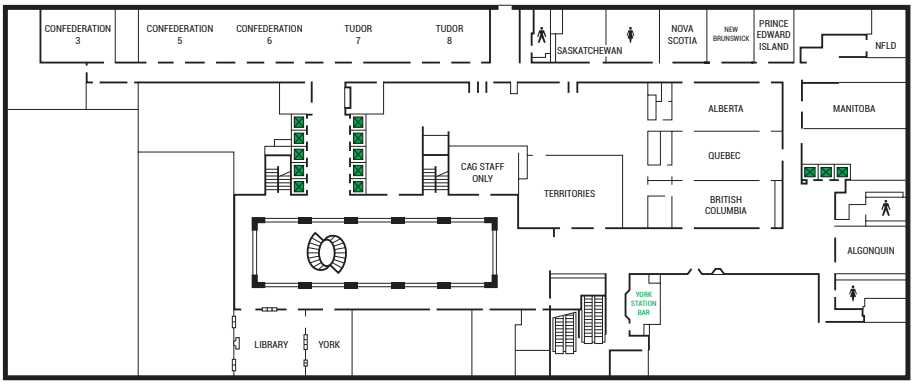
12h45-13h15
Gilead Sciences Canada, Inc. (visit booth #131 for more details)

15h00-15h30
Takeda Canada, Inc.
Case Based Discussions

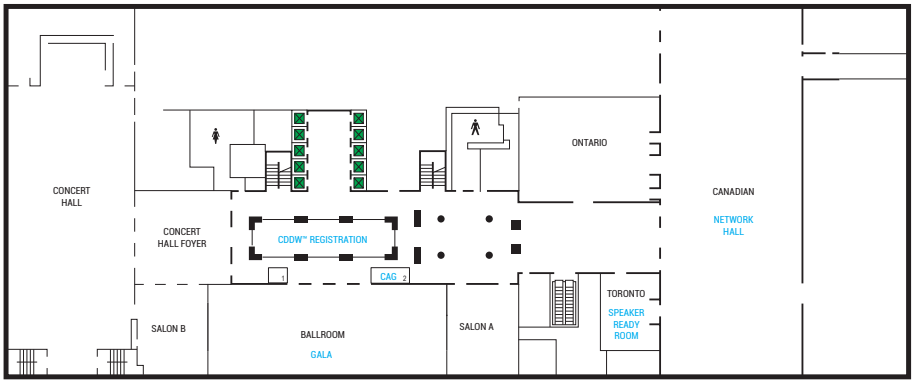
10h30-11h00
Shire Pharma Canada ULC
Tips for Managing Patients Requiring IV Hydration
*Dr. Don Duerksen*

12h45-13h15
Ferring Pharmaceuticals (visit booth #130 for more details)

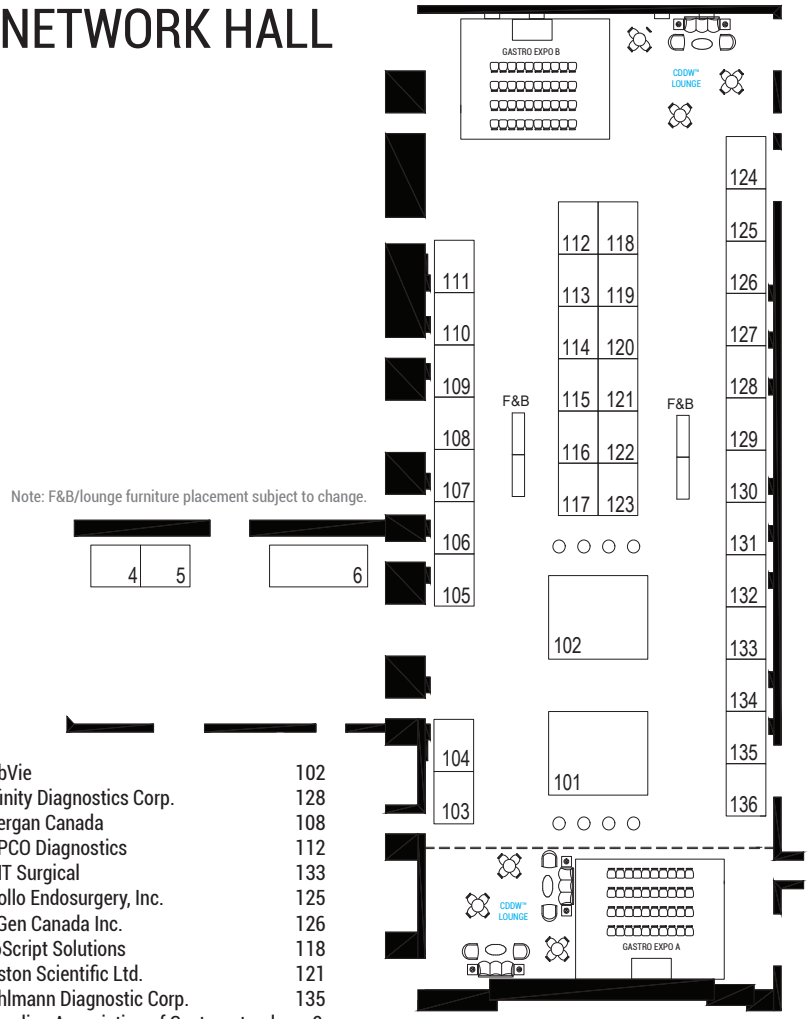
# Main Mezzanine




# Convention Floor



# NETWORK HALL

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Company: **AbbVie**
Address: 8401 Trans-Canada
St-Laurent, QC H4S 1Z1
Contact: Chantal Néron
Telephone: 888-703-3006
Email: chantal.neron@abbvie.com
Booth #: 102

AbbVie is a global, research-based biopharmaceutical company that combines the focus and passion of a leading-edge biotech with the expertise and structure of a long-established pharmaceutical leader. The company's mission is to use its expertise, dedicated people and unique approach to innovation to develop and market advanced therapies that address some of the world's most complex and serious diseases. The company has several core areas of focus, including gastroenterology and hepatitis C. AbbVie aims to help patients live healthier lives and collaborate on sustainable healthcare solutions. For further information, please visit www.abbvie.ca

Company: **AFFINITY Diagnostics Corp.**
Address: 194 Wildcat Road
Toronto, ON M3J 2N5
Contact: Daniel Libertucci
Telephone: 416-650-6300
Email: info@affinitydiagnostics.ca
Booth #: 128

AFFINITY Diagnostics Corp. is a provider of high quality in-vitro diagnostic assays for clinical and research laboratory use. Our Featured Products for CDDW 2018 are the IDK® CALPROTECTIN ELISA, and the PREVENTIS QUANTONCAL point-of-care smartphone device. Fecal Calprotectin is a marker for inflammatory and neoplastic gastrointestinal diseases, and is also an ideal marker for therapy monitoring in IBD patients. The IDK® Calprotectin ELISA enables the differential diagnosis between Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD). The PREVENTIS QUANTONCAL device provides the same performance as the IDK® Calprotectin ELISA, but with the added benefits of at-home testing, and smartphone integration. At AFFINITY, our commitment to providing quality in our products and excellence in our service is the backbone of our business, and the strength of our organization. For more information please e-mail us at: info@affinitydiagnostics.ca

Company: **Allergan Canada**
Address: 85 Enterprise Blvd., Suite 500
Markham, ON L6G 0B5
Contact: Sara Colman
Telephone: 800-668-6427
Email: MR-General_Inquiry@Allergan.com
Booth #: 108

Allergan is a global specialty pharmaceutical company with a full GI portfolio which includes products like VIBERZI®, CONSTELLA®, ASACOL® 800 and SALOFALK®. Additionally, Allergan has an exciting GI pipeline in clinical development, with products for gastroparesis, NASH and IBD.

Company: **Alpco**
Address: 26-G Keewaydin Dr.
Salem, NH 03079 USA
Contact: Bethany Bell
Telephone: 800-592-5726
Email: bbell@alpco.com
Booth #: 112

ALPCO offers a wide range of testing solutions, providing scientists and healthcare professionals with vital tools for advancing research and improving quality of care. Our product portfolio features immunoassays to investigate metabolic disorders, celiac disease, IBD and pancreatic insufficiency including: adiponectin, c-peptide, chromogranin A, zonulin, calprotectin, and pancreatic elastase. Additionally, our therapeutic drug monitoring tools can assess response to biologics for IBD.

Company: **AMT Surgical**
Address: 20 Steckle Place, Unit 16
Kitchener, ON N2E 2C3
Contact: Amanda Habermehl
Telephone: 888-803-6799
Email: info@amtsurgical.com
Booth #: 133

Leading the way in safety and performance, AMT is the leading supplier of surgical systems in Canada. We focus on providing our customers with surgical solutions that optimize patient safety, clinical performance, ease of use and cost-effectiveness.

Company: **Apollo Endosurgery, Inc.**
Address: 1120 S. Capital of Texas Hwy, Bldg. 1,
Ste. 300 Austin, TX 78746
Contact: Sarah Ammons
Telephone: 512-279-5104
Email: sarah.ammons@apolloendo.com
Booth #: 125

Apollo Endosurgery, Inc. is a medical device company focused on less invasive therapies for the treatment of obesity, a condition facing over 600 million people globally, as well as other gastrointestinal disorders. Our device based therapies are an alternative to invasive surgical procedures, thus lowering complication rates and reducing total healthcare costs. Apollo's products are offered in over 80 countries today.

Company: **ATGen Canada Inc.**
Address: 500 boul. Cartier Ouest, Suite 128
Laval, QC H7V 5B7
Contact: Gaétan Huneault
Telephone: 514-557-2791

Email: gaetan@atgenglobal.com
Booth #: 126

ATGen Canada Inc., is an immunodiagnostic company focused on the development of in vitro diagnostic devices for the analysis of patients' immune function. Immunosurveillance performed by lymphoid cells is important in immunity against infections and tumor cells. NK Vue™, the first in vitro diagnostic device developed by ATGen is a Class II In Vitro Diagnostic Device (IVDD) for assessing changes in the immune system which could be indicative of a condition or disease where NK cell activity has been shown to be affected. Nk Vue is the first and only IVDD approved for commercial use in Canada for the measurement of NK cell activity. Please visit www.atgencanada.com to learn more about NK cells.

Company: **BioScript Solutions**
Address: 77 Vaughan Harvey Blvd. Suite 305
Moncton, NB E1C 0K2
Contact: Marla Pisegna
Telephone: 506-260-4224
Email: mpisegna@bioscript.ca
Booth #: 118

The BioScript Solutions group of companies represent a full-service support system for complex drug therapies. BioScript pharmacy is the only Canadian specialty pharmacy with a coast to coast network with pharmacies in all 10 provinces.The trained pharmacists act as an extension of your patient care team. Bioscript simplifies the complicated by providing seamless and integrated case management tools, tracking patient adherence, while ensuring your patients are receiving the best pharmaceutical assistance to support the unique demands of their chronic illness. BioScript Solutions is known to be flexible, and great partner in health.

Company: **Boston Scientific Ltd.**
Address: 6430 Vipond Dr.
Mississauga, ON L5T 1W8
Contact: Kristin Muzylo
Telephone: 888-857-1990
Email:
Booth #: 121

Boston Scientific is dedicated to transforming lives through innovative medical solutions that improve the health of patients around the world.

Company: **BUHLMANN Diagnostics Corp.**
Address: 105 Route 101A, Ste 1
Amherst, NH 03031 USA
Contact: Stacy Smith
Telephone: 603-732-0674 ext 220
Email: sas@buhlmannlabs.com
Booth #: 135

BÜHLMANN has developed into THE CALPROTECTIN COMPANY with highest quality standards and its determination to increase the knowledge and application of fecal calprotectin (fCAL). BUHLMANN Diagnostics Corp is the exclusive North American affiliate for BÜHLMANN Laboratories in Switzerland, offering the BÜHLMANN fCAL® ELISA, BÜHLMANN fCAL® turbo for testing on most clinical chemistry analysers, Quantum Blue® fCAL Rapid Test and IBDoc®, the first self- testing application for fecal calprotectin in IBD patients. Visit www.buhlmannlabs.com or email info@buhlmannlabs.com for more information.

Company: **Canadian Association of Gastroenterology**
Address: 1540 Cornwall Road, Suite 224
Oakville, ON L6J 7W5
Contact: Paul Sinclair
Telephone: 888-780-0007
Email: cagoffice@cag-acg.org
Booth #: 2

Over 1100 members including gastroenterologists, surgeons, pediatricians, radiologists and basic scientists comprise the CAG. CAG members are actively involved in research, education and patient care in all areas of digestive health and disease, contributing to the economic and social health of all Canadians.

Company: **Canadian Digestive Health Foundation**
Address: 2525 Old Bronte Road, Suite 455
Oakville, ON L6M 4J2
Contact: Mackenzie Leavitt
Telephone: 416-729-7569
Email: Mackenzie@CDHF.ca
Booth #: 6

When your patients Google 'Digestive Health,' they are faced with nearly 7 million results. How do they separate the good information from the bad? CDHF.ca is Canada's trusted resource on digestive health. As the foundation of CAG, our mission is to provide value to donors, sponsors and health care professionals through information, programs and awareness initiatives.
Our resources help health care professionals explain complex, science-based information to their patients in easy to understand and engaging ways. Visit us at CDDW™ to learn more about CDHF, and how we can help you and your patients.

Company: **Celgene Inc.**
Address: 6755 Mississauga Road, Suite 600
Mississauga, ON L5N 7Y2
Contact: Sabrina Paiva
Telephone: 289-291-4778
Email: spaiva@celgene.com
Booth #: 110

Celgene Corporation is an integrated global biopharmaceutical company engaged primarily in the discovery,

development and commercialization of novel therapies for the treatment of cancer and other severe immune, inflammatory diseases through gene and protein regulation. For more information, please visit the company's website at www.celgene.ca

Company: **Cook Medical**
Address: 165 Mostar Street
Stouffville, ON L4A 0Y2
Contact: Tony Ranucci
Telephone: 800-668-0300
Email: www.cookmedical.com
Booth #: 113

Since 1963, Cook Group companies have been among the leaders in developing healthcare devices that have improved lives around the world. With sales and marketing offices worldwide, we are at the forefront of medical research and product development in minimally invasive medical device technology for diagnostic and therapeutic procedures.

Company: **Crohn's and Colitis Canada**
Address: 600-60 St. Clair Ave. E.
Toronto ON M4T 1N5
Contact: Emily Cordeaux
Telephone: 416-920-5035 x252
Email: research@crohnsandcolitis.ca
Booth #: 4

Crohn's and Colitis Canada (CCC) was founded in 1974 by a small group of concerned parents hoping to help their children and others living with Crohn's or colitis. Since then, CCC has grown to become the only Canadian volunteer-based charity focused on finding the cures for Crohn's disease and ulcerative colitis and improving the lives of children and adults affected by these diseases. We are one of the top two health charity funders of Crohn's and colitis research in the world, investing over $100 million in research since 1974, leading to important breakthroughs in genetics, gut microbes, inflammation and cell repair as well as laying the groundwork for new and better treatments. We are transforming the lives of people affected by Crohn's and colitis (the two main forms of inflammatory bowel disease) through research, patient programs, advocacy, and awareness. To learn more about us, please visit crohnsandcolitis.ca.

Company: **EndoSoft LLC**
Address: 135 Broadway
Schenectady, NY 12305
Contact: Abhishek Bajaj
Telephone: 518-831-8064
Email: abajaj@endosoft.com
Booth #: 119

EndoSoft provides GI specialty specific enterprise-wide technology solutions to include Hospitals, surgery centers and practices. With over twenty years of experience solving specific healthcare challenges by improving workflow and interoperability. EndoSoft's offerings include EHR developed for specific specialty areas, procedure documentation, image management, infection control, inventory management, scheduling, billing, workflow assessments and reporting.

Company: **Ferring Pharmaceuticals**
Address: 200 Yorkland Boulevard, Suite 500
Toronto, ON M2J 5C1
Contact: Curtis Fichtner
Telephone: 800-263-4057
Email: Curtis.Fichtner@Ferring.com
Booth #: 130

Headquartered in Switzerland, Ferring Pharmaceuticals is a research-driven, specialty biopharmaceutical group that is active in global markets. The company identifies, develops, and markets innovative products in the areas of reproductive health, urology, gastroenterology, endocrinology, and orthopaedics. Ferring has its own operating subsidiaries in nearly 60 countries, employs 5,000 people throughout the world, and markets its products in 110 countries. Ferring Canada's therapeutic focus is on urology, gastroenterology, and reproductive health. To learn more about Ferring or its products, visit www.ferring.ca

Company: **Gastrointestinal Society (Badgut)**
Address: 231-3665 Kingsway
Vancouver, BC V5R 5W2
Contact: Gail Attara
Telephone: 866-600-4875
Email: gail@badgut.org
Booth #: 5

As the Canadian leader in providing trusted, evidence-based information on all areas of the gastrointestinal tract, the Gastrointestinal Society is committed to improving the lives of people with GI and liver conditions by supporting research, advocating for appropriate patient access to health care, and promoting gastrointestinal and liver health. Annually, physicians order ~550,000 of our free pamphlets and our websites draw 750,000+ unique visitors. We hold free BadGut® Lectures on a variety of topics. An annual subscription to our Inside Tract® newsletter is $20.

Company: **Gilead Sciences Canada Inc.**
Address: 6711 Mississauga Rd., Suite 600
Mississauga, ON L5N 2W3
Contact:
Telephone: 905-363-8008
Email: Canada_info@gilead.com
Booth #: 131

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients

suffering from life-threatening diseases. Gilead has operations in more than 30 countries worldwide, with headquarters in Foster City, California. Gilead Sciences Canada, Inc. is the Canadian affiliate of Gilead Sciences, Inc., and was established in Mississauga, Ontario in 2005.

Company: **Innomar Strategies**
Address: 3470 Superior Court
Oakville, ON L6L 0C4
Contact: Susan Arthur
Telephone: 905-847-4310 x7354
Email: sarthur@innomar-strategies.com
Booth #: 111

Innomar Strategies, a part of AmerisourceBergen, is the leading patient support provider in the Canadian specialty biopharmaceutical market. We deliver end-to-end commercialization solutions to improve product access, increase supply chain efficiency and enhance patient care. Strategic consulting, patient support programs, nursing and clinical services, and specialty pharmacy and logistics are just a few of our key areas of specialization. We partner closely with manufacturers, healthcare providers, pharmacies and payers to ensure patients have consistent and reliable access to specialty medication. With our integrated approach and commitment to best-in-class care, Innomar Strategies helps navigate the patient journey to optimize health outcomes. Visit us at www.innomar-strategies.com

Company: **Intercept Pharma Canada Inc.**
Address: 90 Burnhamthorpe Road West,
14th Floor Mississauga, ON L5B 3C3
Contact: Jamie Twiselton
Telephone: 877-559-4278
Email: jamie.twiselton@interceptpharma.com
Booth #: 106

Intercept is a biopharmaceutical company focused on the development and commercialization of novel therapeutics to treat progressive non-viral liver diseases, including primary biliary cholangitis (PBC), nonalcoholic steatohepatitis (NASH), primary sclerosing cholangitis (PSC) and biliary atresia. Founded in 2002 in New York, Intercept now has operations in the United States, Europe and Canada. For more information about Intercept, please visit www.interceptpharma.com.

Company: **Janssen Inc.**
Address: 19 Green Belt Dr
Toronto, ON M3C 1L9
Contact: Shila Murley
Telephone: 416-986-8245
Email: smurley@its.jnj.com
Booth #: 101

Janssen Inc. is a leading healthcare company offering innovative products in areas of high unmet medical need like oncology, immunology, neuroscience, infectious diseases and vaccines, and cardiovascular and metabolic diseases. Janssen Inc., chef de file dans le domaine des soins de santé, offre des produits novateurs là où il existe encore d'importants besoins médicaux sans options thérapeutiques, comme l'oncologie, l'immunologie, la neuroscience, les maladies infectieuses et vaccins, et les maladies cardiovasculaires et métaboliques.

Company: **LABORIE**
Address: 2101 Boulevard Lapiniere
Brossard, QC J4W 1L7
Contact: Christine Frewen
Telephone: 450-671-5901
Email: marketing@laborie.com
Booth #: 109

LABORIE is proud to celebrate 50 years of innovation and commitment to improving the lives of patients suffering from Urologic and Gastrointestinal disorders. LABORIE's product line includes solutions for Urodynamics, Anorectal Manometry, Uroflowmetry, Ultrasound and Pelvic Floor Rehabilitation. For more information on LABORIE products and educational offerings please visit www.laborie.com

Company: **Lupin Pharma Canada Ltd.**
Address: 1155 René-Lévesque Ouest,
Suite 2500
Montréal, QC H3B 2K4
Contact: Isabel Longval
Telephone: 514-866-3863
Email: Isabellongval@lupin.com
Booth #: 115

Lupin Pharma Canada is a subsidiary of Lupin, a pharmaceutical company committed to providing world-class medications. Founded in 1968, the company is named after the Lupin flower and shares the same inherent qualities of strength, determination and nurturing. Lupin, the 3rd largest Indian pharmaceutical company, and the 5th largest pharmaceutical company in the US by number of prescriptions, was established in Canada in 2014. Lupin Pharma Canada is focused on addressing unmet medical needs in gastroenterology by providing the medical community with Zaxine® (rifaximin) to manage patients with hepatic encephalopathy by reducing their risk of recurrence.

Company: **McKesson Canada**
Address: 4705 Dobrin Street
Saint-Laurent, Québec H4R 2P
Contact: Ian Sherwin
Telephone: 416-414-0811
Email: ian.sherwin@mckesson.ca
Booth #: 127

McKesson is in the business of better health and we touch the lives of patients in virtually every aspect of health care. At McKesson Canada, we partner with

insurers, hospitals, physicians' offices, pharmacies, pharmaceutical companies and others across the spectrum of care to build healthier organizations that deliver better care to patients in every setting. We believe in the importance of strong, vital organizations because we know that patients can only be healthy when our system is healthy. Est in 1905 in Montreal, Quebec; McKesson Canada operates in all 10 provinces and 3 territories with 13 distribution centres supplying over 55,000 products. It is the largest pharmaceutical distributor in Canada: we touch over 7,000 pharmacies daily and almost all hospitals, with a National Network of Specialty Pharmacies and close to 90 Infusion clinics performing almost 100,000 infusions annually.

Company: **MedReleaf Corp.**
Address: Markham, ON
Contact: Rebecca Siegal
Telephone: 289-317-1000 x1024
Email: rsiegal@medreleaf.com
Booth #: 132

MedReleaf Corp. is a Canadian owned and operated company licensed by Health Canada for the production and distribution of Medical Cannabis. We operate from our state-of-the-art production facility in Markham, Ontario where we are setting The Medical Grade Standard™. MedReleaf is the first – and only – ISO 9001 certified cannabis producer in North America, and the largest volume provider in Canada. Through extensive clinical research, and in concert with the Canadian medical community, we are dedicated to leading the way in the discovery of medicinal and therapeutic benefits of cannabis, and to sharing this knowledge with the world.

Company: **Medtronic Canada**
Address: 8455 Transcanadienne
St-Laurent, QC H4S 1Z1
Contact: Caroline Robert
Telephone: 877-664-8926
Email: caroline.robert@medtronic.com
Booth #: 103

As a global leader in medical technology, services and solutions, Medtronic helps to improve the lives and health of millions of people each year. We use our deep clinical, therapeutic, and economic expertise to address the complex challenges faced by healthcare systems today. Let's take healthcare Further, Together. Learn more at Medtronic.com. En tant que chef de file mondial du domaine des technologies, des services et des solutions médicales, Medtronic aide à améliorer la santé et la vie de millions de gens chaque année. Nous utilisons notre vaste expertise clinique, thérapeutique et économique pour relever les défis complexes auxquels sont aujourd'hui confrontés les systèmes de santé. Allons plus loin ensemble pour faire progresser les soins de santé. Pour en savoir plus, consultez le site Medtronic.com.

Company: **Merck Canada Inc.**
Address: 16750 Trans Canada Hwy.
Kirkland, QC H9H 4M7
Contact: Debra Manning
Telephone: 514-428-3477
Email: debra.manning@merck.com
Booth #: 105

For more than a century, Merck has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases.
For more information about our operations in Canada, visit www.merck.ca and connect with us on YouTube and Twitter @MerckCanada. Depuis plus d'un siècle, Merck, une entreprise biopharmaceutique mondiale de premier plan, invente pour la vie, produisant des médicaments et des vaccins pour un grand nombre des maladies les plus éprouvantes au monde. Pour de plus amples renseignements à propos de nos activités au Canada, visitez le site www.merck.ca et suivez-nous sur YouTube et Twitter @MerckCanada_FR.

Company: **Mylan EPD**
Address: 85 Advance Road
Toronto, ON M8Z 2S6
Contact: Jose Rodriguez
Telephone: 416-207-1208
Email: josel.rodriguez@mylan.ca
Booth #: 114

Mylan is one of the world's leading global pharmaceutical companies. Our portfolio of more than 2,700 separate products includes generic, brand name and over-the-counter medicines in a variety of dosage forms and therapeutic categories. The company has innovative R&D capabilities and is one of the world's largest active pharmaceutical ingredient manufacturers. Mylan is a global pharmaceutical company committed to setting new standards in healthcare. Our growing portfolio of more than 2,700 separate products includes generic, brand name and OTC medicines. We market our products in more than 165 countries and territories. Our global R&D and manufacturing platform includes more than 50 facilities.

Company: **NKS Health**
Address: 500 – 130 Dundas Street East
Mississauga, Ontario L5A 3V8
Contact: Nancy Simonot
Telephone: 905-232-2322
Email: nsimonot@nkshealth.ca
Booth #: 136

NKS Health is a unique, specialty pharmacy that focuses on injectable, infusion and biologic medications for primarily autoimmune diseases. NKS Health offers new levels of support for physicians and patients by bringing the best monitoring and marker testing from around the world to our patients here in Canada.

Our services include in home training, medication reviews and counselling, home blood work, nutrition expertise, compliance services and high-level customer service delivery. NKS works with the various industry patient support service programs to compliment and add to their existing services.
Our mission statement is to be the premier specialty pharmacy services provider, offering innovative programs, exceptional service and superior value. For our patients, we are committed to achieving better health... NKS Health.

Company: **Olympus Canada Inc.**
Address: 25 Leek Crescent
Richmond Hill, ON L4B 4B3
Contact: Roxanne DeAbreu-Breen
Telephone: 289-269-0204
Email: Roxanne.DeAbreu@olympus.com
Booth #: 123

Olympus Canada is at the forefront of leading edge technology for healthcare professionals to help improve patient outcomes and enhance quality of life. By enabling less invasive procedures for innovative diagnostic and therapeutic endoscopy, Olympus is transforming the future of healthcare. Our GI category delivers innovative technologies including our EVIS EXERA III platform as well as EndoTherapy devices for ESD, EUS, EBUS and ERCP. Visit the Olympus booth to view these technologies and more.

Company: **Oxford University Press, Inc.**
Address: New York, NY 10016

Contact: Matt Turney
Telephone: 212-726-6411
Email: matt.turney@oup.com
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Address: 522 Meloche
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Contact: Sue Khan
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Booth #: 124

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Telephone: 514-787-5114
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Yellowknife, NT X1A 2N1
Contact: Cammy Mailloux
Telephone: 867-669-4379
Email: cammy_mailloux@gov.nt.ca
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Scott Simpson
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## CAG SELECTED CLINICAL PRESENTATIONS FRIDAY, FEBRUARY 9, 08H00-09H30

A1

### MARKERS OF ACTIVATED INFLAMMATORY CELLS ARE ASSOCIATED WITH NON-ALCOHOLIC FATTY LIVER DISEASE AND INTESTINAL MICROBIOTA

K. Schwenger[1], L. Chin[3], A. Chelliah[4], H. Da Silva[5], A. teterina[6], E. Comelli[7], A. Taibi[2], B. Arendt[6], S. Fischer[6], J. Allard[6]

1. University of Toronto, Hamilton, ON, Canada; 2. Nutritional Sciences, University of Toronto, Toronto, ON, Canada; 3. Department of Pathology and Molecular Medicine, Kingston, ON, Canada; 4. Department of Pathology, Cork, Ireland; 5. Sunnybrook Health Sciences Center, Toronto, ON, Canada; 6. Toronto General Hospital, Toronto, ON, Canada; 7. Department of Nutritional Sciences, Toronto, ON, Canada

**Background:** Several mechanisms contribute to the pathogenesis of non-alcoholic fatty liver disease (NAFLD). The intestinal microbiota (IM) and liver immune function cells have been implicated in NAFLD, but data on their potential associations have been scarce.
**Aims:** The aim of this study was to investigate whether there are differences in hepatic inflammatory cell markers between NAFLD and healthy controls (HC), using the antigens CD45, CD163, CD20 and CD3, and to determine whether these markers are associated with specific IM.
**Methods:** This was a prospective, cross-sectional study of adults with biopsy-confirmed NAFLD and healthy controls (HC). Clinical and laboratory data were collected. Fecal IM were assessed by qPCR and immune cells by immunohistochemistry. NAFLD activity score (NAS) was used for disease severity.
**Results:** 42 subjects were studied: 8 HC and 34 NAFLD. Hematopoietic cell marker $CD45^+$ and Kupffer cell marker $CD163^+$ were higher in NAFLD compared to HC, and those with a NAS ≥5 had higher levels of $CD20^+$ cells a marker of B cells versus a NAS of 0 or 1-4. In 39 patients (5 HC, 34 NAFLD) IM was measured: *Faecalibacterium prausnitzii* was negatively correlated with $CD45^+$ ($r$=-0.394, $p$=0.015) and $CD163^+$ ($r$=-0.371, $p$=0.022) cells in the portal tract; *Prevotella* was negatively correlated with $CD20^+$ ($r$=-0.353, $p$=0.028) cells in the liver lobule and Archaea were positively correlated with $CD20^+$ ($r$=0.468, $p$=0.003) in the liver lobule.
**Conclusions:** Hepatic immune cell counts are increased in NAFLD versus HC and associated with disease severity. Specific immune cells in portal or lobular areas correlated with specific fecal IM, suggesting a role for IM in hepatic inflammation.

**Funding Agencies:** CIHR

A2

### GATHERING AND ASSESSING EVIDENCE TO INFORM A GUIDELINE ON SCREENING FOR COLORECTAL CANCER IN INDIVIDUALS WITH A FAMILY HISTORY

D. Leddin[1], D. Lieberman[5], G. Leontiadis[3], F. Tse[3], A.N. Barkun[2], J. Marshall[4], N. Samadder[9], H. Singh[8], J.J. Telford[7], J. Tinmouth[6], A. Abou-Setta[8], A.N. Wilkinson[10]

1. Dalhousie Univ, Halifax, NS, Canada; 2. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 3. McMaster University, Hamilton, ON, Canada; 4. McMaster University Medical Centre, Hamilton, ON, Canada; 5. Oregon Health & Science University, Portland, OR; 6. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 7. University of British Columbia, Vancouver, BC, Canada; 8. University of Manitoba, Winnipeg, MB, Canada; 9. Mayo Clinic, Phoenix, AZ; 10. University of Ottawa, Ottawa, ON, Canada

**Background:** Existing guidelines on colorectal cancer (CRC) screening for individuals with a family history (FH) of CRC or adenoma have not been based on systematic reviews or comprehensive assessment of the quality (=trustworthiness) of evidence (QoE).
**Aims:** To systematically review the literature to inform the ongoing development of a Canadian Association of Gastroenterology-supported Canadian and US guideline on CRC screening for individuals with FH of nonhereditary CRC or adenoma.
**Methods:** Multiple parallel systematic review streams, informed by a series of 10 literature searches, gathered evidence on 4 principal questions around the 1) effect of FH of CRC (or adenoma) on an individual's risk of CRC, 2) age at which screening should begin, 3) recommended screening tests, and 4) recommended testing intervals for individuals with FH of CRC or adenoma. The GRADE approach was used to assess the QoE.
**Results:** The relative risk (RR) of CRC among individuals with FH of 1 first-degree relative (FDR) with CRC was estimated to be approximately 2-fold greater than among those without. The RR increased with an increasing number of FDRs with CRC. A FH of only second-degree relatives was associated with no or minimally elevated risk. The risk of CRC was increased by FH of advanced adenoma, but not with FH of a non-advanced adenoma. The age-specific risk of CRC fell on a continuum: RR increased with decreasing age of affected FDR, and increasing age of the screened individual, but RR was elevated at all ages compared to those with no FH. All the above were of very low QoE. Using data on efficacy (QoE ranging from very low to high), patient preference (very low QoE), and cost-effectiveness (very low QoE), colonoscopy and FIT ranked highest among screening test for individuals with FH of a FDR with CRC. Data on the optimal interval for CRC screening were limited (very low QoE), but suggested a potential benefit of shorter intervals for some individuals with FH compared to those at average risk.
**Conclusions:** A FH of CRC or advanced adenoma is associated with a clinically important increased risk of CRC, which falls on an age continuum.

**Funding Agencies:** Canadian Partnership Against Cancer (CPAC)

A3

**COLORECTAL CANCER DEATHS WHILE AWAITING GASTROENTEROLOGY CONSULTATION AT A CANADIAN ACADEMIC CENTRE**

D. Motomura, T. Kulai, S. Williams

Dalhousie University, Halifax, NS, Canada

**Background:** Delays in access to gastrointestinal (GI) services have long been a concern of practicing gastroenterologists. Triage criteria used at the Queen Elizabeth II Health Sciences Centre (QEII HSC) in Halifax, Nova Scotia, are based on 2006 Canadian Association of Gastroenterology consensus recommendations. The demand for GI services at our academic centre has exceeded available resources and only urgent referrals are being seen within recommended timeframes. Non-urgent referrals are not being seen. Achieving nationally recommended targets for wait times remains a challenge and this raises concern for potential patient morbidity and mortality while awaiting assessment. To our knowledge, no previous studies have documented details surrounding death while awaiting GI consultation.
**Aims:** (1) Outline patient demographics and circumstances of death while awaiting GI consultation at the QEII HSC, (2) describe referrals received on these patients and (3) determine whether cause of death was related to reason for referral.
**Methods:** The Practice Affairs Committee at the QEII HSC is notified when a patient has died while on the GI waitlist. Basic demographic and referral information were collected on each case in addition to details surrounding the cause of death. Two gastroenterologists who are blinded to data collection reviewed original referrals and determined if the referral was triaged appropriately and whether cause of death is related, possibly related or unrelated to reason for referral. In case of disagreement between two physicians in the review process, a third independent physician provided opinion.
**Results:** From March 2015 to September 2017, 39 deaths occurred on the GI waitlist. Mean age was 70.3 years. The majority of referrals (61.5%) came from family physicians and most (92.3%) were felt to be appropriately triaged. The average interval time from referral to death was 348 days (range 4 - 1050 days). In each triage category, patients waited significantly longer than guideline-proposed wait times.
Of the 38 known causes of death, seven (18.4%) cases were directly related to referral diagnosis, while three (7.9%) cases were deemed possibly related. The most common cause of related death was colorectal cancer (n=6, 85.7%), and the most common reason for referral for these patients was anemia (n=4, 57.1%). Inappropriate triaging occurred in one of the seven related cases due to systems error.
**Conclusions:** Significant patient mortality on GI waitlist is due to the primary GI reason for referral. As wait times for GI consultations remain well above national recommendations, this review highlights the need for additional resource allocation towards addressing the growing problem of GI wait times in Nova Scotia.

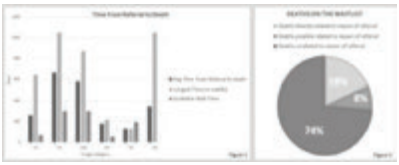


Figure 1. Time from referral to death. C2- Semi Urgent Consult. C3 - Non-Urgent Consult. C3S- Colon Cancer Screening. E2 - Semi Urgent Endoscopy. E3 - Non-Urgent Endoscopy.

Figure 2. Deaths related to original reason for referral

**Funding Agencies:** None

A4

**PERORAL ENDOSCOPIC MYOTOMY IS EFFECTIVE AND SAFE IN NON-ACHALASIA ESOPHAGEAL MOTILITY DISORDERS: AN INTERNATIONAL MULTICENTER STUDY**

M. Khashab[1], M. Masckauchan[2], P. Familiari[3], P. Dragan-ov[4], H. Dakour Aridi[1], J. Cho[5], M. Ujiki[6], R. Rio Tinto[7], H. Louis[7], P. Desai[8], V. Velanovich[9], E. Albéniz[10], A. Haji[11], J. Marks[12], G. Costamagna[3], J. Devière[7], Y. Perbtani[4], M. Hedberg[6], F. Estremera[10], L. Martin Del Campo[12], D. Yang[4], M. Bukhari[1], O. Brewer[1], O. Sanaei[1], L. Fayad[1], A. Agarwal[1], V. Kumbhari[1], Y. Chen[2]

1. Johns Hopkins Medical Institutions, Baltimore, MD; 2. McGill University, Montreal, QC, Canada; 3. Università Cattolica del Sacro Cuore, Rome, Italy; 4. University of Florida, Gainesville, FL; 5. CHA Bundang Medical Center, Seongnam, Korea (the Republic of); 6. NorthShore University Health System, Evanston, IL; 7. Erasme University Hospital, Bruxelles, Belgium; 8. Surat Institute of Digestive Sciences, Surat, India; 9. University of South Florida Morsani College of Medicine, Tampa, FL; 10. Complejo Hospitalario de Navarra, Pamplona, Spain; 11. Kings College Hospital NHS Foundation Trust, London, United Kingdom; 12. University Hospitals Cleveland Medical Center, Cleveland, OH

**Background:** Peroral endoscopic myotomy (POEM) is an effective minimally invasive alternative modality to Heller myotomy for the treatment of achalasia. However, the efficacy of POEM in non-achalasia esophageal motility disorders has not yet been well demonstrated. These disorders include spastic esophageal conditions such as esophagogastric junction outflow obstruction (EGJOO), diffuse esophageal spasm (DES), and Jackhammer esophagus (JE).
**Aims:** The objective of this international multicenter study was to assess the clinical outcomes of POEM in patients with non-achalasia disorders, namely DES, JE, and EGJOO, in a large cohort of patients.



To view enlarged images and tables, please refer to Abstract Library.

**Methods:** This was a retrospective study at 11 centers. Consecutive patients who underwent POEM for EGJOO, DES, or JE between January 2014 and September 2016 were included, patients with achalasia were excluded. Rates of technical success (completion of myotomy), clinical response (symptom improvement and Eckardt score ≤ 3), and adverse events (AEs, severity per ASGE lexicon) were ascertained. LES and cardia myotomy was performed in all cases, although it is unknown if this is essential in patients with DES and JE.
**Results:** A total of 50 patients (56% female; mean age 61.7 years) underwent POEM for EGJOO (n=15), DES (n=17), and JE (n=18). Mean duration of symptoms was 53.2 months and most patients (68%) were treatment naïve. Technical success was achieved in all patients with a mean procedural time of 88.4 ± 44.7 min. The mean total myotomy length was 15.1 ± 4.7 cm. Clinical success was achieved in 93.3% of EGJOO and in 84.9% of DES/JE (p=0.41) with a median follow-up of 195 and 272 days, respectively. Chest pain improved in 88.9% of EGJOO and 87.0% of DES/JE (p=0.88). Mean Eckardt score decreased from 6.2 to 1.0 in EGJOO (p<0.001) and from 6.9 to 1.9 in DES/JE (p<0.001). A total of 9 (18%) AEs occurred and were rated as mild in 55.6% and moderate in 44.4%. These rates were comparable between both groups (13.3% vs 20%, p=0.58).
**Conclusions:** POEM is effective and safe in the management of non-achalasia esophageal motility disorders, which include diffuse esophageal spasm, jackhammer esophagus, and esophagogastric junction outflow obstruction. Although AEs occurred in 18% of patients, none were severe and all complications were managed intraprocedurally or conservatively. Given that DES and JE do not typically have EGJ outflow obstruction, whether LES myotomy is required in these patients remains to be determined and warrants further investigation.

**Funding Agencies:** None

A5

**FIRST-ONSET PSYCHIATRIC DISORDERS IN PREGNANT AND POST-PARTUM WOMEN WITH INFLAMMATORY BOWEL DISEASE IN ONTARIO, CANADA: A POPULATION-BASED STUDY**

S.N. Vigod[1], P. Kurdyak[2], H.K. Brown[3], G.C. Nguyen[4], L. Targownik[5], C. Seow[6], E.I. Benchimol[7]

1. Institute for Clinical Evaluative Sciences, Department of Psychiatry, University of Toronto, Toronto, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Department of Psychiatry, Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; 4. Mount Sinai Hospital Centre for IBD, Department of Medicine, University of Toronto, Toronto, ON, Canada; 5. University of Manitoba IBD Clinical and Research Centre, Department of Medicine, University of Manitoba, Winnipeg, MB, Canada; 6. University of Calgary IBD Centre, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; 7. Institute for Clinical Evaluative Sciences, Children's Hospital of Eastern Ontario IBD Centre, Department of Pediatrics, School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada

**Background:** Inflammation is associated with psychiatric illness, and patients with inflammatory bowel disease (IBD) have elevated risk of anxiety and depression. Pregnancy alters immune functioning, and inflammation may result in psychiatric disorders in pregnancy and postpartum.
**Aims:** Determine risk and predictors of psychiatric disorders in women with IBD during pregnancy and postpartum.
**Methods:** Among all women with a singleton live birth in Ontario 2002-2014 with no history of pre-pregnancy psychiatric disorder, we identified women with IBD using validated algorithms applied to health administrative data (Ontario Crohn's and Colitis Cohort). The primary outcome was any psychiatric disorder during pregnancy or in the first postpartum year (outpatient, emergency or hospitalization). Cox proportionate hazard regression compared risk of psychiatric disorders in those with/without IBD, adjusting for maternal age, year, income, rurality, prenatal care, and C-section, reported as hazard ratios (aHR). In women with IBD only, logistic regression determined predictors of new-onset psychiatric disorder overall, and postpartum.
**Results:** Risk of new psychiatric disorder in 3721 women with IBD was 22.7% vs 20.4% in 798,908 without IBD (aHR 1.12, 95%CI 1.05-1.20). Most healthcare contacts were for depression or anxiety in outpatient primary care settings. Risk was elevated for Crohn's disease (aHR 1.12, 95%CI 1.02-1.23), but not ulcerative colitis (aHR 1.09, 95%CI 0.98-1.21), and post-partum (aHR 1.20, 95%CI 1.09-1.31), but not during pregnancy (aHR 1.04, 95%CI 0.94-1.15). Predictors noted in Table.
**Conclusions:** Women with IBD have increased risk for new-onset psychiatric disorders, especially depression and anxiety, in the peripartum period. Providers should be aware of this elevated risk to increase opportunities for prevention, early identification and treatment.

Predictors of risk of psychiatric diagnosis in pregnant women with IBD

| | Odds Ratio (95% CI) |
|---|---|
| ***Psychiatric disorder in pregnancy or postpartum*** | |
| Age in years (ref: 20 years)[a]<br>25y<br>30y<br>35y<br>40y | <br>0.69 (0.55-0.88)<br>0.56 (0.39-0.80)<br>0.52 (0.35-0.77)<br>0.57 (0.40-0.81) |

| | |
|---|---|
| Year of delivery | 0.95 (0.93-0.97) |
| No. prenatal visits | 1.06 (1.04-1.08) |
| Prenatal care provider (ref: ≥75% care by GP/FP)<br><4 prenatal visits with any physician<br>≥75% care by obstetrician<br>Shared care | <br>0.62 (0.33-1.14)<br>0.54 (0.42-0.69)<br>0.79 (0.62-0.99) |
| Previous IBD admission | 0.81 (0.67-0.99) |
| ***Postpartum psychiatric disorder only*** | |
| Age in years | 0.98 (0.96-0.999) |
| Year of delivery | 0.94 (0.90-0.97) |
| No. prenatal visits | 1.04 (1.02-1.06) |
| Prenatal care provider (ref: ≥75% by GP/FP)<br><4 prenatal visits with any physician<br>≥75% care by obstetrician<br>Shared care | <br>0.42 (0.18-0.96)<br>0.61 (0.46-0.82)<br>0.69 (0.52-0.92) |
| ADG comorbidity score in 2y prior to pregnancy | 1.06 (1.02-1.10) |
| Infant mortality | 12.7 (2.26-70.9) |

[a]Reported at specific ages since association was non-linear. NB infant characteristics not considered for pregnancy and postpartum model since intrapartum events not influenced by post-birth variables

**Funding Agencies:** Medical Psychiatry Alliance

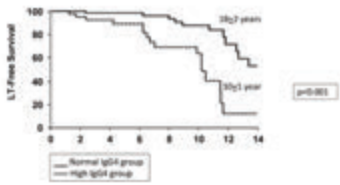
A6

**HIGH SERUM IGG4 IS ASSOCIATED WITH A SHORTER TIME TO CIRRHOSIS DEVELOPMENT, HEPATIC DECOMPENSATION, AND LIVER TRANSPLANTATION IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS**

L. Du[1], A.J. Montano-Loza[3], F. Peerani[2]

1. University of Toronto, Toronto, ON, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Division of Gastroenterology & Liver Unit , University of Alberta , Edmonton, AB, Canada

**Background:** Primary sclerosing cholangitis (PSC) is an immune-mediated biliary disorder of unknown etiology for which there is no effective treatment. Eventually all PSC patients progress to end-stage liver disease and require liver transplantation (LT).
**Aims:** The purpose of this study is to better prognosticate the development of complications related to portal hypertension and the requirement for LT in PSC patients based on IgG4 levels.
**Methods:** We evaluated 121 PSC patients seen at the University of Alberta Hospital between 2002 and 2017. Patients with a radiologic and/or histologic diagnosis of PSC with at least one IgG4 level were included and categorized as high IgG4 group >70 mg/dL or normal IgG4 group ≤70 mg/dL (this IgG4 cut-off value was the best discriminant for LT-free survival in a previous study). The presence of cirrhosis was defined by imaging studies, Fibroscan, or biopsy. Decompensation date was recorded as the first episode of variceal bleeding, ascites, or hepatic encephalopathy. Data is reported as a mean ± standard error for continuous variables and as a percentage for categorical variables. Time to cirrhosis, portal hypertensive complications, and LT-free survival were calculated by Kaplan-Meier methods and compared by the Log Rank (Mantel-Cox) test. Factors associated with LT-free survival were analyzed by Cox regression univariate and multivariable analyses.
**Results:** 121 patients were followed over a period of 7.4±5 years (1-25 years). 78 patients (65%) were male, and the mean age at diagnosis of PSC was 35±16 years. IBD was present in 85 patients (70%) including 59 ulcerative colitis patients, 22 Crohn's disease patients, and 4 type unclassified. High IgG4 levels were found in 41 patients (155±74 mg/dL), and normal IgG4 levels were found in 80 patients (30±19 mg/dL), with a mean number of IgG4 determinations of 2.7±0.2. Patients with high IgG4 levels had higher ALP levels (428±49 *vs.* 279±33 U/L, p=0.01), higher INR (1.2±0.4 *vs.* 1.0±0.2, p=0.05), lower albumin levels (36±1 *vs.* 40±1 g/L, p=0.01), higher PSC Mayo scores (0.64±0.3 *vs.* 0.12±0.2, p=0.04), and higher MELD scores (11±1 *vs.* 9±1, p=0.007). Furthermore, patients with high IgG4 levels had a shorter time to cirrhosis development (9±1 *vs.* 13±1 years, p=0.04) and decompensation (11±1 *vs.* 20±1 years, p=0.05). Lastly, LT-free survival was shorter in patients with high IgG4 levels (10±1 *vs.* 18±2 years, p<0.001, Figure 1). Patients with high IgG4 had an increased risk for LT (HR 3.8, 95% 1.38-12.87, p=0.03), after controlling for age at diagnosis and MELD score.
**Conclusions:** PSC patients with high IgG4 levels have more aggressive disease, reflected by higher ALP levels, MELD scores, and PSC Mayo scores, as well as a shorter time to cirrhosis development, decompensation, and liver transplantation.




To view enlarged images and tables, please refer to Abstract Library.

Figure 1

**Funding Agencies:** None

## CAG/CCC STUDENT PRIZE PAPER PRESENTATIONS FRIDAY, FEBRUARY 9, 10H00-11H30

## CAG Student Prize

A7

### THE ROLE OF PROTEASE-ACTIVATED RECEPTOR-2 IN *GIARDIA* INDUCED DISRUPTIONS OF THE INTESTINAL MUCUS LAYER

E. Fekete[2], C.B. Amat[2], T. Allain[2], M. Saiffeddine[2], M. Hollenberg[2], K. Chadee[3], A. Buret[1]

1. University of Calgary, Calgary, AB, Canada; 2. Biological Sciences, University of Calgary, Calgary, AB, Canada; 3. Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, AB, Canada

**Background:** Disruptions of the intestinal mucus barrier have been implicated in a variety of intestinal disorders. The mechanisms behind these disruptions remain unclear. We recently demonstrated that the enteric parasitic pathogen *Giardia duodenalis* alters the mucus layers of the small and large intestines at least in part via *Giardia* cysteine proteases.
**Aims:** We hypothesized that goblet cell function and mucus disruptions are modulated by activation of protease activated receptor 2 (PAR2), which is highly expressed through the gastrointestinal tract, and is known to regulate mucus production in the airway and stomach. We aimed to determine whether *Giardia's* cysteine proteases cleave and activate PAR2 on intestinal goblet cells, leading to modulation of their mucus producing activity.
**Methods:** The human colonic epithelial cell line LS174T was used for *in vitro* mucus studies. The presence of functional PAR1 or PAR2 was assessed with calcium signaling assays using the specific activating peptides TFLLRN or 2fLIGRLO, respectively. MUC2 mucin gene expression was assessed through quantitative PCR (qPCR) in LS174T incubated with either *Giardia* trophozoites or activating peptides, and with pre-treatment of cells with the PAR2 antagonist p2Pal-218S pepducin. qPCR was also used to measure changes in PAR2 gene expression in response to *Giardia*. Wild type and PAR2 deficient mice were infected with *Giardia* trophozoites. The thickness of the mucus layer was measured by fluorescently staining mucus with fluorescein-coupled WGA, and expression of Muc2 and Muc5ac genes were determined using qPCR.
**Results:** LS174T express functional and responsive PAR2, but little or no PAR1. Treatment of cells with 2fLIGRLO (PAR2 agonist), but not TFLLRN (PAR1 agonist), increased MUC2 gene expression. Incubation of cells with *Giardia* trophozoites also increased MUC2 mRNA production, and this increase was abolished by pre-treatment of cells with a PAR2 antagonist. *Giardia* decreased PAR2 mRNA in LS174T. *Giardia* infection increased the expression of Muc2 and Muc5ac in the colon, and increased Muc5ac expression in the jejunum of wild-type mice compared to uninfected controls. In PAR2-/- mice, *Giardia* infection reduced the expression of Muc5ac, but not Muc2 in the jejunum, but did not affect gene expression in the colon. *Giardia* infection caused a thinning of the mucus layer in wild-type mice. In contrast, the infection induced a thickening of the mucus layer in PAR2-/- mice.
**Conclusions:** Using a model of *Giardia* infection, the findings demonstrate that PAR2 plays a significant role in mucin gene regulation and function in mice and in a human colonic goblet cell line.

**Funding Agencies:** CCCNSERC

## CAG Student Prize

A8

### INFLUENCE OF MATERNAL SSRI EXPOSURE ON THE DEVELOPMENT OF THE ENTERIC NERVOUS SYSTEM

K. Prowse[1], F. Markovic[1], M. Wang[1], R. Borojevic[3], S. Raez Villanueva[1], K. Wiggers[1], A. Holloway[1], E. Ratcliffe[2]

1. Pediatric Gastroenterology, McMaster University, Hamilton, ON, Canada; 2. Pediatrics, McMaster University, Hamilton, ON, Canada; 3. McMaster University, Hamilton, ON, Canada

**Background:** Antidepressants, including selective serotonin reuptake inhibitors (SSRIs) are commonly used during pregnancy. Approximately 7% of women in North America require SSRI in the perinatal period. Perinatal exposure to SSRIs has been shown to disrupt the development of serotonergic signaling pathways in the brain. However, the potential for changes to the enteric nervous system (ENS) over a period of postnatal development has not been explored.
**Aims:** To test the hypothesis that perinatal exposure to SSRIs can influence the development of the ENS.
**Methods:** Female Wistar rats were given fluoxetine (10mg/kg/d) or vehicle (cookie dough) from 2 weeks prior to mating until weaning (postnatal day [P] 21). Offspring were collected from SSRI-treated and control rats on P1, P21 and P6 months to see if changes were persistent. Enteric neurons in the myenteric plexus were visualized in whole mount preparations of jejunum, ileum and colon. Total number (#) of enteric neurons (EN) and serotonergic neurons (SN) were visualized with immunostaining using antibodies to HuC/D and 5-HT, respectively. Percentage of SSRI-expressing enteric neurons were calculated as a percentage of total neurons using image analysis software (Velocity). Female (F) and male (M) offspring were analyzed separately.
**Results:** On P1, no significant differences were found in the total # of EN nor in SN between SSRI-exposed and control offspring in the jejunum, ileum and M colon (n=6-10). However, a significant decrease between the

total # of EN and SN was found in the SSRI-exposed F offspring colon (13.6% vs 9.3%; p=0.04; n=6-9). On P21, no significant differences were found in the total # of EN in the ileum and colon of SSRI-exposed and control offsprings. There was also no significant difference found between the percentage of SN between the SSRI-exposed and control ileum (n=6-10). Significant differences were found in the percentage of SN in both F (1.4% vs 7.6%; p=0.009); n=5-6) and M colons (1.7% vs 6.9%; p=0.002; n=5-8). At 6 months of age, there was no significant difference in the percentage of total # of EN nor in SN between SSRI-exposed and control offspring.
**Conclusions:** Our results suggest that SSRI exposure in the in utero and perinatal period play a role in serotonergic signaling pathways involved in the development of the enteric nervous system of the developing offspring. However, these changes improve over time, which may be attributed to the plasticity of the ENS.

**Funding Agencies:** CCFA Broad Foundation

## CCC Student Prize

A9
**MUCUS BARRIER INTEGRITY IS IMPAIRED BY A DYSFUNCTIONAL MESENCHYME**
V. Reyes-Nicolas, J.M. Allaire, C. Ouellet, R. Servant, V. Pomerleau, P. Garde-Granger, F. Boudreau, N. Perreault

Anatomie et Biologie Cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

**Funding Agencies:** CIHRScholarship Centre de Recherche Médicale de l'Université de Sherbrooke (CRMUS)

## CCC Student Prize

A10
**CORE-1 DERIVED *O*-GLYCOSYLATION OF THE MUCIN MUC2 PLAYS A KEY ROLE IN HOST DEFENSE AGAINST ENTERIC *CITROBACTER RODENTIUM* INFECTION**
L.S. Celiberto[2], J.Y. Chan[2], H.T. Law[2], K. Bhullar[2], L. Xia[3], D.C. Cavallini[4], B. Vallance[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. University of British Columbia, Vancouver, BC, Canada; 3. Oklahoma Medical Research Foundation, Oklahoma, OK; 4. Sao Paulo State University, Araraquara, Sao Paulo, Brazil

**Background:** Enteric bacterial pathogens are a major cause of diarrheal disease in developed as well as developing countries. To infect their hosts, most pathogens need to directly infect the intestinal epithelium, however to do so, they must cross the overlying intestinal mucus layer. Intestinal mucus is predominantly comprised of the mucin Muc2, a highly *O*-glycosylated protein with core 1 and core 3 derived *O*-glycans as its primary constituents. We previously showed that mice lacking Muc2 are highly susceptible to infection by *Citrobacter rodentium*, a mouse specific relative of the bacterial pathogen enterohemorrhagic *E. coli*, with Muc2 deficient mice carrying high pathogen burdens as well as suffering severe intestinal inflammation and epithelial damage. At present, it is unclear whether the protection provided by Muc2 reflects the actions of the Muc2 protein, its glycosylation, or both.
**Aims:** The aim of this study was to explore the role of Muc2 glycosylation in providing host defense in mice challenged with *C. rodentium*, by comparing the susceptibility of mice lacking Muc2, core 1 glycosylation or core 3 glycosylation.
**Methods:** Six to ten week old WT, *C1galt1*$^{f/f}$, *C1galt1*$^{-/-}$, *Core 3*$^{-/-}$ *and Muc2*$^{-/-}$ mice were infected with *C. rodentium* by oral gavage. Mice were monitored daily for morbidity throughout the experiment and were euthanized at day 6 of infection. Several tissues of interest were collected to verify bacterial colonization in the gut and at systemic sites. For histology, colon and cecum tissues were stained with hematoxylin-eosin, mounted on microscope slides and scored based on previously adapted scoring systems.
**Results:** Mice lacking core 3 glycosylation were roughly similar to WT mice in their modest susceptibility to *C. rodentium* infection. In contrast, mice expressing Muc2, but lacking core 1 glycosylation (*C1galt1*$^{-/-}$ mice) were similar to *Muc2*$^{-/-}$ mice in terms of showing increased susceptibility to *C. rodentium* characterized by dramatically increased intestinal and systemic pathogen burdens, greater macroscopic damage to the epithelium, thickening of the colon and shrinkage of the cecum. The results were compared to mice with *loxP* sites flanking *C1galt1* (*C1galt1*$^{f/f}$). Histological samples of *C1galt1*$^{-/-}$ and *Muc2*$^{-/-}$ mice showed significantly higher pathology score in comparison with *C1galt1*$^{f/f}$ demonstrated by severe edema, loss of epithelial integrity, crypt hyperplasia, and goblet cell depletion.
**Conclusions:** This study demonstrates that the protective role played by Muc2 in this model reflects its glycosylation, rather than the protein itself. These findings underscore the need for further exploration of the mechanisms by which the mucus layer protects the intestinal tract from bacterial pathogens and other noxious stimuli.

**Funding Agencies:** CCC, CIHRNSERC

## Honorable Mention

A11
**IMMUNOGLOBULIN G AS A NOVEL SELECTIVE MARKER FOR THE IDENTIFICATION OF INTESTINAL PATHOBIONTS IN PAEDIATRIC INFLAMMATORY BOWEL DISEASES**
H. Armstrong[2], M. Alipour[2], R.S. Valcheva[3], P. Shah[2], D. Zaidi[2], J. Jovel[2], Y. Lou[2], A. Mason[2], G. Wong[2], M.W. Carroll[1], H.Q. Huynh[5], L.A. Dieleman[3], E. Wine[4]

1. Pediatric Gastroenterology, Univeristy of Alberta, Edmonton, AB, Canada; 2. University of Alberta, Ed-

monton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada; 4. Pediatrics, University of Alberta, Edmonton, AB, Canada; 5. Pediatrics, University of alberta, Edmonton, AB, Canada

**Background:** Several studies support a role for gut microorganisms in the development of the common and severely debilitating chronic inflammatory bowel diseases (IBD), Crohn disease (CD) and ulcerative colitis (UC). To date, most studies have examined only samples from stool or inflamed areas, limiting the ability to differentiate between cause and effect. Our recent work examined the uninflamed terminal ileum (TI) in pediatric UC, and showed changes in diversity and composition of bacteria, suggesting that microbes proximal to diseased areas may drive inflammation distally.
**Aims:** As immunoglobulin (Ig)G is increased in IBD and has been shown to bind more selectively to pathogens than its counterpart, IgA, we hypothesized that IgG is formed in response to invasive microbes, and could be used to identify specific taxa involved in IBD pathogenesis. To test this, we isolated IgG-bound intestinal bacteria, identified by 16S rDNA sequencing, and tested their virulence *in vitro*.
**Methods:** TI luminal washes were collected during endoscopy of pediatric IBD patients and non-IBD controls. IgG bound (IgG+) and unbound (IgG-) bacteria were separated and collected using FACS and DNA was extracted for 16S rDNA sequencing (Ilumina MiSeq platform). Virulence of specific IgG-bound bacteria was tested *in-vitro* via gentamycin protection assay, microscopy and qPCR for markers of immune response.
**Results:** Species diversity and microbial composition were reduced in UC compared to non-IBD. Furthermore, the ratio of IgG+/IgG- bacteria increased in CD and UC patients by 2 and 1.5 fold, respectively. Although total abundance of *Burkholderia cepacia*, was comparable in IBD and non-IBD, there was a 2.5 and 4.1 fold increase in the ratio of IgG+/IgG- binding to *B. cepacia* in remission/mild or moderate/severe UC, respectively, compared to non-IBD. *B. cepacia* was previously identified in the ileum of IBD cohorts however, it is not typically recognized as an intestinal pathogen. *B. cepacia* displays pro-inflammatory effects and invasive potential in an *in-vitro* model, supporting its pathobiont potential and further supporting the use of IgG as a marker of pathobionts in IBD.
**Conclusions:** We have demonstrated the ability of IgG-binding to selectively identify previously unrecognized mucosa-associated pathobionts, validated *in-vitro*. Elucidating the role of specific bacterial species in UC pathogenesis will underpin new strategies to improve our ability to direct therapies to those patients most likely to respond.

**Funding Agencies:** CCCCCFA

## Honorable Mention

A12
**INTESINAL TREFOIL FACTOR (ITF) PLAYS CRITICAL ROLES IN INNATE PROTECTION AGAINST, AND RECOVERY FROM, CLOSTRIDIUM DIFFICILE COLITIS**

H. Tang[1], Y. Li[2], J. Nguyen[3], J.A. MacDonald[4], X. Gui[5], P. Beck[1]

1. University of Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada; 5. University of Calgary, Calgary, AB, Canada

**Background:** Clostridium Difficile (Cdif) colitis is a leading cause of morbidity & mortality in many patients including: hospitalized elderly, those with IBD, and immunocompromised. Little is known of the mechanisms involved in protection against, and recovery from, Cdif toxin-induced injury. Histological findings of Cdif colitis include; epithelial disruption, inflammatory cell infiltration, goblet cell depletion & when severe, pseudomembranous colitis (PMC). We previously showed Keratinocyte Growth Factor (KGF) plays protective roles on Cdif exposure. KGF-/- mice had more severe Cdif toxin-induced injury & greater depletion of goblet cells and the goblet cell derived growth factor ITF. Since KGF directly binds the ITF promoter (increasing ITF) and Cdif colitis is associated with goblet cell depletion & loss of ITF we developed the following aim.
**Aims:** We hypothesized that ITF protects against Cdif induced injury and is critical in resolution of Cdif colitis.
**Methods:** Cdif colitis was induced in Sv129 (WT) and $ITF^{-/-}$ mice via intrarectal (IR) Cdif toxin (TcdA/B). In vitro models of toxin exposure, IECs (CaCo2) and fresh human colonic biopsies, were also assessed. Cdif injury/inflammation was assessed via histology, myeloperoxidase activity (MPO), cytokine/chemokine profiles, lactate dehydrogenase (LDH) release & epithelial proliferation/apoptosis balance.
**Results:** IR Cdif toxin resulted in marked depletion in goblet cells & ITF (4h post). Reductions in goblet cell numbers & ITF correlated with severity of injury/inflammation & increased during the resolution phase (24-72 h post). Goblet cell & ITF depletion was also seen in fresh human colon biopies exposed to Cdif toxin. Although $ITF^{-/-}$ mice had similar MPO levels & histological damage as WT mice at 4h post toxin exposure they had marked impairment in recovery from colitis (significantly higher MPO, cytokine/chemokine levels & histological scores at 48h and 72h after toxin exposure vs WT). Loss of ITF also resulted in increased epithelial apoptosis & impaired proliferation following Cdif toxin exposure. Loss of ITF also resulted in a close to 10 fold increased incidence in PMC (1 of 32 wt mice (3%) vs 6 of 24 ITF-/- mice (25%). IR recombinant ITF (rITF) protected WT mice from toxin-induced injury, enhanced recovery & reduced the incidence of PMC. *In vitro* studies showed that rITF decreased Cdif toxin induced cell death (LDH), promoted cell proliferation, enhanced wound repair & altered cell cycle dynamics (enhancing cell survival).
**Conclusions:** In both humans & mice, Cdif toxin induces depletion of goblet cells and ITF. ITF plays important roles in the innate protection against Cdif colitis, and is

critical in mucosal healing following Cdif colitis. These studies may lead to new approaches in the management and prevention of Cdif in patients.

**Funding Agencies:** CIHR

## NOVEL IMMUNOTHERAPIES FOR IBD
## FRIDAY, FEBRUARY 9, 12H30-14H30

A13

### WHOLE EXOME SEQUENCING OF OVER 1000 PEDIATRIC IBD PATIENTS FROM A SINGLE CENTRE IDENTIFIES MONOGENIC FORMS OF IBD.

E. Crowley[2], N. Warner[2], K. Fiedler[2], R. Murchie[2], P. Church[2], T.D. Walters[2], A. Griffiths[2], A. Muise[1]

1. Inflammatory Bowel Disease Center and Cell Biology Program, Division of Gastroenterology, Hospital for Sick Children and Institute of Medical Science, and Department of Biochemistry, University of Toronto, Toronto, ON, Canada; 2. Inflammatory Bowel Disease Center and Cell Biology Program, Division of Gastroenterology, Hospital for Sick Children - Sickkids, Toronto, ON, Canada

**Background:** Inflammatory bowel disease (IBD) has a multifactorial aetiology, with complex interactions between genetic and environmental factors. Recent studies suggest an increasing spectrum of monogenic disease in the very young. The prevalence of these mutations in older children is unknown.
**Aims:** To determine the incidence of monogenic forms of IBD in a typical cohort of pediatric IBD patients and identify any phenotypic characteristics suggestive of a monogenic cause.
**Methods:** 2,431 unique participants underwent whole exome sequencing (WES), including 1,098 IBD probands. This data was interrogated for a panel of 51 genes known to be associated with monogenic IBD. The Genome Analysis Toolkit (GATK) was used to identify highly penetrant rare variants of interest. Sanger sequencing verified variant genotypes. A clinical database was reviewed to ascertain phenotypic characteristics.
**Results:** A single centre retrospective study identified 1,098 index cases, diagnosed over a 12 year period (2003-2015) who underwent WES. 2431 unique participants (302 trios, 31 quads, 29 affected siblings). Of sequenced affected cases, 60% CD, 40% UC/IBD-U. 16% < 6.9 years, 22% 7-10.9 years, 62% > 11 years. Across the 51 genes, 19 protein coding variants predicted to be deleterious were identified in 54 patients, which were high quality and rare (maf <0.01). XIAP, DOCK8 and CYBB were the most commonly identified gene variants within the cohort. Overall, approximately 4.9% of patients in a typical cohort of Pediatric IBD patients were found to have monogenic disease.
**Conclusions:** WES of this largest pediatric cohort to date confirms the highly varied phenotypic spectrum of IBD associated with monogenic disease. Whilst many children with causal VEOIBD mutations were diagnosed < 1 year of age, a significant number of older children were identified. Characterising genotypic-phenotypic features may provoke earlier recognition which will allow novel therapeutic approaches in this paediatric IBD population.

**Funding Agencies:** None

A14

### ACTIVATION OF STROMAL CELL-EXPRESSED NOD2 MODULATES SYSTEMIC DENDRITIC CELL FUNCTION VIA THE PRODUCTION OF GM-CSF

D. Prescott[2], D. Philpott[1], S. Girardin[1]

1. University of Toronto, Toronto, ON, Canada; 2. Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

**Aims:** Polymorphisms in the gene encoding for the pattern-recognition receptor NOD2 confer genetic risk of developing Crohn's disease (CD). However, the mechanisms by which these mutations contribute to the onset of overt inflammation are at this point unclear. Previous studies have shown that dendritic cells (DC) express among the highest levels of NOD2 of any cell type, yet the effects of NOD2 activation on DC function have not been thoroughly assessed. With this in mind, we chose to assess the effects of *in vivo* administration of purified NOD2 ligand on the function and prevalence of specific DC subtype populations.
**Methods:** C57Bl/6 mice were injected *i.p.* with ligands for NOD2 (MDP), NOD1 (FK156), TLR4 (LPS) or TLR2/1 (Pam3CSK4). 24h later, tissues were collected and the populations of DCs present assessed by flow cytometry.
**Results:** Injection of MDP led to a significant increase in the proportion of dendritic cells in the spleen expressing the surface marker CD103 (MDP: 25.4 ± 2.5%, Vehicle: 7.9 ± 0.5%). Closer examination of these cells revealed this to be restricted to a specific subset of splenic DCs ($CD205^+$, $XCR1^+$, $CLEC9a^+$, and $CD8\alpha^+$, also known as cDC1) - a cell type that is known to be an efficient cross-presenter of injested antigens to CD8 T cells. This phenotype was replicated by injection of FK156, a synthetic ligand of the closely related receptor NOD1, while injection of the toll-like receptor ligands LPS and Pam3CSK4 resulted conversely in the significant decrease in the total numbers of cDC1s in the spleen, indicating that this phenomenon is specific to activation of Nod-like receptors (NLRs). Suprisingly, Cre-Lox mouse models indicated that this phenomenon was not dependent on expression of *Nod2* by these DCs themselves. Accordingly, bone marrow chimera experiments indicated that a radioresitant cell was responsible for the detection of MDP in this model. Thus, we examined by qPCR the expression of various immunomodulatory factors within membrane surrounding the peritoneal cavity following MDP adminstration and found a significant increase in the expression of the gene encoding for GM-CSF (15.9 ± 5.2 fold increase over vehicle control), a growth factor known to modulate expression of CD103 on DCs. Further, we found that the injection of recombinant GM-CSF resulted in an increase in CD103 expression on spleen cDC1s in the

same manner as MDP injection, while *Csf2*$^{-/-}$ mice did not respond to MDP, indicating that these two factors are part of the same pathway.
**Conclusions:** Interestingly, deficiencies in GM-CSF signaling has also been implicated in CD pathogenesis. This study is the first to identify a shared biological pathway between GM-CSF and NOD2, suggesting that this pathway might be of vital importance for intestinal immune homeostasis, and could give us insight into the etiology and potential therapy of CD.

**Funding Agencies:** CIHR

## GUT MICROBES, NUTRITION, AND CANCER
## FRIDAY, FEBRUARY 9, 15H00-16H30

A15
**VITAMIN D DEFICIENCY PROMOTES INTESTINAL AUTOPHAGY DYSFUNCTION VIA EPIGENETIC REGULATION INVOLVING MIR142-3P *IN VITRO* AND *IN VIVO***
D.M. Bronte-Tinkew[1], F. Dang[1], A. Hsieh[1], L.H. McGillis[1], I. Verapalan[1], R. Murchie[1], M. Capurro[1], L.K. Greenfield[1], D. Philpott[2], N. Jones[1]

1. Departments of Paediatrics and Physiology, University of Toronto; Cell Biology Program, Peter Gilgan Centre for Research & Learning and Division of Gastroenterology, Hepatology and Nutrition, Hospital For Sick Children, Toronto, ON, Canada; 2. Department of Immunology, University of Toronto, Toronto, ON, Canada

**Background:** Growing evidence from animal and human studies indicate that vitamin D deficiency is an important environmental factor contributing to IBD pathogenesis. The exact mechanism underlying the role of vitamin D in IBD is currently unknown.
**Aims:** We hypothesize that vitamin D deficiency reduces autophagy to promote IBD progression via a mechanism involving the upregulation of specific microRNAs.
**Methods:** To address this hypothesis, C57BL/6 mice were fed either a vitamin D deficient or control chow diet for 5 weeks prior to extraction of the terminal ileum and colon for experimental analysis. Ileal whole tissue was analyzed via Western Blot for changes in autophagy proteins LC3-II and ATG16L1. To further explore this relationship between autophagy proteins and miRNA, bioinformatics target prediction tools were employed to identify miRNA predicted to target ATG16L1 3'UTR. A dual luciferase reporter assay was used to determine whether miR-142-3p directly targets ATG16L1 in intestinal cells. To characterize the functional effect of miR-142-3p, HTC-116 cells and intestinal organoids were transfected with either a miR mimic or the anti-miR. LC3-II and ATG16L1 levels from transfected cells were assessed by immunoblot. In addition, transfected cells were immunostained for LC3-II as a marker of autophagy. Expression of miR-142-3p in ileal whole tissue from vitamin D deficient animals was investigated via qPCR.
**Results:** Ileal whole tissue homogenate from vitamin D deficient animals showed decreased levels of autophagy proteins ATG16L1 and LC3-II, indicating a role for vitamin D in promoting functional autophagy *in vivo*. Bioinformatics target prediction tools confirmed miR 142-3p as a target for ATG16L1. It was also selected for further characterization because of its known elevated expression in animal colitis models. Delivery of miR-142-3p mimic suppressed ATG16L1-3'UTR luciferase activity in HCT-116 cells. There was a reduction in both ATG16L1 and LC3-II protein levels in miR mimic transfected intestinal organoids and HTC-116 cells relative to control cells. In addition, a reduction in LC3 puncta characteristic of autophagosomes was detected in cells transfected with miR-142-3p mimic, when compared to sham-transfected cells. Furthermore, a significant upregulation of miR142-3p expression was detected in the ileum of vitamin D deficient animals as assessed by qPCR.
**Conclusions:** These results indicate that miR142-3p can directly regulate ATG16L1 and repress autophagy. Ongoing studies are assessing the correlation between vitamin D deficiency and ileal mir 142-3p levels in a cohort of paediatric IBD patients. Taken together, our study demonstrates a potential mechanism by which vitamin D deficiency influences IBD pathogenesis.

**Funding Agencies:** CAGCrohns and Colitis

## IMMUNOMETABOLISM AND GASTROINTESTINAL DISEASE
## Saturday, February 10, 08h30-10h30

A16
**FOLLOWING AN ANTI-INFLAMMATORY DIET PREVENTS INCREASES OF FECAL CALPROTECTIN AND ALTERS METABOLOMIC PROFILE OF ULCERATIVE COLITIS PATIENTS, A RANDOMIZED CONTROLLED TRIAL**
A. Hassanzadeh Keshteli[4], K. Madsen[1], C. Nickurak[5], K.I. Kroeker[6], R. Mandal[7], R.S. Valcheva[3], D.S. Wishart[2], S. Veldhuyzen van Zanten[1], B.P. Halloran[2], R. Fedorak[2], L.A. Dieleman[3]

1. University of Alberta, Edmonton, AB, Canada; 2. Biological Science, University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada; 4. Centre of Excellence for Gastrointestinal Inflammation and Immunity Research, University of Alberta, Edmonton, AB, Canada; 5. University of Alberta, Edmonton, AB, Canada; 6. University of Alberta, Edmonton, AB, Canada; 7. University of Alberta, Edmonton, AB, Canada

**Background:** A relationship between ulcerative colitis and diet has been shown in epidemiological and experimental studies.
**Aims:** To investigate the effectiveness of an anti-inflammatory diet for maintenance of remission in UC patients.
**Methods:** In this 6-month randomized control trial, adult UC patients in clinical remission (partial Mayo

score<3) who had a disease relapse within the previous 18 months were randomized to either an "Anti-inflammatory Diet (AID)" or "Canada's Food Guide (CFG)" as the control group.A dietitian provided dietary recommendations to all patients in four face-to-face (baseline, month 1, 3, and 6) and three telephone (month 2,4,5) sessions. Menu plans provided to patients in the AID group were designed to increase dietary intake of fiber, prebiotics, probiotics, anti-oxidants, omega-3 fatty acids and to decrease dietary intake of red or processed meat, added sugar and alcohol. To assess clinical relapse, partial Mayo scoring was done monthly. Monthly 24h dietary recalls were used to assess adherence to the diets. At baseline and month 6 or relapse, fecal calprotectin (FCP), serum CRP, and quality of life were assessed. Metabolomic analysis was performed on urine (GC-MS, DI- LC MS/MS), serum (NMR, DI-LC MS/MS) and stool (NMR) samples collected at baseline and month 6 or relapse.

**Results:** Fifty-three patients were randomized to the two diet groups. The mean age of participants was 41.4±14.7 y and 34 (64.2%) subjects were female. Five(19.2%) patients in the AID and 8(29.6%) patients in the control group relapsed during the trial (P=0.38). Patients following CFG had a statistically significant increase in FCP from baseline to month6/relapse, while patients following the AID showed no significant increase in their FCP over the 6 months (Figure1A). At baseline, the metabolomic profiles of patients randomized to the two groups were similar. However, at 6 months/relapse, the two groups had separated (Figure1B). In comparison to CFG group, patients in the AID group had higher glutamic acid(stool), creatinine (stool), and carnosine (urine) but lower 3-(3-hydroxyphenyl)-3-hydroxypropionic acid (urine), hydroxymandelic acid (urine), phosphatidylcholines (serum), acetone (stool), and Sumiki's acid (urine). In comparison to the CFG group, patients in the AID group had a significant increase in dietary intake of some nutrients including zinc, selenium and phosphorus from baseline to month 6 or relapse.

**Conclusions:** Modification of diet towards an inclusion of anti-inflammatory and reduction of inflammatory foods alters host and microbial metabolic pathways and can help prevent increases in colonic inflammation in UC patients in remission.

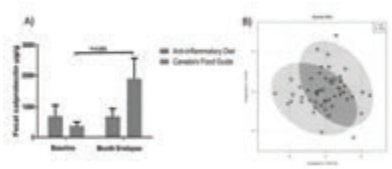


**Figure1.A)** Comparison of changes in fecal calprotectin levels from baseline to month 6/relapse between the two diet groups;**B)** Partial least squares discriminant analysis plot showing a significant difference in the metabolome of patients randomized to the two diet groups at month 6/relapse as identified by metabolites in urine,serum and fecal samples.

**Funding Agencies:** Alberta Innovates Health Solutions

A17

## DIETARY MODULATION OF THE IMMUNE RESPONSE TO CITROBACTER RODENTIUM

M. Yousefi[1], D. Pepin[2], E. Kang[1], L. Zhu[1], B. Willing[2], S. Gruenheid[1]

1. Research Center on Complex Traits, Department of Microbiology and Immunology, McGill University, Montreal, QC, Canada; 2. Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, AB, Canada

**Background:** A leading cause of diarrheal disease is gastrointestinal infection by enteropathogenic and enterohaemorrhagic Escherichia coli (EPEC and EHEC, respectively). Despite evidence of variability in disease severity and clinical outcome of EPEC and EHEC infections, little is known about the mechanisms regulating host susceptibility to these pathogens and the related mouse-specific pathogen *Citrobacter rodentium* serves as a good model to study these mechanisms. Our group has identified a single gene *R-spondin 2* (*Rspo2*) encoding a secreted potentiator of WNT signalling as the common genetic determinant underlying mortality during *C. rodentium* infection. Induction of *Rspo2* during infection of susceptible mice drives uncontrolled proliferation and loss of differentiation of the intestinal epithelium, leading to mortality. We have also recently observed that, in addition to the large impact of host genetics, susceptibility to *C. rodentium* infection is strongly influenced by diet.

**Aims:** Based on our observations and considering the fact that diet could have an impact on the gut microbiota, we aimed to investigate the role of microbiota and nutrition in the susceptibility to *C. rodentium* infection.

**Methods:** To this end, we performed Microbiota analysis, deep immuno-profiling of the gut and gene experession analysis before and during infection with *C. rodentium*.

**Results:** Our data reveals that, diet impacts *C. rodentium* colonization in susceptible mice early upon infection, although bacterial loads equalize at later time points. *Rspo2* induction is attenuated in mice on the resistance-associated diet, correlating with decreased upregulation of some WNT target genes. Microbiota analysis reveals that resistance-associated diet correlates with less diversity of microbial community and more abundance of *Bacteriodes*. Deep immuno-profiling of the susceptible mice on the two different diets reveals an early increase in infiltration of phagocytes to the gut lamina propria in mice on the susceptibility-associated diet. Furthermore, mice on this diet have higher total dendritic cell abundance at realy stages upon infection, which is mostly due to an increase in dendritic cells of a subtype known to induce Th17 cells. Indeed, our data also show that diet mediated susceptibility to *C. rodentium* infection correlates with a more prominent Th17 response, whereas mice on the resistance-associated diet have a more prominent

induction of Tregs and Th22 cells, as well as induction of anti-microbial compounds RegIIIβ and RegIIIγ.
**Conclusions:** These data suggest that different standard mouse chow diets can have large impacts on susceptibility to infection, correlating with changes in microbiota composition and immune status before and during the course of infection. We anticipate that our findings might be applicable towards new dietary and microbial strategies of therapeutic potentials.

**Funding Agencies:** CIHRFerring Postdoctoral Award-Strauss Foundation, Wares Family Postdoctoral Award

## NEURAL MECHANISMS OF PAIN IN GASTROINTESTINAL DISEASE SATURDAY, FEBRUARY 10, 15H30-17H00

A18

### DIETARY ANTIGEN RE-CHALLENGE INCREASES NOCICEPTIVE NEURON EXCITABILITY IN A POST-INFECTIOUS IBS MODEL.

C.D. Lopez Lopez[1], J.O. Jaramillo Polanco[1], J. Aguilera Lizarraga[2], S. Vanner[1], D.E. Reed[1], G. Boeckxstaens[2]

1. Gastrointestinal Diseases Research Unit, Queen's University, Kingston, ON, Canada; 2. Dept. of Gastroenterology, University Hospital Leuven, Leuven, Belgium

**Background:** Infectious gastroenteritis is a risk factor for development of Irritable Bowel Syndrome (IBS). Exposure to the dietary antigen ovalbumin (OVA) during infection with *Citrobacter rodentium* resulted in an increased visceromotor response to colonic distension and increased mucosal permeability following re-challenge with OVA. It is unknown whether colonic immune mediators released following re-challenge of OVA could subsequently increase the excitability of nociceptive neurons.
**Aims:** Determine whether colonic mediators released in response to dietary antigen re-challenge increase excitability of nociceptive neurons and whether the histamine receptor H1 is involved in a model of post infectious IBS.
**Methods:** Mice were infected with *C. rodentium* in the presence (infected OVA/OVA) or absence of OVA (infected saline/OVA) and were subsequently re-challenged with OVA 5 weeks post-infection. A third group of mice were not infected but exposed to OVA and re-challenged with OVA at 5 weeks (non-infected OVA/OVA). Following OVA re-challenge, mice were euthanized and the colons were incubated in media, supernatants were collected after 4 hrs. Supernatants were incubated overnight with nociceptive DRG neurons from control mice. Perforated patch clamp recordings were employed to assess neuronal excitability by measuring rheobase (minimum current to evoke an action potential) and action potential discharge (AP) at twice rheobase. Some DRG neurons were also pre-incubated with the H1 receptor antagonist pyrilamine (1μM) 1 hour prior to incubation with supernatants. Two-way ANOVA with Bonferroni post hoc test were used to analyze the data.
**Results:** Infected OVA/OVA supernatants decreased the rheobase compared to the other two groups (Infected OVA/OVA= 68±4.2 pA* vs Non-infected OVA/OVA= 81.2±4 pA vs Infected saline/OVA = 85.6±4.5 pA; *p<0.05, n= 17-19). Similarly, infected OVA/OVA supernatant also increased action potential discharge at twice rheobase (1.7±0.2* vs 1.2±0.1 vs 1.2±0.1; *p<0.05, n= 17-19). Pyrilamine reversed the effect of infected OVA/OVA supernatant on DRG neurons (rheobase= 88.8±5.5 pA, p < 0.01; AP= 1.3± 0.1, p= NS, n= 16) but had no effect on supernatants from the other two groups.
**Conclusions:** Colonic supernatants following re-challenge with OVA increased excitability of DRG nociceptive neurons only in mice first exposed to OVA at the time of a gastrointestinal infection and this effect was inhibited by an H1 antagonist. This suggests that exposure to a dietary antigen at the time of gastrointestinal infection may prime the immune system such that re-exposure to the antigen induces release of immune mediators (e.g. histamine) resulting in increased pain signalling.

**Funding Agencies:** CIHR

## CELIAC DISEASE: REMOVING THE FOG SUNDAY, FEBRUARY 11, 08H30-10H30

A19

### BACTERIAL PROTEASES INCREASE SENSITIVITY TO DIETARY ANTIGEN THROUGH PAR-2 SIGNALING

A. CAMINERO FERNANDEZ[4], J. McCarville[2], H.J. Galipeau[3], C. Deraison[1], S. BERNIER[2], J.a. Murray[5], B.K. Coombes[2], w. Ruf[6], J. Casqueiro Blanco[7], M. Surette[2], N. Vergnolle[1], E. Verdu[2]

1. U1043, INSERM, Toulouse, France; 2. McMaster University, Hamilton, ON, Canada; 3. Farncombe Family Digestive Health Research Institute, McMaster University, Hamilton, ON, Canada; 4. Farncombe institute, Mcmaster University, Dundas, ON, Canada; 5. Gastroenterology, The Mayo Clinic, Rochester, MN; 6. Johannes Gutemberg University of Mains, Mainz, Germany; 7. Universidad de Leon, Leon, Spain

**Background:** Microbial-dietary-host interactions are generally homeostatic but when dysfunctional, can incite food sensitivities such as celiac disease in genetically predisposed people. However, the specific pathways involved and sequence of events remain poorly understood. We have previously shown that bacterial metabolism of the common dietary antigen, gluten, affects its immunogenicity.
**Aims:** Here we tested whether microbial proteases able to degrade gluten also activate innate immune mechanisms important for the development of food sensitivity.
**Methods:** Clean SPF (Altered Schaedler flora colonized) C57BL/6 and NOD-DQ8 mice were colonized with wild-type (WT) *Pseudomonas aeruginosa* strain PA14 or its *lasB* mutant derivative (lacking elastase activity) and

then sensitized and challenged with gluten. In order to study bacterial-host specific interactions, germ-free mice were also colonized with both *P. aeruginosa* strains (WT and *lasB*) and placed on a gluten-free diet. Finally, SPF protease-resistant PAR2 mutant mice were colonized with WT and *lasB*. Small intestinal microbial composition, proteolytic activity, intraepithelial lymphocyte (IEL) counts, expression of specific innate genes, bacterial infiltration in the mucus layer and villus-to-crypt (V/C) ratios were measured in all mice.
**Results:** *P. aeruginosa* expressing elastase, previously shown to participate in the intestinal metabolism of gluten peptides, produced a PAR-2 pro-inflammatory response associated with increases in IELs in clean-SPF and GF C57BL/6 mice, independently of gluten treatment. This response was characterized by an increased expression of certain genes related to IEL induction and cytotoxicity, barrier function, and autoimmunity including *Ifnγ*, *Tnfα*, *Tgfβ*, *Il6, IL17, IL22* and *Fasl* in the IEL compartment. Moreover, the presence of *P. aeruginosa* expressing elastase also led to shifts in the microbiota composition and bacterial encroachment to the mucosa. In NOD-DQ8 mice, a mouse model of gluten sensitivity, *P. aeruginosa* expressing elastase enhanced gluten immunopathology characterized by a reduction in V/C ratios.
**Conclusions:** Bacterial protease, previously shown to degrade gluten peptides, can directly impact the host immune response through activation of PAR-2 and contribute to small intestinal pathology. This pathway could be targeted therapeutically in genetically susceptible individuals to prevent celiac disease.

**Funding Agencies:** CAG, CIHRFarncombe Institute Postdoctoral Fellowship

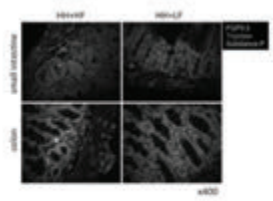
A20

**GUT MICROBIOTA-DIET INTERACTION ALTER INTESTINAL MAST CELL NUMBERS AND DISTRIBUTION IN THE HUMANIZED IBS MOUSE MODEL**

C. Shimbori[3], G. De Palma[2], D.E. Reed[1], M. Pigrau[2], J. Lu[2], Y. Zhang[5], Y. YU[5], N. Jimenez-Vargas[5], J. Sessenwein[7], C.D. Lopez Lopez[6], J.O. Jaramillo Polanco[6], E. Verdu[2], S.M. Collins[2], A.E. Lomax[4], M.J. Beyak[4], S. Vanner[5], P. Bercik[3]

1. GIDRU Wing, Kingston General Hospital, Kingston, ON, Canada; 2. McMaster University, Hamilton, ON, Canada; 3. Medicine, McMaster University, HAMILTON, ON, Canada; 4. Queen's University, Kingston, ON, Canada; 5. GIDRU, Queen's University, Kingston, ON, Canada; 6. Gastrointestinal Diseases Research Unit, Queen's University, Kingston, ON, Canada; 7. Neuroscience, Queens University, Kingston, ON, Canada

**Background:** Growing evidence suggests that immune activation and gut microbiota are involved in the pathophysiology of IBS. We have recently demonstrated that a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) improved symptoms in IBS patients and this was associated with lower urinary histamine and changes in the microbiota composition. A high FODMAP diet in germ-free mice colonized with IBS patient microbiome modulated motility, permeability, and visceral sensitivity. However, the underlying mechanisms are unclear.
**Aims:** To investigate the interactions of host's immune system and intestinal microbiota in response to FODMAPs in the humanized IBS mouse model.
**Methods:** Germ-free NIH Swiss mice were colonized with fecal microbiota from two IBS patients (non-constipation) with a high (HH) or low (LH) urinary histamine (n=24 mice/patient), and one healthy control (HV) (n=8). SPF mice (n=8) were included as additional controls. Mice were assigned to a custom-made low or high FODMAP diet (LF and HF, respectively). Microbiota composition was analysed by 16S rRNA gene sequencing. At sacrifice, intestinal tissues were collected for immunohistochemistry (c-kit staining) and immunofluorescence (tryptase, PGP9.5, and Substance P) detection of mast cell and nerves.
**Results:** HH colonized mice receiving HF diet had increased number of mast cells (c-kit positive cells) in both small intestine and colon compared to HH mice on a LF diet (Effect of diet x microbiota: p=0.041, F(1,32)=4.51 for small intestine, and p=0.029, F(1,30)=5.25 for colon). No differences were observed in the colon and small intestine of LH colonized mice. Immunofluorescent staining of colonic and small intestinal sections revealed high number of tryptase positive mast cells in HH colonized mice on HF diet. Moreover, the majority of the mast cells were in close proximity of nerve fibers (PGP9.5 positive) (Fig 1). In HH colonized mice, colonic mast cell numbers were negatively correlated with the relative abundance of *Adlercreutzia* spp, *Oscillospira* and *Ruminococcus* spp. Similarly, in the small intestine of HH colonized mice, mast cell numbers negatively correlated with the relative abundance of *Blautia, Ruminococcus, and Lactobacillus* spp.
**Conclusions:** A high fermentable diet alters intestinal microbiota composition only in mice colonized with microbiota from a patient with high urinary histamine. These changes are associated with increased numbers of mast cells in both the colon and small intestine. Furthermore, mast cells seem to closely interact with neurons, likely contributing to the functional changes observed in these mice.



**Funding Agencies:** CIHRNIH

## MICROBIOME AND HOST CROSS-TALK IN GASTROINTESTINAL HEALTH AND DISEASE: METAOBOLITES AND MORE
## SUNDAY, FEBRUARY 11, 15H30-17H00

A21

### FERMENTABLE CARBOHYDRATE-MICROBIOME INTERACTIONS IN A MOUSE MODEL OF IBS

G. De Palma[1], D.E. Reed[2], C. Shimbori[1], M. Pigrau[1], J. Lu[1], M. Louis-Auguste[1], Y. Zhang[2], Y. Yu[2], N. Jimenez-Vargas[2], J. Sessenwein[2], C.D. Lopez Lopez[2], J.O. Jaramillo Polanco[2], E. Verdu[1], S.M. Collins[1], K. Madsen[3], A.E. Lomax[2], M.J. Beyak[2], S. Vanner[2], P. Bercik[1]

1. McMaster University, Hamilton, ON, Canada; 2. Queen's University, Kingston, ON, Canada; 3. University of Alberta, Edmonton, AB, Canada

**Background:** The detailed mechanisms underlying IBS are poorly understood. Gut microbiota appears to play an important role in IBS pathogenesis, but little is known about its interaction with specific dietary components. We have previously shown that some patients with IBS improve symptoms when on low FODMAPs diet, which was associated with low urinary histamine.
**Aims:** To investigate mechanisms underlying IBS symptom generation due to the interaction of a high fermentable diet and the intestinal microbiota.
**Methods:** Germ-free NIH Swiss mice were colonized with fecal microbiota from two IBS patients (non-constipation), with either a high (HH) or low (LH) urinary histamine level (n=24 mice/patient), and one healthy control (HV) (n=8). Specific-pathogen free (SPF) mice (n=8) were included as additional controls. Mice were assigned to a custom-made low or high fermentable carbohydrate diet (LF and HF, respectively). GI transit (beads study), cecal volume (CT scan), intestinal permeability (FITC-Dextran) and gut microbiota composition (Illumina sequencing) were assessed. Neuronal excitability by patch clamp recordings of DRG neurons (action potential rheobase) exposed to colonic supernatants and changes in mechanosensitivity of single unit afferent recordings in mouse distal colon were measured.
**Results:** Diet significantly altered gut microbiota composition and diversity only in HH colonized mice. All mice on HF diet (HV, HH, LH, and SPF) had increased cecal volume (Diet effect: $p<0.001$, $F(1,55)=14.097$; microbiota effect: $p=0.019$ $F(3,55)=3.6$) compared to mice on LF diet, more pronounced in mice with HH and LH microbiota. Compared to LF diet, the HF diet induced slower GI transit ($p=0.009$) and increased permeability (FITC-Dextran: $p=0.03$) only in HH colonized mice. HF diet increased neuronal excitability in mice with HH and, to some degree, in LH microbiota, but not in HV and SPF microbiota colonized mice. This increased neuronal excitability was inhibited by specific protease and H1 antagonists. *In vitro* experiments demonstrated that cecal microbiota from HH mice on HF diet produced several fold higher levels of histamine, compared to the microbiota from other groups of mice.
**Conclusions:** High fermentable diet induces changes in gut function in gnotobiotic mice colonized with microbiota from a patient with high urinary histamine. This specific microbiota has the capacity to produce high levels of endogenous histamine, which may contribute to the observed gut dysfunction.

**Funding Agencies:** CAG, CIHR

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## POSTER SESSION 1
## SATURDAY, FEBRUARY 10 18H30-20H00

## ACUTE LIVER INJURY AND HEPATOTOXICITY

A22

### A HIDDEN CAUSE OF DRUG-INDUCED LIVER FAILURE

F. Bergeron[2], T. Hussaini [3], E.M. Yoshida[1], V. Marquez[2]

1. Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 2. Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 3. Vancouver General Hospital, Vancouver, BC, Canada

**Background:** Nimesulide is a non-steroidal anti-inflammatory drug with relative selectivity for cyclooxygenase-2 enzyme marketed in 1985. Nimesulide was never approved for use in Canada, United States, United Kingdom, Australia, or New Zealand due to safety concerns. Multiple reports in the literature have linked nimesulide to severe liver injuries ranging from marked aminotransferase elevation to acute liver failure (ALF), need for liver transplantation, and death. Such reports have led to nimesulide's withdrawal from the market in Finland and Spain in 2002, and in Ireland in 2007; however, it remains widely available in more than 50 countries worldwide. The mechanism for its hepatotoxicity remains unknown.
**Aims:** We report a fatal case of ALF sustained by consumption of a "herbal" product purchased in Canada.
**Methods:** Chart review.
**Results:** A 52-year-old female developed jaundice and malaise with rapid progression to ALF. Her past medical history was significant for type 2 diabetes, hypothyroidism, sickle cell trait, and breast adenocarcinoma in remission. Her medications included metformin, levothyroxine, tamoxifen, and "herbal" medications (Arjun heart tonic, R. Pyine and Hari tablets). She had no risks factors for chronic liver disease and family history was non-contributory. After initial presentation to a community hospital, she was transferred to a liver transplant center where she developed encephalopathy associated with worsening liver function. Serologies were negative for viral, auto-immune, and metabolic etiologies. Acetaminophen and ethanol levels were undetectable. Imaging showed patent hepatic vasculature, normal biliary ducts and hepatic parenchyma. Her clinical status deteriorated further and she underwent an orthotropic liver transplant three weeks after presentation. The liver explant appeared pale and shrunken. Histopathologic examination showed subacute massive paracinar and periportal necrosis compatible with drug-induced liver injury. Since the patient's labeled "herbal" medications did not include hepatotoxic drugs, the "herbal" products were analyzed by our medicinal chemistry lab and revealed presence of high concentrations of nimesulide and chlordiazepoxide within two of the three herbal products. Four days postoperatively, she passed away due to sepsis and multiorgan failure.
**Conclusions:** In Canada, 73% of the population regularly consumes herbal products. The majority (59%) of herbal medicines sold in North America contain ingredients that are not listed on the label. Here, we report a fatal case of ALF sustained by consumption of a commercially available herbal product that contained a known pharmaceutical product that is neither approved nor marketed in Canada. This case highlights the urgent need for governmental regulation and consumer safety policies regarding the manufacture, importation and dispensing of herbal/natural products to prevent serious adverse events.

**Funding Agencies:** None

A23

### A CASE OF ACUTE LIVER DYSFUNCTION DUE TO TRIMETHOPRIM-SULFAMETHOXAZOLE TREATED WITH N-ACETYLCYSTEINE

T.S. Rodriguez, M. Miles, M. McLeod

Dalhousie University, Halifax, NS, Canada

**Background:** Trimethoprim-sulfamethoxazole (TMP-SMX) is commonly prescribed for skin and soft tissue infections. While generally well tolerated in HIV-negative patients, TMP-SMX can lead to drug-induced liver injury (DILI). Most cases are self-limited and resolve quickly with drug discontinuation, but prolonged, severe injury and liver failure can occur. Upon onset of acute liver failure, prognosis is poor without liver transplantation. Currently, there are no specific therapies to prevent progression to acute liver failure in patients with TMP-SMX induced liver injury.
**Aims:** We hope to help raise awareness on DILI due to TMP-SMX and provide evidence for the use of N-acetylcysteine (NAC) to treat acute drug induced liver dysfunction.
**Methods:** We report a case of a young male on TMP-SMX for a purulent soft tissue infection who developed acute liver dysfunction and was successfully treated with NAC.
**Results:** A 17 yo male was prescribed oral TMP-SMX (80 mg/400 mg) for a purulent soft tissue infection and after 30 days of treatment developed jaundice and a rash. He presented to the emergency department with accompanying malaise, weakness, nausea, vomiting and fever. He had no risk factors for viral hepatitis, no history of liver disease, took no other medications and did not drink alcohol or use recreational drugs. Laboratory tests showed elevated total bilirubin (139 µmol/L), transaminases (AST 280 U/L, ALT 1378 U/L), alkaline phosphatase (295 U/L), and lactate dehydrogenase (1162 U/L), with normal white blood cell count (9.6 x 109/L), serum albumin (38 g/L) and INR (1.1). Tests for hepatitis A, B and C were negative. Abdominal ultrasound found no evidence of biliary obstruction. His TMP-SMX was stopped but his condition worsened and

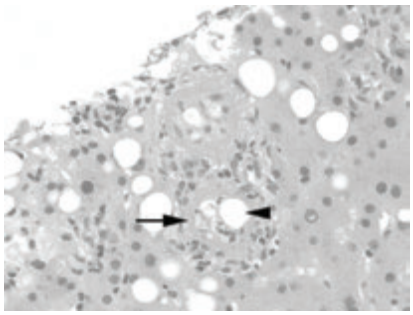
he was transferred to our centre for urgent hepatology assessment. Physical examination revealed scleral icterus and a morbilliform rash over his trunk, back and upper extremities, but no asterixis. Repeat laboratory tests showed increased bilirubin (229 µmol/L), transaminases (AST 1498 U/L, ALT 2045 U/L), lactate dehydrogenase (5302 U/L) and INR (3.2). He underwent a transplant work-up, which did not reveal an alternative cause for his liver dysfunction. He received IV NAC for 72 hours and 4 doses of 10 mg IV vitamin K. NAC was dosed according to our standardized 20-hour protocol and the final infusion rate was continued until his INR was less than 1.5. After 4 days, his INR normalized, his rash and jaundice resolved and he was feeling well enough to be discharged home.
**Conclusions:** Clinicians prescribing TMP-SMX should monitor patients for signs and symptoms of DILI. In the event of acute liver dysfunction due to TMP-SMX, use of NAC may improve outcomes by preventing progression to liver failure, but further research is needed.

**Funding Agencies:** None

A24
**FEVER, CHOLESTATIC HEPATITIS & PNEUMONIA, A COMMON PRESENTATION OF AN UNCOMMON DISEASE: CASE REPORT & LITERATURE REVIEW**
M. Alzahrani[1], J. Walsh[1], K. Qumosani[2], A. Teriaky[3]

1. Western University, London, ON, Canada; 2. Department of Medicine, Western Univesity, LONDON, ON, Canada; 3. Gastroenterology, Hepatology, London Health Sciences Centre , London , ON, Canada

**Background:** Q fever is a zoonotic infection caused by Coxiella burnetii and usually acquired by susceptible patients with common risk factors. The diagnosis is usually delayed. Known manifestations of it include fever of unknown origin, endocarditis, atypical pneumonia, and hepatitis.
**Aims:** To describe an interesting case of Q fever and review the literature on Q fever and its hepatic manifestations.
**Methods:** Patient's informations were extracted from electronic records and included admission notes, laboratory investigations, procedure reports, pathology notes, and clinic reports. In addition, we performed a literature
review using pubmed.
**Results:** We are reporting a case of a 48 years old male with no recognizable risk factor who presented with fever, pneumonia, cholestatic hepatitis, anasarca, and coagulopathy. He did not improve with empiric antibiotic treatment. He had an extensive negative workup and definitive diagnosis was only made after the results of a of liver biopsy showed Q fever's typical finding of a fibrin ring granuloma. He was started on treatment with an 18 month course of doxycycline resulting in full recovery. Reports from different geographical locations indicate that
epidemiological and clinical features of Q fever vary from area to area with most cases presenting as hepatitis being in Europe and more specifically in Spain. North American data showed an increasing number of Q fever cases being reported to the CDC from 19 cases reported in 2000 to 176 cases in 2014. In Canada, the national incidence is not known, but it is notifiable disease in some provinces with a a total of 47 confirmed Q fever cases being reported in Ontario from 2006 to 2011 with a four-fold increase in cases in 2011. Seasonal variation in incidence has been observed. In addition to the fever and other symptoms, a number of hepatic manifestations of Q fever have been described including mild to moderate transaminitis (which is the most common hepatic presentation), cholestatic hepatitis, granulomatous hepatitis, hepatic abscess, triggering of autoimmune
hepatitis/primary biliary cholangitis overlap by Q fever, and acute acalculous cholecystitis.
**Conclusions:** The incidence of Q fever is increasing in North America with a wide spectrum of presenting clinical symptoms. In the presence of atypical hepatitis with exclusion of other causes, investigations should be conducted to rule out Q fever.



Fibrin ring granuloma on liver biopsy (high power)

Funding Agencies: None

## CYTOKINES AND INTRACELLULAR SIGNALS

A25
**COLONIC PROTEASES EVOKE SUSTAINED PAIN SIGNALING VIA A NOVEL ENDOSOMAL PATHWAY IN NEURONS**
N. Jimenez-Vargas[2], N. Bunnett[1], S. Vanner[3]

1. Columbia University, New York City, NY; 2. Queen's University, Kingston, ON, Canada; 3. Queen's University, Kignston, ON, Canada

**Background:** Proteases are increased in IBS patient colonic tissue and have been shown to activate and sensitize nociceptive (pain-sensing) dorsal root ganglia (DRG) neurons. We found that activation of protease

activated receptor 2 (PAR2) on DRG neurons leads to prolonged pain signaling (> 1h). Serine proteases (e.g. trypsin) are major mediators of this response and we identified that trypsin signals through novel pathways that are distinct from cysteine proteases (cathepsin S, elastase). Here we found that trypsin signals by PAR2 endocytosis trafficking to endosomes to induce sustained signaling. It is unknown whether other tissue proteases also act through PAR2 to elicit sustained signaling and if a specific endosomal antagonist can block the effect of proteases in IBS tissues.
**Aims:** 1) to determine if sustained signaling by both serine and cysteine proteases are blocked by the selective PAR2 antagonist I-343 and 2) to determine whether PAR2 in endosomes is a therapeutic target using a novel lipidated PAR2 antagonist that targets endosomes.
**Methods:** DRG neurons from C57BL/6 mice were pre-incubated with trypsin (10 min; 50 nM), elastase (30 min; 390 nM) or cathepsin-S (60 min; 500 nM) and then washed out. Changes in neuronal excitability (rheobase, amount of current to elicit an action potential) was measured using patch clamp recordings, immediately (T=0 min) or after a sustained period (T=30 min). The role of PAR2 was evaluated with PAR2 antagonist I-343 (10 μM) and to evaluate the role of PAR2 in endosomes, we used a lipidated I-343 (MIPS15479). Supernatants containing representative proteases of colonic biopsies were obtained from diarrhea-predominant IBS patients or controls (HC). DRG neurons were pre-incubated with MIPS15479 (30 μM), washed and allowed to recover in antagonist-free medium for 120 min before applying the protease agonists or IBS supernatant. Two-way ANOVA and Tukey's post hoc tests were used to analyze the data.
**Results:** The PAR2 antagonist blocked the sustained (T=30 min) excitability evoked by trypsin (37.5%, $P<0.05$) and cathepsin S (54%, $P<0.001$) whereas the antagonist had no effect on the sustained actions of elastase. In contrast, the immediate excitability (T= 0 min) evoke by all three proteases was completed blocked by the antagonist. IBS-D supernatants also evoked sustained excitability of DRG neurons (decrease 43% in rheobase compared to HC; $P <0.01$) and this effect was blocked by the lipidated PAR2 antagonist MIPS15479. Trypsin-mediated sustained excitability was also inhibited by MIPS15479, but the acute response was unaffected
**Conclusions:** The lipidated PAR2 antagonist blocked the sustained but not immediate excitability evoked by trypsin, consistent with an endosomal action. This antagonist also blocked the sustained protease-PAR2 signaling mediated by IBS tissues, suggesting that this antagonist could be a novel therapeutic agent.

**Funding Agencies:** CCC

A26
**INDUCTION OF A CELLULAR MIGRATION PROGRAM THROUGH PAR2 ACTIVATION IN COLONIC EPITHELIAL CELLS**
A.J. Vegso[2], W. MacNaughton[1]

1. Univ Calgary, Calgary, AB, Canada; 2. Physiology and Pharmacology, University of Calgary, Calgary, AB, Canada

**Background:** Inflammatory bowel disease (IBD) treatments are ineffective for many patients and where they are helpful, lose their efficacy over time. However, the mechanisms that determine mucosal healing, the key goal of therapy, are complex and incompletely understood.
**Aims:** The inflammatory environment is characterized by the presence of several serine proteases that signal through the protease-activated receptors (PARs). PAR2 is ubiquitously expressed in the epithelial cells of the intestinal mucosa, and our previous studies suggest that PAR2 activation serves a protective role consistent with host defence and repair. While our preliminary findings indicate that activation of PAR2 enhances wound healing, we do not know the cellular mechanisms that underlie this response. **We hypothesize that activation of PAR2 induces a cellular migration program in intestinal epithelial cells that enhances mucosal healing.**
**Methods:** T84 colonic epithelial cells were grown to confluence before circular wounds were made by a pipette tip attached to the end of an aspirator. Wounded monolayers were treated with PAR2 activating peptide 2-furoyl-LIGRLO (2fLI, 5 μM) or the control reverse-sequence peptide 2-furoyl-OLRGIL (2fO, 5 μM) and live cell microscopy was utilized to record wound healing over a 24 hr period. A 2fLI concentration-response (0.1 μM – 10 μM) was first performed. A cytokine cocktail consisting of IFNγ (10 ng/mL), TNFα (10 ng/mL), and IL-1β (10 ng/mL) was applied to wounded monolayers with and without 2fLI (5 μM) treatment and wound healing was then assessed. PAR2 activation and cytokine functionality were validated by immunoblot of targets of canonical signaling pathways.
**Results:** PAR2 activation by 2fLI promoted wound healing in a concentration-dependent manner (0.1 μM – 10 μM) compared to 2fO controls at the 24 hr timepoint. 5 μM 2fLI caused the maximal response at the 24 hr timepoint ($p<0.001$). Treatment with a cytokine cocktail also promoted a significantly increased wound healing response compared to the untreated controls ($p<0.05$). Co-stimulation with 2fLI and the cytokine cocktail resulted in an additive wound healing response at the 24 hr timepoint and was significantly greater than individual treatments ($p<0.001$). PAR2 activation resulted in the activation of the ERK/MAPK pathway while the cytokine cocktail activated both the JAK and ERK/MAPK pathways.
**Conclusions:** The data suggest that both PAR2 activation and cytokine treatment promote a wound healing program *in vitro*. An additive wound healing effect occurs upon PAR2 activation in the presence of pro-inflammatory cytokines, which suggest that the inflammatory milieu is integral to initiate a proper wound healing response.

**Funding Agencies:** CCC, CIHR

A27

**ERK/MAPK SIGNALING PROMOTES GOBLET CELL DIFFERENTIATION BY INHIBITING THE NOTCH PATHWAY**

J. Gagné Sansfaçon, A. Langlois, M. Langlois, K. Beaudry, N. Rivard

Anatomie et biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** Several mouse genetic models have suggested an important role for EGF, Wnt, BMP/TGF*beta* and Notch signaling pathways in the renewal and differentiation of intestinal stem cells. EGF and its orthologs TGF*alpha* and epiregulin are factors regulating growth in epithelial tissues through activation of the RAS/RAF/MEK/ERK MAPK signaling pathway. Accordingly, in human and mouse intestines, ERK activity is predominantly found in progenitor cells in the transit-amplifying zone of the crypts where it is thought to control the proliferation/differentiation switch (Aliaga 1999). Indeed, we and others have reported that ERKs are selectively inactivated during absorptive cell differentiation hence supporting the hypothesis that these kinases must be shut down for the initiation of this differentiation process (Lemieux 2011). However, the role of ERK signaling in differentiation of the secretory cell lineage, particularly in Goblet cell differentiation remains to be elucidated.
**Aims:** This study was therefore conducted to analyze the role of ERK/MAPK signaling in the differentiation of intestinal Goblet cells and to elucidate the molecular events involved in this possible regulation.
**Methods:** Goblet cell number and differentiation were analyzed in three mouse models exhibiting sustained activation of ERK/MAPK signaling in intestinal epithelium: mice expressing oncogenic $BRAF^{V600E}$ in intestinal epithelial cells (IECs), mice expressing activated $Shp2^{E76K}$ mutant in IECs and mice knockout for Dusp6 (an inhibitor of ERK). Western blot, qPCR analyses and luciferase assays were performed in goblet-like cells LS174T treated or not with the MEK inhibitor CI-1040 (2 uM).
**Results:** Alcian blue staining in the colon of $BRaf^{V600E}$, $Shp2^{E76K}$ and $Dusp6^{-/-}$ mice reveal a marked increase in the number of Goblet cells in comparison to their control littermates. Interestingly, inhibition of MEK/ERK signaling with CI-1040 significantly reduces *MUC2* transcript levels in LS174T cells. This decrease in *MUC2* expression is associated with decreased transcriptional activity of KLF4 which is involve in Goblet cell terminal differentiation. Most interestingly, we found that inhibition of the MEK/ERK signaling activates the NOTCH pathway as visualized by an increased cleavage of NICD, the NOTCH intracellular domain, and expression of *HES1*, a target gene. This accumulation of NICD and HES1 can be prevent by *gamma*-secretase complex inhibition suggesting a NOTCH-dependent mechanism. Notably, qPCR analyses demonstrated an increased expression of the NOTCH ligands *Delta-like 1* and *Delta-like 4* in CI-1040-treated cells.
**Conclusions:** Taking together, our results strongly suggest that RAF/MEK/ERK signaling pathway promotes Goblet cell differentiation by inhibiting the activation of NOTCH, a pathway known to inhibit the secretory cell fate.

**Funding Agencies:** CIHRFRQS

A28

**SHP-1 REGULATES INTESTINAL EPITHELIUM HOMEOSTASIS BY CONTROLLING ACTIVATION OF BOTH PI3K/AKT AND WNT/β-CATENIN PATHWAYS**

C. Leblanc[4], M. Langlois[2], N. Perreault[3], N. Rivard[1]

1. Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Université de Sherbrooke, Sherbrooke, QC, Canada; 3. Anatomie et Biologie Cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 4. Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** Shp-1 is a tyrosine phosphatase highly expressed in hematopoietic cells and involved in the control of proliferation and differentiation. This phosphatase is also expressed at lower levels in epithelial cells such as intestinal epithelium. Our previous results showed that loss of epithelial Shp-1 leads to an intestinalomegaly associated with increased epithelial cell proliferation. We also noticed that the PI3K/Akt and Wnt/β-catenin pathways were both hyperactivated in IECs from these mice in comparison to controls (Leblanc Faseb J 2017).
**Aims:** However, the role of Shp-1 in this epithelium still remains poorly characterized. So we wanted to determine the contribution of hyperactive PI3K/Akt pathway in these phenotypic alterations.
**Methods:** To determine the contribution of hyperactive PI3K/Akt pathway, we generated mice with a specific deletion of Pten in IEC ($Pten^{IEC\text{-}KO}$ mice) and carefully compared their intestinal phenotype with $Shp\text{-}1^{IEC\text{-}KO}$ mice.
**Results:** Interestingly, both $Shp\text{-}1^{IEC\text{-}KO}$ and $Pten^{IEC\text{-}KO}$ mice develop similar intestinal phenotype: increased proliferation rate, intestinalomegaly and increased Goblet cell number. However, Paneth cell maturation is impaired in $Shp\text{-}1^{IEC\text{-}KO}$ mice but not in $Pten^{IEC\text{-}KO}$ mice. Indeed, decreased gene expression of *Lyz1* and an expansion of intermediate cells are observed in $Shp\text{-}1^{IEC\text{-}KO}$ mice. Since Paneth cells constitute the niche for Lgr5 stem cells in intestinal crypts, we analyzed stem cell activity *ex vivo*, in enteroids isolated from $Shp\text{-}1^{IEC\text{-}KO}$, $Pten^{IEC\text{-}KO}$ and their control littermates. Surprisingly, we observed striking difference in enteroid development: $Pten^{IEC\text{-}KO}$ enteroids grow very well and develop many protrusions in comparison to their respective controls. However, while proliferation is increased in $Shp\text{-}1^{IEC\text{-}KO}$ enteroids, their morphogenesis is clearly impaired; diminution of R-spondin in the culture medium rescues *de novo* crypt formation in Shp-1-deficient organoids.
**Conclusions:** Our results indicate that loss of Shp-1 in

IEC phenocopies many defects that are observed in *Pten*$^{IEC\text{-}KO}$ mice, including intestinalomegaly and abnormal Goblet cell differentiation. However, defects in Paneth cell maturation observed in *Shp-1*$^{IEC\text{-}KO}$ mice is probably triggered by the hyperactivation of Wnt/β-catenin signaling observed in these mice.

**Funding Agencies:** NSERC

## EPIDEMIOLOGY AND THE BURDEN OF ILLNESS

### Poster of Distinction

A29

**THE RISING PREVALENCE OF INFLAMMATORY BOWEL DISEASE IN CANADA: ANALYZING THE PAST TO PREDICT THE FUTURE**

S. Coward[5], F. Clement[10], E.I. Benchimol[1], C.N. Bernstein[2], A. Bitton[4], M.W. Carroll[7], G. Hazlewood[10], S. Jelinski[12], J. Jones[3], E. Kuenzig[1], D. Leddin[3], K. McBrien[10], S. Murthy[8], G.C. Nguyen[6], A. Otley[3], A. Rezaie[11], J. Pena-Sanchez[9], H. Singh[2], L. Targownik[2], G.G. Kaplan[5]

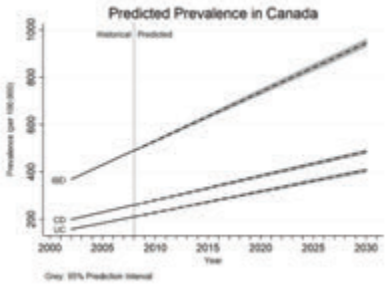
1. Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC), Children's Hospital of Eastern Ontario IBD Centre, University of Ottawa, Ottawa, ON, Canada; 2. CanGIEC, University of Manitoba, Winnipeg, MB, Canada; 3. CanGIEC, Dalhousie University , Halifax, NS, Canada; 4. CanGIEC, McGill University, Montreal, QC, Canada; 5. CanGIEC, University of Calgary, Calgary, AB, Canada; 6. CanGIEC, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 7. CanGIEC, Univeristy of Alberta, Edmonton, AB, Canada; 8. CanGIEC, University of Ottawa , Ottawa, ON, Canada; 9. CanGIEC, University of Saskatchewan, Saskatoon, SK, Canada; 10. University of Calgary, Calgary, AB, Canada; 11. Cedar Sinai Medical Center, Los Angeles, CA; 12. University of Alberta, Alberta Health Services, Edmonton, AB, Canada

**Background:** The prevalence of Inflammatory Bowel Disease (IBD), consisting of Crohn's disease (CD) and ulcerative colitis (UC), is rising in Canada. Because IBD is a complex and costly disease, estimates of changing prevalence over time are necessary to inform the Canadian healthcare system on the evolving burden of IBD.
**Aims:** To analyze historical prevalence and predict the future prevalence of IBD in Canada.
**Methods:** Annual population-based prevalent cohorts from Alberta (2002-2015), Manitoba (1990-2013), Ontario (1999-2014), Quebec (2001-2008), and Nova Scotia (1996-2009) were obtained from the Canadian Gastro-Intestinal Epidemiology Consortium. Data were adjusted based on annual age and sex distribution in Canada. Log binomial regression on adjusted data was performed with either a linear, linear spline, or restricted cubic spline model, depending on model fit, and yielded average annual percentage change (AAPC) with 95% confidence intervals (CI). Predictive models for CD, UC, and IBD to 2030 were calculated for each province, and then combined into a single model for Canada with provincial data from 2002 to 2008. Prediction intervals (PI) were calculated for predicted prevalence.
**Results:** Prevalence of CD, UC, and IBD for each province in 2008 and provincial predicted prevalence in 2018 and 2030 is reported in Table 1. The estimated prevalence of IBD in Canada in 2008 was 489 per 100,000 persons. In Canada, the predicted AAPC after 2008 is: CD: 2.76% (95%CI:2.74-2.78%); UC: 2.90% (95%CI:2.88-2.92%); and IBD 2.88% (95%CI:2.87-2.90%) (Figure 1). The prevalence of IBD in Canada is predicted to climb to 0.95% in 2030 (Table 1, Figure 1), which represents an increase in the number of people with IBD in Canada from 257,564 (95%PI:254,356-260,772) in 2018 to 388,042 (95%PI:381,808-394,276) in 2030.
**Conclusions:** By 2030, 0.95% of the Canadian population is predicted to have IBD. Clinical and policy driven healthcare innovations are required over the next decade to stem the impact of IBD in Canada and ensure these individuals receive the necessary care.

Table 1: Past and Future Prevalence of IBD in Canada (Prevalence per 100,000 persons)

| | IBD | | | CD | | | UC | | |
|---|---|---|---|---|---|---|---|---|---|
| | 2008 | 2018 | 2030 | 2008 | 2018 | 2030 | 2008 | 2018 | 2030 |
| | Actual | Predicted | | Actual | Predicted | | Actual | Predicted | |
| Canada | 489 | 697 | 945 | 259 | 363 | 487 | 210 | 300 | 408 |
| AB | 510 | 646 | 780 | 275 | 317 | 351 | 176 | 222 | 264 |
| MB | 546 | 597 | 664 | 275 | 288 | 307 | 271 | 309 | 357 |
| NS | 860 | 1136 | 1469 | 410 | 516 | 642 | 345 | 543 | 698 |
| ON | 487 | 630 | 782 | 237 | 293 | 350 | 235 | 302 | 372 |
| QC | 429 | 639 | 890 | 270 | 412 | 581 | 159 | 230 | 314 |

AB: Alberta; MB: Manitoba; NS: Nova Scotia; ON: Ontario; QC: Quebec




**Funding Agencies:** CIHRIzaak Walton Killam Memorial Scholarship; Eyes High Doctoral Recruitment Scholarship

## Poster of Distinction

A30

**ETHNIC VARIATION OF PEDIATRIC INFLAMMATORY BOWEL DISEASE IN CANADA**

J. Jeong[1], A. Lee Wing Ngok[1], T.D. Walters[2], A. Griffiths[2], D.R. Mack[2], E.I. Benchimol[2], H.Q. Huynh[2], K. Jacobson[2], A. Otley[2], W. El-Matary[2], C. Deslanders[2], E.G. Seidman[2], M. Sherlock[2], K. Bax[2], J. Critch[2], M.W. Carroll[2], E. Wine[2], S. Lawrence[2], J. Van Limbergen[2], P. Church[2], J. deBruyn[2]

1. University of Calgary, Calgary, AB, Canada; 2. CIDsCaNN, Toronto, ON, Canada

**Background:** Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract with highest prevalence in the Western world. Recent temporal trends in adult and pediatric populations demonstrate increasing incidence in both developed and developing countries. IBD phenotypes may differ between countries and ethnic/racial groups
**Aims:** This study examined ethnic and phenotypic variation of children newly diagnosed with IBD in Canada.
**Methods:** The Canadian Children IBD Network established an inception cohort of children with incident IBD in 13 tertiary-care centers across Canada. Children were categorized into 9 different ethnic groups using a modified Statistics Canada classification method. Demographic characteristics, family history, place of birth, disease phenotype and activity were evaluated. Univariate regression analysis evaluated the association between ethnicity groups. Where appropriate, Wilcoxon rank sum test was used to compare groups.
**Results:** 886 children newly diagnosed with IBD were evaluated. The largest ethnicity groups included Caucasian (71.3%), South Asian (8.6%), Mixed Ethnicity (8.6%), Middle Eastern (3.4%), and African (3.3%). The median age at diagnosis was 12.3 years (IQR 8.8-15 y). The prevalence of IBD subtypes was as follows: Crohn's disease (CD) 60.5%, ulcerative colitis (UC) 28.6% and IBD type Unclassified (IBD-U) 8.7%. South Asians had higher odds of UC compared to non-South Asians (odds ratio [OR] 2.2, 95%CI 1.2–3.8). Using the Paris classification for CD, the prevalence of CD phenotype was as follow: L1 15.9%, L2 19.2%, L3 39.9%, L4a 16.0%, L4b 5.4%. Using the Montreal classification for UC, the prevalence of UC phenotype was as follows: E1 7.1%, E2 4.7%, E3 8.7%, E4 54.9%. The median PCDAI score at diagnosis was 55 (IQR 35-75). The median PUCAI score at diagnosis was 55 (IQR 40–70). Caucasians had higher odds of a positive family history of IBD compared to non-Caucasians (OR 1.7, 95%CI 1.1–2.9), especially maternal history of IBD (OR 2.9, 95%CI 1.3–7.1).
**Conclusions:** Across ethnic groups, South Asians had higher odds of UC compared to non-South Asians. L3 was the most prevalent phenotype in CD and E4 was the most prevalent phenotype in UC. Caucasian ethnicity is associated with higher odds of a positive family history, particularly with a maternal family history of IBD. Further studies are required to evaluate the impact of ethnic variation of pediatric IBD on disease management and prognosis.

**Funding Agencies:** CIHRChILD Foundation

## Poster of Distinction

A31

**DISPARITIES IN THE CARE OF RURAL AND URBAN CANADIANS WITH INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY**

E.I. Benchimol[1], C.N. Bernstein[2], G.C. Nguyen[3], L. Targownik[2], A. Guttmann[4], J. Jones[5], B.K. Potter[6], E. Kuenzig[1], C.A. Catley[7], D. Tanyingoh[8], Z. Nugent[2], N. Mojaverian[7], F. Underwood[8], G.G. Kaplan[8]

1. Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC), Institute for Clinical Evaluative Sciences (ICES), Children's Hospital of Eastern Ontario IBD Centre, Department of Pediatrics, School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada; 2. CanGIEC, University of Manitoba IBD Clinical and Research Centre, Department of Medicine, University of Manitoba, Winnipeg, MB, Canada; 3. CanGIEC, ICES, Mount Sinai Hospital Centre for IBD, Department of Medicine, University of Toronto, Toronto, ON, Canada; 4. ICES, Department of Paediatrics,

Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada; 5. CanGIEC, Department of Medicine, Dalhousie University, Halifax, NS, Canada; 6. ICES, School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada; 7. ICES, University of Ottawa, Ottawa, ON, Canada; 8. CanGIEC, University of Calgary IBD Clinic, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

**Background:** Canada's large geographic area and low population density poses challenges in access to specialized healthcare for remote and rural residents. Inflammatory bowel disease (IBD) (Crohn's disease (CD) and ulcerative colitis (UC)) is less common among rural residents, however disparities in care and outcomes may exist.
**Aims:** Compare health services use and markers of disease control (hospital admissions and surgeries) in rural and urban IBD patients in Canada using population-based health administrative data.
**Methods:** Validated algorithms identified all incident cases of IBD from administrative data in 3 provinces: Alberta (AB) 1999-2008, Manitoba (MB) 1999-2010, Ontario (ON) 1999-2010. We compared rural to urban residents for time to diagnosis, IBD-specific hospitalization, outpatient visits, emergency department (ED) use (ON only), surgical resections (CD) or colectomy (UC), and gastroenterologist (GI) care. Rural/urban status was based on Metropolitan Area and Census Agglomeration Influenced Zones. Multivariable regression compared outcomes in rural/urban residents, controlling for confounders (Table footnote). Provincial results were meta-analyzed to produce overall estimates.
**Results:** See Table. 37,018 urban and 6656 rural residents with incident IBD were included. Rural patients had fewer GI visits, and a smaller proportion of their IBD-specific care provided by GI (39.1% vs 61.4%, P<0.0001). Rural patients were more frequently hospitalized, and used the ED more. There was no difference in outpatient visit rate or risk of first surgery. However, rural patients were more likely to undergo multiple intestinal resections.
**Conclusions:** Rural IBD patients have less use of GI specialists and more need for acute care, suggesting worse outcomes related to disparities in access to specialist care. Innovative methods of delivering GI care to rural IBD patients (such as telehealth, online support, remote clinics) should be explored.

Table. IBD-specific health services utilization in rural patients (ref: urban patients)

| | IBD | Crohn | UC |
|---|---|---|---|
| Time to diagnosis[a] | n/a | 1.01 (0.94-1.07) | **1.11 (1.004-1.22)** |
| Outpatient visit rate[b] | 0.99 (0.93-1.05) | 1.03 (0.98-1.89) | 0.95 (0.87-1.02) |
| Risk of hospitalization[a] | 1.07 (0.94-1.20) | 1.03 (0.92-1.34) | 1.01 (0.94-1.08) |
| Number of hospitalizations[c] | **1.17 (1.02-1.32)** | **1.16 (1.08-1.23)** | 1.16 (0.90-1.42) |
| ED visits[b,d] | **1.54 (1.36-1.73)** | **1.72 (1.47-2.01)** | **1.25 (1.11-1.41)** |
| Risk of surgery[a] | n/a | 0.99 (0.90-1.08) | 0.91 (0.78-1.05) |
| Risk of multiple surgeries (≥2 vs. 1/0 surgeries)[a] | n/a | **1.39 (1.07-1.70)** | n/a |
| Ever seen by GI[e] | **0.47 (0.34-0.61)** | **0.48 (0.47-0.49)** | **0.40 (0.32-0.49)** |
| Number of visits to GI[c] | **0.79 (0.73-0.84)** | **0.80 (0.79-0.81)** | **0.70 (0.65-0.76)** |

Models adjusted for sex, diagnosis age, income; [a]Cox proportionate hazard; [b]Poisson; [c]Negative binomial; [d]Ontario only; [e]Logistic

**Funding Agencies:** CIHRJanssen Future Leaders in IBD Grant, CHEO Research Institute

## Poster of Distinction

A32

**IMPACT OF DISEASE SEVERITY ON HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHEA**

A. Marciniak[1], Y. Mo[2], J. Ma[2], J. Abel[3], R. Carson[3]

1. Former employee of Allergan plc, Buckinghamshire, United Kingdom; 2. Allergan plc, Bridgewater, NJ; 3. Allergan plc, Jersey City, NJ

**Background:** Irritable bowel syndrome with diarrhea (IBS-D) is a chronic gastrointestinal disorder shown to significantly impact patients' health-related quality of life (HRQoL). The relationship between IBS-D disease severity and HRQoL impact is not well understood.
**Aims:** To examine if greater IBS-D disease severity is associated with increased impairment in HRQoL, using baseline data from clinical trials of eluxadoline.
**Methods:** HRQoL was assessed using the disease-specific Irritable Bowel Syndrome Quality of Life (IBS-QoL) and the EuroQol 5-dimension (EQ-5D) questionnaires. The IBS-QoL includes a total score and eight subscale scores, each calculated on a 0–100 scale with higher scores indicating better IBS-specific QoL. The EQ-5D

evaluates five dimensions of health and incorporates these into an overall index score ranging from 0 (worst possible health state) to 1 (best possible health state). IBS-QoL scores were mapped to EQ-5D scores using a validated algorithm. Symptom severity, based on the global symptom score (GSS; on a scale of 0–4 where 0=none and 4=very severe symptoms), was assessed at baseline. IBS-QoL and EQ-5D scores were summarized based on GSS (<3 or ≥3), age (<65 or ≥65 years), sex, and for patients with a GSS ≥3 who also reported inadequate relief of symptoms with loperamide.
**Results:** Patients with GSS ≥3 had a lower mean total IBS-QoL score compared to those with GSS <3 and lower scores across all subscales (Table). Patients with GSS ≥3 also had a lower mean EQ-5D index score compared to those with GSS <3 (0.5 vs. 0.6). Patients with a GSS ≥3 who reported inadequate relief with loperamide treatment (n=249) had greater reductions in HRQoL compared to those with a GSS ≥3 who did not, as indicated by lower IBS-QoL mean scores, overall (36.6 vs. 41.7) and across all subscales. Women generally reported lower IBS-QoL scores than men; no notable differences were observed based on age (Table).
**Conclusions:** Patients with IBS-D with greater disease severity reported increased impairments in HRQoL. IBS-D disease severity may be an important consideration for effective management of IBS-D, highlighting the need for treatments that reduce symptom burden and improve HRQoL.

| IBS-QoL | Total | Female | Male | <65 years | ≥65 years | GSS <3 | GSS ≥3 |
|---|---|---|---|---|---|---|---|
| n | 2404 | 1589 | 815 | 2167 | 237 | 1301 | 1103 |
| Total score, mean | 46.9 | 44.5 | 51.6 | 47.1 | 45.2 | 51.4 | 41.7 |
| Dysphoria | 46.5 | 44.3 | 50.9 | 46.9 | 43.3 | 51.6 | 40.6 |
| Activity interference | 37.3 | 34.6 | 42.6 | 37.8 | 33.1 | 41.6 | 32.3 |
| Body image | 48.8 | 44.5 | 57.0 | 49.1 | 46.1 | 52.4 | 44.5 |
| Health worry | 54.3 | 53.7 | 55.6 | 54.4 | 53.6 | 59.3 | 48.4 |
| Food avoidance | 33.4 | 30.5 | 39.0 | 33.1 | 35.9 | 37.1 | 29.0 |
| Social reaction | 51.1 | 49.5 | 54.4 | 51.2 | 50.7 | 55.6 | 45.8 |
| Sexual | 64.2 | 61.3 | 69.9 | 63.5 | 70.6 | 68.0 | 59.7 |
| Relationships | 57.4 | 55.8 | 60.3 | 57.7 | 54.3 | 62.4 | 51.4 |

**Funding Agencies:** Allergan plc

## Poster of Distinction

A33

### DOES PREGNANCY ADVERSELY IMPACT THE HEALTH-RELATED QUALITY OF LIFE AMONG WOMEN WITH IBD?

N. Rodriguez[4], L. Ambrosio[5], R.T. Sutton[2], L.A. Dieleman[3], B.P. Halloran[1], K.I. Kroeker[3], F. Peerani[1], K. Wong[1], R. Fedorak[1], V. Huang[1]

1. University of Alberta, Edmonton, AB, Canada; 2. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada; 4. Science, University of Alberta, Edmonton, AB, Canada; 5. University of Alberta, Edmonton, AB, Canada

**Background:** Women with Inflammatory Bowel Disease (IBD) are at risk of flaring during pregnancy, and are associated with adverse maternal and neonatal outcomes. In addition, active IBD has been associated with poor health related quality of life (HRQoL). However, whether pregnancy-related changes also influence HRQoL of life is still unknown.
**Aims:** To assess the impact of pregnancy on the health related quality of life (HRQoL) among women with IBD and the impact of IBD disease activity on HRQoL in pregnant women with IBD.
**Methods:** Adult (≧18years) women with Crohn's disease (CD) or ulcerative colitis (UC), and healthy volunteers who were either preconception or pregnant participated in a quality of life research study, and followed until delivery. Participants completed disease activity indices, such as Harvey Bradshaw Index (HBI) for CD or partial Mayo score (pMayo) for UC. Clinically active disease was defined as mHBI ≧5 or pMayo ≧2; whereas c-reactive protein ≧8.0mg/L and fecal calprotectin ≧250mg/kg indicated objectively active disease. Short IBD quality of life (SIBDQ) survey was administered at each time point (preconception, trimester 1, trimester 2, and trimester 3) and compared between groups for diagnosis and disease activity. SIBDQ scores in each time point were compared using independent samples median t-test and differences between categorical variables were analyzed using chi-square test. Statistically significant results were considered to have $p < 0.05$. All statistical analyses were performed using SPSS statistical program, version 24.0.
**Results:** A total of 70 women completed at least one SIBDQ survey during the follow up period. There were 11 (15.7%) healthy volunteers, 36 (52.4%) women with UC, and 23 (32.9%) women with CD. There was no difference in SIBDQ scores at preconception or during pregnancy between healthy women and women with IBD. SIBDQ scores were lower in IBD patients than



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in healthy participants in trimester 2 of pregnancy. Furthermore, SIBDQ scores were significantly lower in patients who had clinically active disease in trimesters 2 and 3. No statistically significant differences were found when patients were grouped by objective disease activity.
**Conclusions:** Overall, HRQoL was reduced in women with IBD and especially during clinically active disease during pregnancy. Women with inactive IBD during pregnancy have similar IBD related quality of life as women without IBD. Our findings encourage further research on the interaction of IBD and pregnancy to improve patient and physician related knowledge in optimizing pregnancy outcomes in IBD patients.

**Funding Agencies:** WCHRI, CEGIIR, University of Alberta Faculty of Medicine

## Poster of Distinction

A34
**TRENDS AND PREDICTORS OF CLOSTRIDIUM DIFFICILE INFECTION AMONG THE CHILDREN OF MANITOBA: A POPULATION-BASED STUDY**
W. El-Matary[2], Z. Nugent[4], B. Yu[5], L. Lix[6], L.E. Targownik[3], C.N. Bernstein[1], H. Singh[2]

1. Uiversity of Manitoba, Winnipeg, MB, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. Internal Medicine, University of Manitoba, Winnipeg, MB, Canada; 4. University of Manitoba, Winnipeg, MB, Canada; 5. University of Manitoba, Winnipeg, MB, Canada; 6. University of Manitoba, Winnipeg, MB, Canada

**Background:** *Clostridium difficile* infection (CDI) is a significant cause of morbidity and mortality in both children and adults. *Clostridium difficile* causes a wide spectrum of clinical illnesses, from asymptomatic colonization and mild diarrhea to pseudomembranous colitis and toxic megacolon. CDI is not adequately characterized in the pediatric age group.
**Aims:** Our objectives were to examine: (a) trends in CDI rates, and (b) predictors of CDIs, including recurrent CDIs, in the pediatric population.
**Methods:** Data were extracted from several validated population-based datasets from the province of Manitoba for the period from 2005 to 2015. CDI was identified from a laboratory-confirmed CDI dataset. Children aged 2-17 years with CDI were matched to children without CDI, based on age, sex, 3-digit residential postal code and duration of coverage with Manitoba Health (MH) prior to the index date (i.e., date of first CDI). Children younger than 2 years of age were excluded on the basis of apparent lack of association between carriage and disease. Rates and time trends of CDIs using previously recommended definitions were determined. Predictors of CDI sub-types were determined using multivariable logistic regression models. CDIs diagnosed in outpatient and hospital settings were identified. Cox regression analysis was used to assess for the potential predictors of CDI, including age, sex, socio-economic status (SES), co-morbidities burden, and medications used.
**Results:** Over the study period, 277 children with CDI were identified and matched with 1314 controls without CDI. After excluding those who had CDI before the age of 2 years old, 193 CDI from 163 children (47% males) were included. Children with and without CDI were followed for 828 and 2753 persons years respectively. There was no significant increase in CDI rates over the observation period. Children with CDI had significantly higher number of outpatient clinic visits compared to controls in the year before CDI diagnosis (p<0.0001). Co-morbid conditions that were more prevalent among children with CDI than matched controls included Hirschsprung's disease (p<0.001) and inflammatory bowel disease (p<0.0001). More than half of CDIs were community acquired and 18.7% were healthcare facility associated. Recurrent CDIs were responsible for 10.4% of CDI episodes (range 2-6 infections). Predictors of recurrence included malignancy (Hazard ratio (HR)= 3, 95% 1.1-8.8), Type 1 diabetes (HR=4.8, 95% CI 1.1-21.4) and neurodegenerative diseases (HR=8.4, 95% CI 1.9-37.5).
**Conclusions:** The incidence of CDI is not increasing among children in Manitoba. Community-acquired CDI is much more common than healthcare facility-associated. Children with malignancy, type 1 diabetes and neurodegenerative disorders are more likely to have recurrent CDI.

**Funding Agencies:** This work was supported with an unrestricted grant from MERCK

## Poster of Distinction

A35
**GENOME WIDE ASSOCIATION STUDY OF ABNORMAL INTESTINAL PERMEABILITY IN HEALTHY FIRST DEGREE RELATIVES OF CROHN'S PATIENTS**
W. Turpin[6], L. Bedrani[6], O. Espin-Garcia[11], M. Smith[6], D. Guttman[6], K. Madsen[3], A. Griffiths[1], P. Moayyedi[2], R. Panaccione[5], H.Q. Huynh[7], L.A. Dieleman[4], A. Steinhart[8], G. Aumais[9], M.S. Silverberg[8], X. Wei[10], A. Paterson[10], K. Croitoru[8]

1. Hospital for Sick Children, Toronto, ON, Canada; 2. McMaster University, Hamilton, ON, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. Medicine, University of Alberta, Edmonton, AB, Canada; 5. University of Calgary, Calgary, AB, Canada; 6. University of Toronto, Toronto, ON, Canada; 7. Pediatrics, University of alberta, Edmonton, AB, Canada; 8. Mount Sinai Hospital, Toronto, ON, Canada; 9. Montreal University, Montreal, QC, Canada; 10. Dalla Lana School of Public Health, Toronto, ON, Canada; 11. Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada

**Background:** Increased intestinal permeability (IP) is thought to be a risk factor for the development of inflammatory bowel disease (IBD). Our recent study has demonstrated that known IBD risk-associated single nucleotide polymorphisms (SNPs) were not associated with IP, while smoking status and age were two inde-

pendent factors associated with increased IP.
**Aims:**
To identify other genetic loci influencing IP, we performed a genome wide association study (GWAS) among healthy first-degree relatives of CD patients with increased and normal IP.
**Methods:**
IP was measured with high-pressure liquid chromatography of timed urine collection after ingestion of two saccharide probes, lactulose and mannitol. For each subject, the lactulose–mannitol ratio (LacMan ratio) was calculated as the fractional excretion of lactulose divided by that of mannitol. A LacMan ratio >0.025 was considered as abnormal IP. Genotyping was performed using the HumanCoreEXOME chip and ImmunoChip platform. Imputation was performed using the Michigan server using the Haplotype Reference Consortium v1.1 panel. Imputation was quality controlled and SNPs with a minor allele frequency < 5% or R square <0.3 were removed. Associations were tested using the gee framework that accounts for family correlation, age (age squared), gender, smoking, and the first three genetic principal components. LacMan ratio was log(10) transformed before statistical analysis.
**Results:**
A total of 1,075 healthy individuals enrolled in the Gene-environment-microbe (GEM) cohort study with both IP and genotyping data were included. In this cohort 17.8% of individuals had abnormal IP. A total of 7.8 million SNPs were imputed and 5.7 million SNPs were included in the analysis after quality control. When the data were not dichotomized (abnormal versus normal IP) the genomic inflation was of 1.03 compared to 1.04 using dichotomized data. No SNP reached genome wide significance ($P > 5\times10^{-8}$). However 58 loci showed suggestive associations e.g. *SGCG*, *RBFOX3*, *PSMG1*, *DAB2, SVIL* ($p<9.1\times10^{-6}$).
**Conclusions:**
We did not find robust genetic wide associations with IP. Although multivariate analysis controlling for major contributing factors to IP showed only a few SNP with nominal association these failed to reach the conventional GWAS threshold ($P< 5\times10^{-8}$). This may be due to the power of the study with only 1,075 subjects.

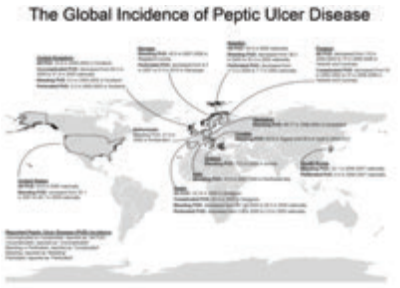
Submitted on behalf of behalf of the CCC IBD GEM Project research team.

**Funding Agencies:** CCC, CIHRThe Helmsley Charitable Trust

A36
**THE GLOBAL INCIDENCE OF PEPTIC ULCER DISEASE AND ITS COMPLICATIONS AT THE TURN OF THE 21ST CENTURY: A SYSTEMATIC REVIEW.**
H. Azhari[2], F. Underwood[2], J. King[1], S. Coward[1], S. Shah[5], S. Ng[4], G. Ho[4], C. Chan[4], W. Tang[4], G.G. Kaplan[3]

1. University of Calgary, Calgary, AB, Canada; 2. Internal Medicine, University of Calgary, Calgary, AB, Canada; 3. Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada; 4. Chinese University of Hong Kong, Hong Kong, China; 5. Vanderbilt University, Nashville, TN

**Background:** The incidence of peptic ulcer disease (PUD) and its complications varies across the world and has changed over the past few decades with the discovery of *H. pylori* as a major etiological factor in the disease pathogenesis, as well as the increasing use of NSAIDs. We conducted a systematic review to determine differences in the worldwide incidence of PUD and its complications in different regions at the turn of the 21st century.
**Aims:** To determine differences in the worldwide incidence of PUD and its complications in different regions at the turn of the 21st century.
**Methods:** We performed a systematic literature search of MEDLINE and PubMed (1 Jan. 2000 – 30 Jun. 2017; 4188 abstracts) to identify observational population-based studies reporting the incidence of PUD or its complications from 2000 or later. PUD was defined as either gastric or duodenal ulcers. Complications of PUD were defined as bleeding or perforation. We created a map to illustrate worldwide differences in the incidence of PUD.
**Results:** Amongst 4188 abstracts screened, 178 full-text articles were identified and 18 incidence studies were retrieved: 14 from Europe, 2 from Asia, and 2 from North America. Figure 1 illustrates the incidence of PUD and complicated PUD throughout the world. The highest annual incidence of all PUD (complicated and uncomplicated) was 141.8 per 100,000 persons in Spain, and the lowest was 23.9 in the UK. The highest annual incidence of bleeding PUD was 72.5 per 100,000 persons in Greece, and the lowest was 8.3 in the UK. The highest annual incidence of perforated PUD was 4.4 per 100,000 persons in South Korea, and the lowest was 2.2 in the UK.
**Conclusions:** This systematic review provides a global overview of the incidence of PUD and its complications at the turn of the 21st century. This disease entity remains a common problem around the world. However, our systematic review highlights the need for incidence data in many regions of the world, particularly from developing countries. Future studies in these regions are required to provide further insight into the geographic patterns of PUD.



**Funding Agencies:** None

A37

**ASTHMA IS NOT ASSOCIATED WITH THE NEED FOR SURGERY IN CROHN'S DISEASE WHEN CONTROLLING FOR SMOKING STATUS: A POPULATION-BASED COHORT STUDY**

E. Kuenzig[1], M. Sadatsafavi[3], A. Avina-Zubieta[3], R. Burne[4], M. Abrahamowicz[4], M. Beauchamp[5], G.G. Kaplan[2], E.I. Benchimol[1]

1. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada; 3. University of British Columbia, Vancouver, BC, Canada; 4. McGill University, Montreal, QC, Canada; 5. Research Institute of the McGill University Health Centre, Montreal, QC, Canada

**Background:** Growing evidence suggests that asthma and Crohn's disease (CD) commonly co-occur. The impact of asthma on the prognosis of CD is not known. Studies evaluating the risk of surgery in CD patients using health administrative data are limited by their inability to adjust for confounding variables not included in these data, such as smoking.
**Aims:** The aim of our study was to assess the impact of asthma on the need for intestinal resection in CD adjusting for smoking status, despite smoking status being unmeasured in health administrative data, using a secondary dataset and novel methodology.
**Methods:** Using population-based health administrative data from Alberta, we conducted a cohort study to assess the impact of asthma on the need for surgery in patients with CD diagnosed between April 1, 2002 and March 31, 2008 (n=2,113). Validated algorithms were used to identify incident CD cases, patients with co-occurring asthma, and intestinal resection surgeries. The association between asthma and intestinal resection was estimated using Cox proportional hazards regression. Smoking status was imputed using a method based on martingale residuals, leveraging information from a secondary dataset in which smoking status was measured. This second dataset included patients enrolled in the Alberta IBD Consortium between 2007 and 2014 who completed environmental questionnaires (n=485). All analyses were adjusted for age, sex, rural/urban status, and mean neighbourhood income quintile.
**Results:** Asthma did not increase the risk of surgery in either the health administrative data unadjusted for smoking status (HR 1.03, 95% CI 0.81 to 1.29) or in the secondary data adjusted for smoking status (HR 0.74, 95% CI 0.50 to 1.37). The association remained non-significant after using the secondary data to impute smoking status in the health administrative data (HR 0.92, 95% CI 0.75 to 1.15).
**Conclusions:** Although asthma is associated with an increased risk of CD, co-occurring asthma was not associated with the risk of surgery in patients with CD. This null association persisted after adjusting for smoking status. This study also demonstrates a novel method to adjust for smoking status in research using health administrative data when it is measured in a smaller secondary dataset.

**Funding Agencies:** CAG, CCC, CIHR

A38

**INCIDENCE OF APPENDICULAR TUMORS TREATED WITH PRIMARY OR DELAYED APPENDECTOMY, COLECTOMY, OR RIGHT HEMICOLECTOMY IN THE ADULT POPULATION IN A REGIONAL ONTARIO HOSPITAL.**

**JASON STRUYK, DR. ARDIT DELIALLISI AND DR IVAN PACHECO**
**WESTERN UNIVERSITY, SHULICH MEDICINE AND DENTISTRY, LONDO, ONTARIO. OWEN SOUND HOSPITAL, DEPARTMENT OF PATHOLOGY, OWEN SOUND, ONTARIO.**
J. STRUYK[1], A. DELIALLISI[1], I. PACHECO[2]

1. UNIVERSITY OF WESTERN ONTARIO, LONDON, ON, Canada; 2. GBHS Owen Sound Hospital, Owen Sound, ON, Canada

**Background:**
Appendicular neoplasms are uncommon to rare tumors of the gastrointestinal tract. Malignant tumor of the appendix account for ~0.5% of all tumors arising from the gastrointestinal tract. Due to their low frequency their true etiopathogenesis and biologic behavior remain poorly understood.
**Aims:** This lack of knowledge has created controversy around the classification of primary epithelial tumors, especially when there is peritoneal spread. Given these discrepancies, we sought to investigate their incidence in the adult population captured by Grey Bruce Health Sciences in order to raise awareness that tumors of the appendix may occur in the setting of acute abdominal pain and as an incidental finding.
**Methods:** The surgical pathology data base (Copath) at GBHS collected over the past 10 years was reviewed to determine the incidence of primary appendicular neoplasms, benign or malignant, in the setting of primary and delayed appendectomy, colectomies, and right hemicolectomy. Appendix removal was the only inclusion criterion. Additional data was collected for cases diagnosed with appendiceal tumors by reviewing Power Chart.Statistical analysis for significant differences will be performed according to the two-tailed Student's t-test for unpaired data and analysis of variance when appropriate. For all determinations, results will be expressed as the mean ± SEM; N will indicate the number of patients. P <0.05 will be considered to be statistically significant.
**Results:** Of the 2301 primary and delayed appendectomies, colectomies, and right hemicolectomies performed in the last 10 years, 68 cases (~2.95%) were diagnosed with an appendicular neoplasm. Aside from common appendiceal tumors, we found two very rare cases of a primary gastrointestinal stromal tumor and a possible primary small cell carinoma. There was a

slight predominance toward females (57%) and 70% of cases occurred after the age of 60. The most common complaint being RLQ pain (59%). Of the 68 total neoplasms, 14 were removed as delayed appendectomies with none being initially suspected of neoplasm. Of all delayed appendectomies performed in the last 5 years, 16% were diagnosed with an appendiceal tumor, as opposed to only 2% of primary appendectomies.
**Conclusions:** We concluded that given the uncommon nature of appendicitis at ages greater than 60 years, these patients, particularly females, who present with RLQ pain should be suspected of a possible appendiceal tumor.

**Funding Agencies:** None

A39
**NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS AND GASTROINTESTINAL BLEEDING: A NETWORK META-ANALYSIS**
A. Dorreen[3], C. Miller[1], M. Martel[1], A.N. Barkun[2]

1. McGill University, Montreal, QC, Canada; 2. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 3. University of Ottawa, Halifax, NS, Canada

**Background:** *Drs. Alastair Dorreen and Corey Miller are co-first authors
Several non-vitamin K antagonist oral anticoagulants (NOACs) have been approved for clinical use. A recent meta-analysis of randomized controlled trials (RCTs) and some observational data have suggested an increased risk of gastrointestinal bleeding (GIB) with dabigatran and rivaroxaban compared to conventional anticoagulation, yet data regarding comparative risk of GIB between NOACs are limited.
**Aims:** To conduct a network meta-analysis to assess the comparative risk of GIB between NOACs.
**Methods:** An initial search for RCTs comparing NOACs to conventional anticoagulation therapy was performed using the EMBASE, Medline, Cochrane and ISI Web of knowledge databases through January 2017. Trials assessing NOACs for the treatment of acute coronary syndrome and other unapproved indications were excluded. The primary outcome of comparison was the risk of GIB via a network meta-analysis with random effects model using the netmeta package in R 3.2 (www.r-project.org).
**Results:** A total of 51 trials were included, randomizing 180,853 patients. When comparing dabigatran vs. apixaban (OR: 1.72, 95% CI: 0.90; 3.30), dabigatran vs. edoxaban (OR: 1.32, 95% CI: 0.66; 2.64), dabigatran vs. rivaroxaban (OR: 1.11, 95% CI: 0.60; 2.04), rivaroxaban vs. apixaban (OR: 1.55, 95% CI: 0.84; 2.87), rivaroxaban vs. edoxaban (OR: 1.19, 95% CI: 0.61; 2.33) and apixaban vs. edoxaban (OR: 0.77, 95% CI: 0.38; 1.55), there was no significant difference in odds of major GIB. Secondary analysis did not reveal any difference in the odds of major GIB when comparing individual NOACs to warfarin, low-dose enoxaparin, placebo or aspirin.
**Conclusions:** Overall, the risk of major GIB was equivalent between NOACs when compared head-to-head in a network meta-analysis. Further high-quality studies are needed to characterize GIB risk among individual NOACs.

**Funding Agencies:** None

A40
**INCIDENCE, CLINICAL FEATURES, AND INVESTIGATION OF ACHALASIA IN NEWFOUNDLAND AND LABRADOR**
K. Woodman, J. Fardy

Memorial University, St. Johns , , Canada

**Background:** Achalasia is a rare esophageal motility disorder of unknown etiology. Patients commonly present with dysphagia, regurgitation and weight loss. Previous epidemiologic studies have suggested an equal male to female ratio and adult onset. Incidence rates range between 0.29 – 1.63/ 100,000 per year. Endoscopic and esophagram findings are often abnormal, however, manometry is required to diagnose achalasia.
**Aims:** This 11-year retrospective study outlines incidence, clinical features, and describes diagnostic findings in incident cases of achalasia in Newfoundland and Labrador.
**Methods:** Patient charts with ICD codes indicating a diagnosis of achalasia between 2005 and 2015 were retrieved from medical records. Charts with a diagnosis of achalasia by manometry prior to 2005 were not reviewed. Patients diagnosed with achalasia based on endoscopy or imaging prior to 2005 were included if their initial diagnostic manometry occurred between 2005 and 2015. The date of diagnosis was recorded as the date of official diagnostic manometry. Epidemiologic data, manometry, endoscopy and esophagram findings were compiled by chart review.
**Results:** 73 cases of achalasia were diagnosed with manometry between 2005 and 2015 in Newfoundland and Labrador. The average age at diagnosis was 52. Males represented 60% of cases. The midpoint incidence of achalasia was 1.42/100,000. Dysphagia occurred in 97% of patients, regurgitation in 73%, weight loss in 71%, chest pain in 22%, and aspiration in 11%. Upper endoscopy was abnormal in 81% of patients. The most common endoscopic finding was narrowing of the gastroesophageal junction followed by dilatation of the esophageal body. Abnormal barium esophagram occurred in 74.0%. An abnormal GEJ was the most common finding on barium esophagram, seen in 64%, followed by esophageal dilatation in 41%. Abnormal manometry was a key feature in all patients.
**Conclusions:** The incidence of achalasia in Newfoundland is similar to the incidence reported by a similar study in Alberta, although higher than reported by studies in Singapore and Iceland. Age and sex distribution is similar to findings in previous studies. Upper endoscopy and barium esophagram were frequently, but not exclusively, abnormal. There were several limitations to the present study, including

suspected cases that were treated without referral for manometry, and lack of access to endoscopy and esophagram records.

**Funding Agencies:** None

A41

**PERIOD PREVALENCE ESTIMATE OF PRIMARY BILIARY CHOLANGITIS IN NOVA SCOTIA**

J. Kiberd[1], C. Burgess[3], M. McLeod[4], K.M. Peltekian[2]

1. Dalhousie University, Halifax, NS, Canada; 2. Atlantic Multi-Organ Transplantation Pogram, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; 3. QEII Health Sciences Center, Halifax, NS, Canada; 4. Dalhousie University, Halifax, NS, Canada

**Background: BACKGROUND**: Primary Biliary Cholangitis (PBC) is a rare autoimmune cause if chronic liver disease. There exists an effective treatment for these patients, ursodeoxycholic acid (UDCA), but unfortunately 30-40% of patients do not have n adequate response or cannot tolerate it. New therapies are currently being researched. A recent Canadian Institute of Health Information report suggested that there are over 500 patients in the Maritime Provinces with PBC, which was much higher than expected. This warranted a review to assess Nova Scotia's current prevalence of PBC as part of a quality assurance and resource planning initiative in our center.

**Aims: AIMS:** As part of a quality assurance initiative, we collected data from the Central Laboratory in Nova Scotia to determine how many patients in our province have PBC.

**Methods: METHODS**: The Central Laboratory database started being routinely used April 2009 and we used data until July of 2017. We considered a positive AMA and an elevated Alkaline Phosphatase to be considered having PBC. Period prevalence was calculated using the population of Nova Scotia during this time period. Median total and direct bilirubin were also calculated.

**Results: RESULTS**: The central lab pull identified 1726 patients who met these criteria since 2009, however most were duplicates. 254 unique patients were identified which gave an estimated prevalence of 0.027% of the population in Nova Scotia. The majority of our sample was female (82%) with a mean age 58.8 years (95%CI: 57.3-60.3 years). Median Alkaline Phosphatase was 161.5 units/L (133-256 units/L). All but two patients had a total bilirubin value with a median value 14 umol/L (IQR: 10-24 umol/L). Of these, 228 (90%) had a direct bilirubin available with a median of 5 umol/L (IQR: 3-12.5 umol/L).

**Conclusions: CONCLUSION**: Our period prevalence estimate is consistent with other estimates that have been published in the current literature. Although the prevalence of PBC is low, many of these patients do not respond adequately to medical therapy and progress to need transplantation. New medical treatment modalities are needed for these patients and other trials are currently being performed.

**Funding Agencies:** None

A42

**IRRITABLE BOWEL SYNDROME IN JORDANIAN MEDICAL STUDENTS**

E. Altamimi[1], H. Alnawayseh[2]

1. Pediatric Department, Jordan University of Science and Technology, Irbid, Jordan; 2. Royal Medical Services, Amman, Jordan

**Background:**
Irritable bowel syndrome (IBS) is one of the commonest diagnoses in medicine. The association with stress is well documented. Studying medicine is a highly demanding and stressful, and postulated to predispose medical students to IBS.

**Aims:** To estimate the prevalence of Irritable bowel syndrome in Jordanian Medical Students using ROME III criteria.
To study the relation between life-style(food,activity, smoking,...) and Irritable bowel Syndrome in Jordanian Medical students.

**Methods:**
This is a cross sectional study included 142 medical students, selected randomly out of four medical schools in Jordan. A confidential, anonymous, and self-administered questionnaire was used to collect personal and sociodemographic data, in addition to the Rome III questionnaires. Rome foundation agreed on using the questionnaires. The study was granted approval by the ethics committee of Faculty of Medicine at Mutah University. All participants give their consent to participate in the study.

**Results:**
300 questionnaires distributed, 160 returned answered, 142 (47.3%) included in the final analysis. 62(43.7%) were females. 30 (22.4%) students met the criteria for IBS diagnosis. Male dominated, with male: female of 2:1.The most common sub-type of IBS was the mixed type comprising half the cases, followed by diarrhea predominant and constipation predominant at 26.7% and 23.3%, respectively.
Eating (Junk Food /Dairy products), level of exercise, smoking and drinking alcohol were not different between IBS students and non-IBS students. In comparison between IBS subtypes, mixed-subtype smoke more frequent than other subtypes, which was statistically significant.12 (40%) of IBS students reported that there symptoms worsen during exam time.

**Conclusions:**
IBS is not uncommon in Jordanian medical students. Males are more affected than females. Life style was not statistically different between IBS students and non-IBS students. Significant number of those students reported worsening of their symptoms on exam time.

**Funding Agencies:** None

## ESOPHAGUS, GASTRIC AND DUODENAL ULCER DISORDERS

### Poster of Distinction

A43

**UTILITY OF A DIFFICULTY SCORE IN PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR TREATING ACHALASIA**

M. Woo, R. Bechara

Queens University, Kingston, ON, Canada

**Background:** Achalasia, a primary esophageal motor disorder characterized by incomplete lower esophageal sphincter relaxation and loss of esophageal peristalsis, results in dysphagia, chest pain, regurgitation and weight loss. Peroral endoscopic myotomy (POEM) is a recently developed method of treating achalasia, less invasively than surgical myotomy.
**Aims:** The objective of this study was to report the early outcomes of a series of patients treated with POEM in a single Canadian center and to assess the correlation between pre- and peri-operative factors and a POEM difficulty score (PDS).
**Methods:** 29 consecutive patients with achalasia (16 men, 13 women, mean age 51.0 +/- 17.4, median duration of symptoms 60 mo [range 10 mo – 600 mo]) from a single tertiary center in Kingston, Ontario underwent 30 peroral endoscopic myotomies (POEM) between March 2016 and Sept 2017. A submucosal tunnel extending from the esophagus to the proximal stomach was created, and then a myotomy (mean length 14.6 ± 3.0 cm in the esophagus and 2.5 ± 0.81 cm in the cardia) of the circular muscle was performed. The mucosal incision was closed with hemostatic clips (median 5, range 4-6 ). The mean operating time was 92.1 ± 30.4 min. Pre- and post-operative assessments included Eckardt scores, timed barium esophagram, endoscopy and manometry.
**Results:** The median Eckardt score pre-procedure was 8 (range 4 - 12). 25 patients underwent follow-up (median duration 10 mo, range 2-18 mo) with post-procedure median Eckardt score of 1 (range 0 - 3). The improvement was statistically significant (Wilcoxon signed ranks $p < 0.001$). The reduction in integrated relaxation pressure (IRP) in 13 patients who underwent follow-up manometry was 13.2 +/- 8.9 mmHg (paired samples t-test $p < 0.001$). 57% (12/21) of patients who underwent follow-up EGD or 24h pH study had evidence of acid reflex.

A difficulty score (POEM difficulty score), consisting of tunnel distension, submucosal oozing, submucosal fibrosis, spastic contractions and tunnel orientation was calculated. The median difficulty score for non-sigmoid (83%) was 1.5 (0-4) and for sigmoid morphology (17%) was 2.5 (1-5). The median difficulty score for type 1 achalasia (3%) was 1, type 2 achalasia (45%) was 1.5 (1 – 2.5) and type 3 achalasia (45%) was 2 (0 – 4).

The PDS strongly correlated with POEM velocity (r=0.83) and this was significant (Spearman's $p < 0.001$). There was no significant correlation with BMI, duration of disease or previous procedures. There were no complications.
**Conclusions:** POEM is a safe, effective and durable method of managing achalasia. A difficulty score has been shown to correlate with POEM velocity and warrants further investigation. In the future, the PDS may be used to aid in the development of formal training protocol for POEM, in addition correlation with pre-procedural variables and post-procedure outcomes will be further investigated.

**Funding Agencies:** None

A44

**IS BLOOD UREA NITROGEN AN INDEPENDENT PREDICTOR OF POSITIVE ENDOSCOPIC FINDINGS IN PRESUMED UPPER GI BLEEDING?**

N. Narula[4], D. Chopra[3], M. Rosenberg[2], P. Moayyedi[1]

1. McMaster University, Hamilton, ON, Canada; 2. Gastroenterology, McMaster University, Thornhill, ON, Canada; 3. Medicine, McMaster University, Hamilton, ON, Canada; 4. neeraj.narula@medportal.ca, Hamilton, ON, Canada

**Background:** Several prognostic scales have been developed for use in upper gastrointestinal bleeding (UGIB), including the Glasgow-Blatchford score, which uses blood urea nitrogen (BUN) as one of eight prognostic variables. However, the test characteristics of BUN in the identification of UGIB or high-risk endoscopic lesions have not been clearly determined.
**Aims:** This study aimed to evaluate if BUN independently predicts the presence of positive endoscopic findings in cases of presumed UGIB and determine a threshold urea level above which it is more likely to identify a source of UGIB on endoscopy.
**Methods:** A crude odds ratio was calculated for odds of bleeding being identified on upper endoscopy based on thresholds of urea>=5, 7.5, 10, 12.5 and 15, compared to values lower than these. Adjusted odds ratios were then calculated using logistic regression to account for the factors that were determined *a priori*. Covariates included in the model were age, sex, hemoglobin, presence of melena, presence of hematemesis, admission in ICU, and use of ASA, warfarin, clopidogrel, or NSAIDS.
**Results:** The odds of identifying UGIB at endoscopy for patients with a urea >=10 was 3.73 (95% CI: 1.90-7.31) times higher than for patients with urea < 10. Variables that were significantly associated with identifying source of bleeding at upper GI endoscopy included male gender and symptoms of melena or hematemesis, after adjusting for the impact of other covariates. BUN >20 is predictive of UGIB in the following settings:



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normal renal function (spec 98%, PPV 0.86), melena (spec 81%, PPV 0.8), NSAID+anticoagulation/ASA use (spec 85%, PPV 0.8), and cirrhotic patients (spec 100%, PPV 1.0). BUN >20 is also predictive of positive EGD findings (spec 87%, PPV 0.8) and high risk lesions (spec 81%, NPP 0.83). A BUN level >20 had 82% specificity for high risk endoscopic lesion requiring intervention, but lower BUN levels were not able to predict EGD intervention. BUN >15 is predictive of UGIB in hematemesis (spec 95%, PPV 0.95) or NSAID users (spec 100%, PPV 1.0). BUN levels >20 had a specificity of 87% for UGIB but poor sensitivity (23%), in contrast to the Glasgow-Blatchford score which is highly sensitive (>90%) but poorly specific (<20%).
**Conclusions:** Overall, the results of this study provide new clinically relevant information regarding the operating characteristics of BUN for UGIB. In males, patients with normal renal function, cirrhosis, NSAID/ASA/AC users, or symptoms of melena and hematemesis, a high BUN level is predictive of positive endoscopic findings in presumed UGIB. A BUN level >20 predicts the need for endoscopic intervention but levels below 20 do not correlate well with the need for endoscopic intervention. BUN level alone is more specific for UGIB when compared to the Glasgow-Blatchford score, which has a higher sensitivity.

**Funding Agencies:** None

A45

**REAL LIFE MANAGEMENT OF PATIENTS PRESENTING WITH UPPER GI BLEEDING IN A TERTIARY CARE EMERGENCY DEPARTMENT - ARE WE DELIVERING THE STANDARD OF CARE?**

S. Sandha[2], M. Bullard[3], B.P. Halloran[1], c. Joseph[4], D. Grigat[4], E. Lang[5], S. Veldhuyzen van Zanten[2]

1. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. Emergency Strategic Clinical Network (ESCN) Alberta Health Services, Calgary, AB, Canada; 5. University of Calgary, Calgary, AB, Canada

**Background:** Upper gastrointestinal bleeding (UGIB) is a common Emergency Department (ED) presentation. Early endoscopic intervention, supported by Glasgow Blatchford Score (GBS) severity, has been shown to reduce re-bleeding rates and lower the morbidity and mortality. However, emergent endoscopy is not necessary for all patients. Low-risk patients can be managed through outpatient follow-up. Other important management issues such as threshold for blood transfusion (Hb <70) and use of oral or intravenous proton pump inhibitor (PPI) therapy also warrant study.
**Aims:** The aim of this study was to review the timing and appropriateness of endoscopy and supportive management such as need for blood transfusion (Hb <70) and proton pump inhibitor (PPI) use in a real life tertiary care site setting compared to standard of care.
**Methods:** A retrospective comparative cohort study was conducted to examine the management of patients presenting with UGIB to the University of Alberta Hospital ED, between January 1 and December 31, 2016 using a chart review methodology. TANDEM and EDIS databases were queried to identify patients using specified ICD 10 codes and CEDIS presenting complaints of vomiting blood or blood in stool/melena. Outcome measures included: patient characteristics, acuity scores including the Glasgow Blanchard Score (GBS) to determine appropriateness for admission and timing of endoscopic intervention, diagnoses, need for blood transfusions and use of oral or intravenous PPIs. Data were entered into a REDCap database. Standard statistical tests were used for data analysis.

**Results:** A total of 200 patients, 59% male (118/200), mean age 59 years (range 18 - 92 years) were included. The average GBS was 8.25. 79% of patients (157/200) underwent endoscopy during the hospital visit: 26% (9/35) of patients with GBS score of 0 to 2 and 78% (129/165) patients with GBS ≥ 3 underwent endoscopy within 24 hours. The two most common endoscopic diagnoses were peptic ulcers (39%, 61/157) and esophageal/gastric varices (18%, 28/157), while 14% (22/157) of endoscopies had a normal diagnosis or mild gastritis. 87 % of patients (174/200) were given IV or oral PPI in the ED whereas the remaining 13% (26/200) did not receive PPI. 37% of patients (74/200) received blood transfusion, but only 53% (39/74) were administered based on the 70 g/L threshold while in 39% (29/74) patients the less restrictive threshold of 90 g/L was used.

**Conclusions:** A majority of UGIB patients presenting to a tertiary hospital ED appropriately received endoscopy within 24 hours based on a GBS score ≥ 3. PPI use was appropriate but a significant proportion of patients received inappropriate blood transfusions.

**Funding Agencies:** Emergency Strategic Clinical Network (ESCN), Alberta Health Services

A46

**THE IMPACT OF CYP2C19 POLYMORPHISM ON PROTON PUMP INHIBITORS DOSING: A RETROSPECTIVE ANALYSIS**

W. Alghamdi[2], R. Kim[1]

1. Division of Clinical Pharmacology and Toxicology, London Health Sciences Centre, Western University, London, ON, Canada; 2. London Health Sciences Centre, Western University, London, ON, Canada

**Background:** Proton pump inhibitors (PPIs) are used in a wide spectrum of gastrointestinal disorders. They undergo significant metabolism by the main enzyme Cytochrome P450 2C19 (CYP2C19). Genetic variation in this enzyme influences the pharmacokinetics of all PPIs. Despite the different challenges with implementing pharmacogenetics-guided therapy in clinical

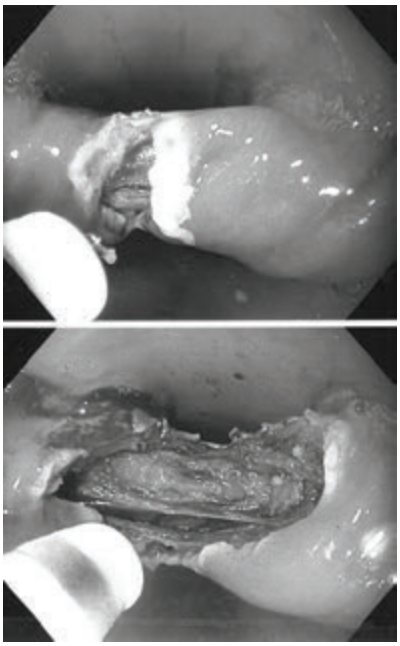
practice, CYP2C19 pharmacogenomics testing is currently available at London Health Sciences Centre (LHSC) as we recognize the major role it plays in drug responses and interactions in different clinical scenarios. However, its role in PPIs response in different gastrointestinal disorder needs further studies.
**Aims:** To investigate the frequency of CYP2C19 polymorphism in our patient population in a tertiary care center in London, Ontario, and its correlation with high and standard PPI dosing. Standard dose was defined as 30 mg per day for lansoprazole and 40 mg per day for pantoprazole. The high dose was defined as a dose that is double the standard dose.
**Methods:** A retrospective chart review was performed of all adult patients who were on CYP-dependent PPIs (lansoprazole and pantoprazole) and underwent CYP2C19 genotype testing in our lab for different indications from January 2010 to July 2017. Statistical testing was conducted to compare high PPI dose group with standard PPI dose group. The primary outcome was to describe the correlation between CYP2C19 genotype and PPI dose.
**Results:** 79 genotyped patients were included in this interim analysis, of whom 22 patients (27.8%) were on high dose PPI and 57 (72.2%) were on standard dose. There was no statistically significant difference between the high dose group and standard dose group in age, gender or BMI. The high dose group patients were more likely to have a previous history of PUD ($p<0.001$), erosions ($p<0.001$) and UGIB ($p=0.002$). Extensive metabolizers (EM) was the most common CYP2C19 phenotype in both groups (81.8% vs. 70.2%; $p=0.29$) with intermediate metabolizers (IM), poor metabolizers (PM) and ultra-rapid metabolizers (UM) identified more in the standard dose group (9.1% vs. 19.3%, $p=0.27$; 4.5% vs. 5.4%, $p=0.9$; 4.5% vs. 5.4%, $p=0.9$; respectively). Patients in the high dose group experienced improvement in their PUD and UGIB more than the standard dose group patients ($p=0.003$ and $p=0.01$, respectively). IM and PM patients were found to be on standard dose PPIs more often but this was not statistically significant.
**Conclusions:** In this interim analysis, there was no statistically significant difference in PPI dosing among CYP2C19 different phenotypes. CYP2C19 genotype testing might have a role in PPI dosing. Future prospective randomized controlled trials are needed to further identify that role. A larger sample size will be presented in the Canadian Digestive Disease Week.

**Funding Agencies:** None

A47
**ENDOSCOPIC ZENKER'S DIVERTICULOTOMY AND MYOMECTOMY:A SINGLE CENTER EXPERIENCE**
N. Suter[1], E. Desilets[2], T. Maniere[3]

1. Université de Montréal, Montreal, QC, Canada; 2. Gastroenterology, Université de Sherbrooke, St-Basile-le-Grand, QC, Canada; 3. Université de Sherbrooke, Greenfiled Park, QC, Canada

**Background:** Zenker's diverticulum is a pseudodiverticulum of the mucosa and submucosa occurring in the posterior pharyngoesophagus through Killian's triangle. Symptoms include dysphagia, secretions, halitosis and weight loss and occur mostly in middle-aged and older adults. Historically, treatment has been extensive neck surgery and eventually rigid endoscopy. Recently, treatment by flexible endoscopic septum division (FESD) has shown excellent success rates with less morbidity[1].
**Aims:** This study aimed to evaluate the clinical response rate and complications of FESD in our single center.
**Methods:** We conducted a single center retrospective study of endoscopic Zenker's diverticulotomy and myomectomy by FESD performed by two different endoscopists between July 2014 and June 2017.
**Results:** Seven patients were included in our analysis, four of which were males. Mean age of patients was 83.7 years (range 73-92). Two patients that were taking an anticoagulant (1 Apixaban, 1 Enoxaparin) and three on Aspirin had stopped their medication the appropriate number of days prior to the procedure. Indication for procedure included severe dysphagia in 6 patients and regurgitation in 1 patient. Patients also complained of regurgitation (3 patients), secretions (2), odynophagia (1), food impaction (1), and weight loss (1). All procedures were performed with a Dual knife (Olympus). Mean diverticular size was 3.3 cm (range 2-6 cm). Mean procedural time was 23.7 min (range 10-36 min). Minimal procedural bleeding occurred in two cases and no perforation was noted. Four procedures were conducted under general anesthesia and 3 under conscious sedation. Mean follow up duration was 2 months for 6 patients (range 1-5 months), one patient was lost on follow-up. Four patients reported complete recovery of initial symptoms, and two major improvement. No patient required a second procedure or surgery.
**Conclusions:** In our retrospective analysis of flexible endoscopic diverticulotomy, we showed a good response rate, with no severe complication rendering this procedure very safe and effective for symptomatic Zenker's diverticulum.



The septum of the diverticulum is exposed with the diverticuloscope and dissected with the Dual Knife

**Funding Agencies:** None

A48

**PROPHYLACTIC ENDOTRACHEAL INTUBATION IN CRITICALLY ILL PATIENTS WITH UPPER GASTRO-INTESTINAL BLEED: A SYSTEMATIC REVIEW AND META-ANALYSIS**

K. Bishay, D. Chaudhuri, P. Tandon, V. Trivedi, P.D. James, E.M. Kelly, K. Thavorn, K. Kyeremanteng

Gastroenterology and Hepatology, University of Ottawa, Ottawa, ON, Canada

**Aims:** To compare clinical outcomes and perform a cost analysis of prophylactic endotracheal intubation compared to no intubation in upper gastrointestinal bleeding (UGIB).
**Methods:** EMBASE, MEDLINE, and the Cochrane Central Register of Controlled Trials were used to identify studies through June 2017. Studies performed comparing prophylactic intubation to no intubation in UGIB in adults were included. Studies were excluded that did not report on at least one of the a priori established clinical outcomes. Two authors collected and assessed the data independently. Data on mortality, length of stay (LOS), cardiac complications and rates of pneumonia was collected. DerSimonian-Laird random effects models were used to calculate the inverse variance-based weighted, pooled treatment effect across studies.
**Results:** Seven studies (five manuscripts and two abstracts) were identified including a total of 5662 patients. Prophylactic intubation conferred increased mortality compared to no intubation (odds ratio [OR], 2.59; 95% CI [1.01 – 6.64], P = 0.05; $I^2$ = 94%). The hospital LOS was higher in the prophylactic intubation group (mean difference [MD], 0.96 days; 95% CI [0.26 – 1.67], P = 0.007; $I^2$ = 0). The prophylactic intubation group had significantly higher rates of pneumonia (OR, 6.58; 95% CI [4.91 – 8.81], P <0.0001; $I^2$ = 0%) and significantly higher rates of cardiac complications (OR, 2.11; 95% CI [1.04 – 4.27], P = 0.04; $I^2$ = 6%). There was a trend towards increased ICU LOS in the prophylactically intubated group, though this difference was not statistically significant. Using a previously published costing method based on length of stay, the prophylactically intubated group incurred costs of $9020 per patient (95% CI: 6962 – 10609) compared to $7510 per patient (95% CI: 6486 – 8432) in the non-intubated group.

**Conclusions:** Prophylactic intubation in UGIB is associated with higher rates of pneumonia, cardiac complications, hospital LOS and overall mortality. Furthermore, it shows a trend towards higher cost and longer ICU LOS. Because the studies included in this review were retrospective, further large prospective trials are needed to evaluate this topic further.

**Funding Agencies:** None

A49

**PRELIMINARY RESULTS: RETROSPECTIVE ANALYSIS OF THE LONG-TERM OUTCOMES OF PATIENTS WITH T1B ESOPHAGEAL CANCER**

J. Yonge[1], C. Galorport[1], F. Donnellan[2], R.A. Enns[1]

1. University of British Columbia, Burnaby, BC, Canada; 2. Gastroenterology, Vancouver General Hospital, Vancouver, BC, Canada

**Background:** Endoscopic mucosal resection (EMR) is commonly performed for dysplasia/early adenocarcinoma within the setting of Barrett's esophagus. Cancers that invade the submucosa (T1b) can be further subdivided into SM1, SM2, and SM3, depending on the depth of invasion into the submucosa. Invasive adenocarcinoma significantly increases the risk of lymph node metastasis, which is of critical importance if endoscopic treatment is the only therapy planned. Accurate prediction of lymph node status is therefore crucial in order to determine the appropriate method of treatment (surgery or endoscopic) for early lesions.
**Aims:** This study aims to assess the long-term outcomes of patients who have had treatment for a T1b esophageal adenocarcinoma and to determine the extent of lymph node involvement as assessed through surgical specimens or long term clinical/radiological follow up. Additionally, factors associated with lymph node metastasis will be evaluated.
**Methods:** A retrospective chart review of patients with T1b esophageal cancer between 01/05-05/17 was performed at St. Paul's Hospital. Data collected

includes demographics, endoscopy dates, indication, findings, imaging, characteristics of the cancer (depth and extent of penetration, size of lesion, differentiation, lymphovascular invasion), method of resection, and follow-up. The study is being performed at 4 sites which deal with most of the esophageal cancers in British Columbia. The data collected presently is just from one site, the other three sites are pending.
**Results:** Out of 313 patients that had a specimen removed from the esophagus, 3.5% (11/313) were found to have a T1b esophageal cancer. 9% (1/11) of patients with T1b cancer were found to have positive lymph nodes. 18% (2/11) of patients had a recurrence with an average of 2.5 years from the initial cancer (range 1 to 4 years). Recurrent disease was managed palliatively in 1 patient and by EMR in another. 36% (4/11) patients underwent transhiatal esophagectomy, with no recurrence.
**Conclusions:** Only 9% of patients have had evidence of lymph node involvement in this small group with T1b esophageal adenocarcinoma. Additional data is being collected to evaluate the results in a Provincial manner and will be presented.

**Funding Agencies:** None

A50
**VARIATION IN DIAGNOSTIC CRITERIA FOR LYMPHOCYTIC ESOPHAGITIS: A SYSTEMATIC REVIEW**
M. Habbal, M.A. Scaffidi, M. Ramaj, A. Almazroui, R. Khan, T. JEYALINGAM, A. Shetty, M.J. Abunassar, S.C. Grover

University of Toronto, Toronto, ON, Canada

**Background:** Lymphocytic esophagitis (LyE) is a novel clinicopathologic entity, that presents as dysphagia, with an endoscopic appearance similar to eosinophilic esophagitis. There is no standard histologic definition used in the literature.
**Aims:** To determine the variation of the histologic criteria used to diagnose LyE.
**Methods:** We conducted a systematic review in the Embase, MEDLINE, and SCOPUS databases. Studies were included if they used a histologic diagnostic criteria for LyE in human patients.
**Results:** We identified 29 relevant studies. There is a growing literature on LyE (Fig 1). Diagnostic criteria are summarized in Table 1. For IELs, 15 studies (52%) included a cut-off, with 3 (10%) that specified CD3 positive staining and 16 (55%) that specified localization in peri-papillary fields. In addition, 6 studies (21%) included the presence of spongiosis in their criteria and 28 studies (97%) specifed granulocytes should be rare or absent.
**Conclusions:** There is considerable variation in criteria used to diagnose LyE, highlighting the need for consensus guidelines.

Table 1. Diagnostic criteria for LyE used in the literature

| Author | Year | Diagnostic (IEL/hpf) | Peri-papillary IELs | Presence of spongiosis | Absence of granulocytes | CD3 stain of IEL specified |
|---|---|---|---|---|---|---|
| Pleet | 2017 | NS | Yes | Yes | N/F | NA |
| Ebach | 2011 | >50 | No | No | <1 IEGs: 50 IELs | NA |
| Rubio | 2017 | ≥40 | No | No | ≤14 eos per hpf | Yes |
| Ichiya | 2017 | ≥40 | No | No | ≤14 eos per hpf | Yes |
| Kissiedu | 2016 | ≥20 | Yes | Yes | N/F | NA |
| Haque | 2012 | NS | Yes | Yes | N/F | Yes |
| Putra | 2016 | > 62,46,41* | No | No | ≤1 per 2 hpf | NA |
| Pasricha | 2016 | ≥10 | No | No | 0 | NA |
| Truskaite | 2016 | ≥40 | No | No | ≤14 eos per hpf | Yes |
| Basseri | 2013 | ≥50 | Yes | No | N/F | NA |
| Rubio | 2006 | NS | Yes | No | N/F | Yes |
| Xue | 2015 | NS | No | No | ≤12 | NA |
| Tanaka | 2013 | >20 | No | No | N/F | NA |
| Cohen | 2012 | >20 | No | No | N/F | NA |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| | | | | | | |
|---|---|---|---|---|---|---|
| Rubio | 2016 | ≥40 | No | No | NA | Yes |
| Sutton | 2014 | >50 | No | No | <1 IEGs :50 IELs | NA |
| Gonza-lez-Cordero | 2016 | >20 | No | No | N/F | NA |
| Purdy | 2008 | NS | Yes | No | N/F | NA |
| Jideh | 2016 | NS | Yes | Yes | N/F | NA |
| Zhang | 2016 | NS | Yes | No | N/F | Yes |
| Hendy | 2013 | NS | Yes | No | N/F | NA |
| Kasirye | 2012 | NS | Yes | No | N/F | NA |
| Van-gimalla | 2016 | NS | Yes | Yes | 0 eos | NA |
| Man-daliya | 2012 | NS | Yes | No | N/F | Yes |
| Sloan | 2016 | >20 | No | No | N/F | Yes |
| Niewi-arows-ki | 2016 | NS | Yes | Yes | N/F | NA |
| Figue-iredo | 2014 | NS | Yes | No | N/F | NA |
| Maeji-ma | 2016 | NS | Yes | No | N/F | Yes |
| Basseri | 2010 | ≥50 | Yes | No | N/F | NA |

*0-2, 5, and 10 cm above the gastroesophageal junction, respectively eos: eosinophils IEGs: intraepithelial granulocytes NA: not available N/F: none to few granulocytes NS: not specified


**Figure 1.** Line plot of the number of studies on LyE

**Funding Agencies:** None

A51

**RARE CAUSES OF DYSPHAGIA: A CASE SERIES**

E.Y. Liu, E. Vantomme, S. Bhasin

College of Medicine, University of Saskatchewan, Regina, SK, Canada

**Background:** Dysphagia is the sensation of difficulty swallowing and is a common clinical problem that warrants prompt evaluation, diagnosis, and management. Dysphagia has a large differential diagnosis including mechanical obstruction and neurological pathology.
**Aims:** We aim to report a series of unusual cases of dysphagia to remind readers to have an index of suspicion for atypical etiologies of dysphagia.
**Methods:** Three cases were identified in clinical practice and included in this case series.
**Results:** Case 1
A 61-year-old male presents with a 4-month history of progressive solid and liquid oropharyngeal dysphasia and 20-pound weight loss. Nasopharyngeal laryngoscopy and gastroscopy did not reveal structural abnormality. CT neck and chest showed diffuse idiopathic skeletal hyperostosis (DISH).The C3-4 osteophyte formed a shelf-like projection anteriorly measuring up to 1.8 cm which compressed the posterior hypopharynx at the level of the epiglottis, likely impeding epiglottic inversion (Fig. 1a). The patient tolerated percutaneous endoscopic gastrostomy tube insertion with no complications and will seek surgical consultation for treatment of DISH.

Case 2
A 30 year-old female snowboarder fell 15 feet onto hard-packed snow and sustained soft tissue injuries to her left hip and chest wall. Forty-eight hours later, she developed retrosternal pleuritic chest pain and progressive dysphagia and odynophagia. CT chest/abdomen showed no abnormalities; however, gastroscopy revealed several partial-thickness esophageal tears with visible muscle fibers just above the gastroesophageal junction (Fig. 1b). She was treated conservatively for 3 days with NPO, intravenous pantoprazole and intravenous piperacillin-tazobactam with no complications.

Case 3
A 72-year-old female presented with dysphagia, odynophagia and melena stool. She had a thoracic stent graft exclusion of a ruptured thoracic aneurysm 2 months ago, which was complicated post-operatively by methicillin-susceptible Staphylococcus aureus bacteremia and thoracic epidural abscess. CT angiography showed type 1 endoleak at the inferior margin of the thoracic aortic stent. Gastroscopy showed a bleeding aortoesophageal fistula (Fig. 1c). Due to patient frailty no further surgery was recommended and she was offered palliative treatment.
**Conclusions:** Dysphagia is a non-specific clinical symptom that has a broad differential diagnosis. The workup of dysphagia must be focused to the patient's history; in these three cases, a rare diagnosis was considered in the clinical context and appropriate management was promptly initiated. In order to make these diagnoses, there must be an index of suspicion for uncommon causes of dysphagia. This case series reminds the clinician that patients can present with time-sensitive and life threatening disease with a primary symptom of dysphagia, and consideration for uncommon etiologies is crucial in delivering prompt management to these patients.

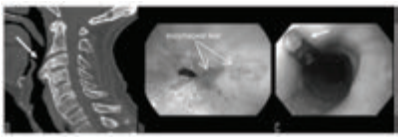


**Figure 1.** a) 61-year-old male with DISH presents with oropharyngeal dysphagia due to prominent C3-4 osteophyte projecting anteriorly and compressing the posterior hypopharynx. b) 30 year-old female with dysphagia and odynophagia due to isolated partial-thickness esophageal tears from deceleration injury. c) 72-year-old female with dysphagia and odynophagia secondary to aortoesophageal fistula due to infected thoracic aortic stent graft.

**Funding Agencies:** None

A52
**ENDOSCOPIC CLOSURE OF PERFORATED PEPTIC ULCER IN A PATIENT WHO WAS A CHALLENGING CANDIDATE FOR SURGICAL MANAGEMENT**
R. Bechara[2], V.V. Kanagasabai[1]

1. Gastroenterology, Queen's University, Kingston, ON, Canada; 2. Gastroenterology, Queens University, Toronto, ON, Canada

**Background:** The incidence of peptic ulcer disease (PUD) in developed countries has overall decreased but is still seen commonly in patients above the age of 60. The commonest complication of PUD is hemorrhage (73%) followed by perforation (9%) and obstruction (3%). Perforated peptic ulcer (PPU) is associated with a mortality of at least 25%. Traditionally, PPU is managed surgically, however the postoperative course is also associated with a high risk of complications and mortaliy.
**Aims:** To describe the first case report of endoscopic loop and clips closure technique used for perforated gastric ulcer, augmented by video.
**Methods:** We describe a case of a 68 year old patient with complicated past medical and surgical history who presented 9 days post small bowel resection for a partial small bowel obstruction with an acute abdomen. CT scan demonstrated a large collection in the left upper quadrant and free air, confirming perforation. He was brought to the Operating theatre emergently for an exploratory laparotomy due to his unstable status. As he had a "frozen abdomen" from severe adhesions from previous surgeries, the surgery team was unable to repair the perforation. The left upper quadrant was irrigated and a sump drain inserted. Repeat CT scan post op showed features consistent with persistent perforation. The Gastroenterology team was consulted for endoscopic closure of the perforations. Two perforated gastric ulcers were successfully repaired with the loop and clips technique. Repeat endoscopy after showed complete healing of the defects. This case presentation is augmented by video.
**Results:** This is the first report of the endoscopic loop and clips closure technique used for a perforated gastric ulcer, with successful outcomes. PPU is associated with a high rate of mortality and morbidity and traditionally is managed emergently by surgery. Post operative mortality for PPU is estimated to be 6-10%, and is 3 to 5 times higher in the elderly population. Endo et al first described the loop and clips technique in 2004. In the literature, multiple other techniques are described for endoscopic closure of defects
**Conclusions:** PUD is commonly seen in the elderly population, PPU is a rare but dangerous complication. In our patient, who was a challenging candidate for surgical management, endoscopic repair of PPU with the loop and clips technique was successful. In select patients perhaps endoscopic repair of PPU with the loop and clips technique may be a simple and feasible alternative to operative management and its associated high risk of complications, costs of prolonged hospital stay and mortality.

**Funding Agencies:** None

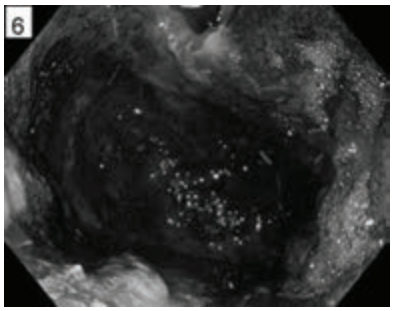
A53
**DIFFUSE PHLEGMONOUS GASTRITIS**
A. Aruljothy, S. Camilleri-Broet, S. Mayrand, L. Ferri, T. Bessissow

McGill University Health Center, Montreal, QC, Canada

**Background:** Phlegmonous gastritis is a rare inflammatory disease of the stomach caused by suppurative exudate, associated with a high mortality rate with treatment delay. Thus, strong clinical suspicion and recognition of this disease is key to the diagnosis and prompt management.
**Aims:** Describe a case of diffuse phlegmonous gastritis

presenting as ischemic gastritis and shock.
**Methods:** Case report
**Results:** A 78 year-old Haitian male with hypertension, dyslipidemia, and a coronary artery bypass grafting presented to the emergency room (ER) with epigastric pain and diarrhea. His temperature was 37.1, with a blood pressure 76/45, heart rate 108, distended abdomen, epigastric tenderness without peritoneal signs, leukocytosis of 18.3 x $10^9$/L, CRP 15.8 mg/L, and lactate 8.8 mmol/L. A computed tomography (CT) showed a distended stomach with circumferential wall thickening, and gastrohepatic ligament fat stranding. Gastroscopy showed a diffuse friable, dusky gastric mucosa with multiple ulcerations, and spontaneous bleeding suspicious for ischemic gastritis versus malignancy. Biopsy showed necrotic tissue and no malignancy. In the ICU, he improved with intravenous fluids, 5 days of Piperacillin and Tazobactam, pantoprazole, and was investigated for vasculitis which was negative. A CT angiogram showed patent abdominal arteries. Repeat endoscopy showed patchy healing of the antrum and body with necrotic areas at the fundus. Biopsy showed increased eosinophils suggestive of eosinophilic gastritis, and no H. pylori. He improved on conservative management and was discharged with pantoprazole BID but returned to the ER 10 days later with dysphagia, vomiting, and a 50lbs weight loss. Gastroscopy showed a stomach with diffuse nodularity, pus, and remaining large antral ulcerations. Biopsy revealed gastric mucosa with eosinophils. Infectious Diseases was consulted and excluded latent TB and parasitic infection (no peripheral eosinophilia, negative Strongyloides and stool cultures). He was discharged on prednisone for presumed eosinophilic gastritis but his symptoms and endoscopy did not improve, prednisone was stopped after a 2 month taper.

On 1 month follow-up, gastroscopy showed persistent diffuse nodular, friable gastric mucosa, and a large antral ulcer. Biopsy showed no eosinophilic gastritis, but evidence of H. pylori. He was rehospitalized for malnutrition and symptom control with a working diagnosis of phlegmonous gastritis in the healing phase and remained on pantoprazole BID. He was discharged with 14-days of H. pylori eradication therapy and was seen in 5 weeks with symptom resolution. Repeat endoscopy showed healed mucosa with diffuse scarring and histology confirmed no H. pylori and healed mucosa.
**Conclusions:** Phlegmonous gastritis may present with shock and ischemic-like endoscopic features and requires prompt recognition and treatment with broad-spectrum antibiotics and conservative management.




**Funding Agencies:** None

A54
**DUODENAL DUPLICATION CYST PRESENTING AS OBSCURE OVERT GASTROINTESTINAL BLEEDING**
M. Albabtain[1], R. Bechara[2]

1. Gastroenterology, Queen's University, Kingston, ON, Canada; 2. Gastroenterology, Queens University, Toronto, ON, Canada

**Background:** Duodenal duplication cysts are very rare congenital malformations that usually present in childhood with recurrent pancreatitis, biliary or duodenal obstruction. Overt bleeding in an adult secondary to a duodenal duplication cyst is an exceedingly rare diagnosis.
**Aims:** We report a case of duodenal duplication causing recurrent gastrointestinal bleeding that was successfully managed with endoscopic excision.
**Methods:** A detailed review of the case and the literature was undertaken.
**Results:**
A 67-year-old lady was referred to the GI clinic with a long history of iron-deficiency anemia since childhood and intermittent melena with unknown etiology. She had multiple upper and lower endoscopic examinations which failed to reveal the etiology of anemia or melena. In September 2016, she had frank melena and an acute hemoglobin drop 70g/L from 99g/L and an urgent upper endoscopy was performed. The endoscopic description was that of two visible lumens at the start of the second part of the duodenum. A culprit lesion was found as an adherent clot on a polypoid protuberance at the distal end of one the lumens. This was managed with Epinephrine injection.

A second look endoscopy with transparent hood was performed and demonstrated the ampulla sitting on a septum that separated the true lumen and the lumen of the duodenal duplication cyst. The duodenal duplication cyst was resected in two pieces, during which arterial bleeding was encountered, which was managed with soft coagulation end hemostatic clips. The patient subsequently had no further recurrence of melena and iron deficiency anemia has resolved. Pathology demonstrated a duodenal duplication cyst.
**Conclusions:** This case represents the successful

excision of a duodenal duplication cyst with an atypical presentation, in addition to having both ends of the cyst open, which exhibits a unique endoscopic appearance of a double lumen.

**Funding Agencies:** None

## FIBROGENESIS, PORTAL HYPERTENSION, COMPLICATIONS OF CIRRHOSIS

A55

### PREDICTORS OF ENDOSCOPIC HIGH RISK ESOPHAGEAL VARICES IN COMPENSATED CIRRHOSIS: CAN WE AVOID FIBROSCAN?

G. Huard, J. Hercun, M. Bilodeau, J. Bissonnette, J. Giard

liver diseases, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada

**Background:** Patients with cirrhosis are at risk of developing esophageal varices (EV). Recently, criteria based on elastography and platelet count (Baveno VI criteria) have been adopted and included in practice guidelines to circumvent screening endoscopy (EGD). However, elastography measurement is not widely available.
**Aims:** The aim of the study was to determine predictive factors excluding liver stiffness in order to predict high-risk EV in patients with compensated cirrhosis.
**Methods:** Retrospective chart review of all compensated cirrhotic adult patients who underwent screening EGD at Saint-Luc Hospital between 01/2014 and 12/2016. Patients with decompensated cirrhosis (ascites, hepatic encephalopathy, jaundice), past history of EV/TIPS or liver transplantation, acute upper gastointestinal bleeding, acute alcoholic hepatitis were excluded. High-risk EV were defined as medium or large EV and/or presence of red wale signs. Splenomegaly was defined as a spleen ≥ 13 cm on imaging. Thrombopenia was defined as a platelet count < 150 x $10^9$/L. Baseline characteristics, laboratory values and EGD findings were analyzed.
**Results:** A total of 463 patients were included. The median (IQR) age was 60.2 (13.4) years and the majority were males (n=289; 62.4%). The most frequent causes of liver disease were chronic hepatitis C infection (n=117; 25.3%) and non-alcoholic steatohepatitis (n=112; 24.2%). At screening EGD, the median (IQR) MELD score was 7.5 (2.7), the median (IQR) platelet count was 154 (87) x $10^9$/L, and 203 (43.8%) patients had splenomegaly. A total of 45 (9.7%) patients had high-risk EV at screening EGD. In multivariate analysis adjusting for age and gender, the following variables were predictive of high-risk EV: thrombopenia (OR 4.7; p= 0.001) and splenomegaly (OR 3.8; p=0.001). MELD > 6 score was not predictive of high-risk EV (OR 1.7; p=0.337). Among the 172 patients having normal spleen size and platelet count ≥ 150 x $10^9$, only 2 (1.2%) patients had high-risk EV at screening EGD. The presence of splenomegaly and/or thrombopenia had a sensitivity of 95.6% and a negative predictive value of 98.8% for the presence of high-risk EV at screening endoscopy.
**Conclusions:** In compensated cirrhosis, the combination of normal spleen size and normal platelet count translates into a 98.8% chance of absence of high-risk EV at screening EGD. Using these criteria, 172 (37.1%) screening EGD could have been avoided in our population. Therefore, the use of elastography is not mandatory in the decision of recommending screening EGD in patients with compensated cirrhosis.

**Funding Agencies:** None

A56

### LEVELS OF AGREEMENT BETWEEN PATIENT AND PRACTITIONER LED MALUTRITION SCREENING TOOLS IN CIRRHOSIS

T. Eslamparast[1], L. Taylor[2], N. Shommu[3], A. Kumar[2], K. Farhat[4], Q. Fitzgerald[2], P. Tandon[4], M. Raman[2]

1. Medicine, University of Alberta, Edmonton, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada

**Background:** Malnutrition is prevalent in cirrhosis, and tools to screen for nutrition risk are available, however, screening is seldom implemented in clinical practice. Time constraints in a clinic setting may provide one explanation for this omission. Accurate, easy to use patient-led nutrition screening tools may increase use of nutrition screening.
**Aims: Research objectives:**
1. To identify the agreement between a patient-led and health practitioner led nutrition-screening tool, the nutrition prioritizing tool (NPT).
2. To identify agreement between the patient led NPT and registered dietitian (RD) assigned gold-standard royal free hospital subjective global assessment score (RFH-SGA assessment tool).
**Methods:** A cross-sectional survey and RD-led interview were completed on 68 patients with diagnosed cirrhosis from Edmonton and Calgary cirrhosis clinics and inpatients. Patients completed the online patient led NPT, and were subsequently interviewed by a research assistant and a RD to determine the practitioner led NPT and RFH-SGA gold standard assessment score.
**Data Analyses:** Proportions of patients in each category were examined and kappa measure of agreement analyses were conducted to identify if there was a statistically significant difference between assessment methods.
**Results:** See Table 1 for a comparison of the results from the 3 scales. Both the practitioner led NPT (Kappa = 0.37, p<0.001) and RFH-SGA (0.07, p=0.173) were not in agreement with the patient led NPT results. Considering that patients with any degree of nutrition risk should be referred for further assessment, all screens were collapsed into two categories, low risk and increased risk. While this did not improve the kappa levels the sensitivity of the patient led NPT compared to the RFH-SGA was 69% and the specificity was 87%.



To view enlarged images and tables, please refer to Abstract Library.

**Conclusions:** Many patients with cirrhosis (67% using RFH-SGA) would likely benefit from consultation with a RD. Patients in the 3 nutrition risk categories identified by the patient-led NPT screening tool were not in agreement with the practitioner led screening NPT categories or the gold-standard RFH-SGA, although the sensitivity and specificity of the test was acceptable. Further examination of other patient led measures with higher levels of agreement with the RFH-SGA is warranted.

Table 1. Malnutrition scores on three different scales in cirrhosis

| Scales | Low risk % (n) | Mild to moderate risk % (n) | High to severe risk % (n) |
|---|---|---|---|
| Patient-led NPT | 50 (34) | 9 (6) | 41 (28) |
| Practi-tioner-led NPT | 27 (18) | 21 (14) | 53 (36) |
| RFH-SGA | 34 (23) | 49 (33) | 18 (12) |

NPT Nutrition prioritizing tool, RFH-SGA Royal free hospital-subjective global assessment

**Funding Agencies:** None

A57

**ACUTE VARICEAL GASTROINTESTINAL BLEEDING DOES NOT INFER POOR SURVIVAL COMPARED TO NON-VARICEAL BLEEDING IN PATIENTS WITH CIRRHOSIS: A RETROSPECTIVE, OBSERVATIONAL STUDY**

P. Tandon[1], K. Bishay[1], S. Bishay[2], D. Yelle[4], I. Carrigan[3], K. Wooller[4], E.M. Kelly[1]

1. Division of Gastroenterology and Hepatology, The Ottawa Hospital, Ottawa, ON, Canada; 2. Ottawa Hospital Research Institute, University of Ottawa, Ottawa, ON, Canada; 3. University of Ottawa, Ottawa, ON, Canada; 4. Division of General Internal Medicine, The Ottawa Hospital, Ottawa, ON, Canada

**Background:** Acute upper gastrointestinal bleed (UGIB) in cirrhosis is associated with significant morbidity and mortality. The most frequent cause of UGIB in cirrhosis is acute variceal bleed (AVB), though non-variceal bleed (NVB) may also occur. Whether there exists differences in mortality and clinical outcomes between AVB and NVB is unknown.
**Aims:** To evaluate differences in clinical outcomes, such as mortality, intensive care unit (ICU) stay, and need for transfusion between AVB and NVB in patients with cirrhosis presenting with UGIB.
**Methods:** All patients over the age of 18 with cirrhosis who presented to The Ottawa Hospital with UGIB and underwent upper endoscopy were included. AVB was defined as presence of varices on endoscopic examination with at least high-risk stigmata such as cherry-red spots or red-wale markings. NVB was defined as other etiology of UGIB such as peptic ulcer disease, portal hypertensive gastropathy, esophagitis, and dieulafoy lesions. The primary outcome was the risk of mortality of AVB and NVB in cirrhotic patients presenting with UGIB. We also compared hospital length of stay (LOS), 30-day hospital readmission, ICU admission, requirement for transfusion, and baseline characteristics such as demographics, cirrhosis complications, and presenting laboratory investigations between the two groups. Descriptive statistics were calculated using chi-square test and t-test with R v3.3.
**Results:** From 2014-2016, a total of 117 patients with cirrhosis were admitted with UGIB, 75 with AVB and 42 with NVB. The median age in the AVB group was 54.69 compared to 60.64 in the NVB group (p=0.001). There were no significant differences in gender or active alcohol use in both groups. The median model of end-stage liver disease (MELD) score was not significantly different in the AVB group (15.13, IQR 11.03-17.60) vs. the NVB group (15.09, IQR 10.92-23.21) (p=0.649). The risk of mortality was 13.3% in the AVB group compared to 9.5% in the NVB group (p=0.543). There was no significant difference in ICU admission (29.3% for AVB vs. 16.7% for NVB, p=0.128) or need for transfusion (65.3% for AVB vs. 54.8% for NVB, p=0.26). Patients who had AVB were more likely to have a history of previous esophageal varices (62.7%) compared to those who presented with NVB (38.1%) (p=0.011). There were no differences in history of hepatic encephalopathy, spontaneous bacterial peritonitis, and ascites in both groups. Hospital LOS was not significantly different for the AVB group (4.95, IQR 3.65-6.90) and NVB group (5.05, IQR 2.65-8.59) (p=0.42).
**Conclusions:** Our results found no difference in mortality, hospital LOS, and need for ICU between AVB and NVB. A history of known esophageal varices may predict future AVB whereas an older age may predict NVB in cirrhosis.

**Funding Agencies:** None

A58

**POPULATION CHARACTERISTICS AND OUTCOMES OF CARE IN PATIENTS WITH DECOMPENSATED CIRRHOSIS ADMITTED TO MEDICAL SERVICES AT THE OTTAWA HOSPITAL**

D. Yelle[1], I. Carrigan[1], K. Wooller[2], E.M. Kelly[2]

1. University of Ottawa, Ottawa, ON, Canada; 2. The Ottawa Hospital, Ottawa, ON, Canada

**Background:** Patients with decompensated cirrhosis have increased healthcare needs and consequentially greater healthcare utilization. Whether specific types of decompensating events including ascites, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy (HE), variceal bleeding (VB), and hepatorenal syndrome (HRS) are associated with greater risk of hospital readmission is unclear.

**Aims:** We aim to describe an inpatient cohort admitted with decompensated cirrhosis at a single tertiary care center and evaluate important clinical endpoints including length of stay (LOS), inpatient mortality and 30-day readmission rates (R-30) by presence and type of liver decompensation events.
**Methods:** Patients with decompensated cirrhosis admitted to a medical service at TOH between July 2014-2016 were identified using ICD codes. Cirrhosis and decompensating events were confirmed by chart review.
**Results:** Of the 302 patient admissions reviewed to date, 190 were first presentation to TOH with decompensated cirrhosis. Among those, 40.5% consumed alcohol in the prior week, and 62.6% of patients had one or more pre-existing complications of cirrhosis (ascites 53.7%, HE 25.8%, SBP 6.8%, VB 12.6%, HRS 1.1%). The average MELD-Na on admission was 19.2 (SD 6.8) for all unique patients. Admissions were complicated by ascites in 70.5%, HE in 25.5%, VB in 20.5%, SBP in 9.5%, and HRS in 5.8%. Patients with ascites, HE and HRS had significantly longer LOS compared to those without: ascites median LOS 6.9 days (IQR 4.0-17.5, p = 0.025), HE 8.7 (4.5-22.0, p = 0.046), HRS 20.7 (11.7-26.9, p = 0.0022). VB trended towards prolonging LOS but not significantly (median 5.29, IQR 3.28-6.89, p=0.051). SBP did not significantly impact LOS (median 12.1, IQR 4.9-24.0, p = 0.13). R-30 was significantly greater in those with HE (37.5%, p=0.008) compared to those without, while other in-hospital decompensating events did not significantly impact R-30 (ascites 23.9%, p=0.72; SBP 27.8%, p=0.63; HRS 9.1%, p=0.26; VB 18.0%, p=0.65). Pre-existing HE was also a significant predictor of R-30 (34.7%, p=0.026). Overall inpatient mortality rate was 19.0%. Inpatient mortality was greatest in those with an in-hospital diagnosis of HRS (72.7%, p<0.0001), followed by SBP (55.6%, p<0.0001) and ascites (19.0%, p=0.002). Mortality rates were not significantly different in patients with HE and VB compared to those without (18.8%, p=0.89; and 20.5%, p=0.94, respectively).
**Conclusions:** In our cohort, patients admitted with decompensated cirrhosis have high in-hospital mortality, prolonged LOS and increased risk of 30-day readmission. Decompensating events, notably HE, negatively impact hospital outcomes such as LOS and R-30, while HRS, SBP and ascites are associated with increased mortality. Future work will target strategies to improve the care for these patients.

**Funding Agencies:** None

A59

## QUALITY OF CARE OF PATIENTS WITH DECOMPENSATED CIRRHOSIS ADMITTED TO A MEDICAL SERVICE AT THE OTTAWA HOSPITAL

D. Yelle[2], I. Carrigan[2], K. Wooller[1], E. Kelly[1]

1. The Ottawa Hospital, Ottawa, ON, Canada; 2. University of Ottawa, Ottawa, ON, Canada

**Background:** Cirrhosis is an increasingly prevalent condition associated with growing healthcare costs and resource utilization related to several possible complications of the disease including ascites, spontaneous bacterial peritonitis (SBP), hepatorenal syndrome (HRS), hepatic encephalopathy (HE), and variceal bleeding (VB). Inconsistencies are known to exist in the management of patients with cirrhosis. Evidence-based quality indicators (QIs) recently developed to help clinicians guide management of cirrhosis are now correlated with outcomes such as readmission and mortality.
**Aims:** We seek to evaluate adherence to defined QIs at TOH and measure the association with subsequent outcomes such as length of stay, inpatient mortality, and 30-day readmission rates.
**Methods:** Patients with decompensated cirrhosis admitted to a medical service at TOH between July 2014-2016 were identified using ICD codes, and a retrospective cohort study using electronic charts is underway. Predictive validity of the QIs used is being assessed by measuring the relationship between QI adherence and patient outcomes.
**Results:** Of the 302 admissions reviewed to date, 291 were visits related to decompensated cirrhosis (190 unique patients). Among those, mean length of stay was 12.2 days (median 6.2, IQR 3.2-14.7) and the 30-day readmission rate was 24.4%. Gastroenterology consultations were obtained in 47.8% of visits. Among patients with variceal upper GI bleeding, the following QIs were met: endoscopy performed within 24h in 81.0%, octreotide instituted within 12h in 86.8%, and antibiotic prophylaxis given in 94.1%. Among patients with ascites, paracentesis was performed during admission in 60.8%, albumin was infused after large-volume paracentesis in 88.7%, spontaneous bacterial peritonitis (SBP) was treated with appropriate antibiotics in 96.4%, and secondary antibiotic prophylaxis post-SBP was prescribed in 38.5%. In patients with overt hepatic encephalopathy, a search for and correction of all precipitating factors was documented in 35.2%, while medical therapy at discharge was appropriate in 64.8% of cases.
**Conclusions:** Patients admitted to TOH with decompensated cirrhosis have prolonged stay in hospital and high readmission rates. Adherence to predefined QIs is variable and may be related to both patient and provider factors (understanding, education, coordination and timeliness of care). Focused interventions are warranted in several areas to help improve outcomes.

**Funding Agencies:** None

A60

## PREDICTIVE FACTORS OF INTENSIVE CARE UNIT ADMISSION AND MORTALITY IN CIRRHOTIC PATIENTS WITH UPPER GASTROINTESTINAL BLEEDS

K. Bishay[2], P. Tandon[1], S. Bishay[4], D. Yelle[2], I. Carrigan[5], K. Wooller[1], E.M. Kelly[3]

1. The Ottawa Hospital, Woodbridge, ON, Canada; 2. The Ottawa Hospital, Ottawa, ON, Canada; 3.

Gastroenterology and Hepatology, University of Ottawa, Ottawa, ON, Canada; 4. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 5. University of Ottawa, Ottawa, ON, Canada

**Background:** Acute upper gastrointestinal bleeds (UGIB) are the most common emergency condition managed by gastroenterologists in the emergency department. Several pre-endoscopic scoring systems have been developed to predict clinical outcomes in patients presenting with UGIB, however these have not been validated in predicting outcomes in UGIB in cirrhotic patients.
**Aims:** The objective of this study is to elucidate patient factors at presentation that are associated with admission to the intensive care unit (ICU) or mortality in cirrhotic patients presenting with UGIB.
**Methods:** All patients over the age of 18 with known cirrhosis presenting with a first presentation of UGIB were eligible for inclusion into this study. A sequential retrospective analysis of patients presenting to The Ottawa Hospital between 2014 and 2016 was performed to collect baseline characteristics at admission including demographics, etiology and complications of cirrhosis, vital signs, blood work, model of end stage liver disease (MELD) score, active alcohol or intravenous drug use, length of stay, transfusion requirement. Patients were stratified by need for ICU or mortality. Descriptive statistics were calculated using chi-square and t-test with R v3.3.
**Results:** A total of 117 patients with cirrhosis presenting with an UGIB were included, 31 of which were admitted to the ICU or died during admission and comprised the ICU/death group. There were no significant differences between baseline characteristics including age, gender, cirrhosis etiology, and active alcohol or current injection drug use. The presence of variceal bleeding was similar was similar between groups (ICU/death: 74.2% vs 60.5%, P=0.172). At admission, the ICU/death group had lower systolic blood pressure (108.5 vs 120.5, P=0.004), higher white blood cell count (12.9 vs 7.9, P=0.006), higher INR (1.7 vs 1.4, P<0.001), higher bilirubin (62.0 vs 27.0, P=0.001), lower albumin (23.0 vs. 26.0, P=0.001) and a higher MELD score (18.14 vs 13.43, P<0.001). The proportion of patients requiring blood transfusion was higher in those with ICU/death (87.1% vs 52.3%, P=0.001). Hospital length of stay was also longer in this group (6.9 vs 4.8 days, P=0.028).
**Conclusions:** Among cirrhotic patients presenting with UGIB, the presence of impaired synthetic liver function and elevated MELD score is associated with more severe outcomes and predictive of the need for ICU admission and in hospital death.

**Funding Agencies:** None

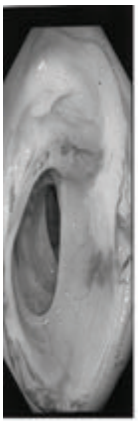
A61
**COLORECTAL ANASTOMOTIC VARICES IN A PATIENT WITH PORTAL HYPERTENSION: A CASE REPORT AND REVIEW OF THE LITERATURE**

G. Sasson[2], E. Yong[3], H. Steinhart[1]

1. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 2. University of Toronto, Toronto, ON, Canada; 3. Sunnybrook Hospital, University of Toronto, Toronto, ON, Canada

**Background:** Ectopic varices (EV) account for 5% of variceal bleeding. Anastomotic varices (AV) are a rare form of EV that have been predominantly described in small bowel. To our knowledge colorectal AV have not been described. We describe a case of colorectal AV hemorrhage in a patient with portal hypertension (PH) treated with endoscopic band ligation (EBL).
**Aims:** To gain insight into the incidence, location and optimal treatment of AV.
**Methods:** Case report and literature review.
**Results: Case report:** A 63 year old woman with alcoholic cirrhosis presented with recurrent lower GI bleeding (LGIB) 2 years following sigmoid resection and primary colorectal anastomosis for colorectal cancer. Colonoscopy demonstrated anastomotic neovascularization with prominent submucosal vessels suggestive of varices, without high risk stigmata. Her symptoms resolved without intervention. She returned 5 weeks later with recurrent LGIB; sigmoidoscopy revealed AV with stigmata of recent hemorrhage successfully managed with single EBL. The next episode of LGIB occurred over 2 years later; colonoscopy revealed AV with visible erosions treated with EBL. She attended subsequent EBL sessions until variceal extinction. After several months, she presented on 3 occasions over a 2-month period for LGIB in the context of alcohol binges. AV with erosions were visualized at each episode, however there was no active bleeding or endoscopic intervention.
**Literature review:** A PubMed and Cochrane Database of Systematic Reviews search produced publications describing varices at surgical sites, most of which were peristomal. There were 4 cases of esophagojejunal AV, 13 cases of gastroduodenal AV, and 3 cases of jejunal varices after hepatico- or choledochojejunostomy. The most distal anastomosis reported was a case series of 10 patients with PH who underwent ileal pouch-anal anastomosis; none developed pouch variceal bleeding. The lack of colonic variceal involvement, particularly of the descending and sigmoid colon, may relate to their anatomical distance from, and indirect drainage to, the portal vein, resulting in indirect transmission of venous pressure.
Management of AV is controversial. Endoscopic intervention with N-butyl-2-cyanoacrylate is efficacious in small bowel AV. Transjugular intrahepatic portosystemic shunt and percutaneous transhepatic obliteration is beneficial in EV. Surgical resection or transcatheter embolization can be effective, however perioperative morbidity and mortality is high. To our knowledge, EBL for colorectal AV has not been described. This treatment modality appears to be useful for temporary hemostasis but rebleeding rates appear to be high.
**Conclusions:** A case report of colorectal AV is

presented. EBL achieved temporary hemostasis but rebleeding rates were high.



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## HORMONES, TRANSMITTERS, GROWTH FACTORS

### Poster of Distinction

A62
**BMP SIGNALING IN FOXL1⁺ CELLS IS A KEY TO THE INTESTINAL STEM CELL NICHE HOMEOSTASIS**
R. Servant[4], C. Jones[1], F. Boudreau[3], N. Perreault[2]

1. Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Anatomie et Biologie Cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 3. Anatomie et biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 4. Anatomie et Biologie Cellulaire , Unversité de Sherbrooke, Sherbrooke, QC, Canada

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## IMMUNOBIOLOGY AND LIVER TRANSPLANTATION

A63
**TRANSPLANTATION OF A LIVER ALLOGRAFT FROM A HEPATITIS C VIRUS (HCV) SEROPOSITIVE DONOR WITH PREVIOUS SUSTAINED VIROLOGIC RESPONSE TO AN UNINFECTED RECIPIENT SUFFERING STEROID REFRACTORY ACUTE GRAFT REJECTION WITH NO EVIDENCE OF HCV TRANSMISSION**
R.A. Mitchell[1], T. Hussaini [5], A. Yau[1], M. Krajden[3], A.J. Wright[4], C. Scudamore[2], V. Marquez[1], Z. Erb[1], E.M. Yoshida[1]

1. Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 2. Division of General Surgery, University of British Columbia, Vancouver, BC, Canada; 3. Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada; 4. Division of Infectious Diseases, University of British Columbia, Vancouver, BC, Canada; 5. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada

**Background:** The goal of treating chronic hepatitis C virus (HCV) infection is sustained virologic response (SVR). There is concern that despite achieving SVR, replication-competent HCV may be sequestered at low levels within the liver and could theoretically reactivate with immunosuppression.
**Aims:** We report transplantation of a HCV seropositive liver donor, who achieved SVR, into a seronegative patient without HCV reactivation despite profound immunosuppression.
**Methods:** Retrospective chart review.
**Results:** We present a 21-year-old male who was HCV seronegative and received a liver transplant from a donor who had been treated for HCV and achieved SVR. The liver recipient, despite developing severe acute graft rejection and undergoing intense immunosuppression with T-cell depleting antibodies, did not become HCV RNA positive with a follow up period of 8 months. The recipient was HCV seronegative before transplant, but became HCV seropositive immediately post-transplant. The antibodies were undetectable after 97 days, in keeping with a passive antibody transmission or B lymphocyte transmission with the graft.
**Conclusions:** To the best of our knowledge, this is the first reported case of an HCV seropositive liver allograft transplanted into a HCV negative recipient. This case, therefore, is an encouraging and novel step in liver transplantation, and demonstrates that SVR may be closer to a true "cure" of HCV in the donor population and that, even in circumstances of very potent immunosuppression in the recipient, this SVR is sustained. To our knowledge, this case also contains the first documented example of an HCV antibody decay phenomenon in the recipient post-liver organ transplant.

**Funding Agencies:** None

A64
**BURKITT LYMPHOMA AFTER PEDIATRIC LIVER TRANSPLANTATION**
N. Laverdure[2], S. Collardeau[1], N. Patey[2], A. Lachaux[1], F. Alvarez[2]

1. HFME, Bron, France; 2. CHU Ste Justine, Montreal, QC, Canada

**Background:** Burkitt lymphoma (BL) is a post-transplant lymphoproliferative disorder (PTLD) different from other monomorphic PTLDs (M-PTLDs).
**Aims:** We report clinical presentation and pathologic findings in 6 pediatric cases.
**Methods:** We included patients that undergone a liver transplantation (LT) at Sainte Justine Hospital (Montreal) or in The Children hospital of Lyon, from 1991 to 2017, (aged ≤18 years). During this period, 10 patients presented monomorphic PTLDs (M-PTLDs), 6 of which were Burkitt lymphoma (BL).
**Results:** The median age at transplantation, for the 6 children (5 boys, 1 girls) with BL, was 21.5 months (range 6 – 159 months), and biliary atresia was the main indication (3/6). BL had an abdominal presentation in majority of cases (5/6).
Patients displayed a monomorphic population of small to intermediate-sized, non-cleaved, lymphoid elements with a "starry-sky" pattern. The immune-phenotype in patients available for analysis was CD20+ (n =6/6), CD10+ (n = 6/6), Bcl-6+ (n = 6/6), Ki-67/MIB-1 proliferation index (n = 5/5), and negative for TdT (n = 5/5). Pre-transplant Epstein-Barr virus serology was negative in 4 patients (n = 4/6). At the time of BL diagnosis, all patients showed high EBV viral loads estimated by quantitative PCR testing between 16000 and $20^6$ copies/ ml. The PCR was positive since a median time of 26.5 months (range, 1-40 months).
The median time from transplantation to diagnosis was 33 months (range, 3-46 months). All patients were currently alive after chemotherapy, with median disease-free time of 14.5 years from diagnosis (range, 2-19 years).
**Conclusions:** Post-transplant-BL is strongly associated with high EBV viral loads and represented a distinct monomorphic PTLD. Managed aggressively with decreased immunosuppression and specific chemotherapy must lead to a favorable outcome. These data also lead to discuss the modality of monitoring and the establishment of early treatment, with anti CD 20, for transplanted patients who retain high EBV viral loads.

**Funding Agencies:** Ste Justine Foundation, Servier Laboratory

## IMMUNOLOGY AND INFLAMMATORY BOWEL DISEASE

### Poster of Distinction

A65
**HNF4A IS A KEY REGULATOR OF THE EPITHELIAL STEM CELL NICHE.**
C. Jones[1], F. Boudreau[2]

1. Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Anatomie et biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** HNF4α is a transcriptional factor downregulated in intestinal bowel diseases (IBD). Epithelial deletion of HNF4α in the mouse intestine leads to spontaneous intestinal inflammation. Those observations suggest that HNF4α could play an important role in epithelial homeostasis. The intestinal crypt is the functional compartment responsible for the maintenance of this homeostasis. Proliferation of stem cells is essential for the mucosa healing following injuries, while Paneth cells are important regulators of this process through the secretion of stem cell niche factors including WNT3, a key activator of the canonical WNT/β-catenin pathway.
**Aims:** We aimed to investigate if HNF4α could play an intrinsic role in stem and Paneth cells for the maintenance of the epithelial niche in intestinal crypts.
**Methods:** Villin-Cre/HNF4α$^{loxp/loxp}$ and the hydroxytamoxifen (4OHT) inducible Villin-Cre ERT2/HNF4α$^{loxp/loxp}$ mouse models were used in this study. Isolated crypts were processed for protein and RNA isolation. Enteroids were derived from these models and used for RNAseq and qPCR experiments.
**Results:** Enteroids were derived from jejunal crypts of inducible Villin-Cre ERT2/HNF4α$^{loxp/loxp}$ mice. Induction of HNF4α deletion with 4OHT led to degeneration of these enteroids starting 5 days after the deletion, an observation reminiscent of enteroids derived from the Villin-Cre/HNF4α$^{loxp/loxp}$ mouse model. EdU incorporation assays showed a decrease in the proliferative rate of enteroids 4 days following HNF4α deletion. RNAseq was next performed on RNA isolated from enteroids induced for HNF4α deletion after 2 and 4 days in culture. Transcriptomic analysis identified more than a thousand of genes differentially expressed following the deletion of HNF4α under these conditions. A significant reduction of WNT3 was predicted, an observation that was further confirmed by qPCR and Western in jejunal crypts of HNF4α mutant mice. To measure the functional relevance of WNT3 reduction during enteroids degeneration, a rescue experiment was performed. WNT3A supplementation was able to maintain HNF4α deleted enteroids in culture. Transcriptomic analysis of WNT3A-treated enteroids showed rescue for 85% of the genes identified to be modulated in enteroids deleted for HNF4α. To further verify if HNF4α may contribute to Paneth cell differentiation, enteroids committed to differentiate into the Paneth lineage were deleted for HNF4α. Gene transcript expression of Paneth cell markers (Defa3, Defa5, Defa20, Defa21-22, Lyz and WNT3) were all downregulated in the absence of HNF4α as opposed to EpHB3, which was not significantly modulated.
**Conclusions:** This study identifies HNF4α as a key regulator of Paneth cell function for maintenance of the epithelial stem cell niche. These observations provide a novel mechanistic loop for which the intestinal epithelial healing process could be dependent following stress-related injuries.

**Funding Agencies:** CIHRCCC-Vertex

## Poster of Distinction

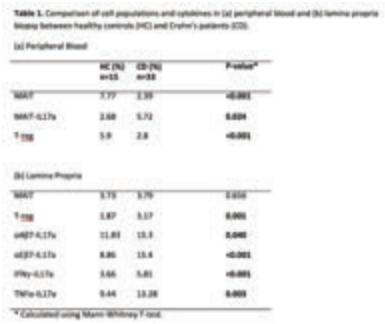
A66

**CHARACTERIZATION OF PERIPHERAL BLOOD AND LAMINA PROPRIA LYMPHOCYTES IN CROHN'S DISEASE.**

N. Power, T. Jeyalingam, M. Filice, M. Smith, M.S. Silverberg, A. Steinhart, G.C. Nguyen, P. Zezos, K. Croitoru

Mount Sinai Hospital Centre for Inflammatory Bowel Disease, Toronto, ON, Canada

**Background:** Stimulation of the intestinal immune system is an important contributor to the pathogenesis of Crohn's disease. This includes possible changes in regulatory T cells (Tregs), mucosal-associated invariant T cells (MAIT), and helper T cells (Th cells).
**Aims:** We aimed to characterize and compare T-lymphocyte subpopulations in the peripheral blood and intestinal lamina propria (LP) of healthy individuals and those with Crohn's disease (CD).
**Methods:** Peripheral blood and LP biopsy specimens of the colon and ileum were collected from 33 patients with CD and 15 healthy controls (HC). Lymphocytes were isolated from the peripheral blood (PBL) and LP (LPL) and cell surface phenotype and intracellular cytokines were analyzed by flow cytometry. Specifically, we assessed markers of T cells (CD3+), Tregs (CD4+CD25+CD127-), MAIT cells (CD3+CD8+CD161high, Vα7.2+), and cells expressing α4β7 and αEβ7 integrins (Beta7+, CD103+). Cells were also stimulated with PMA and ionomycin for 4 hours at 37ºC and analyzed for cell surface phenotype and intracellular cytokine expression using Ab to IFNγ, TNFα, and IL17a.
**Results:** When compared to HC, we found a decrease of MAIT and Tregs in the peripheral blood of CD patients (2.39% vs. 7.77%, P=0.0008; 2.8% vs. 5.9%, P<0.0001). In inflamed tissue of CD patients there was an increase in Tregs as compared to both HC and non-inflamed tissue of CD patients (3.17% vs. 1.87%, P= 0.0013; 3.17% vs. 1.86%, P=0.011). Interestingly, MAIT cell levels in LPL of HC were not significantly different from that of CD patients (3.73% vs 3.79%, P=0.6558). MAIT cells in the blood of CD patients produced more IL17a than MAIT cells from HC (5.72% vs. 2.68%, P=0.0242). Furthermore, we saw an increase in production of IL17a from α4β7 + and αEβ7 + cells in CD patients (15.3% vs. 11.83%, P=0.0401; 15.4% vs. 8.86%, P=0.0002) as well as an increase in LPL co-producing IFNγ and IL17a (5.81% vs. 3.66%, P=0.0003) and TNFα and IL17a (13.28% vs. 9.44%, P=0.0028), when compared to HC, regardless of disease activity.
**Conclusions:** These data show that peripheral blood lymphocyte phenotype differs from gut LPL in HC and in CD. The increase in IFNγ-IL17a and TNFα-IL17a producing LPL suggest a disease state shift from Th1 cells to Th17 cells in CD. Taken together, these results suggest that intestinal Th17 cells can transition into Th1-like cells and pro-inflammatory stimuli may promote this conversion. It remains to be shown if therapy restores the balance of Th1 and Th17 cells. Together, these results provide insight into the immune profile of CD patients at baseline, prior to biologic treatment.



**Funding Agencies:** AbbVie

## Poster of Distinction

A67

**RAPID REDUCTION IN ANXIETY SCORES IN IBD PATIENTS AFTER INFLIXIMAB INFUSION IS ASSOCIATED WITH CHANGES IN KYNURENINE/TRYPTOPHAN METABOLISM**

C. Seiler[1], C. Avila[1], R. Khana[1], E. Springer[1], C. James[1], D. Armstrong[1], J. Marshall[3], S.M. Collins[1], M.I. Pinto-Sanchez[2], P. Bercik[1]

1. McMaster University, Hamilton, ON, Canada; 2. Medicine, McMaster University, Hamilton, ON, Canada; 3. McMaster University Medical Centre, Hamilton, ON, Canada

**Background:** Patients with inflammatory bowel disease (IBD) frequently suffer from psychiatric comorbidities, mainly anxiety and depression. Infliximab, an anti-TNFα antibody, is commonly used for treatment of colitis. There are anecdotal reports of IBD patients having improvement in mood only hours after infliximab infusion, well before intestinal mucosal healing could occur.
**Aims:** To evaluate the immediate effects of infliximab infusion on intestinal and extra-intestinal symptoms and immune markers in IBD patients.
**Methods:** IBD patients attending the McMaster University and Charlton infusion clinics were enrolled in the study. Patients were examined at baseline (day 0), 1 day, and 7 days after the infliximab infusion. We assessed anxiety and depression (HAD and STAI-Y scales), disease specific quality of life (SIDBQ), as well as disease activity scores using the Harvey Bradshaw Index (HBI) or the Mayo Score. Serum C-reactive protein (CRP), kynurenine, tryptophan, and serotonin levels were measured at each visit.
**Results:** We enrolled 41 IBD patients (Crohn's disease = 35, Ulcerative Colitis = 5, indeterminate colitis = 1; median age 33 yrs, median disease duration 9 yrs). Disease activity decreased at day 1 compared to

baseline (p=0.01), but this was not sustained at day 7. Anxiety scores (HADS-A) decreased significantly at day 1 (p=0.006), and remained lower at day 7 (p=0.009). An improvement in quality of life (SIBDQ) was seen only at day 7 (p=0.017). The decrease in anxiety scores strongly correlated with the improvement in quality of life (SIBDQ r=-0.81; p<0.001) at day 1 and day 7. The kynurenine/tryptophan ratio decreased significantly at day 1 (p=0.025) and remained lower at day 7 (p=0.047). However, CRP levels did not change during the study period.
**Conclusions:** Infliximab infusion induces rapid changes in anxiety and disease activity. We hypothesise that this effect is central, mediated through changes in kynurenine/tryptophan metabolism, and not through improvement of gut inflammation.

**Funding Agencies:** CIHR

## Poster of Distinction

A68
**INVESTIGATING THE ROLE OF INTESTINAL EPITHELIAL CELL NF-κβ SIGNALLING IN CD8 T CELL RESPONSE TO MURINE NOROVIRUS**
B.k. Hardman[2], L. Osborne[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. Microbiology/Immunology, University of British Columbia, Vancouver, BC, Canada

**Background:** The intestinal lumen constitutes the site of highest contact between a mucosal surface and non-self matter. IECs serve dual functions: acting as a physical barrier, as well as working in conjunction with innate and adaptive immune cells to form a dynamic sensory organ that surveys luminal contents and responds to threats. Nuclear Factor kappa β (NF-κβ) is a major regulator of inflammation in response to physical damage and pathogenic events. NF-κβ signalling can be induced through Inhibitor of Kappa Kinase α or β (IKKα and IKKβ). Previous research has shown differential effects between IEC NF-κβ induction through IKKα or IKKβ in DSS-induced colitis and in response to intestinal infections with bacteria or helminths. Currently, the significance of IEC NF-κβ signalling through IKKα and IKKβ during intestinal viral infection is unknown.
**Aims:** This research will examine the impact of IKKα or IKKβ ablation specifically in IECs on the magnitude and localization of CD8 T cell responses to acute Murine Norovirus (MNV). Virus specific CD8 T cells will be quantified and phenotypically characterized by flow cytometry. Immunofluorescent microscopy will be used to examine the localization of responding CD8 T cells. It is anticipated that the combination of these complementary techniques will highlight the importance of IEC signalling during immune responses in this highly dynamic environment.
**Methods:** Mice lacking either IKKα or IKKβ in IECs were injected with virus-specific mCherry+ CD8 T cells and then infected with MNV-CW3, a strain that recapitulates characteristics of human Norovirus infection, including intestinal exposure, systemic spread, and acute clearance. At the peak of the antiviral T cell response (day 8), intestines and spleen were harvested and immune populations were analyzed. A combination of flow cytometry and immunofluorescent microscopy were used to characterize the CD8 T cell response in terms of individual cell phenotype and localization, respectively.

**Results:** Flow cytometry data from spleen and intestinal CD8 T cells demonstrate a decreased number and impaired activation of antiviral CD8 T in mice lacking IEC intrinsic IKKα.
**Conclusions:** This finding identifies a role for IEC NF-κβ signalling in shaping the viral response by influencing activation of responding CD8 T cell population in response to intestinal viral infection. Furthermore, the systemic deficiency in responding cell numbers suggests that signalling from the intestinal epithelium is critical not just for local responses but also in organism wide immunity to intestinal pathogens.

**Funding Agencies:** CIHR

## Poster of Distinction

A69
**THE MOLECULAR LANDSCAPE IN ULCERATIVE COLITIS**
K. Madill-Thomsen[4], V. Jovanovic[5], J. Venner[6], K. Famulski[3], S. Withecomb[2], M. Parkes[2], A. Thiesen[4], R. Fedorak[1], P. Halloran[3], B.P. Halloran[4]

1. Los Alamos National Laboratory, Edmonton, AB, Canada; 2. Medicine, University of Alberta, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 5. Gastroenterology, University of Alberta, Edmonton, AB, Canada; 6. University Of Queensland, Brisebane, Queensland, Australia

**Background:** Ulcerative colitis (UC) is a chronic, idiopathic inflammatory condition affecting the colonic epithelium, with the inflammasome, T cells, complement activation, and microbiome dysbiosis contributing to pathogenesis.
**Aims:** We applied a previously established method of microarray molecular analysis to a set of 71 UC biopsies (from 61 patients), to elucidate the molecular changes associated with active UC, specifically comparing UC to T-cell mediated rejection (TCMR), as a prototype of a sterile, T-cell mediated disease.
**Methods:** 71 for-cause UC colonic biopsies were collected at the U of A Hospital in Edmonton, AB and Cedars-Sinai Hospital in LA, California. These biopsies were processed using Affymetrix GeneChip microarrays and the data analyzed in R programming language. Gene expression data was displayed using volcano plots (showing the fold change and association between the genes and endoscopic Mayo score) and heatmaps (showing expression of the top 30 genes in a cell panel). We then analyzed overexpression of the top genes using the DAVID tool[1], and compared the results to similar results for top genes overexpressed in TCMR.

**Results:** The volcano plot (Figure 1) showed strong associations between the endoscopic Mayo score and decay accelerating factor (CD55), and moderate associations with calprotectin genes (S100A8/S100A9), with lesser associations for effector T cell transcripts (i.e. CTLA4, interferon gamma (IFNG), and chemokine ligand (CXCL13)), many IFNG inducible transcripts, inflammasome transcripts (CASP1), and toll-like receptors (TLR5). NLRP3 (incriminated in mouse UC models) did not pass the IQR filter and was not significant. Expression of the top genes in a cell panel showed primary expression in monocytes, macrophages, and dendritic cells, with some expression in epithelial and endothelial cells, while minimal expression was found in CD4/CD8 T cells, or in NK cells. Pathway analysis showed major differences between pathway terms.
**Conclusions:** Our findings show that while transcripts associated with cognate T cell inflammatory processes (TCMR) are expressed in UC, there are substantial differences between the pathogenesis of a pure T cell-mediated disease and UC. In our cohort, the top genes associated with the endoscopic Mayo score in UC were not those associated with effector T cells: T cell-associated transcripts were only moderately associated with the Mayo score, and pathway analysis showed significant differences between TCMR and UC, which is much more an inflammatory environment with strong associations to CD55. This suggests that cognate T cell recognition is present in UC but supplemented by a second source of inflammation.

**REFERENCES:**
1. Huang et al. Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. Nature Protocols (2009).

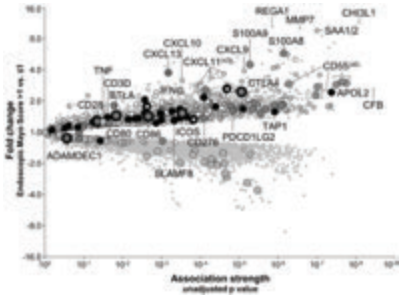



**Figure 1.** Molecular landscape of UC by volcano plot. Samples towards upper right have high association and fold change, indicating a significant association with endoscopic Mayo score, while samples towards the middle left are not strongly associated.

**Funding Agencies:** None

A70
**MOLECULAR ARCHETYPE HETEROGENEITY IN ULCERATIVE COLITIS BIOPSIES**
K. Madill-Thomsen[3], S. Withecomb[3], M. Parkes[3], V. Jovanovic[2], J. Venner[1], R. Fedorak[2], P. Halloran[3], B.P. Halloran[1]

1. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 2. Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** The assessment of patients with ulcerative colitis (UC) remains a challenge despite rapidly evolving medical therapy. Current assessment with endoscopic scoring and histopathology lacks the granularity to correlate strongly with response to therapy.
**Aims:** Utilizing a microarray based system for colonic epithelial assessment we looked for stratification of endoscopically similar UC biopsies using molecularly heterogeneous archetypes.
**Methods:** Molecular data from 71 UC biopsies (from 61 patients) was obtained from microarray analysis. The top 300 genes correlating with the endoscopic Mayo score (2/3 vs 0/1) were used for an unsupervised analytical method called archetypal analysis, and grouped the biopsies into three distinct clusters. Logistic regression modeling was used to compare archetype scores or cluster membership to endoscopic Mayo score and PC1 in predicting mucosal healing. A contingency table was generated to show evidence of mucosal healing within each of the archetype clusters. We then assessed a subset of biopsies from the original set of 71 (selected due to the availability of biopsies before and after therapy, all on TNF therapy) plus one IBDU case. Patients were classified as 'responders' (Mayo 2/3 score to Mayo 0/1 score by last obtained biopsy or scope) or 'non-responders' (Mayo 2/3 score that did not decrease to 0/1 by last obtained biopsy or scope).
**Results:** We found three unique groups of biopsies using archetypal analysis (A1: lack of inflammation, A2: inflammation and response to wounding, A3: inflammation). Logistic regression showed that the only models with statistically significant predictive value (p-value < 0.05) were those that contained archetype scores or cluster membership. Response rates differed between archetype clusters with statistical significance (Table 1), while the mayo score distribution within these clusters was not statistically different. In our subset of serial biopsies, the majority of initial biopsies were found to have an A2 archetype, moving to an A1 archetype in follow-up that mirrored response to treatment (Figure 1).
**Conclusions:** This archetypal analysis suggests there is potentially important heterogeneity in UC biopsies that is not accessible by endoscopic Mayo score. Serial biopsies showed dynamic shifts in the archetype composition between biopsies. This may be a useful tool for both initaillly prognosticating patients and assessing response to treatment over time with increased granularity and reliablity.

UC Patient Response to Therapy Assessed by Initial Archetype Cluster


To view enlarged images and tables, please refer to Abstract Library.

| Archetype Cluster (Total cases) | # of cases improved* |
|---|---|
| A1 (4) | 4 (100%) |
| A2 (16) | 10 (62%) |
| A3 (6) | 1 (17%) |

All cases had a Mayo score of 2-3 on initial endoscopy. *score of 0-1 on follow up endoscopy . Pearson's Chi-Squared = 7.222, df = 2, p = 0.027

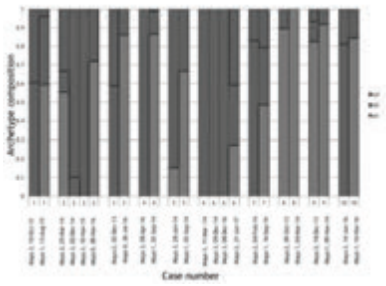


Figure 1. Stacked and group bar charts showing archetype composition of biopsies in 10 UC patients taken over time (2-4 serial biopsies/patient).

**Funding Agencies:** None

## Poster of Distinction

A71

**ASSOCIATION OF PREOPERATIVE CORTICOSTEROID USE WITH ADVERSE POSTOPERATIVE OUTCOMES IN PATIENTS UNDERGOING ILEAL POUCH ANAL ANASTOMOSIS FOR ULCERATIVE COLITIS**

A. Rumman[1], A. Alnahas[2], T.D. Jackson[2], G.C. Nguyen[1]

1. Division of Gastroenterology, Department of Medicine, University of Toronto, Toronto, ON, Canada; 2. Department of Surgery, University of Toronto, Toronto, ON, Canada

**Background:** Inflammatory bowel disease (IBD) patients are frequently treated with steroids prior to surgery. Steroid use has been associated with perioperative complications
**Aims:** We characterized the association between preoperative steroid use and postoperative complications in a large prospective cohort of IBD patients undergoing single-step ileal pouch anal anastomosis (IPAA).
**Methods:** We identified ulcerative colitis patients who underwent open or laparoscopic colectomy with IPAA surgery in the American College of Surgeon's National Surgical Quality Improvement Program (ACS-NSQIP) between 2005 and 2012. We compared the risk of postoperative complications and 30-day mortality between preoperative steroid users and non-users.
**Results:** A total of 2736 patients were included in the analysis: 1623 (59.3%) were male, mean age at the time of surgery was 41 years (standard deviation, SD = 14), and the majority of patients had ulcerative pancolitis (89.9%). Laparoscopic surgery was used in 965 (35.3%) cases. Preoperative steroid use was encountered in 1104 (40.4%) patients. Preoperative steroid use was associated with higher rate of major (26.2% vs. 19.4%, p <0.001) and overall (32.7% vs. 26.2%, p <0.001) postoperative complications as well as a higher 30-day re-operation rate (8.2% vs. 5.6%, p = 0.006) and a slightly longer mean length of stay (8.1 vs. 7.5 days, p = 0.004). After adjustment for age, sex, smoking status, body mass index, functional status, preoperative weight loss and anemia, coexisting diabetes, and emergent status, preoperative steroid use was associated with higher risk of postoperative complications (OR, 1.48; 95% CI: 1.23–1.78, p <0.001). The difference was driven by higher rate of infectious complications (34.1% vs. 28.2%, p <0.001) and venous thromboembolism (VTE, 6.1% vs. 2.9%, p <0.001) in steroid users. Thirty-day readmission rate (16.1% vs. 16.4%, p = 0.981) and mortality rate (0.4% vs. 0.1%, p = 0.184) did not differ significantly between steroid users and non-users.
**Conclusions:** The use of preoperative steroids is associated with a higher risk of postoperative sepsis and VTE in ulcerative colitis patient undergoing colectomy and single-step IPAA. Increased infection control measures and VTE prophylaxis may reduce adverse events in these patients.

**Funding Agencies:** None

A72

**INFLAMMATORY BOWEL DISEASE TRAINING DURING ADULT GASTROENTROLOGY FELLOWSHIP: A NATIONAL SURVEY OF CANADIAN PROGRAM DIRECTORS AND TRAINEES**

A. Rumman[3], K. Pivovarov[4], K.J. Fortinsky[4], G.C. Nguyen[2], Z. Gallinger[1]

1. The Mount Sinai Hospital, New York, NY; 2. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 3. Department of Medicine, University of Toronto, Toronto, ON, Canada; 4. University of Toronto, Toronto, ON, Canada

**Background:** Clinical training in inflammatory bowel disease (IBD) is a major component of adult gastroenterology fellowship. As Canadian residency programs adopt a competency-by-design (CBD) training model, there is a need to identify core competencies in IBD training.
**Aims:** This study aims to identify priorities and deficiencies in IBD clinical training among residents and program directors (PDs).
**Methods:** Using an online and paper based platform, we administered a 15-question PD survey and 19-question trainee survey and assessed 22 proposed IBD competencies. The survey was previously developed and administered to US gastroenterology trainees and PDs.

**Results:** Surveys were completed by 9/14 (62.3%) PDs and 44 trainees. Both trainee years were equally represented (22 residents in each year of training). All respondents were based at university teaching hospitals with full time IBD faculty on staff. All training programs surveyed offered an additional year of advanced IBD fellowship training. Dedicated IBD rotations were not offered by over half of training programs, and IBD exposure was mostly commonly encountered in inpatient rotations.
Overall, only 14 (31.2%) trainees were fully satisfied with the level of IBD exposure during training. Thirty-six (81.8%) trainees reported being comfortable with inpatient IBD management, whereas only 23 (52.3%) trainees reported being comfortable with outpatient IBD management. There was a strong concordance between the proportion of PDs ranking a competency as essential and trainee comfort in that area (Pearson's rho 0.59; p=0.004). Fewer than half of trainees reported comfort in 11/22 (50%) proposed competencies. Identified areas of deficiency included phenotypic and endoscopic classification of IBD, inpatient management of severe active IBD, perianal disease management, monitoring biologic therapy, and extra-intestinal manifestations of IBD.
**Conclusions:** Only one-third of Canadian gastroenterology trainees are fully satisfied with the level of IBD exposure under the current training model. Furthermore, several IBD core competencies appear to be inadequately covered during training. Our findings, which parallel previously published US data, highlight the need for additional focus on IBD during gastroenterology fellowship. It is possible that the optimal treatment of patients with IBD may require advanced specialists.

**Funding Agencies:** None

## Poster of Distinction

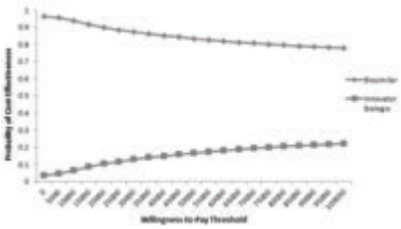
A73

### COST-EFFECTIVENESS OF INFLIXIMAB BIOSIMILAR COMPARED TO ORIGINATOR INFLIXIMAB FOR THE MANAGEMENT OF CROHN'S DISEASE

C.L. Beilman[1], C. Ma[2], C. McCabe[1], R. Fedorak[1], B.P. Halloran[1]

1. Department of Medicine, University of Alberta, Edmonton, AB, Canada; 2. Medicine, University of Calgary, Calgary, AB, Canada

**Background:** Originator infliximab (marketed as Remicade) was the first biological therapy approved in patients with Crohn's Disease (CD), and has been proven to be effective for the induction and maintenance of remission in patients with moderate-to-severe disease. Due to its recent patent expiry, an infliximab biosimilar (infliximab-dyyb, marketed as Inflectra) has been introduced in Canada. Recent trials have shown that switching from originator infliximab to its biosimilar is not inferior to continued treatment with originator infliximab, however the molecular complexity and sensitivity to changes in manufacturing of biologics makes it difficult to verify the similarity of biosimilars to their respective originator biologic. Nevertheless, the lower price of infliximab biosimilar compared to originator infliximab has the potential to result in large cost savings for patients with CD.
**Aims:** The aim of our study was to compare the cost-effectiveness of infliximab biosimilar (Inflectra) to originator infliximab (Remicade) for the management of CD.
**Methods:** A Markov model was developed to simulate the clinical pathway of patients with moderate-to-severe CD after initiating either originator infliximab or infliximab-dyyb. We calculated the cost and effectiveness of both treatments arms over a 5-year time horizon. Loss of response rates were obtained using the CD data from the NOR-SWITCH non-inferiority trial. Transition probabilities between health states and utility values for each health state were obtained from a review of the literature. The cost of health states were accessed with the CIHI patient cost estimator, and the drug costs of Remicade and Inflectra were determined by the Alberta Health and Wellness Drug Benefit List. Deterministic and probabilistic sensitivity analysis was performed on all key variables.
**Results:** Using a 5-year time horizon, originator infliximab costs $190,632 per patient and yields 3.63 quality-adjusted life years (QALYs). Infliximab-dyyb costs $128,306 per patient and yields 3.15 QALYs. Using a willingness-to-pay (WTP) threshold of $50,000 per QALY, infliximab-dyyb has a 83% probability of being cost-effective, whereas originator infliximab has a 17% probability of being cost-effective. The cost-effectiveness of each treatment at a range of WTP thresholds is shown in Figure 1.
**Conclusions:** Infliximab biosmilar resulted in large cost savings despite similar effectiveness to originator infliximab for patients with moderate-to-severe CD. Based on the results of our model, the mainstream usage of infliximab biosimilar (Inflectra) may help reduce the economic burden associated with CD.



Cost-effectiveness acceptability curve demonstrating the probability that each treatment option is cost-effective at a range of willingness-to-pay thresholds.

**Funding Agencies:** The Centre of Excellence for Gastrointestinal Inflammation and Immunity Research

A74

**COST-EFFECTIVENESS OF VEDOLIZUMAB COMPARED TO INFLIXIMAB FOR THE MANAGEMENT OF MODERATE-TO-SEVERE ULCERATIVE COLITIS**

C.L. Beilman, R. Fedorak, B.P. Halloran

Department of Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Ulcerative colitis (UC) is a relapsing and remitting condition, characterized by inflammation and ulceration in the colon and rectum. Biologic therapies have shown to be effective in inducing and maintaining remission in patients with UC, however there is no general consensus regarding which biologics should be used as first-line therapy for patients with UC. In order to decide which biologics should be used, the cost of the drugs needs to be taken into consideration. Infliximab and vedolizumab are commonly used biologics for UC, however it is unknown which biologic is more cost-effective as first-line therapy for patients with moderate-to-severe disease.
**Aims:** The aim of our study was to compare the cost-effectiveness of vedolizumab to infliximab for the management of moderate-to-severe ulcerative colitis.
**Methods:** A Markov model was constructed to simulate the clinical disease course of UC patients after initiating either infliximab or vedolizumab. Drug costs were obtained from the Alberta Health Drug Benefit List, and the remaining costs were determined from the CIHI Patient Cost Estimator. Transition probabilities were attained from a review of the literature, and loss of response and complication rates for infliximab and vedolizumab were obtained from the ACT and GEMINI trials, respectively. Previously published utility values were used to assess patient's quality of life in each disease state. Our main analysis used a time horizon of 5 years due to the lack of long-term data on these therapies. Time horizons of 10 and 15 years were assessed in our sensitivity analysis by extrapolation. Probabilistic sensitivity analysis was performed to characterize uncertainty related to all input parameters.
**Results:** Using a 5-year time horizon, vedolizumab costs $107,667 per patient and yields 2.23 quality-adjusted life years (QALYs). Infliximab costs $127,883 per patient and yields 2.30 QALYs. At a willingness-to-pay (WTP) threshold of $50,000 per QALY, probabilistic sensitivity analysis revealed that vedolizumab had a 69% probability of being cost-effective, and infliximab has a 31% probability of being cost-effective. Sensitivity analysis results for 10- and 15-year time horizons are displayed in Table 1.
**Conclusions:** Infliximab and vedolizumab as first-line therapies have similar effectiveness, however vedolizumab's lower cost results in it being considered more cost-effective compared to infliximab for the management of UC.

Table 1. Cost and effectiveness of infliximab versus vedolizumab for ulcerative colitis patients using multiple time horizons

| Time Horizon | Cost (CA$) | | | Effectiveness (QALYs) | | |
|---|---|---|---|---|---|---|
| | Infliximab | Vedolizumab | Incremental | Infliximab | Vedolizumab | Incremental |
| 5 years | $127,883 | $107,667 | $20,216 | 2.30 | 2.23 | 0.07 |
| 10 years | $186,021 | $155,617 | $30,403 | 4.59 | 4.54 | 0.05 |
| 15 years | $225,148 | $187,579 | $37,569 | 5.73 | 5.68 | 0.06 |

**Funding Agencies:** The Centre of Excellence for Gastrointestinal Inflammation and Immunity Research

A75

**ROLE OF LRRK2 IN INFLAMMATORY BOWEL DISEASE**

j. rocha[2], c. sun[2], M. Glogauer[2], D. Philpott[1]

1. University of Toronto, Toronto, ON, Canada; 2. Immunology, University of Toronto, TORONTO, ON, Canada

**Background:**

Variants of the leucine-rich repeat kinase 2 (*LRRK2*) are associated with an increased susceptibility to Parkinson disease but also Crohn's disease (CD).
**Aims: The present research is designed to develop a comprehensive understanding of the role of LRRK2 in immune system modulation, and how dysfunction of this pathway may lead to the development of CD.**
**Methods:** WT and LRRK2-deficient neutrophil were infected with Gram-positive Bacteria (*Listeria monocytogenes*-LM) in a gentamicin protection assays and colony-forming unit assessment will determine the competence of LRRK2 deficient cells for bacterial phagocytosis as well as killing capacity ). To examine how LRRK2 is involved in the generation of ROS during the respiratory burst, we will first examine if neutrophil from LRRK2-KO mice have altered ROS generation upon infection with LM and addition of PMA. We evaluate in vitro the ability of neutrophils from LRRK2-KO versus WT mice to transmigrate *in vitro* in a transwell assay using fMLP as a chemattractant. Also, we investigate the peritoneal cells (by FACS analysis) after injection of different microbial stimuli including FK105 (NOD1 ligand), MDP (NOD2 ligand) and LPS (TLR4 ligand) and anti-cd3 model of ielitis.
**Results:** We found that LRRK2 KO mice have a defect in migration of neutrophils to the peritoneal cavity

after injection of different microbial stimuli including FK10565 (NOD1 ligand), MDP (NOD2 ligand) and LPS (TLR4 ligand). Neutrophils from LRRK2 mice were compromised in their ability to transmigrate in vitro in a transwell assay using fMLP as a chemoattractant. Chemotaxis was also compromised. In parallel, we designed experiments to examine reactive oxygen species (ROS) produced in response to infection of myeloid cells with bacteria. Neutrophils from LRRK2 KO mice infected with *Listeria monocytogenes* were less able to restrict bacteria growth compared to WT cells. Consistent with these findings, cells from LRRK2 KO mice produced lower levels of ROS following bacterial infection. In order to determine whether myeloid cell migration is compromised in vivo during inflammation, we performed experiments in WT and KO mice looking at different models of ileitis/colitis.
**Conclusions:** With this work we will further characterize the role of LRRK2 in intestinal homeostasis and mucosal barrier maintenance, including how its deficiency may predispose an individual to developing CD.

**Funding Agencies:** CAG, CIHR

A76
**UPPER ENDOSCOPY AND HISTOLOGY IN THE DIAGNOSIS OF PEDIATRIC INFLAMMATORY BOWEL DISEASE**
B. Chen, Z. Hamilton, M. Hasosah, R. Katz, A. Lakhani, O. Popescu, K. Jacobson

BC Children's Hospital, Vancouver, BC, Canada

**Background:** Upper gastrointestinal(GI) endoscopy and biopsy has been recommended as part of the initial evaluation of children with suspected inflammatory bowel disease(IBD). It is known that upper GI tract inflammation can be found in both Crohn's disease CD) and ulcerative colitis(UC). However, criteria and classification of IBD of the upper GI tract is lacking. To date, specific upper GI tract histologic findings associated with CD include granulomas and focally enhanced active gastritis.
**Aims:** To perform a retrospective histologic review of biopsies collected at time of diagnosis from the upper GI tract of pediatric patients with known CD and UC to determine specific upper GI histologic features for differentiation of CD and UC.
**Methods:** Patients between 2 and 17 years diagnosed between 1998 and 2014 with either CD or UC were eligible for inclusion. All underwent both upper endoscopy and colonoscopy at time of diagnosis. A pathologist blinded to IBD diagnosis reviewed H&E slides of esophageal, antral, gastric body and duodenal biopsies taken at the initial assessment before treatment. From each site, these histologic findings were recorded: focal, multifocal or diffuse inflammation, superficial or deep inflammation, acute or chronic inflammation, focally enhanced gastritis, multinucleated giant cells and granulomas. Results were summarized as means. The Student's t test and $\chi^2$ test were utilized to compare difference between the two groups. $p<0.05$ was accepted as statistical significance.
**Results:** A total of 158 patients, 87 with CD and 71 with UC were included. Mean age was 11.5 years(range-2 to 17 years). CD patients were slightly older(mean age 12.2 vs. 10.8 years in UC, p=0.013). 59% of CD patients had ileocolonic disease and 79% had inflammatory disease. The majority of UC patients (69%) had pancolitis at diagnosis.
Macroscopically normal upper GI endoscopy was present in 58/158(37%) patients [41(26%) UC, 17(11)% CD]. Of the CD patients with grossly normal endoscopy, granulomas were present in 5/17 patients. 30%(n=26) of CD patients had upper GI granulomas (5% esophagus, 18% body, 30% antrum and 2% duodenum). Chronic inflammation (deep, superficial and focal) of the upper GI tract was present in a significantly higher proportion of CD patients than UC patients(94% vs.78%, p=0.004, Figure 1). In the antrum, chronic deep and superficial inflammation were more common in CD than UC patients (deep-41% vs.7%, superficial-55% vs.18%, p<0.001). Focally enhanced gastritis was seen in only 3 patients (2 UC, 1 CD).
**Conclusions:** In addition to the presence of granulomas, chronic superficial or deep inflammation of the upper GI tract may be a diagnostic clue in making a diagnosis of CD. However, aside from granulomas, such features may also be present in patients with UC. Focally enhanced gastritis was not a prominent feature in CD patients.

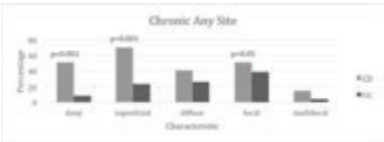



**Figure 1.Comparison of chronic inflammation characteristics found on upper GI biopsy in CD (n=87) and UC (n=71) patients**

**Funding Agencies:** None

A77
**TAPEWORM PARASITE *HYMENOLEPIS DIMINUTA* PROTECTS YOUNG MICE FROM EXPERIMENTAL COLITIS BY A RECALL MEMORY RESPONSE WITH WORM ANTIGEN**
F. Lopes[2], A.J. Shute[3], A. Wang[4], D.M. McKay[1]

1. Physiology & Pharmacology, Uni. Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. Phisiology and Pharmacology, University of Calgary , Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada

**Background:** Lack of exposure to helminth parasites, as predicted by the hygiene hypothesis, would contribute to the development of auto-inflammatory disease. Previous studies revealed that infection with rat tapeworm, *H. diminuta,* reduced the severity of di-nitrobenzene sulphonic acid (DNBS)-induced colitis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in adult mice. There has been a significant increase in pediatric onset IBD in Canada. Consequently the hypothesis that infection with this helminth would exert an anti-colitic benefit in young mice was tested.
**Aims:** To determine if three-week old (young) mice can expel *H. diminuta* and are protected from DNBS-induced colitis, and if an anti-colitic response could be elicited by systemic antigen challenge of previously infected mice (i.e. evoking an immunological memory response).
**Methods:** Three- and eight-week old (adult) Balb/c mice were orally infected with 5 cysticercoids of *H. diminuta* to assess infectivity and TH2 immunity. Young mice were infected with *H. diminuta* and 8 or 10 days later received 1.5 mg of DNBS intra-rectally. Colitis was assessed 72h post-DNBS by: 1) colon length, 2) disease activity score, 3) histopathology, and 4) concanavalin-A stimulated cytokine production from spleen cells. Finally, the ability of re-challenge with helminth antigen (HdE) after early life infection to protect mice from DNBS-induced colitis was tested.
**Results:** Young and adult mice evoked Th2 responses and successfully expelled *H. diminuta*, although worm expulsion was delayed by ~2 days in young mice compared to adults. The young mice developed DNBS-colitis as determined by all indicator of disease. Colitis was less severe in young mice infected 10 but not 8 days before DNBS-treatment, and was associated with an increased capacity to make interleukin (IL)-4 and IL-10. Mice infected 28 days prior to DNBS were not protected, but injection of these mice the with (ip., 500 µg) resulted in less disease and boosted splenic output of IL-4 and IL-10. Immunological memory was confirmed by increased serum anti-*H. diminuta* IgG.
**Conclusions:** Young mice rejected *H. diminuta* and were protected from DNBS-induced colitis. Exposure *H. diminuta* antigen treatment after early life infection protects against colitis in later life. We present these preliminary data in support of the putative value of helminth therapy in early onset IBD, and reveal that triggering of anti-helminth immunological memory can treat IBD later in life.

**Funding Agencies:** Yamanashi Scholarship, NSERC CREATE Host-Parasite Interactions scholarship

A78
**INHIBITION OF DAPK-1 PROMOTES INTESTINAL BACTERIA TRANSLOCATION AND INCREASES SEVERITY OF DSS-INDUCED COLITIS**
F. Lopes, A. Wang, D.M. McKay

University of Calgary, Calgary, AB, Canada

**Background:** Epithelial intestinal barrier is a first-line of defense often compromised in inflammatory bowel disease (IBD). Lumen-derived commensal bacteria enter the mucosa and are likely important in etiology and pathophysiology of the disease. Genome wide association studies have identified that mutation is autophagy genes (e.g. ATG16L1 and IRG1) is a susceptibility trait for IBD. Death-associated protein kinase (DAPK)-1 is a regulator of autophagy and a polymorphism in the DAPK-1 gene was reported in some patients with IBD.
**Aims:** The aim of this study was to analyze if the inhibition of DAPK-1 would increase the severity of colitis.
**Methods:** Balb/c mice received 2.5% (wt./vol.) DSS or normal water and were treated daily i.p. with the DAPK-1 pharmacologic inhibitor DAPK6 or vehicle for 5 days. Colitis was assessed by standard indices: disease activity score (DAS), colon length and weight loss and histopathology. Intestinal barrier function was assessed by the number of aerobic bacteria within the mesenteric lymph nodes (MLN), spleen and colonic mucosal.
**Results:** With this low dose of DSS, as expected, mice experience a mild or negligible inflammation and there were not obvious increases in DAS or intestinal barrier function in Balb/c mice. However, animals treated with DSS and DAPK6 presented with a significant increase in the severity of colitis, showing higher DAS, shorter colon length, and greater weight loss in comparison with naïve control, DAPK6/water- and DSS/vehicle-treated mice groups. Also, DSS+DAPK6 treatment resulted in increased translocation of aerobic bacteria into the colonic mucosal, MLN and the spleen. Finally, the inhibition of DAPK-1 alone (i.e. DAPK6/water treatment) resulted in shortening of the colon and loss of body weight.
**Conclusions:** DAPK-1, a component of the autophagy cascade, is important for normal gut homeostatic activity and for limiting the severity of colitis, likely via inactivation of bacteria via xenophagy.

**Funding Agencies:** CAG, CIHRAlberta Innovates, Allergan

A79
**FECAL SHORT CHAIN FATTY ACID COMPOSITION IN CROHN'S DISEASE PATIENTS CONSUMING A DIVERSIFIED COMPARED TO NON-DIVERSIFIED DIET**
M. Raman[4], L. Taylor[4], R. Panaccione[4], S. Ghosh[1], R. Reimer[4], N. Shommu[4], R. Fedorak[2], K. Madsen[3]

1. Gastrointestinal Section, Imperial College london, London, United Kingdom; 2. Los Alamos National Laboratory, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. University of Calgary, Calgary, AB, Canada

**Background:** Patients with Crohn's Disease (CD) are at increased risk of nutritional deficiencies that are multifactorial in etiology, and may include poor dietary diversity. Short chain fatty acids (SCFA) are known to have anti-inflammatory properties. Nutrition status and dietary diversity have been shown to impact the gut microbiome, however the effect of dietary diversity on fecal SCFA composition in CD is understudied.
**Aims:** (1) To describe the baseline fecal SCFA profiles in patients with CD in remission who consume a diversified diet (DD) compared to patients who consume a non-diversified diet (NDD); (2) To describe

the changes in fecal SCFA in patients with CD in remission who consume a NDD following a 3-month dietary intervention.
**Methods:** Patients with CD were recruited prospectively at the University of Calgary. All patients were in remission as confirmed by ileo-colonoscopy within 6 months of study entry and normal fecal calprotectin levels. A NDD was defined as fewer than 3 daily servings of fruits and vegetables, dietary fiber ≤ 15g/day, red meat intake ≥ 3 weekly servings. Patients recorded dietary intake using a 3-day food record that was analyzed by the study Registered Dietitian. Patients consuming a NDD were provided a personalized dietary intervention by the RD for 3 months to improve dietary diversity and maintained weekly food diaries to assess compliance. SCFA were measured in stool samples at baseline and after 3 months by gas chromatography.
**Results:** Twenty participants were recruited (14 DD, females: n=11; 6 NDD, females: n=4). Compared with the CD group consuming a DD group at baseline, CD patients consuming a NDD had lower levels of fecal propionate (μmol/ml) (1.56±0.59 vs 2.35±0.18; p=0.08), lower levels of iso-butyrate (0.12±0.05 vs 0.24±0.02; p=0.03), and iso-valeric acid (0.15±0.06 vs 0.36±0.04; p=0.01). Following a 3-month dietary intervention, a significant increase in fecal propionate was observed from baseline to 3-months (1.56± 0.59 vs. 2.06± 0.55; p <0.05) with trends towards increased acetate (7.46±0.6 to 9.57±1.2; p=0.06) and iso-butyrate (0.12±0.05 to 0.25±0.08; p=0.07). In the NDD group, non-significant increases in fecal acetate and propionate were observed from baseline to 3 months.
**Conclusions:** CD patients consuming a non-diversified diet have reduced levels of fecal SCFA compared with patients consuming a more diversified diet. We have demonstrated that initiation of a structured dietary intervention to enhance dietary diversity will significantly increase fecal SCFA (propionate) levels. Clinical studies are underway to document the efficacy effects of this intervention.

**Funding Agencies:** Broad Foundation

A80
**MALT1 BLOCKS IL-1β-MEDIATED INTESTINAL INFLAMMATION**
M. Monajemi[1], Y. Pang[1], S. Menzies[3], L.M. Sly[2]

1. UBC, Vancouver, BC, Canada; 2. Pediatrics, UBC, Vancouver, BC, Canada; 3. BC Children Hospital Research Institue, Vancouver, BC, Canada

**Background:** Primary immune deficiencies are often accompanied by intestinal inflammation. A patient with severe combined immunodeficiency and dramatic inflammation along the gastrointestinal tract was diagnosed with a homozygous mutation in MALT1. Malt1 acts both as a scaffolding protein and a protease. The consequences of MALT1 immunodeficiency have largely been attributed to its role in lymphocytes. However, macrophages play an important role in gut inflammation and Malt1 is activated in macrophages downstream of toll-like receptor 4 and dectin-1. The effect of MALT1 deficiency in macrophages and its contribution to gut inflammation has not been investigated.
**Aims:** We hypothesized that Malt1 deficiency in murine macrophages increases susceptibility to DSS-induced colitis by increasing pro-inflammatory cytokine production. To address this hypothesis, we will determine:
1) whether Malt1 deficient mice are more susceptible to DSS-induced intestinal inflammation than wild type mice, and
2) the role of Malt1 expression and activity in pro-inflammatory macrophage responses.
**Methods:** *Malt1*$^{+/+}$ and *Malt1*$^{-/-}$ mice were subjected to DSS-induced colitis and sacrificed for histology, immunohistochemistry, and tissue cytokine analyses by ELISA. *Malt1*$^{+/+}$ or *Malt1*$^{-/-}$ murine bone marrow-derived macrophages were differentiated with macrophage colony-stimulating factor and wild type macrophages were untreated or treated with the Malt1 inhibitor mepazine; followed by stimulation with LPS or curdlan. Cytokines were assayed by ELISA and whole cell lysates were analyzed by western blot, and in a Malt1 activity assay.
**Results:** In vivo, Malt1 deficiency exacerbated DSS-induced colitis in mice. Macrophage stimulation increased Malt1 protein expression but decreased Mat1 activity. Malt1 deficient murine macrophages produced more IL-1β than wild type macrophages and pharmacological inhibition of Malt1 protease activity increased some pro-inflammatory cytokine production in response to innate immune stimuli.
**Conclusions:** Taken together, our studies suggest that Malt1 deficiency contributes to intestinal inflammation *in vivo* by increasing macrophage pro-inflammatory cytokine production. In future studies, we will investigate the cell-specific contribution of Malt1 deficiency in macrophages using myeloid-specific *Malt1*$^{-/-}$ mice. These studies will provide critical information about the cell specific role of Malt1 and possible side effects of MALT1 inhibitors currently used for lymphoma treatment.

**Funding Agencies:** CIHRBCCHR Graduate Award

A81
**FUNCTIONAL ANALYSIS IMPLICATING SAMD9 MUTATION FOR INTESTINAL INFLAMMATION IN PATIENTS WITH MIRAGE SYNDROME AND INFLAMMATORY BOWEL DISEASE**
T. Ishige, C. Guo, N. Warner, J. Pan, K. Hossain, N. Dhingani, R. Murchie, A. Muise

Cell Biology, The Hospital for Sick Children, Toronto, ON, Canada

**Background:** MIRAGE syndrome is caused by heterozygous mutation in the *SAMD9* gene. The syndrome is characteristic of enteropathy, and is often fatal within the first 2 years of life. However, the

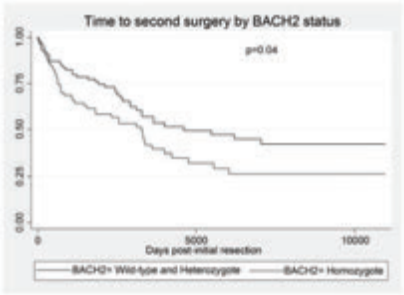
pathogenesis of enteropathy in the syndrome is unknown.
**Aims:** We present a case of MIRAGE syndrome (gestational age 35 weeks, birth weight 1330g) who developed restriction of growth, adrenal hypoplasia, genital anomaly, and enteropathy at the time of birth. Sigmoidoscopy showed longitudinal ulcers in rectum. Aim of this study is (1) to identify whether SAMD9 mutation is involved in early onset inflammatory bowel disease (IBD), and (2) to investigate the involvement of SAMD9 mutation in colitis.
**Methods:** (1) Whole exome sequence (WES) results performed for IBD patients and their families in The Hospital for Sick Children were reviewed. Mucosal expression of SAMD9 in patients' biopsy samples were investigated by immunohistochemistry.
(2) We assessed difference in TNF-alpha responsiveness between wild type (WT) or mutated (R1293W) SAMD9 using stably expressing HEK293 cell lines. Difference in apoptosis were measured using western blotting and Caspase assays.
**Results:** (1) Among our WES data, 3 patients from 2 families (2 ulcerative colitis, 1 colonic Crohn's disease) had mutation in *SAMD9* gene. Biopsy samples from IBD patients showed increased SAMD9 signals by immunohistochemistry, whereas those from MIRAGE syndrome patient and these 3 patients showed decreased signals.
(2) R1293W expressing cells showed increased expression of cleaved Poly ADP-ribose polymerase (PARP) when compared with WT and control. X-Linked inhibitor of apoptosis (XIAP), a known apoptosis inhibitor involves in early onset IBD, were decreased in R1293W mutations. Caspase assay showed increased caspase 3/7 activity in mutated cell lines. Apoptosis was also observed in pathology of the patient's intestinal mucosal biopsy specimen.
**Conclusions:** SAMD9 might be a novel gene associated with development of pediatric IBD. Suppression of XIAP might result in increased apoptosis and intestinal inflammation observed in patients with SAMD9 mutation.

**Funding Agencies:** None

A82
**A *BACH2* GENE VARIANT IS ASSOCIATED WITH POST-OPERATIVE RECURRENCE OF CROHN'S DISEASE**
M. Laffin, R. Fedorak, E. Wine, B. Dicken, K. Madsen

University of Alberta, Edmonton, AB, Canada

**Background:** Crohn's disease often requires intestinal resection, which is not considered curative. Repeat surgical intervention is necessary in over half of the patients following their initial operation. Although many genetic loci are implicated in Crohn's disease, few have been associated with post-resection recurrence.
**Aims:** To identify genetic factors that predict recurrence of CD following intestinal resection.
**Methods:** A cohort of Crohn's disease subjects who underwent intestinal resection was analyzed to determine genetic and clinical factors associated with post-resection recurrence. Genotype was assessed at eight loci associated with adaptive immunity (*SMAD3, IL10RB, IL15RA, BACH2, IL12B, IL18RAP, IFNGR2*, and *JAK2*). Univariate and multivariate survival analyses were performed using a log-rank test and Cox-proportional hazard model, respectively.
**Results:** 191 Crohn's disease subjects with 11.2 years mean post-operative follow-up were included. 46% experienced a surgical recurrence. Factors associated with increased incidence of recurrence included male gender(p=0.05), and shortened time to first intestinal surgery(5.0 vs 7.3years p=0.03), while inflammatory disease behaviour was associated with a lower chance of repeat surgery(p<0.01). Of the loci assessed on multivariate analysis, homozygosity for a risk allele at *BACH2* (rs1847472) was significantly associated with disease recurrence(HR-1.24 CI-1.00-1.54 p<0.05).
**Conclusions:** We identify *BACH2* as a susceptibility locus for post-operative recurrence of Crohn's disease in our cohort. *BACH2* is critical in the differentiation and function of T-cells, as a regulator of B-cell activity, and is associated with several dysregulated immunologic phenomena. Its identification as a risk locus in post-operative Crohn's disease recurrence suggests a potential role for regulatory T cells, effector T cells, humoral immunity, and immunologic memory in the development of this disease process.




**Funding Agencies:** CIHR

A83
**CHROMOFUNGIN DECREASES INTESTINAL INFLAMMATION AND REGULATES DENDRITIC CELLS MARKERS**
K. Kapoor[1], N. Eissa[1], M.F. Rabbi[2], L. Kermarrec[1], G. Gupta[2], J. uzonna[2], C.N. Bernstein[1], J. Ghia[2]

1. Immunology, University of Manitoba, Winnipeg, MB, Canada; 2. Immunology and Internal Medicine Section of Gastroenterology, University of Manitoba, Winnipeg, MB, Canada

**Background:** Ulcerative colitis (UC) is characterized by altered levels of chromogranin-A (CHGA) and a dysregulation of dendritic cells (DCs). CHGA, a prohormone protein, can be cleaved into several bioactive peptides including chromofungin (CHR: $CHGA_{47-66}$) encoded by CHGA Exon-IV. Previously, we

demonstrated that CHR is reduced in active UC patients and protects against intestinal inflammation through modulation of the macrophages plasticity. Thus, we hypothesized that CHR regulates other antigen presenting cells functions like DCs during the progression of colitis.
**Aims:** We aimed to investigate the association between CHR and DCs in patients with active UC, and underlay the effect of CHR treatment on DCs functions in dextran sulfate sodium (DSS)-induced colitis.
**Methods:** mRNA levels of CHR (CHGA Exon-IV) and its association with DCs markers (interleukin (IL)-23, IL-12p40, CD86, CD11C, CRR7, CD74, IL-12A) were quantified in colonic biopsies of patients with active UC and healthy individuals. Colitis was induced in C57BL/6 mice (7-8 weeks) by 5% DSS (wt./vol.) for 5 days. Intra-rectal administration of CHR (2.5 mg/kg/day) started one-day before induction of colitis and lasted for 6 days. Disease activity index (DAI), macroscopic and microscopic scores were assessed. Colonic levels of interleukin (IL)-23, IL-12p40, cluster of differentiation (CD) 86, CD11C, C-C chemokine receptor (CCR)7, CD74 and IL-12A were determined using ELISA and/or RT-qPCR. *In-vitro*, splenic $CD11c^+$ cells were isolated from naïve and colitic mice, cultured overnight in the presence or absence of CHR ($10^{-6}$ M) and CD40, CD80, and CD86 markers were quantified using flow cytometry.
**Results:** In patients with active UC, CHR level is reduced and showed a negative relationship with DCs markers; *IL23* (r= -0.3725), *IL12p40* (r= -0.3706), *CD11C* (r= -0.4647), *CRR7* (r= -0.3709), *IL12A* (r = -0.4253), *CD86* (r= -0.6765), and CD74 (r= -0.3647). *In-vivo*, CHR treatment reduced the severity of the colitis and is associated with a significant decrease in colonic levels of IL-23, IL-12p40, and CD86, and without significant changes in the levels of CD11c, CCR7, CD74, and IL-12A. *In-vitro*, CHR treatment reduced CD40 and CD80 expression in splenic $CD11c^+$cells isolated from colitic mice when compared with PBS-treated group. No differences were detected in the expression of CD86.
**Conclusions:** CHR regulates the development of colitis, and modulates $CD11c^+$ cells markers of immune activation. Further studies are warranted to understand the possible effects of CHR on the crosstalk between $CD11c^+$ cells and T-cells. These findings provide the foundation of future potential therapeutic strategies in UC.

**Funding Agencies:** Mindel and Tom Olenick Scholarship in Gastroenterology

A84

**INTERACTION OF SEROTONIN WITH PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR-GAMMA IN ANTIMICROBIAL PEPTIDE PRODUCTION IN GUT**

E.Y. Kwon, H. Wang, W.I. Khan

Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

**Background:** Serotonin (5-hydroxytryptamine; 5-HT), is a neurotransmitter and hormone that regulates various gut physiological functions. Enterochromaffin (EC) cells are the main producer of gut 5-HT, and tryptophan hydroxylase 1 (*Tph1*) is the rate-limiting enzyme of 5-HT biosynthesis. There is increasing evidence that gut function as well as pathology rely on interactions with gut microbiota. β-defensins are major class of antimicrobial peptides (AMPs) expressed by colonocytes, maintaining mucosal barrier integrity by shaping gut microbiota composition. Peroxisome proliferator activated receptor-gamma (PPAR-γ), a ligand-inducible transcription factor, has been shown to influence AMP secretion. It is reported that 5-HT inhibit PPAR-γ expression in pulmonary artery smooth muscle cells, providing a crucial link between 5-HT and PPAR-γ regulation. As intestinal epithelial cells express 5-HT receptors, we hypothesize that 5-HT released from EC cells down-regulates PPAR-γ expression, which subsequently inhibits β-defensin production from neighbouring intestinal epithelial cells
**Aims:** To determine whether 5-HT inhibits β-defensin production by down-regulating PPAR-γ signalling
**Methods:** We measured PPAR-γ, mouse β-defensin (mBD)-1 and mBD-3 levels in colonic tissues of naïve *Tph1*$^{-/-}$ mice (which have significantly lower 5-HT in gut), wild-type (WT) littermate (*Tph1*$^{+/+}$), and *Tph1*$^{-/-}$ administered with either 5-hydroxytryptophan (5-HTP; precursor of 5-HT) or PPAR-γ antagonist (GW-9662). Colonic epithelial (HT-29) cells were treated with 5-HT to determine direct role of 5-HT in PPAR-γ expression along with subsequent changes in human β-defensin (hBD)-1 and hBD-2 levels. In addition, cells were treated with 5-$HT_3$, 5-$HT_4$, 5-$HT_7$ receptor antagonists and extracellular signal-regulated kinase-1 and -2 (ERK1/2) inhibitor.
**Results:** We observed higher expression of PPAR-γ along with up-regulation of mBD-1 and mBD-3 in *Tph1*$^{-/-}$ mice, compared with WT littermates; while replenishing 5-HT synthesis by 5-HTP decreased PPAR-γ and β-defensin expression in *Tph1*$^{-/-}$ mice. *Tph1*$^{-/-}$ mice administered with GW-9662 showed decreased expression of both mBD-1 and mBD-3. Treatment of HT-29 cells with 5-HT receptor antagonists revealed that 5-$HT_7$ receptor, but not 5-$HT_3$ or 5-$HT_4$ receptor, plays an important role in mediating inhibitory action of 5-HT on PPAR-γ expression and subsequent β-defensin production. ERK1/2 inhibitor (PD98059) restored hBD-1 and hBD-2 production in 5-HT treated cells
**Conclusions:** Our results illustrate 5-HT released from EC cells activates 5-$HT_7$ receptor and down-regulates PPAR-γ expression through ERK1/2-depedent pathway, which subsequently inhibits β-defensin production from intestinal epithelial cells. This study exemplifies novel information on the interaction between 5-HT and PPAR-γ in relation AMP production in the context of intestinal innate response

**Funding Agencies:** CIHR

A85



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**SEMAPHORIN-3E AMELIORATES INTESTINAL INFLAMMATION BY REGULATING EXPRESSION OF TIGHT JUNCTION PROTEIN AND PROINFLAMMATORY MEDIATORS**

L. Kermarrec[2], N. Eissa[2], A. Soussi Gounni[1], C.N. Bernstein[1], J. Ghia[3]

1. Uiversity of Manitoba, Winnipeg, MB, Canada; 2. Immunology, University of Manitoba, Winnipeg, MB, Canada; 3. Immunology and Internal Medicine Section of Gastroenterology, University of Manitoba, Winnipeg, MB, Canada

**Background:** Ulcerative colitis (UC) is characterized by an alterations of tight junction (TJ) barrier and immune responses that result in abnormal passages of exogenous antigens such as gut-derived bacterial lipopolysaccharides (LPS). Semaphorin-3E (Sema3E) and its receptor plexin D1 (PLXD1R) are key regulators of epithelia and immune systems
**Aims:** To investigate Sema3E activity in human and animal model of colitis and its effects on the intestinal epithelial cell functions
**Methods:** Sema3E mRNA level and its correlation with TJ proteins and mucosal healing mediator (Kruppple-Like Factor [KLF]-5) were quantified in human rectal biopsies. PLXD1R expression was quantified by immunofluorescence/RT-qPCR in Caco2 epithelial cell line and mice colonic tissues. Proliferation, metabolism, viability and wound healing properties were evaluated after 24 hours of treatment with Sema3E recombinant protein (100ng/ml). TJ proteins and KLF-5 were quantified by RT-qPCR in Caco-2 cells pretreated with Sema3E for 24 h and challenged with LPS (1µg/ml) for additional 24 h. Dextran sulfate sodium (DSS)-colitis was induced in BL6/57 mice for 5 days. Sema3E treatment (10µg/kg/day/intra-peritoneal) started at day 5 after induction of colitis and lasted for 4 days. Disease activity index (DAI), macroscopic and histological scores were assessed. mRNA and protein levels of pro-inflammatory cytokines and KLF5 were quantified.
**Results:** Sema3E is reduced in active and mild UC patients and has strong positive correlation with *CLDN1 (r = 0.54, P =0.03), ZO-1 (r = 0.53, P = 0.03), CADH1 (r = 0.60, P =0.01), OCLDN (r = 0.64, P =0.008), KLF-5 (r = 0.52, P =0.03), TLR2 (r = - 0.6147, P =0.0103)* and *TLR4 (r = - 0.5794, P =0.0207)*. PLXD1R is expressed by Caco2 cells and mice colonic tissue. Sema3E accelerated significantly the epithelial cells migration when compared to control group. No significant changes on epithelial cells proliferation, metabolism and viability were detected. Compared to LPS-induced inflammation, Sema3E treatment increased the expression levels of TJ proteins (*Cldn1, Zo-1, ECadh1, Ocldn*) and *Klf5*, and decreased *Tlr2* without significant changes in *Tlr4*. Sema3E treatment decreases DAI, macroscopic and histological scores in DSS-induced colitis compared with control. *Il6* and *Mcp1* were significantly decrease in colitic mice treated with Sema3E when compared to untreated mice. *Il1bTnfa* tend to decrease whereas *Klf5* tends to increase. No changes in colonic levels of *Tlr2, Tlr4, Cldn1, Zo-1 and Ocldn were* detected.
**Conclusions:** Sema3E regulates intestinal inflammation through epithelial cells barrier markers in human and cell line and reduces experimental inflammation and proinflammatory mediators. These findings may lead to improved therapeutic strategies in the treatment of UC by restoring Sema3E level in UC patients.

**Funding Agencies:** CCC, CIHR

A86

**NON-PREBIOTIC EFFECTS OF RHAMNOGALACTURONAN ON INTESTINAL EPITHELIAL BARRIER FUNCTION AND WOUND HEALING**

C.H. Baggio[2], M. Gordon[2], A. Nascimento[3], T. Cipriani[3], W. MacNaughton[1]

1. Univ Calgary, Calgary, AB, Canada; 2. Physiology and Pharmacology, University of Calgary, Calgary, AB, Canada; 3. Federal University of Parana, Curitiba, Brazil

**Background:** Dietary fibre comprises a complex group of polysaccharides that are indigestible but are fermented by gut microbiota, promoting beneficial effects to intestinal mucosa indirectly. However, studies have shown that polysaccharides also have direct effects on intestinal epithelial barrier function. Recently, we found that rhamnogalacturonan (RGal), a polysaccharide isolated from *Acmella oleracea*, protected mice against DSS colitis. However, the underlying mechanism of action of RGal remains unclear.
**Aims:** We aimed to verify whether RGal directly enhances intestinal epithelial barrier function and promotes wound healing to maintain tissue health.
**Methods:** Monolayers of human colonic epithelial Caco-2 cells were mounted in Ussing chambers and treated apically with RGal (10-1000 µg/ml). Transepithelial electrical resistance (TER) and FITC-dextran flux were measured. In a calcium-switch assay, the epithelial monolayers were temporarily exposed to zero calcium conditions (calcium-free buffer containing the calcium chelator, EGTA) to disassemble tight junctions. RGal (10-1000 µg/ml) was added during calcium-free conditions and its effect on barrier recovery during the return to Ca-containing buffer was assessed. FITC-dextran permeability was also evaluated in Caco-2 cells stimulated with IFNg plus TNF-a (25 ng/ml, basolateral) and co- or post-treated with RGal (1000 µg/ml, apical) for 48 or 24 h, respectively. Immunofluorescence staining was performed for evaluation of tight junction proteins, occludin and ZO-1. Finally, to evaluate wound healing, scratch wounds were performed on cell monolayers treated with RGal (10-1000 µg/ml) at 0 and 24 h. Wound healing was assessed over 48 h using the IncuCyte live cell imaging system.
**Results:** Apical treatment of cells with RGal (1000 µg/ml) significantly increased TER and reduced FITC-dex-

tran flux compared to control. Additionally, apical addition of RGal accelerated tight junction reassembly in the calcium switch assay. Exposure to cytokines enhanced FITC-dextran flux and disrupted tight junction protein localization. Co- and post-treatment of cells with RGal (1000 µg/ml) reversed this effect on FITC-dextran flux by 13 and 16% at 60 min, respectively, and preserved the occludin and ZO-1 distribution. In the wound healing assay, RGal at concentration of 1000 µg/ml enhanced wound healing by 28% at 48 h compared to control group, under 10% serum but not serum free conditions.
**Conclusions:** We demonstrated that RGal increased barrier function through acceleration of tight junction assembly, prevented cytokine-induced barrier dysfunction, and was able to increase wound healing *in vitro*. Elucidation of RGal mechanisms of action could lead to new approaches to the treatment of inflammatory diseases of the gut that are characterized by compromised epithelial barrier function.

**Funding Agencies:** CIHR

A87
**MACROPHAGE-ACTIVATED INFLAMMASOME MEDIATES RECOVERY OF INTESTINAL EPITHELIAL CELLS DURING INFECTION**
M. Bording-Jorgensen[2], H. Armstrong[3], E. Zwaigenbaum[1], E. Wine[1]

1. Pediatrics, University of Alberta, Edmonton, AB, Canada; 2. Physiology, University of Alberta, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada

**Background:** Nod-like receptor protein-3 (NLRP3) inflammasomes have been linked to various inflammatory conditions such as inflammatory bowel diseases (IBD). Conditions associated with the inflammasomes are typically characterized by an overabundance of interleukin (IL)-1β with the exception of IBD, where its dysregulation results in hypoproduction. The mouse pathogen *Citrobacter rodentium*, which causes IBD-like colitis, is used to understand the dynamic relationship between pathogens, the inflammasome and the epithelial barrier. We have recently shown that ATP-activated macrophages increase clearance of *C. rodentium in vitro.* Our hypothesis is that inflammasome activation will increase macrophage recruitment and facilitate protection of the epithelial barrier.

**Aims:** The aim was to determine the role the inflammasome plays during macrophage-epithelial interaction during *C. rodentium* infection
**Methods:** Mouse colonic epithelial cells (CMT-93) were seeded on the bottom of collagen coated transwells until tight junctions were formed using transepithelial electrical resistance (TEER). The CMT-93 cells were infected with *C. rodentium* on the apical membrane. ATP and LPS were used to activate the inflammasome in macrophages with YVAD as an inhibitor and added to the basolateral membrane, with tight junction permeability measured using TEER. Immunofluorescence was done using confocal microscopy looking at tight junction proteins ZO-1, occluding and claudin 1. Adherence of *C. rodentium* to the epithelial barrier was assessed using serial dilutions and plating on LB agar at 37°C overnight.
**Results:** ATP-activated macrophages were increased at the apical membrane during *C. rodentium* infection of epithelial cells. Tight junction proteins Claudin-1, Occludin, and ZO-1 were found on macrophages using immunofluorescence. The presence of epithelial ZO-1 rings were observed during *C. rodenitum* infection through immunofluorescence. *C. rodentium* adherence was found to be significantly reduced, together with an increase in epithelial TEER recovery; this was inhibited using YVAD.
**Conclusions:** These data suggest that the inflammasome is an important mediator for pathogen clearance by macrophages. Some individuals with Crohn Disease that have a decreased ability to produce IL-1β may be more susceptible to infection, as they cannot clear a pathogen. Furthermore, the role of the epithelial cell in this relationship is critical to understanding why the epithelial barrier in IBD patients is disrupted.

**Funding Agencies:** CCCCCA

A88
**NLRP3 DRIVES INTESTINAL INFLAMMATION-ASSOCIATED FIBROSIS**
J. Tjong[2], Y. Li[1], J.A. MacDonald[1], D. Muruve[1], P. Beck[1]

1. University of Calgary, Calgary, AB, Canada; 2. Medicine, University of Calgary, Calgary, AB, Canada

**Background:** Fibrosis is one of the most common causes of surgery in inflammatory bowel disease (IBD) and the mechanisms of fibrosis in IBD are not well understood. Nucleotide-binding oligomerization domain (NOD)- like receptors, including NLRP3, are cytosolic protein sensors involved in inflammatory pathways and implicated in IBD pathogenesis. We have shown NLRP3 drives fibrosis in the heart and kidney; however, its role in intestinal fibrosis is unknown. We hypothesize that NLRP3 drives inflammation associated with intestinal fibrosis.
**Aims:** 1) To determine, *in vitro*, if intestinal fibroblasts lacking NLRP3 are phenotypically distinct from wild type fibroblasts.
2) To assess intestinal fibrosis of NLRP3-deficient and wild type mice in a model of chronic colitis.
3) To investigate intestinal NLR expression in IBD patients and healthy controls.
**Methods:** Primary colonic myofibroblasts were isolated from wild-type (WT) and Nlrp3-/- mice. Cells were treated with pro-fibrogenic cytokine TGF-beta and downstream signalling was assessed by western blot. To investigate the role of NLRP3 in intestinal fibrosis in vivo, WT and Nlrp3-/- mice were given 3 cycles of low percent (w/v) dextran sulfate sodium (DSS) in water for

5 days, followed by a two-week recovery period. In addition, we investigated the expression of NLRP3 transcripts in patients with IBD by qPCR of cDNA from mucosal biopsies.
**Results:** TGF-beta signalling is attenuated in Nlrp3-/- colonic myofibroblasts as phosphorylation of Smad2, a downstream TGF-beta signalling protein, was reduced in Nlrp3-/- myofibroblasts compared to WT. Nlrp3-/- myofibroblasts also had lower TGF-beta-induced connective tissue growth factor (CTGF) compared to WT. Nlrp3-/- mice are more susceptible to cyclical DSS treatment with significantly greater weight loss and mortality compared to WT. Marked intestinal fibrosis was induced with the cyclical DSS protocol and those with most severe fibrosis were Nlpr3-/- mice. NLRP3 transcript levels were significantly increased in Crohn's Disease (CD) patients compared to normal controls, but not in ulcerative colitis (UC) patients.
**Conclusions:** Our data suggest that loss of NLRP3 leads to reduced response to TGF-beta in colonic myofibroblasts. Similar to its role in the kidney and heart, NLRP3 may potentiate TGF-beta signalling in the gut. Further insights into the mechanisms of intestinal fibrosis will significantly impact the development of new tools that will help with assessing and treating patients with IBD complications.

**Funding Agencies:** CIHR

A89
**FUNCTIONAL ANALYSIS OF NEUTROPHIL CYTOSOLIC FACTOR 4 (*NCF4)* IN THE PATHOGENESIS OF PEDIATRIC INFLAMMATORY BOWEL DISEASE**
V. Batura[1], N. Moradin[2], G. Leung[2], C. Guo[2], R. Murchie[2], N. Warner[2], A. Muise[2]

1. University of Toronto, Toronto, ON, Canada; 2. The Hospital for Sick Children, Toronto, ON, Canada

**Background:** Inflammatory bowel disease (IBD) can arise because of various genetic, environmental, immunological and microbial factors, however, the precise pathological mechanisms leading to IBD remains elusive. Recent advances in genomics have identified multiple genes that cause monogenic IBD. Genetic variants in the Nicotinamide Adenine Dinucleotide Phosphate (NADPH) oxidase have been reported to increase susceptibility of Very Early Onset Inflammatory Bowel Disease (VEOIBD). This multi-protein enzyme complex is involved in the production of superoxide anions ($O_2^-$), causing a respiratory burst that leads to the formation of hydrogen peroxide and hypochlorous acid for bactericidal activity. A notable histopathological feature of a subset of Crohn's Disease (CD) patients is the formation of granulomas in the gastrointestinal (GI) tract. This is also commonly seen in Chronic Granulomatous Disease (CGD). CGD patients are unable to mount a respiratory burst to defend against bacterial infections.
**Aims:** In this study, two sisters are reported with CD who were diagnosed at ages 7 and 14. Whole exome sequencing identified an autosomal recessive nonsense variant in the *NCF4* gene, leading to the truncation of the $p40^{phox}$ protein, a component of the NADPH oxidase. This study investigated whether this truncation leads to impaired phagocyte oxidase activity which may contribute to the onset of pediatric IBD.
**Methods:** Co-immunoprecipitation (Co-IP) and immunofluorescence (IF) were used to study the effect of this mutation on the interaction of $p40^{phox}$ with other proteins within the cell. Chemiluminescence assays were used to measure stimuli (PMA and zymosan) induced-oxidative burst over time in RAW264.7 macrophages that stably expressed the wild type and truncated forms of $p40^{phox}$. Finally, bacterial killing assays were used to test the ability of these macrophages in pathogen clearance.
**Results:** Co-IP showed a loss of interaction between truncated $p40^{phox}$ and $p67^{phox}$, a component of the NADPH oxidase responsible for formation of a fully activated enzyme. Furthermore, this mutation causes its mislocalization to early endosomes, compared to the cytoplasm location of wild type $p40^{phox}$. Finally, chemiluminescence assays show impaired oxidative burst in macrophages stably expressing truncated $p40^{phox}$.
**Conclusions:** Taken together, these results suggest that impaired oxidative burst, as a result of this mutation, may be the cause of defective pathogen clearance leading to severe bacterial infections, as seen in the patients. Further validation, using bacterial clearing assays and neutrophils as another model, is warranted to confirm these results.

**Funding Agencies:** CIHRThe Leona M. and Harry B. Helmsley Charitable Trust

A90
**THREE PATIENTS WITH INFLAMMATORY BOWEL DISEASE DIAGNOSED WHILE BEING TREATED WITH SECUKINUMAB FOR PSORIASIS**
T. Shukla[1], J. McCurdy[1], S. Fahim[1], A. Rostom[2]

1. The Ottawa Hospital , Ottawa, ON, Canada; 2. The Ottawa Hospital , Ottawa, ON, Canada

**Aims:** We report three cases of inflammatory bowel disease (IBD) in patients on secukinumab, an anti-IL-17A antibody, for psoriasis.
**Methods:** Case Review
**Results:** Patient one: 49 year old female, with a history of psoriasis managed with secukinumab, presented to hospital with a six-day history of bloody diarrhea. C-reactive protein was >190 mg/L and erythrocyte sedimentation rate was 70 mm/hr. Colonoscopy showed severe colitis. Pathology showed cryptitis, crypt abscesses, crypt architectural irregularity, without granulomatous lesions. She was started on intravenous steroids during her hospitalization and on infliximab for maintenance IBD therapy. Her secukinumab was discontinued.

Patient two: 54 year old male with psoriasis that was managed with secukinumab. The patient developed

symptoms of diarrhea, occurring 6-7 times per day, shortly after secukinumab exposure. Colonoscopy showed severe pancolitis. Histology showed patchy chronic inflammation, consistent with IBD. He was started on adalimumab and methotrexate therapy, and achieved clinical remission. Secukinumab was discontinued.

Patient three: 28 year old male on secukinumab therapy for his psoriasis with good clinical response. Shortly after starting secukinumab he developed diarrhea symptoms, having 3-4 loose bowel movements per day. Fecal calprotectin was elevated at 563.8 mg/kg. Colonoscopy and histology showed colonic mucosa with focal active cryptitis and non-necrotizing granulomas. Secukinumab was discontinued and he was started on ustekinumab for his psoriasis, with clinical response.

**Conclusions:** The role of secukinumab in Crohn's disease has been investigated in a randomised double-blind placebo-controlled trial, which showed IL-17A blockade was not effective in the treatment of Crohn's disease and resulted in more adverse events when compared to placebo (Hueber et al). In this study, six severe drug-related adverse events were reported in the secukinumab group and one such event in the placebo group; five of these events were worsening of Crohn's disease. The current evidence suggests that IL-17A blockade is efficacious in psoriasis. A pooled analysis of ten phase II and III studies in patients with plaque psoriasis showed an overall favorable safety profile. In this analysis, three cases of Crohn's disease were reported among individuals on secukinumab (Malakouti et al).

Our cases of inflammatory bowel disease diagnosed in three patients on secukinumab for psoriasis highlight the complex and multifaceted role of the Th17 pathway. The Th17 inflammatory response can be either protective or exacerbating depending on the organ system involved.

**Funding Agencies:** None

A91

**T CELL-SPECIFIC DELETION OF NOD2 DOES NOT INFLUENCE MICROBIAL RESILIENCE FOLLOWING ANTIBIOTIC EXPOSURE OR MUCOSAL DAMAGE**

K. Marshall[2], A. Goethel[2], K. Croitoru[1]

1. Mount Sinai Hospital, Toronto, ON, Canada; 2. Immunology, University of Toronto, Faculty of Medicine, Toronto, ON, Canada

**Background:** The cause of inflammatory bowel disease (IBD) involves interactions between host genetics, the environment and the gut microbiota. Environmental perturbations, such as antibiotics, induce transient shifts in the microbiota, which may alter T cell-mediated immune responses. We previously found that *Nod2* knockout mice show a delayed microbial recovery following antibiotic treatment, and that this altered microbiota influenced the response to T-cell induced mucosal damage in the small intestine.

**Aims:** We sought to determine if deletion of *Nod2* specifically in $CD4^+$ T cells would play a role in antibiotic induced dysbiosis and resilience of the microbiota and whether this could lead to an altered immune response.

**Methods:** Adult $Nod2^{Flox}$ and $Nod2^{\Delta CD4}$ mice received either control or amoxicillin [200 mg/L] *ad libitum* for one week, followed by control water for four weeks. Stool samples were collected weekly to monitor changes in the gut microbial community. On day 35, small intestinal mucosal damage was induced by an intraperitoneal injection of 50µg anti-CD3.

**Results:** On day 0, the gut microbiota of $Nod2^{Flox}$ and $Nod2^{\Delta CD4}$ littermates did not differ. Antibiotic treatment induced a reduction in the abundance of Firmicutes, including Lactobacillus and Clostridia, whereas Gamma-Proteobacteria and Bacteroidaceae increased compared to water-treated controls on day 7. Anti-CD3 injection induced mucosal damage resulting in increased levels of IFNγ and IL-17 in the small intestine, however there were no differences between genotypes or treatments. Myeloperoxidase, a measure of neutrophil activity, was significantly increased in $Nod2^{Flox}$ mice as compared to $Nod2^{\Delta CD4}$ littermates; however, this difference was ablated if the mice had previously received antibiotics.

**Conclusions:** Our data indicates that while *Nod2* is involved in microbial resilience and small intestinal mucosal damage, specific deletion of *Nod2* in T cells does not recapitulate the phenotype. Together, this suggests that other (non-$CD4^+$ T) cells are involved in the response to antibiotic-induced perturbations of the gut microbiota. Furthermore, altered microbial composition can influence neutrophil activity during mucosal damage in the small intestine.

**Funding Agencies:** Department of Immunology, University of Toronto

A92

**ANTI-TNF DOSE AUGMENTATION FREQUENTLY OCCURS IN THE ABSENCE OF OBJECTIVE EVIDENCE OF DISEASE ACTIVITY**

E. Elias, A. Oketola, C.N. Bernstein, H. Singh, L. Targownik

University of Manitoba, Winnipeg, MB, Canada

**Background:** Anti tumor necrosis factor therapy (anti-TNF) is widely used in patients with moderate to severe CD and UC. When symptoms persist, anti-TNF dose is often increased or the dosing interval shortened. Evidence supporting the effectiveness of dose augmentation is of low quality and dose augmentation imparts a significant additional cost of care. Persons with persistent gastrointestinal symptoms ascribed to IBD may not have evidence of ongoing inflammation; hence, dose augmentation may not be expected to benefit those without inflammation.

**Aims:** We sought to determine the extent to which clinicians routinely assessed the presence of active inflammation prior to undertaking anti-TNF dose augmentation.
**Methods:** Medical records of all IBD patients prescribed anti-TNF therapy from 2007-2016 by 8 of 23 Manitoba gastroenterologists were reviewed and demographics, disease characteristics, and IBD treatments recorded. Patients who underwent anti-TNF dose augmentation were further reviewed for the presence of any objective assessment of inflammatory activity, including laboratory investigations (CRP, ESR, albumin, ferritin, hemoglobin, fecal calprotectin), cross-sectional abdominal imaging, and endoscopy.
**Results:** 529 patients receiving anti-TNF therapy were identified, of whom 151 had anti-TNF doses increased on 195 occasions (117 CD, 34 UC). 51 patients (43.6%) with CD had penetrating disease while 16 patients (47.1%) with UC had pancolitis. Mean age at diagnosis was 25.5 years and 50.3% of patients were female. There was no difference in demographics, disease phenotype, or baseline lab values between patients who received dose augmentation and those who did not. Patients were assessed for biochemical evidence of disease activity in the 90 days preceding dose augmentation on 134 of 195 occasions (68.7%), however the results of these investigations were abnormal in only 23 cases (11.8%). Cross-sectional imaging was performed in 11 cases (5.6%) and revealed active disease in 8 (4.1%). Endoscopy was performed prior to dose augmentation on 28 occasions (14.4%) with 24 (12.3%) revealing active disease. Overall, objective evidence of inflammatory activity was present in only 48 of 195 dose augmentation events (24.6%), no objective evidence of inflammation was present in 95 (48.7%), and in 52 (26.7%), anti-TNF dose was increased without any investigation being performed.

**Conclusions:** Anti-TNF dose augmentation routinely occurs in the absence of objective evidence of active inflammatory disease. This represents a target for ongoing quality improvement to optimize care of persons with IBD requiring anti-TNF based therapies, given the significant economic burden of unjustified and potentially unnecessary dose augmentation.

**Funding Agencies:** None

A93
**NO INCREASE IN IMMUNOMODULATOR USE IN COMBINATION WITH ANTI-TNF THERAPY IN THE POST SONIC ERA**
E. Elias, A. Oketola, L. Targownik, H. Singh, C.N. Bernstein

University of Manitoba, Winnipeg, MB, Canada

**Background:** The SONIC trial in 2010 definitively proved the superiority of anti tumor necrosis factor (anti-TNF) therapy in combination with thiopurines over anti-TNF monotherapy in persons with moderate to severe CD. Despite high-quality evidence supporting combination therapy, there is a scarcity of data about the impact of this trial on the utilization of combination therapy (anti-TNF plus thiopurines or methotrexate) in clinical practice.
**Aims:** We assessed the prevalence of combination therapy usage by all Manitoba gastroenterologists both pre and post publication of the landmark SONIC trial in 2010.
**Methods:** All 23 prescribers of anti-TNF medications for IBD in Manitoba agreed to participate in the study. Patient charts were reviewed, with demographics, disease characteristics, and prior IBD treatments recorded from time of first contact with a gastroenterologist. The pre-SONIC group was defined as persons who received their first anti TNF treatment between 2005 and 2009, and the post-SONIC group as those who started treatment between 2011 and 2015; subjects starting therapy in 2010 were excluded. The proportion of subjects using combination therapy was compared between the pre-SONIC and post-SONIC patient populations.

**Results:** 1,070 patients were identified, of whom 673 met the inclusion criteria . 226 patients started treatment pre SONIC and 447 post SONIC. Pre SONIC, 50.0% received combination therapy compared with 48.3% post SONIC (p=0.68). The proportion of patients receiving adalimumab increased from 12.3% in the pre-SONIC period to 33.2% post-SONIC (p<0.00001); Adalimumab users were as likely as infliximab users to receive combination therapy. Choice of immunomodulator differed pre and post SONIC. Of those who received combination therapy pre SONIC 80.0% received a thiopurine, versus 91.2% post SONIC (p=0.04). Of patients treated with anti-TNF monotherapy, 41.9% pre SONIC and 41.4% post SONIC had no record of any immunomodulator therapy before starting anti-TNF treatment (p=0.94). There were no differences in demographics, clinical characteristics, or markers of disease activity/severity between pre and post SONIC groups, or between combination therapy and anti-TNF monotherapy groups.
**Conclusions:** We were unable to detect increased prevalence of combination therapy among anti-TNF users in the post-SONIC era. This represents a potential opportunity for quality improvement initiatives to optimize care of persons with IBD requiring anti-TNF based therapy.

**Funding Agencies:** None

A94
**SHIP-MICROBIOME INTERACTIONS IN INTESTINAL INFLAMMATION**
P. Dobranowski, S. Menzies, L.M. Sly

Pediatrics, UBC, Vancouver, BC, Canada

**Background:** Immune regulating Src homology domain 2-containing inositol phosphatase (SHIP) protein levels and activity are reduced in patients with the chronic

intestinal inflammatory condition, Crohn's disease (CD). SHIP deficient ($^{-/-}$) mice develop spontaneous CD-like ileal inflammation beginning at 4 weeks of age. Several groups have associated the microbiome with the pathogenesis of CD, where the loss of other immune regulating genes such as NLRP6, NLRP12, and NOD2 result in microbial population changes and intestinal inflammation in mice. However, the microbiome of SHIP$^{-/-}$ mice has not been examined.
**Aims:** To investigate whether SHIP attenuates ileal inflammation by maintaining microbial diversity and protective commensal populations.
**Methods:** Bacterial DNA was extracted from stool and colonic, cecal, and ileal contents of SHIP$^{-/-}$ and SHIP$^{+/+}$ mice at 4 and 8 weeks of age. Bacterial load was quantified by qPCR and normalized by 16S *rrn* gene copy number. V4-V5 hypervariable regions of the 16S rRNA gene were sequenced with the Illumina MiSeq platform and fastq files were imputed using QIIME 1.9. Microbial diversity metrics and relative abundance measures were generated with data rarefied to 5500 sequences per sample. Abundance measures were normalized by *rrn* gene copy count. Metabolomic data were obtained by PICRUSt v1.1.1 and directly measuring short chain fatty acid concentrations of ileal contents using gas chromatography.
**Results:** Bacterial DNA was extracted from a total of 94 samples. No significant differences were observed in bacterial loads between age and genotype groups, indicating that ileal inflammation in SHIP$^{-/-}$ mice is not associated with bacterial overgrowth. Reductions in microbial alpha-diversity were seen in 8 week old SHIP$^{-/-}$ microbiomes as measured by number of OTUs and chao1. Separation of clusters were seen between 8 week old SHIP$^{-/-}$ and SHIP$^{+/+}$ during principle component analysis, but not at 4 weeks old. 8 week old SHIP$^{-/-}$ microbiota showed reductions in the unclassified Bacteroidetes family S24-7. Non-significant changes in abundances were seen at the genus-level. Reduced amino acid metabolism and elevated glutathione and lipid metabolism in 8 week SHIP$^{-/-}$ samples were predicted with PICRUSt, consistent with other models of intestinal inflammation. Modest reductions in butyric acid and propionic acid and elevations in branched chain fatty acids were found after the onset of inflammation.
**Conclusions:** Significant changes in bacterial diversity, populations, and metabolism were only observed after the onset of inflammation. Similar but non-significant changes to the microbiome were observed prior to the onset of inflammation. Taken together, these results suggest that SHIP deficiency is sufficient to drive changes in the intestinal microbiome, which may contribute to, and are amplified by intestinal inflammation.

**Funding Agencies:** CIHR

A95

**INFLAMMATORY PROTEASES DRIVE A MIGRATORY INTESTINAL EPITHELIAL PHENOTYPE THROUGH THE GENERATION OF BIOACTIVE PEPTIDE FRAGMENTS OF E-CADHERIN**

M. Gordon[1], A. Chauvin[2], F. Boisvert[2], W. MacNaughton[1]

1. Physiology and Pharmacology, University of Calgary, Calgary, AB, Canada; 2. Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** The inflammatory microenvironment in the gut contains a variety of proteases which are known to be increased in patient samples in both IBD and CRC. How these proteases and their proteolytic peptide products contribute to wound resolution has been poorly elucidated. A cellular switch from a "barrier" to a "migration/repair" phenotype is required for healing in IBD, but is also a hallmark of tumorigenesis. Proteolytic degradation of epithelial E-cadherin (Ecad) is necessary for this process, we have been studying the biological activity small peptide fragments of Ecad generated by neutrophil elastase, an inflammatory protease elevated in IBD. We have been studying the ability of proteases to induce a switch in the colonic epithelium from a barrier to a repair phenotype (epithelial to mesenchymal transition [EMT]) characterized by increased migration and disrupted homeostasis.
**Aims:** To test the hypothesis that inflammatory proteases process Ecad into small bioactive peptides that contribute to wound resolution.
**Methods:** Recombinant Ecad was incubated with neutrophil elastase (NE) *in vitro* to produce NE-dependent Ecad peptides. Six of these peptides shared partial homology with Ecad peptides identified by mass spectrometry in IBD patient samples, and were chosen for further characterization. Peptides were synthesized and assayed for their ability to alter wound healing capacity, proliferation, cell spreading, and cytotoxicity in Caco-2 cells using the IncuCyte™ live-cell imaging system for 48 hours following exposure to 1, 10, and 100 mg/mL concentrations of peptides. All analysis was done using the IncuCyte™ ZOOM platform in conjunction with ImageJ software.
**Results:** We have identified 6 Ecad peptides produced by neutrophil elastase activity that appear to be increased in IBD patient tissue. We have characterized these peptides to have novel biological roles in altering wound resolution and proliferation rates, with 3 peptides showing significantly increased wound healing capacity at at least one concentration. These 3 peptides (KAADTDPTAPPYD, NRNTGVISVV, and LPPEDDTRDNV) showed improved wound closures of approximately 7-10% under serum free conditions and 5-10% under full serum conditions compared to controls. Preliminary data also suggests that these peptides appear to have a positive effect on proliferation rates, and appear to alter cellular morphology of cells to that of a more flattened cell type, typical of repair programming of cells to cover a denuded area.
**Conclusions:** Our data reveal a novel role for proteolytic processing of Ecad under inflammatory conditions, producing bioactive peptides that drive a wound-healing phenotype in epithelial cells in response to damage.

**Funding Agencies:** CIHRUniversity of Calgary Faculty Seed Grants

A96

**MACROPHAGES DERIVED FROM BLOOD MONOCYTES OF PATIENTS WITH IBD TREATED WITH IL-4 ARE DEFECTIVE IN THEIR CAPACITY TO PROMOTE EPITHELIAL WOUND REPAIR IN VITRO**

T.S. Jayme[2], A. Wang[3], P. Beck[2], D.M. McKay[1]

1. Physiology & Pharmacology, Uni. Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. University of Calgary, Calgary, AB, Canada

**Background:** We have shown that adoptive transfer of an IL-4 stimulated alternatively activated macrophage (AAM) (i.e. M(IL4)) can inhibit colitis in mice. Analyses of other mouse models of inflammation have shown that the AAM is important for wound healing: deletion of this macrophage can exacerbate disease by impairing wound repair. Extrapolating to IBD, we hypothesized that monocytes from patients with IBD, during active inflammation, would be impaired in their ability to convert to M(IL4)s and that this could contribute to impaired wound repair, thus promoting disease.
**Aims:** To assess the ability of M(IL4)s to promote epithelial wound repair in an *in vitro* assay and determine if monocytes from patients with IBD can be converted to M(IL4)s with a wound repair capacity.
**Methods:** Human blood-derived macrophages from healthy donors (HD) and patients with inflammatory bowel disease (Crohn's disease active, n=4; Crohn's disease inactive, n=7; ulcerative colitis active and inactive, both n=3) were exposed to IL-4 (10 ng/ml; 48h) or left unstimulated (controls). Expression of M(IL4) markers were assessed by qPCR (CD206, CD14, CCL18) or ELISA (CCL18). Confluent Caco2 epithelial cell monolayers were wounded with a razor blade and treated with supernatants from HD or IBD M(IL4)s and wound repair was measured ($\mu m^2$) 48h later. TGFβ in M(IL4) supernatants was measured by ELISA, and the effect of adding anti-TGFβ antibodies to the wound repair assay tested.
**Results:** M(IL4)s from healthy donors showed increased expression of CD206 and CCL18, and reduced CD14. Supernatants from these M(IL4)s increased epithelial wound repair (36±14%) (n=8, $p<0.05$) compared to baseline, had increased TGFβ (353±78 pg/ml) compared to control macrophages (204±71 pg/ml) (n=11, $p<0.05$), and were significantly inhibited in the ability to drive epithelial wound repair with addition of anti-TGFβ antibodies. Similarly, monocytes from patients with clinically inactive IBD converted to M(IL4) s with an ability to increase epithelial wound repair (32±32%.). This was not observed with monocytes from patients with active disease that failed to induce CD206 expression or promote wound repair (2 ± 10%) .
**Conclusions:** Human M(IL4)s enhance epithelial wound repair, in part, via TGFβ. The inability of IL-4 treated macrophages to promote wound repair in individuals with active IBD suggests that a similar deficiency *in vivo* would contribute to lack of mucosal healing and ongoing inflammation.

**Funding Agencies:** CCCNSERC Host-Parasites Interactions

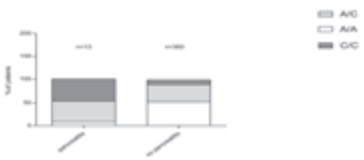
A97

**HLA-DQA1-HLA-DRB1 POLYMORPHISM IS A MAJOR PREDICTOR OF AZATHIOPRINE-INDUCED PANCREATITIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

A. Wilson[3], L. Jansen[1], R. Rose[2], J.C. Gregor[2], T. Ponich[2], N. Chande[2], R. Khanna[2], B. Yan[5], V. Jairath[2], N. Khanna[2], M. Sey[2], M.D. Beaton[1], K. McIntosh[4], W. Teft[2], R. Kim[2]

1. Gastroenterology & Hepatology, London Health Sciences Centre, London , ON, Canada; 2. The University of Western Ontario, London, ON, Canada; 3. Gastroenterology, University of Western Ontario, London, ON, Canada; 4. Department of Medicine, Western University, London, ON, Canada; 5. Medicine, Gastroenterology, Western University, London, ON, Canada

**Background:** Azathioprine (AZA)-induced pancreatitis is an unpredictable and dose-independent adverse event affecting 2-7% of patients with inflammatory bowel disease (IBD) patients treated with AZA. There are no tools in clinical practice to identify at-risk individuals; however, a genome wide association study (GWAS) identified a strong association between the Class II HLA gene region polymorphism (rs2647087) and AZA-induced pancreatitis.
**Aims:** To independently confirm the findings of the GWAS in an IBD cohort, to evaluate its utility in clinical practice and to offer a novel AZA treatment algorithm for IBD based on pharmacogenomic principles.
**Methods:** A retrospective cohort study evaluated 373 AZA-exposed IBD patients from a tertiary care academic centre in London, Canada. All subjects underwent screening for the single nucleotide polymorphism (SNP) rs2647087 mapped to the HLA-DQA1*02:01-HLA-DRB1*07:01 haplotype and were sub-divided based on the presence (n = 13) or absence (n = 360) of an AZA-induced pancreatitis diagnosis. The risk of AZA-induced pancreatitis was assessed based on rs2647087 genotype.
**Results:** The risk of pancreatitis during AZA-therapy was highly predictable and genotype dependent: 0.53% for wild-type (A/A), 4.25% (OR=4.19, 95%CI 1.02-36.45, p=0.044) for heterozygous (A/C), and 14.63% (OR=15.83, 95%CI 3.80-145.26, p=0.0001) for homozygous variant (C/C) patients.
**Conclusions:** The class II HLA region (at rs2647087) is an important marker of AZA-induced pancreatitis risk. We propose a simple and clinically implementable algorithm based on rs2647087 and TPMT genotypes for AZA selection and dosing for patients with IBD.



Genotype frequency stratified based on the presence or absence of pancreatitis. Genotypes are expressed as a percentage of the total population of the pancreatitis cases (n =13) and controls (n = 360).

**Funding Agencies:** CAG, CCC, CIHRCancer Care Ontario

A98

**PLASMA BIOMARKER MAY DETECT DISEASE-DEPENDENT ALTERATIONS IN GUT MICROBIOTA IN IBD: A PILOT STUDY**

S.M. Nelson[2], K. McIntosh[1], R. Kim[1], A. Wilson[1], V. Jairath[1], C. Schmerk[1], Y. Liao[1], W.A. Teft[1]

1. Department of Medicine, Western University, London, ON, Canada; 2. Internal Medicine, Western University, London, ON, Canada

**Background:** Ulcerative colitis (UC) is chronic, often relapsing, remitting inflammation affecting the rectum to proximal colon. UC activity is linked to reduced gut microbial diversity. Trimethylamine-N-oxide (TMAO) is a quantifiable plasma metabolite produced from dietary choline and carnitine through a microbial-mammalian pathway. A previous study by our group demonstrated decreased plasma TMAO was associated with UC. It was hypothesized that changes in the gut microbial profile accounted for differences in plasma TMAO concentrations.
**Aims:** To evaluate the gut microbial profile of subjects with UC and healthy controls to determine if it is predictive of plasma TMAO concentrations.
**Methods:** Thirty-three subjects (13 control (C), 20 UC) were recruited and informed consent was obtained. Demographic and disease activity data were collected. Liquid chromatography-tandem mass spectrometry was used to measure TMAO and dietary choline plasma concentrations. A combined 132 sigmoid colon pinch biopsies were taken during colonoscopy to quantify the mucosal-adherent microbial profile. The abundance of five bacterial genera (*Bacteroides prevotella (Bp), Clostridium XIV (CXIV), Bifidobacterium longum (Bl), Lactobacillus (L), Enterobacteriaceae (E)*), representative of the 4 main bacterial phyla present in the gastrointestinal tract, were quantified from biopsies using real-time PCR.
**Results:** TMAO plasma concentrations were reduced in UC compared to healthy controls (UC: 1.027±0.896, C: 5.478±3.655, p <0.001) and when adjusted for dietary choline plasma concentrations (UC: 0.149±0.232, C:0.643±0.388, p<0.0001). Relative to the total microbiome, *Enterobacteriaceae*, *Lactobacillus* and *Clostridium XIV* were decreased in the UC population compared to the control population (*E:* UC: 0.714±1.67, C: 1.16±2.49, p=0.28; *L:* UC: 0.035±0.043, C: 0.042±0.057, p=0.72; *CXIV*, UC: 1.16±1.51, C: 2.82±5.09, p=0.28). Conversely, in the UC population, *Bacteroides prevotella* and *Bifidobacterium longum* were increased relative to the total microbiome (*Bp:* UC: 6.37±7.22, C: 3.59±2.53, p=0.15; *Bl:* UC: 0.32±-0.51, C: 0.11±0.15, p=0.11). Studies of the microbiome did not reach statistical significance.
**Conclusions:** This pilot study shows that TMAO plasma concentrations are significantly reduced in patients with UC, even when normalized for choline plasma concentrations. Microbial profiles appear to be different in individuals with UC compared to a healthy population. TMAO-producing *Enterobacteriaceae*, *Lactobacillus* and *Clostridium XIV* were under-represented compared to the total microbiome in individuals with UC. This suggests that differences in the gut microbial profile in UC versus healthy individuals may be detectable by a plasma-based biomarker. Expansion of the sample size is needed to confirm these findings.

**Funding Agencies:** CAG, CCC, CIHR

A99

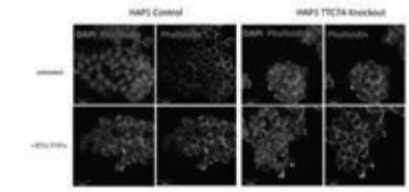
**RESCUING TTC7A MUTANT PHENOTYPES ASSOCIATED WITH *VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE* (VEO-IBD)**

S. Jardine[3], G. Leung[2], C. Guo[2], R. Murchie[2], N. Dhingani[4], N. Warner[2], J. Pan[1], A. Muise[1]

1. Hospital for Sick Children , Toronto, ON, Canada; 2. The Hospital for Sick Children, Toronto, ON, Canada; 3. Cell Biology, The Hospital for Sick Children, TORONTO, ON, Canada; 4. Biochemistry, University of Toronto, Toronto, ON, Canada

**Background:** Very early onset inflammatory bowel disease (VEOIBD) is a severe disease presenting in children <6 years. Patients with *TTC7A* mutations present with apoptotic enterocolitis, disrupted intestinal architecture, multiple intestinal atresias, and/or combined immunodeficiency. There are few effective treatment options for these patients, and infant fatality is common. Rare autosomal recessive variants for tetratricopeptide repeat domain 7A (TTC7A) have been uncovered in the most severe forms of VEOIBD. The role of TTC7A in the pathogenesis of VEOIBD is largely unknown.
**Aims:** The rising prevalence of IBD in Canada is driven by the rapidly increasing incidence (~60%) in children. Compounded with poor responses to standard IBD therapies, the need for therapies motivates researchers to seek effective treatment options. **We hypothesize that TTC7A dysfunction results in aberrant intestinal phenotypes related to VEO-IBD.** My research aim is to define *TTC7A* mutant phenotypes in cell-based and zebrafish models; thus, allowing for phenotypic screening and discovery of drugs for use in clinical settings. *The*

*overall research goal is to identify compounds that can rescue aberrant phenotypes induced by the TTC7A defect via high throughput drug screening.* Since research on TTC7A's function is scarce, identifying drugs with known targets may provide some insight into TTC7A's cellular functions, and in VEO-IBD as a whole.
**Methods:** Mutant phenotypes were characterized using CRISPR engineered TTC7A knockout HAP1 cells. Assays revolving around apoptosis and cell adhesion were used in a manner amenable to high throughput screening (HTS). For example, 96-well fluorescent and luminescent assays using caspase 3 /7 luciferases. TTC7A mutant zebrafish with fluorescently stained GI tracts allowed for peristaltic activity analyses. HTS using libraries containing FDA approved drugs identified drugs that could rescue TTC7A-related aberrant phenotypes
**Results:** Aberrations in a range of phenotypes were observed in TTC7A i*n vitro* models including round and small morphologies, altered f-actin organization, poor adhesion, compromised viability, and increased susceptibility to apoptosis. Homozygous TTC7A zebrafish show reduced gut motility, narrow intestinal lumens, and increased apoptotic cells. Drug screening has identified several (hits) drugs capable of rescuing TTC7A phenotypes. These drugs will be validated in orthogonal assays as well as in patient derived intestinal organoids.
**Conclusions:** Defining the TTC7A mutant phenotype has provided targets for identifying drugs for use in clinical settings. Furthermore, these findings could elucidate the functional pathways of this relatively uncharacterized protein. Drugs capable of rescuing TTC7A defects could increase patient prognosis and uncover functional pathways contributing to VEOIBD.




**F-actin is upregulated and staining pattern resembles cells in early apoptosis in TTC7A knockout cells.** HAP1 control and TTC7A knockout staining at 40x,1slice with a spinning disk confocal. Nuclei and actin structures were stained with DAPI and phalloidin, respectively. Bottom panels were treated with IFN$\gamma$ and TNF$\alpha$ pro-inflammatory cytokines for 48 hours.

**Funding Agencies:** CIHR

A100

**PANCREASTATIN WORSENS INTESTINAL INFLAMMATION BY INDUCING CLASSICALLY ACTIVATED MACROPHAGES (M1) THROUGH SUPPRESSION OF STAT3**

N. Eissa[1], L. Kermarrec[1], G. Hendy[2], C.N. Bernstein[3], J. Ghia[2]

1. Immunology, University of Manitoba, Winnipeg, MB, Canada; 2. Departments of Medicine, Physiology, and Human Genetics, McGill University, Montreal , QC, Canada; 3. Internal Medicine Section Gastroenterology, Winnipeg, MB, Canada

**Background:** Chromogranin-A (CHGA) levels are increased in inflammatory bowel disease (IBD) and murine models of colitis. CHGA is cleaved in several peptides including the immunoregulatory pancreastatin (PST: $CHGA_{273-301}$), which encodes by CHGA exon-VII. Classically activated macrophages (M1) and signal transducer and activator of transcription (STAT) 3 play significant roles in the pathophysiology of IBD. Previously we showed that *Chga*-knockout mice (*Chga*$^{-/-}$) exhibited a significant decrease in the severity of colitis correlated with a reduction of M1 activity.
**Aims:** we aimed to investigate the activity of PST in patients with active ulcerative colitis (UC) and the underlying mechanisms in dextran sulfate sodium (DSS)-induced colitis using *Chga*$^{-/-}$ mice to define the effect on macrophages activation and migration
**Methods:** Serum and colonic protein levels of PST were quantified in Patients with UC & healthy individuals. Expression of CHGA Exon-VII expressing PST and its correlation with M1 markers (IL-1β, IL-6, TNF-α, MCP-1) and STAT3 levels were determined in human colonic tissues. Colitis was induced in *Chga*$^{+/+}$ and *Chga*$^{-/-}$ mice by administrating DSS (5%, 5 days). PST treatment (2.5 mg/kg/day) or vehicle (Phosphate Buffered-Saline 1%) started 1-day before colitis induction and lasted for 5-days. Disease activity index, macroscopic scores, and serum C-reactive protein were evaluated. Colonic M1 markers and phosphorylated STAT3 levels were assessed using ELISA/RT-qPCR. PST (200ng/ml) treated-naïve peritoneal macrophages were exposed for 6 h to LPS (100ng/ml) to promote M1. M1 markers were quantified. In vitro chemotaxis activity of PST (200ng/ml) on naïve macrophages were assessed by transwell migration assay using MCP-1 (30ng/ml) as a chemoattractant.
**Results:** Patients with UC exhibited a 10-fold increase in colonic and serum levels of PST compared with healthy individuals. PTS also positively correlated with proinflammatory macrophages (M1) mediators and negatively with STAT3. Experimentally, colonic levels of PST elevated in *Chga*$^{+/+}$ mice with DSS-induced colitis. Administration of PST worsened the severity of colitis associated with an increase of M1 macrophages cytokine and chemokines, and a decrease of STAT3 level in *Chga*$^{+/+}$ and *Chga*$^{-/-}$ mice. In vitro, peritoneal M1 associated cytokines significantly increased in PST-conditioned *Chga*$^{-/-}$ M1 that linked to a reduction in STAT3 level. In undifferentiated macrophages, PST dramatically enhanced macrophages migration.
**Conclusions:** The aggravation of intestinal inflammation exists only in the presence of PST, and its absence leads to a reduction of disease severity, a decrease of M1 activation and an increase in STAT3. Targeting PST may lead to a novel therapeutic strategy in IBD.

**Funding Agencies:** CCC, CIHRResearch Manitoba, Canada

A101

**ARPC1B-DEFICIENT B CELLS DISPLAY ABERRANT SPREADING BEHAVIOUR**

G. Leung[2], N. Warner[3], R. Murchie[4], A. Muise[1]

1. Hospital for Sick Children , Toronto, ON, Canada; 2. The Hospital for Sick Children, Toronto, ON, Canada; 3. The Hospital for Sick Children, Toronto, ON, Canada; 4. The Hospital for Sick Children, Toronto, ON, Canada

**Background:** ARPC1B-deficiency is a newly described genetic condition with an early age of onset and is clinically similar to Wiskott-Aldrich syndrome (WAS). Nearly all affected patients experience colitis that is eosinophilic in nature, and their immunological profiles show increased peripheral $CD19^+$ cells, IgE, IgA, and detectable auto-antibodies. ARPC1B is a member of the Arp2/3 actin nucleating complex, which is activated by WAS protein and is the rate-limiting step in branched actin polymerization. It is expressed by haematopoietic cells and is important for regulating a dynamic cytoskeleton for essential functions such as migration and intracellular transport.
**Aims:** There are currently no data addressing the loss of ARPC1B and its effect on B cell function specifically. We intend to characterize how ARPC1B deficiency affects B cell activation *in vitro*.
**Methods:** EBV-transformed lymphoblastoid (B cell) lines were generated from PBMCs derived from patients and their first-degree relatives. B cell receptor (BCR) internalization was assessed by flow cytometry. Cell spreading was activated by receptor cross-linking: B cells were added to anti-human IgG-coated chamber slides and allowed to spread (2-20 min), then fixed and stained with phalloidin which binds filamentous (F)-actin. Images were acquired and analysed in ImageJ.
**Results:** Our group identified three patients harbouring mutations in *ARPC1B*: one with a severe phenotype (Pat 1) accompanied by a homozygous 2 bp insertion (c.387_388insCT [L90fs]) resulting in truncation, and two brothers with mild (Pat 2)/very mild (Pat 3) phenotypes caused by 2 homozygous SNPs (c.434C>T [A105V]; c.832G>A [A238T]). In B cell lysates, immunoblots confirmed the loss of ARPC1B in Pat 1, and reduced protein in Pat 2/3 compared to controls; this pattern was inversely correlated with expression of its isoform, ARPC1A. Flow cytometric analysis of phalloidin-stained B cells showed significantly reduced F-actin in all affected patients, while BCR expression was higher (internalization was not affected). Interestingly, a small proportion of unstimulated B cells from Pat 1 spontaneously adhered to tissue culture-treated surfaces after 2 d. Moreover, spreading assays demonstrated that a higher number of B cells from Pat 1 stuck down with no effect on spreading area. Upon closer inspection, structured illumination microscopy of phalloidin-stained B cells revealed a divergent spreading phenotype, with fewer extensive protrusions in cells from Pat 1.
**Conclusions:** B cells deficient in ARPC1B have an inherent defect affecting their activity *in vivo*, BCR expression, and spreading behaviour *in vitro*. Further characterization is warranted to define the mechanism underlying this phenotype and its implications in the development of early onset IBD.

**Funding Agencies:** CAG, CIHRHelmsley Charitable Trust

A102

**TOLERABILITY OF USTEKINUMAB IN INDUCTION AND MAINTENANCE FOR THE TREATMENT OF CROHN'S DISEASE**

E.V. Loftus[2], B.D. Sattin[1], D. Jacobstein[5], C. Gasink[6], S. Sloan[6], B.G. Feagan[4], J.F. Colombel[3]

1. Janssen Inc, Toronto, ON, Canada; 2. Mayo Clinic, Rochester, MN; 3. School Of Medicine, Mount Sinai Medical Center , New York, NY; 4. Robarts Clinical Trials Inc, London, ON, Canada; 5. Janssen Research & Development, LLC, Spring House, PA; 6. Janssen Scientific Affairs, LLC, Horsham, PA

**Background:** Tolerance to therapy is critical for pts to receive the maximal treatment benefit. In Phase 3 clinical trials for ustekinumab (UST) for moderate to severe Crohn's disease (CD), UNITI-1 enrolled anti-TNF failures and UNITI-2 enrolled conventional therapy failures. In UNITI-1, 36.4% had previous intolerance (infusion-related reactions [IRR], delayed hypersensitivity reactions, or injection site reactions [ISR]) that led to discontinuation of the anti-TNF. UNITI-2 enrolled pts that were not intolerant to anti-TNFs, but some were intolerant to immunomodulators (39%) or corticosteroids (15%).
**Aims:** Here we assess tolerability as measured by IRR, delayed hypersensitivity, or ISR to UST in the Phase 3 CD trials.
**Methods:** All enrolled pts in UNITI-1 and UNITI-2 were given an intravenous (IV) induction infusion of UST 130mg, UST ~6 mg/kg, or placebo (PBO). The IM-UNITI maintenance study began 8 weeks after IV induction; UST IV responders were randomized to UST 90mg SC Q8W, UST 90mg SC Q12W, or PBO. Non-randomized patients, included non-responders to placebo who received 130mg IV UST, then continued to UST 90mg SC Q12W maintenance therapy; non-responders to IV UST who received UST 90 mg SC, then continued UST 90 mg SC Q8W in maintenance; and IV placebo responders who received placebo SC in maintenance.
**Results:** Overall, IRR were infrequent: 4.0 % and 1.9 % of all pts in UNITI 1 & 2, respectively, experienced infusion reactions to the single IV dose. There were no differences in IRR between PBO & UST, or between UST doses (UNITI 1 IRRs in 2.0%, PBO and 4.5% UST 130mg and 3.6%, UST ~6 mg/kg; UNITI 2 IRRs in 2.9%, PBO and 2.4% UST 130mg and 1.4%, UST ~6 mg/kg). During IM-UNITI, in non-randomized pts who were non-responders to placebo induction and received a 130mg IV injection, IRR to PBO and UST were similar and infrequent (2.5% and 1.8%, respectively). There were no anaphylactic or delayed hypersensitivity reactions to any IV dose.
After SC administration, ISRs were infrequent and not different across groups. In the combined (randomized

and non- randomized) population, ISRs were 1.7 % with PBO, and 3.0% with UST. No serious ISRs were reported. The most common ISR was erythema, reported in 1.1 % of PBO, and 1.7% of UST. There were no anaphylactic or delayed hypersensitivity reactions to any SC dose. Amongst randomized pts, ISRs were infrequent and consistent between groups. ISRs occurred in 3/418 (0.7 %) of all UST 90mg Q12W injections and in 12/599 (2.0 %) of all UST 90mg Q8W injections. One pt in the entire phase 3 program discontinued therapy due to ISR.
**Conclusions:** In a broad population of pts with Crohn's disease, many of whom were intolerant to previous therapies, UST had a tolerable profile. Rates of IRR and ISR were minimal, and were not different between groups, nor populations.

**Funding Agencies:** Janssen Research & Development, LLC funded this study

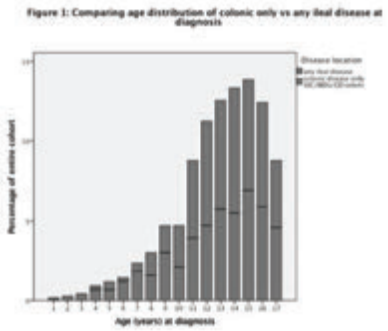
A103

**PHENOTYPIC VARIATION IN PEDIATRIC IBD BY AGE: A MULTI-CENTRE INCEPTION COHORT STUDY OF THE CANADIAN CHILDREN IBD NETWORK**

J. Dhaliwal[11], P. Church[11], D.R. Mack[10], H.Q. Huynh[9], K. Jacobson[8], W. EL-MATARY[7], J. deBruyn[6], A. Otley[5], C. Deslandres[4], M. Sherlock[3], J. Critch[2], K. Bax[12], E.G. Seidman[1], M. Rashid[5], P. Jantchou[4], R. Issenman[3], A. Muise[11], E.I. Benchimol[10], E. Wine[9], M.W. Carroll[9], S. Lawrence[8], J. Van Limbergen[5], T.D. Walters[11], A. Griffiths[11]

1. Montreal Children's Hospital, McGill University, Montreal, QC, Canada; 2. Division of Gastroenterology, Janeway Children's Health and Rehabilitation Centre, Memorial University of Newfoundland, St. John's, , Canada; 3. Division of Gastroenterology & Nutrition, McMaster Children's Hospital, Hamilton Health Sciences, Hamilton, ON, Canada; 4. Division of Gastroenterology, Hepatology and Nutrition, Department of Paediatrics, CHU Sainte-Justine, Montréal, QC, Canada; 5. Division of Gastroenterology & Nutrition, IWK Health Centre, Department of Pediatrics, Dalhousie University, Halifax, NS, Canada; 6. Division of Pediatric Gastroenterology, Department of Pediatrics, Faculty of Medicine, University of Calgary, Alberta Children's Hospital, Calgary, AB, Canada; 7. Section of Gastroenterology, Department of Pediatrics, Max Rady College of Medicine, University of Manitoba, Winnipeg, MB, Canada; 8. Division of Gastroenterology, Hepatology and Nutrition, B.C. Children's Hospital, Vancouver, BC, Canada; 9. Division of Pediatric gastroenterology and Nutrition, Department of Pediatrics, University of Alberta, Stollery Children's Hospital, Edmonton , Edmonton, AB, Canada; 10. Children's Hospital of Eastern Ontario IBD Centre, Department of Pediatrics, University of Ottawa, Ottawa, ON, Canada; 11. Division of Gastroenterology, Hepatology and Nutrition, Department of Paediatrics, Hospital for Sick Children, Toronto, Toronto, ON, Canada; 12. Children's Hospital of Western Ontario, University of Western Ontario, London, ON, Canada

**Background:** The Paris classification of pediatric IBD divides "pediatric-onset" IBD (A1, Montreal classification) into A1a (diagnosis <10 years) and A1b(≥10and< 17y). The Montreal A1 category was arbitrarily defined, but the Paris division was based on variation in spectrum of IBD localization with age, any ileal disease being uncommon prior to age 9-10y. Other variations in phenotypic spectrum with age have not been rigorously examined.
**Aims:** To examine the variation with age of IBD type, location, severity in a large national multi-centre prospectively accrued pediatric inception cohort of new onset IBD.
**Methods:** Patients aged <17y presenting with new onset IBD at 12 participating academic pediatric IBD centres were enrolled in an inception cohort study of the Canadian Children Inflammatory Bowel Disease Network. Baseline and longitudinal phenotypic and demographic data were collected. IBD type was diagnosed as Crohn's disease(CD), ulcerative colitis(UC), or IBD unclassified(IBDU) using clinical, endoscopic and histologic criteria. Location was based on macroscopic disease, identified by colonoscopy and MR enterography. Baseline disease activity categorized by physician global assessment and measured by PCDAI or PUCAI. Mann-Whitney and Kruskal-Wallis tests were applied as appropriate.
**Results:** Between April 2014 and June 2017, 1146 children (median(IQR)age 13y(11-15); 57% male; CD:62%; UC:29%; IBDU:9%) were enrolled. Colon only disease (UC/IBDU or CD-colon) was the predominant IBD phenotype until diagnosis age 11y(p=0.004), with a progressive increase thereafter in the percentage children with any ileal or other small bowel CD(Figure1). In the CD cohort overall, macroscopic location was 19%L1; 27%L2; 54%L3. L2 disease predominated until age 12y(p=0.001), when both L1 and L3 (any ileal disease) became more common. In the UC cohort the extent of disease was 9% E1; 6% E2; 11% E3; 74% E4; this distribution was consistent across all ages. The male:female ratio for the entire cohort was 1.3:1, and in both UC and CD, gender distribution was similar across all ages. Among children with UC, there was no variation in PGA of disease severity (mild:22%; moderate:42%; severe:34%; fulminant:2%) by age at diagnosis. In CD overall, severity was mild:26%; moderate:44%; severe:29%; fulminant;1%, but mild-moderate disease severity predominated until age 7y(p=0.01).
**Conclusions:** Our data confirm the predominance of colon only IBD in younger children and support the Paris designation of A1a as early onset pediatric IBD. A spectrum of disease severity at diagnosis is seen across all ages.




**Funding Agencies:** CIHRC.H.I.L.D Foundation (Children with Intestinal and Liver Disorders)

A104

**PREGNANCY OUTCOMES IN WOMEN WITH INFLAMMATORY BOWEL DISEASE AND EXPOSURE TO BIOLOGICS - A PROSPECTIVE COHORT STUDY**

S. Wang[2], J. Pena-Sanchez[3], S. Fowler[1]

1. Department of Medicine, Division of Gastroenterology, University of Saskatchewan, Saskatoon, SK, Canada; 2. Department of Medicine, University of Saskatchewan, Saskatoon, SK, Canada; 3. Department of Community Health & Epidemiology, University of Saskatchewan, Saskatoon, SK, Canada

**Background:** Inflammatory bowel disease (IBD) has a peak incidence rate in women of reproductive age. Biologic agents are commonly used in IBD management. However, prospective safety data on biologics exposure in the pregnant population remain limited.
**Aims:** To assess baseline differences, and to compare obstetrical and neonatal outcomes in women with IBD who are exposed and non-exposed to biologics during pregnancy.
**Methods:** Since November 2014, pregnant women with ulcerative colitis (UC) or Crohn's disease (CD) were enrolled in a prospective registry. Patients were assessed every trimester, and at three, six, and 12-months post-partum. Disease activity, pregnancy complications, and delivery and newborn outcomes were recorded. Women were divided into exposed (adalimumab [ADA], infliximab [IFX], vedolizumab [VDZ], or ustekinumab [UST]) and non-exposed (no medications or 5-aminosalicylic acid [5-ASA]) groups. Patients taking only immunomodulators were excluded. Mann–Whitney U and Fisher's exact tests were used to identify differences between groups.
**Results:** To date, 36 patients have been enrolled in the study, totalling 38 pregnancy events. Sixteen pregnancy events were exposed to biologics: 9 (56.2%) ADA, 4 (25.0%) IFX, 2 (12.5%) VDZ, 1 (6.2%) UST. Twenty-two pregnancy events were not exposed: 8 (36.4%) 5-ASAs and 14 (64.6%) no medications. Within the exposed and non-exposed groups, 13 (81.3%) and 14 (63.6%) women had CD, respectively. The exposed group had fewer patients with a smoking history (1 [6.3%] vs 11 [50.0%], p=0.04), while a higher proportion had an annual household income above $100,000 (11 [78.6%] vs 7 [35.0%], p=0.012). No differences were observed between groups for adverse pregnancy diagnoses (gestational hypertension and diabetes, preeclampsia/eclampsia), post-partum infections, and neonatal outcomes (low birth weight, prematurity, and infections). Disease relapse during pregnancy (5 [31.3%] vs 8 [36.4%], p=0.74) and steroid use (4 [25%] vs 3 [13.6%], p=0.42) were similar between exposed and non-exposed groups, respectively. Caesarian section (CS) occurred in 7 (46.7%) of exposed and 10 (62.5%) of non-exposed group (p=0.38), while 6 (16.7%) patients in total had active perianal disease. There was a trend towards significance for increased emergency CS within the non-exposed (6 [37.5%]) compared to exposed group (1 [6.7%], p=0.08). No significant difference was observed for breast feeding rates between groups.
**Conclusions:** Biologics exposure does not appear to be associated with adverse pregnancy and neonatal outcomes. Higher socioeconomic status was linked to women using biologics during pregnancy. A high CS rate was also observed overall while few had an IBD-related indication. Future studies should explore any barriers to accessing biologics in Canada, and the propensity for CS in women with IBD.

**Funding Agencies:** Saskatchewan Health Research Foundation (SHRF)

A105

**CANADIAN WOMEN WITH IBD ARE MORE LIKELY TO GIVE BIRTH TO LOW BIRTH WEIGHT INFANTS**

L.E. Targownik[8], E.I. Benchimol[1], C. Seow[7], G.C. Nguyen[3], J. Pena-Sanchez[6], J. Jones[2], A. Metcalfe[9], C. Dolovich[5], C.N. Bernstein[4], H. Singh[5]

1. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. Medicine, Dalhousie University, Halifax, NS, Canada; 3. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 4. Uiversity of Manitoba, Winnipeg, MB, Canada; 5. University of Manitoba, Winnipeg, MB, Canada; 6. University of Saskatchewan, Saskatoon, SK, Canada; 7. Medicine, University of Calgary, Calgary, AB, Canada; 8. Internal Medicine, University of Manitoba, Winnipeg, MB, Canada; 9. University of Calgary, Calgary, AB, Canada

**Background:** Inflammatory bowel disease (IBD), a chronic inflammatory disease, often develops in adolescence and young adulthood, thus affecting many women in their childbearing years. Data are conflicting on the effect of IBD on gestational outcomes. Population-based data evaluating perinatal outcomes among Canadian women with IBD in the modern era are lacking.

**Aims:** We sought to determine whether there is an

increased likelihood of prematurity and/or low birth weight among infants born to Canadian women with IBD in a population based provincial dataset

**Methods:** We used the University of Manitoba IBD Epidemiologic Database to identify all women in Manitoba between the ages of 15 to 45 with either Crohn's disease (CD) or ulcerative colitis (UC) between 1984-2014. Women with IBD were matched to non-IBD controls in a 1:10 ratio on age and neighbourhood of residence at the time of IBD diagnosis. Live birth events were identified in the maternal record and linked to the neonatal record to obtain the estimated gestational age and birth weight. Prematurity was defined as gestational age less than 37 weeks. Infants weighing less than 2500g at birth were considered to have low birth weight (LBW), and those weighing between 2500-3000g were classified as low-normal birth weight (LNBW). The proportion of all LBW and premature babies among all babies born was calculated for IBD (stratified for CD and UC) and controls.

**Results:** There were 3172 women with IBD (1,827 CD, 1,345 UC) matched to 27,184 non-IBD controls (15,802 matched to CD cases, 11,382 matched to UC cases), 1495 infants (878 CD, 617 UC) were born to women with IBD, compared with 14,006 infants born to controls (8,362 CD controls, 5,644 UC controls). 3.5% of infants born to women with CD were premature, compared with 1.9% of controls (p=0.0043); There was no significant difference in the likelihood of prematurity among babies born to women with UC compared with their controls (2.9% vs. 2.3%, p>0.2).
The probability of having a LBW infant was higher among both women with CD and UC compared with controls (CD: 7.8% vs 3.4%, p=0.0004; UC: 7.0% vs 3.1%, p=0.0033). There was also a higher prevalence of LNBW babies among CD (17.5% vs 10.9%, p=0.0008) and UC (18.2% vs 12.5%, p=0.009). Neither maternal age at birth nor era of birth were associated with prematurity, LBW, or LNBW

**Conclusions:** Canadian women with IBD are at increased risk of having LBW and LNBW infants, and women with CD specifically have a higher chance of giving birth prematurely. Further work is required to determine the disease and treatment related factors which may predispose to the development of these adverse birth outcomes.

**Funding Agencies:** American College of Gastroenterology and the Canadian Gastrointestinal Epidemiologic Consortium

A106

**SAFETY OF USTEKINUMAB WITH AND WITHOUT CONCOMITANT CORTICOSTEROIDS OR IMMUNOSUPPRESSANTS IN PATIENTS WITH MODERATELY-TO-SEVERELY ACTIVE CROHN'S DISEASE**

B.E. Sands[1], C. Gasink[3], D. Jacobstein[4], E. Ott[5], Y. Lang[6], P. Ramachandran[4], S. Ghosh[2]

1. Icahn School of Medicine at Mount Sinai, New York, NY; 2. Gastrointestinal Section, Imperial College london, London, United Kingdom; 3. Janssen Scientific Affairs, LLC, Horsham, PA; 4. Janssen Research & Development, LLC, Spring House, PA; 5. Janssen Research & Development, LLC, Spring House, PA; 6. Janssen Research & Development, LLC, Spring House, PA

**Background:** Ustekinumab (UST), a monoclonal antibody to IL-12 and 23, was recently approved for the treatment of moderate-severe CD.
**Aims:** Here we report safety data with and without concomitant use of Immunomodulators(IMM) and corticosteroids(CS) in induction and maintenance in pts pooled from the Phase 2 and 3 CD studies.
**Methods:** Percentages of pts experiencing safety events (AEs, SAEs, infections, and deaths) were assessed with and without concomitant IMM or CS use at baseline after IV ustekinumab (UST) or placebo (PBO) induction (8 weeks) and were then also compared with SC UST or PBO maintenance (up to 44 weeks) from the Phase 2 and 3 CD clinical studies. Pts who received IV UST (doses included: 130mg flat dose and 1, 3, 4.5, & 6 mg/kg) during the PBO-controlled induction period (Week 0-8) were pooled from 2 Phase 2 (C0379T07 & CERTIFI) and 2 Phase 3 (UNITI-1 and 2) clinical studies (total n= 1,986). For maintenance, SC UST (combining 90mg q8w and q12w) and PBO were pooled and compared in the randomized responder populations (ie responders to IV UST induction) from the maintenance phase of the Phase 2 CERTIFI (Week 8 to Week 22) and Phase 3 IM-UNITI (Week 0 to Week 44) studies (total n= 541).
**Results:** No death occurred in either the induction or maintenance phases in any groups. Through 8 weeks of induction, the percentages of pts with AEs, SAEs, and infections were similar between UST and PBO both on and off IMM and CS: across all 4 subgroups, for UST, 58-63% had AEs, 4-7% had SAEs, and 19-23% had infections and for PBO, 56-66% had AEs, 5-9% had SAEs, and 21-26% had infections. In maintenance, proportions of pts experiencing AEs, SAEs, and infections were generally similar between UST and PBO groups both on and off IMM and CS,: across all 4 subgroups, for UST, 72-82% had AEs, 9-10% had SAEs, and 41-43% had infections and for PBO, 77-87% had AEs, 9-15% had SAEs, and 37-49% had infections. Proportions of pts on CS in both the UST and PBO groups experienced slightly higher rates of AEs compared with those not on CS (UST, 82% vs 74%, respectively; PBO, 87% vs 76%, respectively). Additionally, PBO pts on CS also experienced slightly higher rates of SAEs (15%) and infections (49%) than the other groups (9-12% with SAEs; 37-43% with infections).
**Conclusions:** No differences in safety data were identified based on the use of concomitant IMMs or CSs in UST-treated pts with either IV induction or with SC maintenance compared to PBO. The concomitant use of IMM or CS during either IV induction or SC maintenance treatment with UST did not adversely

impact the previously reported favorable safety profile of UST in moderate to severe CD pts, although concomitant CS did result in slightly higher rates of events during maintenance, particularly in the PBO group.

**Funding Agencies:** Janssen Research & Development, LLC funded this study

A107

**TOLL LIKE RECEPTOR 9 LIMITS INTESTINAL INFLAMMATION AND PROMOTES MICROBIOTA BASED COLONIZATION RESISTANCE DURING CITROBACTER RODENTIUM INFECTION**

H. Yang[2], H. Yu[4], G. Bhinder[6], N.R. Ryz[3], H. Yang[2], A. Fotovati[2], D.L. Gibson[5], S.E. Turvey[2], G. Reid[2], B. Vallance[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Pediatrics, BC Children's Hospital Research Institute, Vancouver, BC, Canada; 3. Child and Family Research Institute, Vancouver, BC, Canada; 4. Paediatrics, Research Institute, BC Children's Hospital, Vancouver, BC, Canada; 5. Biology, UBC Okanagan, Kelwona, BC, Canada; 6. University of British Columbia, Vancouver, BC, Canada

**Background:** Mammalian cells express a variety of toll-like receptors (TLRs) to detect and respond to microbial pathogens, such as enteropathogenic and enterohemorrhagic *E. coli* (EPEC and EHEC), two important human pathogens that are major causes of diarrheal diseases worldwide. Since EPEC and EHEC are human-specific, *Citrobacter rodentium*, a natural extracellular pathogen of mice has been widely used as a surrogate organism to study the role of immunity (including TLRs) in promoting host defense against EPEC and EHEC. These enteric pathogens share similar virulence strategies allowing them to directly infect the apical surface of the intestinal epithelium, resulting in host-driven intestinal inflammation.
**Aims:** This study explored the potential role of TLR9, a receptor that recognizes unmethylated CpG dinucleotides present in bacterial DNA, in promoting host defense against *C. rodentium* infection.
**Methods:** HEK293 cells co-transfected with the TLR9 and its reporter genes were treated with genomic DNA isolated from *C. rodentium* and the activity of the reporter was measured via a colorimetric assay. 8-12 week-old male and female wildtype (WT) C57BL/6J and TLR9 deficient *(Tlr9$^{-/-}$)* mice were infected by oral gavage using 2 x $10^8$ colony forming units (CFU) of streptomycin-resistant wildtype *C. rodentium*. Mice were monitored daily. An *in vivo* imaging system (IVIS) was used to visualize the colonization of *C. rodentium* in intact intestinal tissues. The mice were euthanized at day 6 post-infection and samples (cecum, colon and feces) were collected for further analysis such as CFU, histology, immunostaining, Western blot and quantitative PCR analysis.
**Results:** *Tlr9$^{-/-}$*mice infected with *C. rodentium* suffered exaggerated mucosal damage and carried significantly higher intestinal pathogen burdens as compared to WT mice. *C. rodentium* infection also induced increased intestinal inflammatory and antimicrobial responses, as well as hyper-activation of NF-κB signaling in *Tlr9$^{-/-}$*mice. These changes were associated with more rapid depletion of the intestinal microbiota in *Tlr9$^{-/-}$*mice as compared to WT mice. Intriguingly, antibiotic based depletion of the gut microbiota in WT mice before *C. rodentium* infection increased their susceptibility to the levels seen in *Tlr9$^{-/-}$* mice.
**Conclusions:** Our results indicate that TLR9 suppresses intestinal inflammatory and antimicrobial responses during an enteric infection, thereby promoting microbiota-mediated colonization resistance against *C. rodentium* infection.

**Funding Agencies:** CCC, CIHRNSERC, MITACs

A108

**USTEKINUMAB IV INDUCTION RESULTS IN CROHN'S DISEASE SYMPTOM IMPROVEMENT WITHIN THE FIRST WEEK IN ANTI-TNF REFRACTORY PATIENTS**

W. Sandborn[1], B. Yeager[4], C. Gasink[3], T. Hoops[4], L. Gao[4], Y. Wang[3], D. Jacobstein[5], S.D. Lee[6], S. Hanauer[2]

1. University of California San Diego, La Jolla, CA; 2. University of Chicago, Chicago, IL; 3. Janssen Scientific Affairs, LLC, Horsham, PA; 4. Janssen Scientific Affairs, LLC, Horsham, PA; 5. Janssen Research & Development, LLC, Spring House, PA; 6. University of Washington, Seattle, WA

**Background:** In both the UNITI-1&2 Crohn's disease (CD) studies, a single 6mg/kg Ustekinumab (UST) IV infusion showed significantly greater rates of clinical response & remission vs placebo, and significant reductions in CDAI (and >70 pt reduction)[1] by the first post-baseline visit at Wk 3.[2]
**Aims:** It remains to be determined how soon patients see benefit (ie. before Wk 3).
**Methods:** Patient (pt) CDAI diary daily data (day -7 to +14) from the UNITI-1 study of pts who had previously failed TNF antagonists were compiled and analyzed post-hoc for the 3 pt-reported CDAI components (stool frequency[SF], abdominal pain[AP], & general well-being[WB]). Mean change in these daily scores with IV UST 6 mg/kg and 130mg were compared vs. placebo (PBO), as were 2-item SF+AP PRO2 weekly, over the 7d prior, weighted either 1:1 or as a CDAI subscore (assessed by mean change, and as % of pts with >50pt improvement). Ranked transformation was used to compare groups for all analyses.
**Results:** IV UST induced significant improvement in all 3 components within the first 2 wks, with AP first significantly better than PBO on d2 for both UST doses, and consistently significantly better than PBO from d6 through d14 for 6mg/kg and from d8 through d14 for 130mg. Mean improvement in SF was first significantly better than PBO on d7 for UST both doses, while this occurred on d8 for WB. Week 1 and 2 SF+AP with CDAI weighting was significantly improved for both UST doses vs PBO at d7 and d14, & SF+AP added with equal

1:1 weight was significantly improved for both UST doses at d14. 29.3% of 6mg/kg & 31.4% of 130 mg groups attained ≥50pt improvement in CDAI solely based on SF&AP components over the second week vs 18.8% in the PBO group ($p<0.05$ and $p<0.01$, respectively).
**Conclusions:** Even in the refractory CD population of previous anti TNF failures in UNITI 1, symptom relief based on individual pt-reported CDAI components began to show significant improvement as early as 1 day post UST infusion, and was seen consistently among all 3 components by d8 with both IV UST doses, confirmed by consistent PRO2 benefit in the second week. These findings support previously reported significant early efficacy seen at the post-baseline (Wk3) visit in the UNITI induction studies.[2]
[1]Best WR, et al. Gastroenterology 1976;70:439-44
[2]Feagan BG, et al. N Engl J Med 2016;375:1946-60

**Funding Agencies:** Janssen Research & Development, LLC funded this study

A109
**PREGNANCY OUTCOMES IN WOMEN EXPOSED TO USTEKINUMAB IN THE CROHN'S DISEASE CLINICAL DEVELOPMENT PROGRAM**
E. Scherl[1], D. Jacobstein[2], C. Murphy[2], E. Ott[3], C. Gasink[4], D.C. Baumgart[5], B. Abraham[6]

1. New York Presbyterian Hospital Weill Cornell Medicine, New York, NY; 2. Janssen Research & Development. LLC, Spring House, PA; 3. Janssen Research & Development, LLC, Spring House, PA; 4. Janssen Scientific Affairs, LLC, Horsham, PA; 5. Charité Medical School of the Humboldt-University of Berlin, Berlin, Germany; 6. Houston Methodist Hospital and the Weill Cornell Medical College, Houston, TX

**Background:** Ustekinumab (UST) has been approved for moderate to severe Crohn's Disease (CD) in adult patients (pts). While no adverse developmental outcomes (pre-& postnatal) were observed in animal studies of UST, limited data exist, including previously reported outcomes in psoriasis (PsO) pts, concerning the effects of UST on human pregnancies[1].
**Aims:** To characterize pregnancy outcomes in women exposed to UST during pregnancy, data from the UST CD clinical development program (CDP) are presented.
**Methods:** Pregnancies reported with maternal use of UST (typical terminal half-life of approx 3 weeks) from 5 CD studies were evaluated: 2 Phase 2 (C0379T07:n=131; CERTIFI:n=526) & 3 Phase 3 (UNITI-1:n=769 & UNITI-2:n=640, from which 1,281 continued on maintenance in IM-UNITI).
**Results:** 877 female pts received ≥1 IV or SC dose of UST, and 26 maternal pregnancies were reported (despite agreeing to adequate birth control). UST treatment was discontinued upon the report of pregnancy in all cases. Mean maternal age was 27.6 years (range 19-43) and mean duration of UST exposure prior to the reported pregnancy was 76±62.1 weeks. Pregnancy outcomes were reported for 24 of 26 pregnancies, including 15 (62.5%) live births (LBs), 4 (16.7%) spontaneous abortions (SAs), and 5 (20.8%) elective abortions. All 4 SAs occurred in the 1st trimester. Mean maternal age was older for pts who had SAs (33.0±2.94 years) vs. LBs (27.6±3.75 years) and median UST treatment duration was longer for pts who had SAs (80 weeks) vs. LBs (56 weeks). Among the LBs, there were no congenital anomalies; 1 infant had a single episode of transient hypoglycaemia treated with oral supplement. No safety signals emerged with neonatal outcomes with gestational age of 38.2±1.3 weeks (n=12), mean 5 min-APGAR of 9.8±0.45 (n=5), and mean birth weight of 6.6±1.6 pounds (n=13).
**Conclusions:** While the rate of SA's was generally comparable to the rate previously reported in PsO data, the small number of pregnancies among women with CD with prenatal exposure to UST precludes definitive interpretation of the data. In this case series, SAs were associated with older maternal age, and longer duration of UST exposure prior to the reported pregnancy was not associated with adverse outcomes. However, the limited available data from the UST CD program requires additional research to determine pregnancy and newborn safety.
[1]Cather JC, Rahawi KW, Schaufelberger BW, Chan D, Horn EJ, Goyal K. Pregnancy outcomes in women exposed to ustekinumab in the psoriasis clinical development program. *Journal of the American Academy of Dermatology*. 2014;70(5).

**Funding Agencies:** Janssen Research & Development, LLC funded this study

A110
**USE OF PROBIOTICS, PREBIOTICS AND DIETARY FIBRE SUPPLEMENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE**
M. Silva[1], R. Chibbar[3], E. Wine[2], J. Walter[1], K. Goodman[1], A.H. Keshteli[1], R.S. Valcheva[1], L.A. Dieleman[1]

1. Medicine, University of Alberta, Edmonton, AB, Canada; 2. Pediatrics, University of Alberta, Edmonton, AB, Canada; 3. Gastroenterology, University of British Columbia, Kamloops, BC, Canada

**Background:** Inflammatory bowel diseases (IBD) are chronic inflammatory conditions of the intestines likely induced by abnormal immune response to resident intestinal bacteria in genetically susceptible hosts. Probiotics, prebiotics and dietary fibres alter the gut microbiota and improve its function, thus potentially counteracting the development of inflammation. Although the role of these compounds in the prevention and management of IBD is relatively understudied, anecdotal evidence suggests widespread, undocumented use of these supplements by patients. Investigating the use of probiotics and prebiotics by IBD patients and association with disease severity may allow for optimization of therapy and improved clinical outcomes.
**Aims:** To assess if the self-motivated intake of probiotics, prebiotics and dietary fibre supplements is

associated with the disease severity in patients with IBD.
**Methods:** We conducted a cross-sectional study of patients with a diagnosis of IBD in the University of Alberta IBD clinic. Using a 20-item questionnaire we collected data from patients on demographics, disease characteristics and knowledge and use of probiotics, prebiotics and dietary fibre supplements. We used a chart review to ascertain the occurrence of flares, disease duration and objective markers of inflammation such as fecal calprotectin (FCP) as indicators of disease severity.
**Results:** In this study, 100 participants (45% females) with a known diagnosis of IBD (47% Crohn's disease, 34% ulcerative colitis, 19% IBD-unclassified) completed questionnaires. Large proportions of participants were knowledgeable about probiotics (88%) and dietary fibres (76%), but less about prebiotics (42%). The majority of users had Crohn's disease (42% CD vs. 35% UC, p=0.33). 66% of surveyed patients had used these products as an alternate therapy. Disease flares in the last two years did not have an effect on usage (73% users vs. 71% non-users, p=0.8). The use of alternative therapies was higher in patients with longer history of IBD (77% in those with a duration >5 years vs. 22% in those with a duration <5 years, p=1.0). Close to half of patients (48%) with a fecal calprotectin (FCP) >250 µg/g (an indicator of acute disease) during the preceding six months reported supplement use, compared to 52% with FCP values below this value (P=0.11).
**Conclusions:** This study shows that a large proportion of IBD patients are interested in alternative therapies for IBD. Increased flare frequency and objective markers of inflammation did not have an effect on usage. However, longer disease history was the main factor influencing the search for a "cure" by the patients. These microbiota-altering strategies have the ability to affect disease outcomes, therefore clinicians and researchers should identify and document their use.

**Funding Agencies:** CIHR

A111
**ANALYSIS OF GUT MICROBIOME OF HEALTHY INDIVIDUALS THAT GO ON TO DEVELOP CELIAC DISEASE**
L. Bedrani[2], W. Turpin[2], O. Espin-Garcia[2], M. Smith[3], D. Guttman[2], W. Xu[2], K. Croitoru[1]

1. Mount Sinai Hospital, Toronto, ON, Canada; 2. University of Toronto, Toronto, ON, Canada; 3. Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada

**Background:** Celiac disease (CeD) is characterized by inflammation of the small intestine due to an intolerance to the gliadin fraction of gluten. Studies have identified a strong genetic component with disease. Several genetic variants have been located within genes of the HLA region, in fact, 85-95% of CeD subjects carry at least one variant of the HLA-DQ2 and/or HLA-DQ8 allele.However, carriers of these variant do not necessarilydevelop the disease. Indeed, although about 40% of the general population are thought to carry the HLA risk allele, only 2-5 % of healthy carriers will develop CeD over time. Recent findings suggest that the microbiota is a contributing factor toward the onset of CeD, however no preexiting celiac microbial signature has been identified.
**Aims:** In this study, we assess the pre-disease fecal microbiome composition of CeD patients.
**Methods:** As part of the ongoing GEM Project, we identified 15 subjects who self reported developing CeD. The diagnosis of CeD was supported by the presence of at least one genetic variant associated with CeD. Genotyping was performed using the HumanCore-EXOME chip and imputed to the 1KG genome imputation panel. Seven subjects had bacterial 16S rDNA from stool sequenced using MiSeq Illumina platform after amplification of the V4 hypervariable region. Closed reference operational taxonomic unit picking was performed against GreenGenes database (v 13_8) using QIIME (v1.9) pipeline.Four controls matched for Age, gender, and DQ2.2, DQ2.5, DQ4, and DQ8 allele. The relative abundanceof 230 taxa were compared using a conditional logistic regression. Covariates of the model included total number of reads per sample.
**Results:** Relative abundance of the genus Coprococcus and of an unknown genus of the Peptostreptococcacae family were higher in the CeD individuals (p <0.05). Alpha diversity, as assessed by the Shannon index was similar between the two groups.
**Conclusions:** These findings suggest an increase in Coprococcus and of an unknown genus of the Peptostreptococcacae family in prediseasesamples of CeD patients, although the p values did not survive correction for multiple testing. The potential implication of these difference remain to be confirmed but suggest the possibility of a microbiome driven initiation of disease.

Submitted on behalf of behalf of the CCC IBD GEM Project research team.

**Funding Agencies:** CCC, CIHR

A112
**THE VALIDITY OF PATIENT-LED SELF-SCREENS FOR IDENTIFYING MALNUTRITION IN INFLAMMATORY BOWEL DISEASE**
T. Eslamparast[1], K. Farhat[2], L. Taylor[3], N. Shommu[4], A. Kumar[5], Q. Fitzgerald[6], K. Kroeker[1], M. Raman[3], P. Tandon[2]

1. Medicine, University of Alberta, Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada; 5. University of Calgary, Calgary, AB, Canada; 6. University of Calgary, Calgary, AB, Canada

**Background:** Malnutrition is common in Inflammatory Bowel Disease (IBD) and is associated with significant morbidity and mortality. Identification of high-risk patients using an efficient, and sensitive screen is the first step to dietitian referral for nutritional assessment and intervention.
**Aims:** To determine the validity of patient led self-screens against a dietitian-led subjective global assessment (SGA) to detect malnutrition in IBD patients.
**Methods:** Adult patients were prospectively recruited from IBD clinics in Edmonton and Calgary. Patients completed 4 self-screening questionnaires: abridged Patient-generated Subjective Global Assessment (abPG-SGA), Malnutrition Universal Screening Tool (MUST), Canadian Nutrition Screening Tool (CNST) and Malnutrition Screening Tool (MST). A dietitian blinded to the results of the screens carried out a gold standard nutritional assessment using the SGA.
**Results:** A total of 95 IBD patients (60 Crohn's (CD) and 35 Ulcerative colitis (UC)), 52% male were assessed. According to Harvey-Bradshaw Index and partial Mayo scores, 14% of CD and 28% of UC patients had moderate to severe disease. The most common symptoms affecting dietary intake in this patient population were diarrhea (33%), pain (32%), poor appetite (24%) and fatigue (22%). According to the dietitian –led SGA, 21% of patients (15% Crohn's, 31% UC) were moderately to severely malnourished. Patients classified themselves at moderate to high risk of malnutrition in 50% of cases (abPG-SGA), 37% (MUST), 15% (CNST), 21% (MST). Of the 4 screening tools, the abPG-SGA had the best test characteristics (see Table 1).
**Conclusions:** The abPG-SGA is a promising nutrition screening tool in patients with IBD. It is time-efficient and can be completed by patients in the waiting room. With the high sensitivity and high negative predictive value for malnutrition detection, all patients who screened at risk of malnutrition would be appropriately referred for further assessment. This tool has been successfully utilized in other chronic disease populations. Future clinical practice should integrate the abPG-SGA into routine IBD nutrition screening.

Measures of validity of the abPG-SGA, MUST, CNST and MST against the dietitian-administered SGA in IBD

| Patient-led self-screens | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| abPG-SGA | 100 | 64 | 42 | 100 |
| MUST | 55 | 68 | 31 | 85 |
| CNST | 45 | 85 | 45 | 85 |
| MST | 20 | 87 | 29 | 80 |

abPG-SGA abridged patient generated subjective global assessment, MUST malnutrition universal screening tool, CNST Canadian nutrition screening tool, MST malnutrition screening tool, SGA subjective global assessment, PPV positive predictive value, NPV negative predictive value

**Funding Agencies:** None

A113
**LINKING GENE-ENVIRONMENT INTERACTIONS IN IBD: VITAMIN D-MEDIATED REGULATION OF AUTOPHAGY**
L.H. McGillis[1], S. Johnson[1], D. Bronte-Tinkew[1], F. Dang[2], D. Philpott[3], N. Jones[1]

1. The Hospital for Sick Children, Toronto, ON, Canada; 2. Gastroenterology, The Hospital for Sick Children, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada

**Background:** The incidence of IBD has risen dramatically over the past decade, indicating a role for environmental factors in disease onset. Growing evidence from animal and human studies indicate that vitamin D deficiency is an important environmental factor contributing to IBD pathogenesis, although the exact mechanism involved remains unknown. Autophagy is a pathway that has gained interest for its recently established role in IBD pathogenesis. Previously in our lab, we have shown that inducing vitamin D deficiency in wildtype C57Bl/6 mice causes a significant down-regulation of autophagy proteins ATG16L1 and LC3II in the intestine.
**Aims:** We aim to elucidate the relationship between vitamin D deficiency and IBD by exploring the effect of vitamin D on intestinal autophagy. We hypothesize that vitamin D deficiency plays a role in the dysregulation of autophagy in the intestine.
**Methods:** To complement our previous findings and to directly assess the effect of vitamin D on intestinal epithelial cells and autophagy, we employed *in vitro* experiments using murine intestinal epithelial (MODE-K) cells and murine intestinal organoids. Cells were incubated with increasing concentrations of the active form of vitamin D. Western blotting was performed to evaluate autophagy markers ATG16L1 and LC3II, as well as the vitamin D receptor (VDR), a vitamin D responsive gene.
**Results:** As expected, a significant and dose-dependent increase in VDR expression was detected in cells incubated with vitamin D. Furthermore, a trend towards increased ATG16L1 was detected in vitamin D treated cells.
**Conclusions:** Our findings suggest that vitamin D upregulates the autophagy protein ATG16L1 providing a potential mechanism by which vitamin D deficiency modulates IBD pathogenesis. Given this interesting interaction between vitamin D and autophagy, the next step of this project is to assess the effect of vitamin D deficiency in the context of IBD susceptibility Nod2 mutations.

**Funding Agencies:** CCCOGS, Restracomp

A114

**SYSTEMATIC REVIEW AND META-ANALYSIS: ENDOSCOPIC AND HISTOLOGIC PLACEBO RATES IN INDUCTION AND MAINTENANCE TRIALS OF ULCERATIVE COLITIS**

C. Ma[1], L. Guizzetti[2], R. Panaccione[1], R. Fedorak[3], C.E. Parker[2], T. Nguyen[2], R. Khanna[4], B.G. Feagan[4], V. Jairath[4]

1. University of Calgary, Calgary, AB, Canada; 2. Robarts Clinical Trials, London, ON, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. Western University, London, AB, Canada

**Background:** Treatment targets in ulcerative colitis (UC) have evolved to include normalization of objective endoscopic and histologic endpoints. Minimizing the endoscopic and histologic placebo response and remission rate is critical for the conduct of efficient randomized controlled trials (RCTs) and development of new treatments, in order to maximize ability to detect differences between active comparator and placebo.
**Aims:** To quantify the endoscopic and histologic placebo response and remission rates in induction and maintenance UC RCTs and to identify trial design factors influencing these rates.
**Methods:** MEDLINE, EMBASE, and the Cochrane Library were searched from inception through March 1, 2017 for placebo-controlled RCTs of adult patients with UC treated with aminosalicylates, immunosuppressants, corticosteroids, biologics, and oral small molecules. Endoscopic and histologic placebo response and remission rates for induction and maintenance trials were pooled using a random-effects model. Patient- and trial-level covariates were evaluated by constructing stratum-specific rates of placebo response/remission and by random-effects meta-regression analysis.
**Results:** Placebo endoscopic response/remission rates were reported in 45 induction and eight maintenance trials; placebo histologic response/remission rates were reported in nine induction trials. Pooled estimates for placebo induction endoscopic remission, induction endoscopic response, and maintenance endoscopic remission rates were 25% [95 confidence interval (CI): 22-30%], 36% [29-43%], and 20% [16-24%], respectively. The pooled histologic remission rate in induction trials was 16% [10-25%]. Disease severity, disease duration, trial setting, trial phase, class of active comparator, trial follow-up duration, and endoscopic subscore criterion for trial inclusion were not predictive of placebo endoscopic or histologic remission rates.
**Conclusions:** Pooled placebo endoscopic and histologic response and remission rates vary according to whether trials are designed for induction or maintenance. Potential strategies to further reduce these rates include standardization of histologic scoring as well as the definitions used for response and remission.

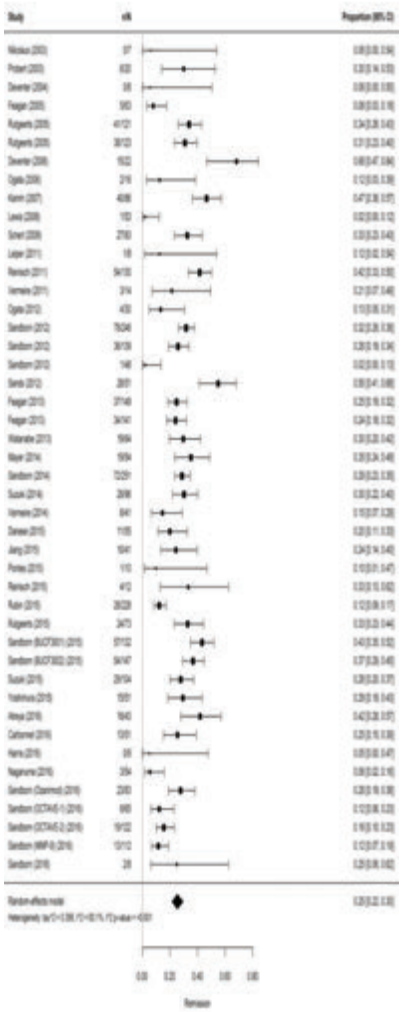


**Figure 1:** Forest plot of induction trials reporting placebo endoscopic remission rates, pooled using random-effects model.

**Funding Agencies:** None

A115

**CLINICAL, RADIOGRAPHIC, AND ENDOSCOPIC REMISSION WITH VEDOLIZUMAB TREATMENT IN CROHN'S DISEASE**

P. Kotze, C. Ma, A. Almutairdi, A. Al-Darmaki, S. Devlin, G.G. Kaplan, C. Seow, K.L. Novak, C. Lu, J. Ferraz, M.J. Stewart, M.c. Buresi, M. Mathivanan, J. Heatherington, M. Martin, R. Panaccione

Inflammatory Bowel Disease Unit, University of Calgary,

Calgary, AB, Canada

**Background:** Vedolizumab is a gut-specific alpha-4-beta-7 integrin antagonist that has demonstrated efficacy in induction and maintenance of clinical response and remission in Crohn's disease randomized controlled trials.
**Aims:** To evaluate the symptomatic and objective response and remission rates achieved with vedolizumab therapy in Crohn's disease in the real-world setting.
**Methods:** A retrospective cohort study was performed at the University of Calgary of adult (≥18 years) CD patients receiving vedolizumab induction between 2012 and 2017. All patients received standard induction therapy with vedolizumab 300mg IV at weeks 0, 2, and 6 and were subsequently advanced onto a scheduled maintenance vedolizumab IV regimen. The primary outcome was achievement of clinical or objective remission at 3, 6, and 12 months after induction. Clinical remission was defined by complete absence of symptoms and no need for corticosteroids. Objective remission was defined by achievement of steroid-free endoscopic mucosal healing or complete normalization of radiographic appearance on contrast-enhanced ultrasound or CT/MR enterography.
**Results:** We identified 122 CD patients treated with vedolizumab. Mean follow-up was 43.4 weeks (SD 30.8 weeks). 68.9% (84/122) of patients had previously failed anti-TNF therapy; 18.9% (23/122) of patients had failed at least three previous biologic therapies. Steroid-free clinical remission at 3 months, 6 months, and 12 months was 19.8% (22/111), 22.1% (21/95), and 22.1% (15/68), respectively. Steroid-free objective remission occurred in 11.5% (6/52), 21.2% (14/66), and 18.9% (7/37) patients at 3, 6, and 12 months, respectively. Mucosal healing on endoscopy was achieved by 22.2% (6/27), 33.3% (14/42), and 25.9% (7/27) of patients at 3, 6, and 12 months, respectively. Thirty-three patients (27.0%) required dose escalation during maintenance therapy to 300mg IV every 4 weeks; 23 patients required dose escalation to optimize primary response and 10 patients required dose escalation for secondary loss of response.

An adverse event was reported in 35 patients (28.7%). The most common adverse events were infections (16/122, 6.6%) and infusion reactions (8/122, 6.6%). Serious adverse events requiring drug discontinuation or hospitalization were reported in 8 patients (6.6%). Two deaths occurred in the cohort: one patient developed cholangiocarcinoma in the context of pre-existing primary sclerosing cholangitis and a second patient died from metastatic renal cell carcinoma which had been diagnosed prior to vedolizumab.
**Conclusions:** In this cohort of patients with highly refractory CD, vedolizumab was effective for inducing steroid-free clinical, endoscopic, and radiographic remission.

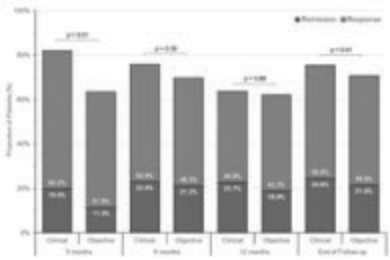


**Figure 1:** Clinical and objective response and remission with vedolizumab

**Funding Agencies:** None

A116
**LOSS OF RESPONSE TO VEDOLIZUMAB MAINTENANCE THERAPY IN CROHN`S DISEASE**
C. Ma, P. Kotze, A. Almutairdi, A. Al-Darmaki, S. Devlin, G.G. Kaplan, C. Seow, K.L. Novak, C. Lu, J. Ferraz, M.J. Stewart, M.c. Buresi, M. Mathivanan, J. Heatherington, M. Martin, R. Panaccione

Inflammatory Bowel Disease Unit, University of Calgary, Calgary, AB, Canada

**Background:** Vedolizumab is a gut-specific alpha-4-beta-7 integrin antagonist that has demonstrated efficacy in induction and maintenance of clinical response and remission in Crohn's disease randomized controlled trials.
**Aims:** To evaluate the long-term maintenance of response achieved with vedolizumab therapy in Crohn's disease in the real-world setting.
**Methods:** A retrospective cohort study was performed at the University of Calgary of adult (≥18 years) CD patients responding to vedolizumab within 6 months of standard induction therapy (vedolizumab 300mg IV at weeks 0, 2, and 6) followed by a scheduled maintenance vedolizumab IV regimen. The primary outcome was composite loss of response (LOR) in follow-up, defined by worsening symptoms requiring vedolizumab dose escalation, rescue medical therapy with corticosteroids or immunomodulators, or vedolizumab discontinuation. Survival analysis with Kaplan-Meier plots was performed to assess median time to LOR and probability of LOR in follow-up.
**Results:** 109 CD patients with symptomatic response within 6 months to vedolizumab induction therapy were followed for a mean duration of 46.3 weeks (SD ±31.3 weeks). Mean Harvey Bradshaw Index (HBI) at induction was 6.3 (± 3.2); 68.8% (75/109) of patients had previously failed biologic therapy and 45 patients (41.3%) had previously failed multiple biologic agents.

Composite loss of response occurred in 36 patients (33.0%) in follow-up at a mean time of 35.2 weeks (± 20.9 weeks). Dose escalation of vedolizumab to 300mg IV every four weeks was required in 22 patients (20.1%)

to optimize primary clinical response in the context of ongoing symptoms despite every eight week therapy. Dose escalation for secondary loss of response occurred in 10 patients (9.2%) at a mean time of 38.9 weeks (± 5.0 weeks). Addition of rescue corticosteroids or immunomodulators was attempted in six patients (5.5%). Vedolizumab was discontinued due to loss of response in 22 patients (20.2%); mean time to drug discontinuation was 42.3 weeks (± 23.3 weeks).

At 52 weeks, the probability of developing a composite loss of response was 36.7% [95% CI: 26.6 – 49.2%]. The probability of continuing on vedolizumab therapy at 52 weeks among initial symptomatic responders was 75.6% [95% CI: 62.8 – 84.5%].
**Conclusions:** Over three quarters of patients who respond symptomatically to vedolizumab induction therapy continue on treatment at one year, but 1/3 of patients will experience a loss of response and approximately 20% will discontinue treatment due to loss of response during maintenance therapy.

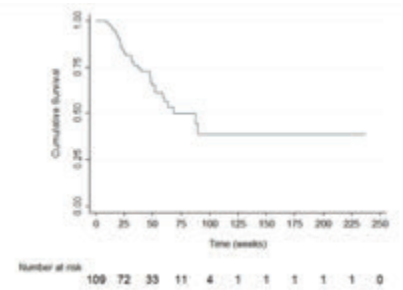



**Figure 1:** Kaplan-Meier survival curve for probability of composite loss of response among 109 Crohn's disease patients with primary clinical response/ remission within 6 months of induction.

**Funding Agencies:** None

A117
**SQUAMOUS CELL CARCINOMA (SCC) IN A PATIENT WITH FISTULIZING CROHN'S DISEASE (CD): AN UNUSUAL CAUSE FOR HYPERCALCEMIA**
M. Rai[1], S. Al Ghamdi[2], K. Erin[2], C. Kenneth[2]

1. Internal Medicine, Queen's University, Kingston, ON, Canada; 2. University of Toronto, Toronto, ON, Canada

**Background:** Fistulizing disease in CD is a common occurrence, affecting up to 50% of CD patients after 20 years. Malignant transformation is a rare complication in perianal fistulas, and has also been reported to arise from enterocutaneous fistulae (EF).
**Aims:** We present a patient with complex fistulizing CD who presented with hypercalcemia secondary to a rapidly enlarging invasive abdominal SCC.
**Methods:** A comprehensive literature search identified 2 cases of SCC associated with EFs in patients with CD. Neither of these patients presented with metabolic abnormalities.
**Results:** A 44-year-old with a history of longstanding ileocolonic penetrating CD underwent multiple small bowel resections and was on home TPN for short gut syndrome. For the past several years her CD was managed with Azathioprine monotherapy, she was biologic-naïve. She presented with a 4-month history of a progressive lower abdominal pain. A CT scan initially revealed a complex mass in the lower abdomen and pelvis measuring 8.3 x 9.6 x 7.5 cm, with a fluid attenuating center encasing small bowel and spreading anteriorly into the abdominal wall. An infectious collection was initially suspected, but she did not respond to 2 courses of antibiotics. She continued to develop progressive lower abdominal pain and increased persistent purulent discharge originating from a long-standing EF. Blood work revealed chronic iron deficiency anemia (Hb 80g/L, ferritin 15 pmol/L) normal white blood cell count and platelets, negative inflammatory markers, low albumin (30 g/L) and elevated corrected calcium (3.9mmol/L). Phosphate, magnesium and PTH levels were normal. MRI revealed the abdominal mass had grown over 2 weeks to 13.6 x 13.1 x 15.4 cm with internal necrosis and invasion to the urinary bladder, colon, anterior abdominal wall, pelvic sidewall and uterus. Percutaneous biopsy showed invasive SCC with negative p16 staining, making HPV-associated SCC less likely. CT scan of her chest did not reveal a lung primary and a bone scan was normal. The origin of the tumour was thought to be her longstanding EF. Due to the extent of the mass, she was not a candidate for surgical intervention. The patient's hypercalcemia was treated with intravenous fluids and bisphosphonates and was patient was started on neoadjuvant chemoradiation.
**Conclusions:** SCC of the anus and skin have been reported in CD. SCC development in Crohn's disease patients with chronic fistulas is a rare entity with a poor outcome. Delayed wound healing, constant mucosal regeneration with high cell turnover rates or immunosuppressive therapies may play a role in malignant transformation. Physicians should be aware of the malignancy potential in patients presenting with persistent pain, unhealing fistulas and metabolic abnormalities, as delayed diagnosis contribute to limited treatment options and poor outcomes.

**Funding Agencies:** None

A118
**PATTERNS AND MOTIVATIONS FOR MARIJUANA USE AMONGST PATIENTS WITH INFLAMMATORY BOWEL DISEASE**
S. Pi[4], G. Rosenfeld[3], A. Wong[1], C. MacDonnell[1], C. Enns[1], R.A. Enns[2], B. Bressler[1], Y. Leung[1]

1. Pacific Gastroenterology Associates, Vancouver, BC, Canada; 2. Medicine, St Paul, Vancouver, BC, Canada; 3. Medicine, UBC, Vancouver, BC, Canada; 4. Internal Medicine, University of British Columbia, Vancouver, BC,

Canada

**Background:** Marijuana contains over 60 compounds which interact with cannabinoid receptors throughout the gastrointestinal (GI) tract. This is the proposed mechanism by which marijuana exerts its effects as an analgesic, appetite stimulant, anti-emetic, and motility modulator. Self-medication for the alleviation of GI symptoms with marijuana is common. Despite its pending legalization, there is a paucity of Canadian data that summarizes the patterns and motivations behind marijuana use amongst patients with IBD.
**Aims:** The purpose of this study is to investigate the patterns and motivations of marijuana use amongst patients with IBD.
**Methods:** An electronic survey was used to assess 161 patients with IBD at a tertiary outpatient gastroenterology clinic. Patients completed the survey in clinic or at home using a web link. Exclusions: Age <18, incomplete surveys, or repeat surveys as evidenced by IP address. The short-inflammatory bowel disease questionnaire (SIBDQ) was used to evaluate quality of life (QoL).
**Results:** *Patterns of use.* Amongst patients with UC and CD, 44/71 (62%) and 75/89 (84%) of patients report using at some point in their life with 25/71 (35%) and 45/89 (51%) using within <6 months, respectively. The most common route of use was inhalation 45/70 (64%). 37/70 (53%) report using at least once per week, with 17/37 (46%) within this group using daily. 16/70 (23%) reported a total duration of use <6 months. 35/70 (50%) have been using >5 years.

*Motivations for use amongst patients using within <6 months.* 37/70 (53%) primarily use for recreation, 27/70 (39%) primarily use for treatment of symptoms, and 5/70 (7%) report using for both. For symptoms, common reasons for use included poor appetite in 15/32 (47%), abdominal pain/bloating in 14/32 (44%), diarrhea in 6/32 (19%), post-prandial discomfort in 6/32 (19%), and nausea in 3/32 (9%). 32/34 (94%) who use marijuana for symptoms agree that it helps. Amongst patients with CD or UC, there was no statistical significant difference between marijuana vs. non-marijuana users in mean SIBDQ scores.
**Conclusions:** Marijuana use is common amongst IBD patients and will likely increase in the near future. Despite 94% of patients endorsing that marijuana helps with their symptoms, this does not translate into a better QoL when compared to non-users. Gastroenterologists are in a unique position to educate patients on the risks and benefits of marijuana use especially with the impending legalization and ongoing health claims from the marijuana industry.

**Funding Agencies:** None

A119
**THERAPUTIC DRUG MONITORING IN PATIENTS WITH ULCERATIVE COLITIS TREATED WITH GOLIMUMAB**
Z. Bahreini[1], J.C. Gregor[1], P. Walton-Mennill[2]

1. University of Western Ontario, London, ON, Canada;
2. University of Western Ontario, London, ON, Canada

**Background:** Anti-tumor necrosis factor (TNF) is a mainstay of treatment in patients with inflammatory bowel disease (IBD) who are refractory to traditional therapies. The most recent anti-TNF that obtained its marketing license for treatment of ulcerative colitis (UC) is Golimumab (GLM). Other anti-TNF drugs in this category include Infliximab and Adalimumab. These 2 drugs have validated algorithms with respect to Therapeutic Drug Monitoring (TDM) and dose optimization strategies however such algorithms are not yet available for GLM. The PURSUIT trial strongly suggested that high GLM trough levels correlated with patients' improvement and resulted in higher rates of clinical response and remission. Although, there is no consensus on what constitutes an adequate trough level, a recent review article in Therapeutic Advances in Gastroenterology, has suggested a trough level of 2.5 $\mu$g/ml to optimize clinical response.
**Aims:** To determine the proportion of patients with ulcerative colitis treated with GLM in the IBD clinic at Western University who have obtained adequate trough levels of GLM.
**Methods:** This is a retrospective cross-sectional analysis of GLM trough levels and antibodies to GLM (ATG) in patients with ulcerative colitis on GLM maintenance therapy treated between December 2015 and October 2017.
**Results:** 40 patients were initiated on GLM in the study period and 11 patients remained on the drug at the end of the study period. TDM was available on 11 patients. The most common initial maintenance regimen was 100 mg every 4 weeks with one patient receiving a lower dose and two patients receiving the drug more frequently. The mean GLM trough level was 2.58 $\mu$g/ml with a median of 1.43 $\mu$g/ml. Only 3/11 (27%) of patients had a trough level above the level suggested for optimal clinical response. All patients did have measurable drug levels although one patient had a level of only 0.1 $\mu$g/ml on 50 mg every 4 weeks that increased to only 0.15 $\mu$g/ml when the dose was doubled. 3 patients with trough levels below 2.5 $\mu$g/ml had their dose doubled, resulting in a mean increase of 1.27 $\mu$g/ml or 142% but only 1/3 obtained a level above 2.5 $\mu$g/ml. None of the patients had measurable levels of ATG.
**Conclusions:** Although ATG appear to be rare with GLM administration, the traditional dosing regiment appears to produce trough levels that may not be adequate for an optimal clinical response. Use of an initial maintenance dose higher than 100 mg every 4 weeks may prove to be a more effective strategy.

**Funding Agencies:** None

A120
**PEDIATRIC TO ADULT TRANSITION OF CARE IN IBD: ESTABLISHING THE CURRENT STANDARD OF CARE AMONGST CANADIAN ADULT ACADEMIC GASTROENTEROLOGISTS**
N. Jawaid[1], N. Bollegala[2]

1. Internal Medicine, University of Toronto, Toronto, ON, Canada; 2. GI, Women's College Hospital, Toronto, ON, Canada

**Background:** Current consensus on pediatric to adult IBD transition is influenced primarily by pediatric gastroenterologists. While transition extends to age 25, there has not been a systematic effort to define current standard of care amongst adult gastroenterologists providing IBD transition care.
**Aims:** The purpose of this study was to establish current transition practices across Canada amongst adult gastroenterologists in high volume GI centers.
**Methods:** Within Canada, only 8 provinces have large pediatric centers, thought to care for the majority of pediatric onset IBD. There are 14 adult GI academic centers across Canada, thought to receive the majority of pediatric to adult IBD transfers of care. Adult gastroenterologists with an interest in pediatric to adult IBD transition were identified through research and clinical networks. A total of 10 semi-structured interviews representing 8 adult GI centers across 6 provinces were conducted to reflect practice patterns at the highest volume transition centers across Canada. Questions focused on the transition process – referral practices, information transfer and access to multidisciplinary resources. Subjective assessments were identified as well as transition-related quality indicators. The interviews were audio-recorded, transcribed and coded for qualitative thematic analysis.
**Results:** Transition practices were divided into a transition clinic (n=3) vs. direct transfer to an adult gastroenterologist (n=5). The majority of transition patients were referred to academic centers with the notable exception of British Columbia. The volume of transferring patients ranged from 12 to 100 per year, most averaged 30-40 patients/year. Transfer of information was optimized with a pediatric-adult electronic medical record system. Only one program did not have access to an IBD nurse but the majority lacked consistent access to a multidisciplinary team. Strongest attributes related to healthcare providers interested in transition and meaningful transfer of information from pediatrics. Major areas for improvement included increased resource allocation. All participants agreed that a consensus-based guideline standardizing adult-phase transfer and transition would be beneficial. Potential quality indicators included adherence, wait time, depression/anxiety scores and patient education.
**Conclusions:** This Canadian survey of adult gastroenterologists representing high volume adult IBD transition centers reveals that practice patterns vary but ideally involve a dedicated transition clinic with access to multi-disciplinary resources. A consensus-based guideline and quality indicators may assist in standardizing adult-phase transition and optimizing outcomes.

**Funding Agencies:** None

A121

## ULTRASOUND VERSUS ENDOSCOPY, SURGERY OR PATHOLOGY FOR THE DIAGNOSIS OF SMALL BOWEL CROHN'S DISEASE AND IT'S COMPLICATIONS

N. Bollegala[2], G.C. Nguyen[1]

1. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 2. GI, Women's College Hospital, Toronto, ON, Canada

**Background:** The diagnosis of Small Bowel Crohn's Disease (SBCD) is challenging given poor endoscopic accessibility. Ultrasound (US) represents an accessible, cost-effective, minimally invasive, radiation-free diagnostic option.
**Aims: Primary objective:** To determine the diagnostic accuracy of US in SBCD compared to endoscopic visualization (enteroscopy, VCE or ileocolonoscopy), surgery and/or pathology. **Secondary objective:** To determine the accuracy of US in determining the presence of SBCD-related complications (fistula, abscess, stricture).
**Methods:** MEDLINE, EMBASE and CENTRAL were searched for prospective cohort studies. Full-text review and data extraction were performed by a single reviewer. Studies were assessed for their methodological quality using the QUADAS criteria.
**Results:** 1082 unique references were identified. 20 studies were finally included. All studies were at low-moderate risk of bias. Trans-abdominal US (TAUS) yielded moderately high sensitivity and specificity for the diagnosis of SBCD and its post-operative recurrence. Detection was more accurate for severe post-operative recurrence. The diagnostic accuracy of US in stricture and abscess detection was high. Contrast enhancement improved the detection of abscess. The diagnostic detection of fistulas had moderate accuracy. Entero-enteric and entero-mesenteric fistulas were most accurately identified.
**Conclusions:** US is an accurate radiological modality to diagnose SBCD in those with known or suspected disease. It can be used with success to diagnose post-operative recurrence and can be used accurately to identify complications, especially with the aid of contrast enhancement.

**Funding Agencies:** None

A122

## CHARACTERIZING A LOST-TO-FOLLOW-UP COHORT AMONGST PATIENTS DIAGNOSED WITH PEDIATRIC ONSET INFLAMMATORY BOWEL DISEASE IN THE PEDIATRIC TO ADULT TRANSFER OF CARE.

N. Bollegala[5], E.I. Benchimol[1], A. Griffiths[2], A. Kovacs[7], H. Steinhart[3], X. ZHAO[6], G.C. Nguyen[4]

1. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. Hospital for Sick Children, Toronto, ON, Canada; 3. Mount Sinai Hospital, Toronto, ON, Canada; 4. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 5. GI, Women's College Hospital, Toronto,

ON, Canada; 6. University of Ottawa, Ottawa, ON, Canada; 7. Oregon Health and Science University, Portland, OR

**Background:** Pediatric onset inflammatory bowel disease (IBD) is a high-risk phenotype that requires transfer to an adult gastroenterologist at age 18. Under-developed emotional and cognitive skills in the transition-aged population can affect adherence rates, especially during periods of remission. A recent study evaluating patients with pediatric onset IBD requiring transfer of care to an adult gastroenterologist identified a relatively large lost to adult gastroenterology (GI) follow-up (LTF) group.
**Aims:** The purpose of this study was to characterize those patients with pediatric onset IBD who are LTF in the first five years of adult care and identify risk factors for their non-compliance.
**Methods:** This was a population-based retrospective cohort study using health care administrative data from Ontario, Canada. A cohort of patients with pediatric onset IBD was identified and health resource utilization during a 5-year post-transfer period was analyzed. Patients LTF were compared to those patients actively followed by a gastroenterologist in terms of health resource utilization. The primary outcome of this study comprised Emergency Department (ED) utilization. Secondary outcomes included hospitalizations, surgeries, ambulatory visits, endoscopic and radiological investigations.
**Results:** 2043 patients with pediatric onset IBD were identified. 1696 were followed by an adult GI in the post-transfer period. 306 patients were never seen by an adult GI. 41 patients were never seen by any adult health care provider in the post-transfer period. Patients in the loss to follow-up group were significantly younger, more likely to be male, have ulcerative colitis (UC) and reside in an urban environment. Overall, there were no significant differences found in ED use, total ambulatory care visits (aside from the expected drop amongst GI follow-up), hospitalizations, endoscopic procedures or radiological procedures between exposure groups. Multivariable negative binomial logistic regression revealed that the LTF group was less likely to be seen in the ED and admitted to hospital.
**Conclusions:** A relatively large LTF group with pediatric onset IBD was characterized in this study. 5-year follow-up reveals no evidence of increased health resource utilization. More work is needed to further define this population, identify barriers to follow-up and whether outcomes such as quality of life, productivity etc. are affected by their non-compliance.

**Funding Agencies:** CCC

A123
**PERINATAL FACTORS AND RISK OF INFLAMMATORY BOWEL DISEASE IN THE OFFSPRING: A SYSTEMATIC REVIEW AND META-ANALYSIS**
F. Gentilcore[1], M. Chartier[1], M. Rousseau[2], S. Girard[1], S. Wei[1], A. benedetti[3], A. Nuyt[1], P. Jantchou[1]

1. Gastroenterologie, Hépatologie et Nutrition, CHU Ste-Justine, Montreal, QC, Canada; 2. INRS-Institut Armand-Frappier, Laval, QC, Canada; 3. Departments of Medecine and Epidemiology, Biostatistics & occupational Health, McGill University, Montreal, QC, Canada

**Background:** It has been hypothesized that exposure to environmental factors during critical windows of immune maturation may interfere with the immune system development and influence the subsequent risk for inflammatory bowel disease (IBD).
**Aims:** To summarize the available data of the literature and perform a meta-analysis regarding the association between perinatal factors and the subsequent risk for Crohn's disease (CD) or ulcerative colitis (UC) in the offspring.
**Methods:** We systematically searched the following electronic databases: Embase, PubMed, Medline, EBM Reviews to identify observational studies on the association between perinatal factors and IBD in the offspring up to April 2017. A meta-analysis was performed using RevMan 5 to obtain a combined effect measure and the 95% CI with random effects models. Pooled adjusted odds ratios (OR) with 95% confident intervals were calculated by combining the inverse of their variance for each factor.
**Results:** Twelve studies (5 cohort studies and 7 case-control studies) were identified out of 1852 studies reviewed. Maternal diabetes during pregnancy was associated with an increased risk for CD **[OR(95% CI): 1.67 (1.18-2.36)]** but not UC. Maternal age >35 years was associated with an increased risk for CD **[1.65 (1.02-2.66)]** but a decrease risk for UC **[0.92 (0.86-0.98)].** The following perinatal factors were not associated with the risk for IBD: maternal infection, pre-eclampsia, birth weight, preterm, and low APGAR score. (See Table 1.)
**Conclusions:** This meta-analysis suggests opposite associations between advanced maternal age and risk for CD or UC. In addition, diabetes during pregnancy appears to be associated with an increased risk for CD in the offspring.

Odds ratio, 95% confident intervals number of studies per factors

| Factors | Inflammatory Bowel Diseases | Crohn | Ulcerative Colitis |
|---|---|---|---|
| Infections during pregnancy | N=3, I2=86% 1.52 (0.58-3.99) | N=3, I2=72% 1.46 (0.44-4.86) | N=3, I2 =52% 1.65 (0.89-2.71) |
| Preeclampsia | N= 4, I2 =0% OR: 0.95 (0.69-1.31) | N= 2, I2 =91% 2.30 (0.20-27.02) | N=2, I2 =0% 1.02 (0.50-2.10) |

| | | | |
|---|---|---|---|
| Diabetes | N=2, I2 =0% 1.00 (0.41-2.47) | N=2, I2 = 0% 1.67 (1.18-2.36) | N=2, I2 =0% 0.98 (0.66-1.45) |
| Maternal age >35 years | N=5, I2 =12% 1.08 (0.87-1.33) | N=4, I2 =82% 1.65 (1.02-2.66) | N=2, I2 =0% OR: 0.92 (0.86-0.98) |
| Preterm Birth | N=8, I2 =48% 0.98 (0.80-1.20) | N=7, I2 =0% 0.93 (0.78-1.09) | N=5, I2 =0% 0.83 (0.63-1.11) |
| Birth weight < 2500g | N=4, I2 =0% 1.07 (0.87-1.31) | N/A | N/A |
| APGAR score < 8 | N= 2, I2 =0% 1.12 (0.75-1.66) | N=2, I2 =0% 1.11 (0.74-1.66) | |

**Funding Agencies:** None

A124

**UNDERSTANDING THE ROLE OF LRBA AND CHARACTERIZING THE PHENOTYPE OF LRBA-DEFICIENCY IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

Z. Omary[3], J. Pan[4], N. Warner[7], R. Murchie[5], C. Guo[6], F. Safi[1], J. Brumell[2], A. Muise[1]

1. Hospital for Sick Children, Toronto, ON, Canada; 2. Cell Biology, Hospital for Sick Children, Toronto, ON, Canada; 3. Biochemistry, University of Toronto, Toronto, ON, Canada; 4. SickKids, Toronto, ON, Canada; 5. SickKids, Toronto, ON, Canada; 6. SickKids, Toronto, ON, Canada; 7. Sickkids, Toronto, ON, Canada

**Background:** The prevalence of inflammatory bowel disease (IBD) in the Western hemisphere is increasing. IBD is a family of autoimmune diseases causing inflammation in the gastrointestinal tract which typically presents in two major forms: Crohn's disease or ulcerative colitis. The pathogenesis of these diseases is driven by several factors including environmental stress, dysbiosis of the gut microbiota, and genetic susceptibility.

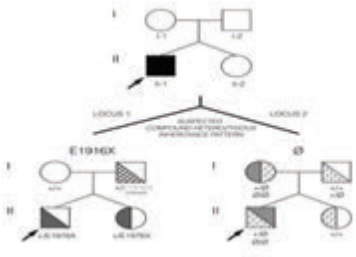
Recent research has identified a growing number of IBD-risk loci in various genes, including a novel interesting IBD-related gene is *Lipopolysaccharide Responsive Beige-Like Anchor* (*LRBA*). LRBA-deficiency results in immunodeficiency, autoimmunity, defective B cell differentiation, and hypogammaglobulinemia. In our own pediatric patient cohort, we have identified a patient with a rare damaging variant in *LRBA* (chr4: CC/AA; E1916X, exon 36) through whole-exome sequencing. Little is known about the function of LRBA but there seems to be a consensus that LRBA may be a scaffold or adaptor protein and has a role in endosomal trafficking.

**Aims:** To study the significance of this mutation on the functional role of LRBA and its potential effect on deregulating autophagy is being investigated.

**Methods:** BioID biotinylation tagging experiments were performed on HEK293T cells overexpressing FLAG-LC3B, which identified LRBA as one of the highest fidelity hits among the many autophagic proteins. This interaction will be confirmed by performing co-immunoprecipitation. To characterize the phenotype of LRBA-deficiency, apoptosis assays on HAP1 LRBA-KO cell line will be performed. In addition, immunofluorescence and staining for autophagy markers, such as LC3B and p62 will be performed to determine if LRBA-deficient cells have an autophagy defect.

**Results:** The BioID results indicated that LC3B may be in close proximity to LRBA. We suspect that LRBA co-localizes with LC3B and that they may interact in a larger complex during the fusion of the endosome and autophagosome. Furthermore, the phenotype in the HAP1 LRBA-KO cell line shows a morphological difference compared to the HAP1 wildtype cell line. More studies will be performed to confirm an apoptotic and/or autophagy defect in LRBA-deficient cells.

**Conclusions:** Our data suggest that a loss of LRBA expression may lead to defects in autophagy, which in turn may contribute to the IBD phenotype observed in LRBA-deficient patients.




**Funding Agencies:** CIHRThe Leona M. and Harry B. Helmsley Charitable Trust

A125

**PERICARDITIS AND 5-ASA EXPOSURE IN INFLAMMATORY BOWEL DISEASE: TWO PAEDIATRIC CASE REPORTS**

A. Lozano Ruf[2], T.D. Walters[1], P. Church[1]

1. GI, Hepatology and Nutrition, Hospital For Sick Children, Toronto, ON, Canada; 2. The Hospital for Sick Children, Toronto, ON, Canada

**Aims:** 5-aminosalicylic acid-containing products are often used as first-line treatment in inflammatory bowel disease (IBD). Pericarditis has been reported as a



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rare extraintestinal inflammatory manifestation of IBD and as a side effect of 5-ASA, when it usually occurs soon after starting the drug. Clinical presentations range from asymptomatic pericardial effusions to potentially life-threatening cardiac tamponade. Recognition as a possible side effect of 5-ASA necessitating cessation is important.
**Methods:** We report two paediatric cases presenting with chest pain and fever, elevated cardiac enzymes and electro/echocardiographic evidence of pericarditis. Infectious causes of pericarditis were excluded.
**Results:** One of the patients received 5-ASA for one month prior to developing pericarditis, whereas the other received 5-ASA for eighteen months. In the second case, the patient soon had a flare of colitis symptoms, and so treatment was restarted five days later. Pericarditis symptoms recurred within six days and 5-ASA was immediately stopped with prompt resolution of symptoms. Both patients then went on to receive maintenance therapy with infliximab, with good effect.

**Conclusions:** Pericarditis in inflammatory bowel disease is a rare occurrence with a multifactorial origin. The pathophysiology of 5-ASA induced pericarditis is not completely understood. Treatment includes prompt cessation of the drug, supportive care, and close monitoring for complete resolution of cardiovascular symptoms. Given the common use of 5-ASA in the treatment of IBD, physicians should keep this potentially severe complication in mind.

**Funding Agencies:** CAG

A126
**SERUM ADALIMUMAB LEVELS IN CROHN DISEASE**
M. Gandhi[2], L. Stitt[2], J.C. Gregor[1]

1. Medicine, Los Alamos National Laboratory, London, ON, Canada; 2. Medicine, Western University, London, ON, Canada

**Aims:** Tests measuring serum adalimumab levels are not widely available. We aim to evaluate whether serum adalimumab levels correlate with disease severity in patients with Crohn disease. Additionally, as the test is expensive, we aim to see if clinical and biochemical markers can be used as a surrogate for adalimumab levels.
**Methods:** A retrospective chart review was performed on Crohn disease patients that had a measured adalimumab level. One hundred forty-nine patients were identified between January 2015 and August 2017 at London Health Sciences Center. Disease severity was determined using the Harvey-Bradshaw Index (HBI).
**Results:** Out of 149 patients, 100 were in remission. Mean trough adalimumab level was 8.7 and 6.5 for remission and active disease groups respectively. Patients in remission had a mean weight of 78.4kg compared to 101.4kg in patients with active disease. Serum adalimumab levels correlated with HBI, weight and log CRP. The respective pearson correlation coefficients were r= -0.19 (p=0.018), r= -0.24 (p=0.005), r= -0.40 (p=0.0004). There were no statistically significant correlations between trough adalimumab level and albumin. Nor were there any significant correlations between HBI and weight, albumin or log CRP. Similar results were seen when stratified based on weekly (n=32) or biweekly dosing (n=117).
**Conclusions:** Higher trough adalimumab levels correlated with lower disease activity, lower weight and lower CRP in patients with Crohn disease. Patients with higher disease burden and increased weight may benefit from empiric weekly dosing of adalimumab. These results also lend support for increasing adalimumab dosing in non-responders. Ultimately, larger studies with prospective data may yield more helpful information.

**Funding Agencies:** None

A127
**ANTI-TNF VS SURGICAL MANAGEMENT OF ABDOMINAL PHLEGMON IN CROHN'S DISEASE: A RETROSPECTIVE ANALYSIS**
T. Jeyalingam[2], S. O'Donnell[3], T. Chawla[1], K. Erin[4], G.C. Nguyen[2], M.S. Silverberg[2], A. Steinhart[2], K. Croitoru[2]

1. Department of Medical Imaging, Mount Sinai Hospital, Toronto, ON, Canada; 2. Mount Sinai Hospital Centre for Inflammatory Bowel Disease, Toronto, ON, Canada; 3. Department of Gastroenterology, The Royal London Hospital, Bartshealth NHS Trust, London, United Kingdom; 4. Department of Surgery, Mount Sinai Hospital, Toronto, ON, Canada

**Background:** Penetrating Crohn's disease (CD) can lead to the development of abdominal phlegmon and abscesses. Phlegmon formation can be addressed with antibiotic therapy, percutaneous drainage, or surgical resection. The role of anti-tumor necrosis factor (anti-TNF) treatment in this scenario is less well established. In particular, it is not clear how anti-TNF therapy affects need for surgical resection.
**Aims:** Penetrating Crohn's disease (CD) can lead to the development of abdominal phlegmon and abscesses. Phlegmon formation can be addressed with antibiotic therapy, percutaneous drainage, or surgical resection. The role of anti-tumor necrosis factor (anti-TNF) treatment in this scenario is less well established. In particular, it is not clear how anti-TNF therapy affects need for surgical resection.
**Methods:** A retrospective chart review was conducted of all CD patients over age 18 presenting with abdominal phlegmon or abscess between the years 2000 and 2017 at Mount Sinai Hospital. Patients were excluded if the clinical record was incomplete or they lacked follow up, had perianal or post-operative phlegmon/abscess, or had greater than 2 previous intestinal resections or prior anti-TNF exposure. Patient demographics, treatment history, need for and timing of surgery (and any post-operative complications) were

extracted and statistical analyses performed.
**Results:** Seventy cases of abdominal phlegmon complicating CD meeting inclusion/exclusion criteria were identified. Mean age at CD diagnosis was 21.2 years and average disease duration at phlegmon presentation was 10.5 years. Of 70 cases, initial treatment in 8 (11.4%) involved antibiotics alone, 50 (71.4%) received antibiotics followed by surgical resection within a period of 5.2 months, and 12 (17.1%) received antibiotics followed by anti-TNF. Of those who had first-line anti-TNF, 7 out of 12 (58.3%) went on to require surgery within an average follow up of 5.0 years, while 12 out of 50 (24.0%) of those who had first-line surgery went on to receive anti-TNF therapy within an average follow up of 8.6 years. Thus, patients who received first-line anti-TNF were significantly more likely to require a second intervention than those who had first-line surgery (58.3% vs. 24.0%, P=0.02). Surgical complications were not significantly different between those who did and did not receive pre-operative anti-TNF (28.6% vs. 12.2%, P=0.25).
**Conclusions:** In the management of Crohn's patients with abdominal phlegmon, our data suggests that while pre-operative anti-TNF therapy is safe and may delay surgical intervention, its use does not obviate the need for surgery altogether.

**Funding Agencies:** None

A128
**DIAGNOSTIC YIELD OF CAPSULE ENDOSCOPY AND INFLAMMATORY BOWEL DISEASE SEROLOGY IN PATIENTS WITH ISOLATED COMPLEX PERIANAL FISTULAS**
R. Weng[1], R. Sy[2], B. Macdonald[2], J. McCurdy[2]

1. University of Ottawa Faculty of Medicine, Ottawa, ON, Canada; 2. The Ottawa Hospital, Ottawa, ON, Canada

**Background:** Complex perianal fistulizing disease is difficult to manage and can lead to significant morbidity. When it occurs in the absence of luminal inflammation, isolated perianal fistulizing disease (IPD) may represent an early manifestation of Crohn's disease (CD) or idiopathic cryptoglandular fistulas, referred to as fistula in ano. Currently, there are no diagnostic tests to distinguish between these etiologies, which make treatment decisions difficult.
**Aims:** Our objectives are to 1) investigate if there is an incremental benefit of capsule endoscopy (CE) above and beyond CTE/MRE for detecting small bowel inflammation, and 2) identify the percentage of patients with positive serologic markers for inflammatory bowel disease (IBD).
**Methods:** Consecutive patients referred to a tertiary IBD center with recurrent IPD were included in this observational study. Recurrent IPD was defined as 2 or more episodes of perianal abscesses or persistent perianal fistula drainage for 3 or more months. Patients required complex fistula anatomy by MRI, and a normal luminal evaluation by ileocolonoscopy and CTE/MRE. Patients exposed to non-steroidal inflammatory drugs within 1 month or immunosuppressive medications within 1 year before CE were excluded. Patients underwent CE using PillCam® SB2 and IBD serology from Prometheus Laboratories. CE results were analyzed by Rapid Reader version 2.0 using a predefined data extraction sheet. Diagnosis of luminal CD required one of the following in 1 or more segment(s) of small bowel: diffuse erythema, linear/circumferential ulcers, 3 or more aphthous ulcers, or stenosis.
**Results:** Nineteen patients; 11 males and 8 females, with a median age of 46 years (range 26-80) were included. The fistula anatomy included trans-sphincteric (n=7, 39%) and inter-sphincteric (n=5, 28%). Fistula hyperenhancement was present in 14 patients (78%); and an abscess in 7 (39%). IBD serology was available for 17 patients; 9 (53%) with at least 1 positive marker, 5 (29%) with 2 or more positives, and 2 (12%) with 3 or more positives. Anti-FlaX IgG was the most frequent positive marker. All 19 patients underwent CE without complication. Overall, 3 patients (16%) met our criteria for luminal CD based on presence of 3 or more apthous ulcers. The median Lewis score was 450 (range 17-1518). Two of these patients had IBD serology testing; one had 3 positives, and the other had 0 positives.
**Conclusions:** Based on this observational study in patients with IPD, IBD serological markers are frequently positive, and CE appears to add a small incremental benefit over CTE/MRE for identifying small bowel inflammation.

**Funding Agencies:** None

A129
**THE ROLE OF BACTERIAL HTPG IN HOST-MICROBIOME INTERACTIONS IN CROHN'S DISEASE**
E.C. Finlayson-Trick[1], J. Connors[2], S. Whitehouse[2], A. Stadnyk[1], J. Van Limbergen[2]

1. Microbiology and Immunology, Dalhousie University, Halifax, NS, Canada; 2. Pediatric Gastroenterology and Nutrition, IWK Health Centre, Halifax, NS, Canada

**Background:** The bacterial chaperone high temperature protein G (HtpG), a homolog of eukaryotic heat shock protein 90 (Hsp90), functions to protect bacteria by stabilizing proteins against a variety of environmental stresses. We recently observed increased abundance of HtpG amongst several metagenomic pathways associated with sustained remission in pediatric Crohn's disease patients treated with exclusive enteral nutrition (Dunn *et al.*, 2016). HtpG and other chaperones from several bacteria have been reported to induce the production of CXCL8 in human fibroblasts, endothelial cells, and monocytes (Shelburne *et al.*, 2007). Bacterial heat shock proteins (e.g. Hsp65) have been reported to protect against colitis in mice (Gomes-Santos *et al.*, 2017). Understanding the impact of bacterial HtpG on intestinal immune responses will provide important mechanistic insight into how HtpG


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may promote sustained remission following exclusive enteral nutrition.
**Aims:** To establish the degree of impact that HtpG has on innate immune functions of intestinal epithelial cells.
**Methods:** HT-29 cells (a human colon adenocarcinoma cell line) were treated with *Bacteroides fragilis* recombinant (r) HtpG (2 µg/ml or 10 µg/ml), or media alone for 24 hours. CXCL8 cytokine expression was measured from HT-29 supernatants using an ELISA assay.
**Results:** Preliminary data indicate that lower concentrations of rHtpG result in increased CXCL8 cytokine expression in HT-29 cells. In comparison to the media control, CXCL8 expression in cells treated with 2 µg/ml rHtpG was markedly increased and greater than cells treated with 10 µg/ml rHtpG.
**Conclusions:** We found that lower concentrations of bacterial HtpG, as observed in pediatric Crohn's disease patients unable to sustain remission, resulted in increased expression of CXCL8 in intestinal epithelial cells. These findings may be of particular relevance to the subset of Crohn's disease patients who have an innate immune dysfunction associated with lower neutrophil chemotaxis (Marks *et al.*, 2006).

**Funding Agencies:** CIHR

A130
**CHARACTERIZATION OF GASTROINTESTINAL TRACT PATHOLOGY IN PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY DISORDER (CVID)**
A. Rumman[1], S. Al Ghamdi[1], R. Khan[1], A.A. Bukhari[1], M.A. Scaffidi[1], A. Almazroui[1], M.J. Abunassar[2], S. Betschel[2], S.C. Grover[2]

1. Gastroenterology, University of Toronto, Toronto, ON, Canada; 2. Medicine, St. Michael's Hospital, Toronto, ON, Canada

**Background:** Common variable immunodeficiency disorder (CVID) is the most common symptomatic primary immunodeficiency disorder. Patients with CVID are reported to have a significant burden of infectious and inflammatory gastrointestinal (GI) diseases.
**Aims:** This study aims to characterize the incidence and clinical profile of GI pathology in a cohort of CVID patients.
**Methods:** We conducted a retrospective cohort study of all CVID patients followed at an tertiary care hospital between January 2005 and July 2017. Using a standardized data collection tool, we performed chart reviews to identify CVID patients with GI complaints, infections and medication use, as well as patients undergoing endoscopic investigations. Patients with inflammatory bowel disease (IBD) were identified. Baseline demographic and clinical characteristics relating to CVID stage and treatment were also collected.
**Results:** A total of 106 patients were identified and included in the final analyses. Mean age at study inclusion was 52.8 (standard deviation, SD = 14.8), mean age at CVID diagnosis was 38.7 (SD = 16.0 years) and 43/106 (40.6%) were male. Mean IgG level was 9.0 (SD = 3.6 g/L). Most patients (98.1%) were on IVIG replacement therapy, and 56/106 (52.8%) were on chronic steroid therapy. GI symptoms (abdominal pain, change in bowel habits, or weight loss), were reported by 67/106 (63.2%) patients. GI infections were encountered as follows: C. difficile infection in 4 (3.8%), chronic giardiasis in 14 (13.2%), bacterial enterocolitis in 8 (7.5%), CMV colitis in 3 (2.8%) and H. pylori infection in 4 (3.8%). Proton pump inhibitor use was reported by 29.2% of patients and exposure to an antibiotic to treat a GI-related infection was reported by 37.7% of patients. Seven patients (6.6%) had elevated transaminases. Colonoscopy was performed in 52 (49.1%) patients. Of those, 27 (51.9%) had an inflammatory colitis based on either endoscopic or histologic abnormalities. Based on a standardised review of endoscopic and histologic reports, we classified the disease phenotype as follows: 9 (8.5%) with Crohn disease, 2 (1.9%) with ulcerative colitis, 11 (10.4%) with indeterminate colitis, and 5 (4.7%) with microscopic colitis.
**Conclusions:** Patients with CVID have a significant burden of both infectious and inflammatory GI pathology. Clinical and demographic predictors of developing significant GI pathology have not been identified. Further studies are needed to delineate predictors and outcomes of GI pathology in this patient population.

**Funding Agencies:** None

A131
**HOW EFFECTIVE IS COLONOSCOPIC BALLOON DILATION IN ANASTOMOTIC AND NON-ANASTOMOTIC STRICTURES OF CROHN'S DISEASE?**
W. Alghamdi[1], N. Chande[1], N. Khanna[2], J.C. Gregor[1]

1. Gastroenterology Devision/Department of Medicine, London Health Sciences Centre, Western University, London, ON, Canada; 2. St. Joseph's Health Care London, Western University, London, ON, Canada, London, ON, Canada

**Background:** Stricture formation is a common and challenging complication of Crohn's disease (CD) with a significant impact on disease management. Treatment options include medical therapy, surgical resection or strictureplasty. Another less invasive approach is colonoscopic balloon dilation (CBD).
**Aims:** To assess the efficacy and safety of CBD in our cohort of Crohn's disease patients with strictures.
**Methods:** From January 2006 to March 2016, we conducted a retrospective chart review of CD patients in our practice who underwent CBD. The primary outcomes were technical and clinical success of CBD. Technical success was defined as subjective improvement in the stricture and the ability to pass the scope through it post-dilation. Clinical success was defined as subjective clinical improvement at follow up visits. Secondary outcomes included post-CBD

complication rate, surgery-free survival and repeat CBD-free survival.
**Results:** A total of 123 patients with 152 strictures were included in the analysis. The mean age of the sample patients was 48.5 years (range 20-86). 63.2% of patients were females. Anastomotic strictures were the cause in (52.6%). Medications used at the time of CBD include biologic therapy in 30.3%, immunomodulators (azathioprine, methotrexate and 6-mercaptopurine) in 30,9%, steroids in 27.6% and 5-ASA derivatives in 7.2%. The median dilation diameter was 15 mm. 73% of the procedures had technical success while 88.8% had clinical success. CBD of primary strictures was more likely to achieve technical success (80.6% vs. 66.3%; p=0.047) but not clinical success (90.3% vs. 87.5%; p=0.59). Two patients experienced post-CBD bleeding (requiring hospitalization and blood transfusion) while another two patients experienced self-limited pain. Dilated secondary strictures were more likely to undergo a repeat-CBD (38.8% vs. 31.9%; p=0.38) and post-CBD surgery (28.8% vs. 25%; p=0.6) when compared to primary strictures.
**Conclusions:** Overall, CBD is an effective treatment option for CD strictures with more success in primary strictures. Serious complications were encountered, although not insignificant, at a low rate.

**Funding Agencies:** None

A132
**DEVELOPMENT OF THE TUMMY-CD, A SYMPTOMS-BASED DISEASE ACTIVITY PATIENT REPORTED OUTCOME (PRO) FOR PEDIATRIC CROHN'S DISEASE**
M.B. Crane[1], A. Grant[1], J. Hyams[6], N. Croft[5], D.R. Mack[3], S. Hussey[7], F. Sylvester[8], H.Q. Huynh[2], D. Turner[9], A. Otley[4]

1. Gastroenterology, IWK Health Centre, Halifax, NS, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Pediatrics, University of Ottawa/CHEO, Ottawa, ON, Canada; 4. Pediatrics, Dalhousie University, Halifax, NS, Canada; 5. Queen Mary University of London, London, United Kingdom; 6. Connecticut Children's Medical Center, Hartford, CT; 7. National Children's Research Centre, Dublin, Ireland; 8. UNC School of Medicine, Chapel Hill, NC; 9. Shaare Zedek Medical Center, Jerusalem, Israel

**Background:** In accordance with recent regulatory guidance which mandates patient reported outcomes (PRO) [without a proxy] for use in clinical trials, elucidating the signs and symptoms that children with Crohn's disease deem important when referencing their level of disease activity is important.
**Aims:** We now report the first stage in developing the TUMMY-CD index, a PRO for pediatric Crohn's disease.
**Methods:** Concept elicitation interviews were performed with children and teens who have Crohn's disease and their caregivers in 9 international centers (Canada, USA, Ireland, UK, Israel). Interviews were recorded, transcribed verbatim, and analysed using qualitative analytic techniques. Items were ranked based on frequency of endorsement and rated level of importance according to participants. Items endorsed in over 6% of participants will be carried forward to Phase 2 of study. Disease activity was categorized using the Pediatric Crohn's Disease Activity Index (PCDAI).
**Results:** A population of 59 children aged 4-17 years (52% male, 80% inactive disease, 14% mild disease, 6% moderate to severe disease), and 56 caregivers were interviewed. Of the signs and symptoms reported, 13 were endorsed in over 6% of participants in either the child or caregiver group. The items that will be explored in the next phase of this study, in decreasing order of endorsement are: Abdominal pain (100% child, 83% caregiver), Diarrhea (53% child, 54% caregiver), Fatigue (49% child, 63% caregiver), Appetite (25% child, 36% caregiver), Nausea +/- Vomiting (24% child, 20% caregiver), Bloody Stool (20% child, 34% caregiver), Joint Pain (14% child, 27% caregiver), Weight loss (9% child, 14% caregiver), Perianal Disease (7% child, 4% caregiver), Constipation (5% child, 7% caregiver), Mood (3% child, 13% caregiver), Pallor (3% child, 11% caregiver), and Mouth Sores (3% child, 9% caregiver). No significant difference was found in the symptoms reported by children experiencing higher or lower disease activity, complicated [penetrating and/or stricturing] versus inflammatory disease behavior, or among caregivers with varying levels of education . Children under 7 years had difficulty reporting symptoms, and therefore an Observer Reported Outcome (ObsRO) will be created for this group.
**Conclusions:** From this first stage of the development of the TUMMY-CD Index, 13 signs and symptoms were significantly endorsed by children with Crohn's disease and their caregivers. These items will be explored in a second phase, where vocabulary and response options will be determined. Once validated, the TUMMY-CD Index can supplement objective outcome measures in future clinical trials.

**Funding Agencies:** NASPGHAN Foundation; Investigator-initiated Grant from AbbVie

A133
**THE INCIDENCE OF DEEP REMISSION INCLUDING HISTOLOGIC NORMALIZATION IN LONGSTANDING UC**
S. Shaffer, C.N. Bernstein

University of Manitoba, Winnipeg, MB, Canada

**Background:** The primary treatment goal in UC is to maintain clinical remission, and endoscopic mucosal healing. Up to 40% of those with mucosal healing have persistent histologic inflammation. Reduced histologic inflammation is associated with decreased risks of relapse, hospitalization, corticosteroid use, colectomy, and neoplasia. Some persons with UC may completely normalize their colon histology. It is unknown what patient characteristics, disease extent, or treatment characteristics are associated with histologic normalization and whether normalization can impact on clinical outcomes.

**Aims:** To assess the rate of dysplasia in patients with UC who achieve endoscopic and histologic normalization on at least two consecutive colonoscopies compared to the rest of the cohort.
**Methods:** A retrospective chart review was undertaken, of a referral clinic's patients from 1994 to 2017. Patients included were those diagnosed with UC, with at least 1 colonoscopy undertaken in the referral clinic. Data extracted from the chart included: age, sex, date of diagnosis, date of last follow-up, endoscopic extent of disease, severity of disease, colon histology, medication history, all dysplasia surveillance colonoscopies, and presence/absence of dysplasia. Dedicated GI pathologists then reviewed biopsies to confirm normalization.
**Results:** A total of 350 individuals' charts were reviewed, with 294 meeting the inclusion criteria. 108 patients had at least 1 normal colonoscopy with normal histology. 28 of these 108 had two consecutive normal colonoscopies and histology. Comparing those with 2 normal colonoscopies to all others (including with 1 normal colonoscopy) there was no statistical difference in the medications used, duration of medications or age at diagnosis, but disease duration was longer for those with 2 consecutive normal colonoscopies (20.5 years vs 15.7, p = 0.02). The mean number of colonoscopies was 5.4 for those with two consecutive normal colonoscopies, vs 3.1 (p<0.001). No dysplasia occurred after 2 consecutive normal endoscopies compared to 18 (6.8%) cases of dysplasia in the comparison cohort. For those with at least one normal colonoscopy, 5 (6.3%) developed dysplasia at some point.
**Conclusions:** Persons who develop deep remission manifested by 2 consecutive colonoscopies with normal endoscopy and normal histology have a lower risk of dysplasia (0 in this cohort). Having 1 colonoscopy with normal histology was not protective against developing dysplasia. In persons with 2 consecutive normal colonoscopies by endoscopy and histology dysplasia surveillance intervals should be lengthened.

**Funding Agencies:** None

A134
**ANTI-IL-12/23P40 ANTIBODIES FOR MAINTENANCE OF REMISSION IN CROHN'S DISEASE**
S.C. Davies[1], T. Nguyen[3], J. MacDonald[3], C.E. Parker[2], V. Jairath[2], K. Reena[2]

1. Schulich School of Medicine and Dentistry, London, ON, Canada; 2. Robarts Clinical Trials, London, ON, Canada; 3. Cochrane IBD Group, London, ON, Canada

**Background:** Ustekinumab (CNTO 1275) is a monoclonal antibody that targets the standard p40 subunit of cytokines interleukin-12 and interleukin-23 (IL-12/23p40), which are involved in the pathogenesis of Crohn's disease.
**Aims:** To assess the efficacy and safety of anti-IL-12/23p40 antibodies for maintenance of remission in Crohn's disease.
**Methods:** A comprehensive search of MEDLINE, EMBASE, The Cochrane Central Register of Controlled Trials, and The Cochrane IBD Group Specialized Register through September 2016 was completed. Randomized controlled trials (RCTs) in which monoclonal antibodies against IL-12/23p40 were compared to placebo or another active comparator in adult patients with active Crohn's disease were identified for inclusion.
**Results:** Two RCTs (n=542) met the inclusion criteria. However, the two studies were not pooled due to differences in time points for analysis. One study (n=145) compared doses of 1, 3, and 6 mg/kg of ustekinumab to placebo for 22 weeks. There was no statistically significant difference in remission rates in this study (RR=0.80, 95% CI 0.63 to 1.02, low-quality evidence). However, ustekinumab was statistically superior to placebo in rates of clinical response (RR=0.53, 95% CI 0.36 to 0.79, low-quality evidence). The other included study (n=259) compared doses of 90 mg of ustekinumab administered every 8 weeks and every 12 weeks to placebo for 44 weeks. Ustekinumab was shown superior to placebo in maintenance of remission in both 90 mg every 8 weeks and every 12 weeks (RR= 0.73, 95% CI 0.58 to 0.92, moderate-quality evidence and RR=0.80, 95% CI 0.65 to 0.99, moderate quality evidence respectively). Ustekinumab was also shown to be superior to placebo with respect to clinical response in the 8 and 12 week dosing groups (RR=0.73, 95% CI 0.56 to 0.94, low-quality evidence and RR=0.75, 95% CI 0.58 to 0.97, low-quality evidence respectively). Data on adverse effects was pooled from both studies and showed there was no statistically significant differences in incidence of adverse events (AE) or serious adverse events (SAE) (RR=0.94, 95% CI 0.86-1.03, low quality of evidence and RR=0.69, 95% CI 0.42 to 1.15 respectively).
**Conclusions:** Low to moderate quality evidence suggests that ustekinumab is effective for maintenance of clinical response when administered for 22 and 44 weeks and maintenance of clinical remission when administered for 44 weeks. Ustekinumab appears to be safe with no increased risk of AE's, SAE's or withdrawal due to AE's. Further studies are required to increase the quality of evidence available for the use of ustekinumab in the maintenance of moderate to severe Crohn's disease.

**Funding Agencies:** Cochrane IBD Group and Summer Opportunities Research Program, Schulich School of Medicine and Dentistry

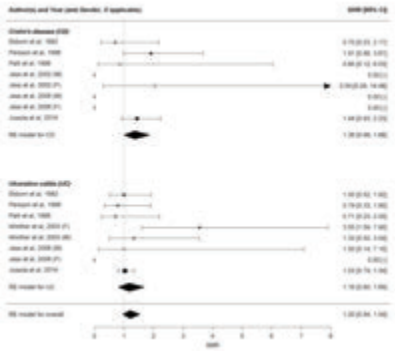
A135
**INCIDENCE OF SUICIDE IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS.**
C. Zhang[3], G. Byrne[2], T. Lee[2], J. Singer[2], D. Giustini[2], B. Bressler[1]

1. Pacific Gastroenterology Associates, Vancouver, BC, Canada; 2. University of British Columbia, Vancouver, BC, Canada; 3. Medicine, University of British Columbia, Burnaby, BC, Canada

**Background:** Patients with inflammatory bowel disease (IBD) have higher incidence of psychosocial disorders including depression. As suicide is the most severe manifestation of depression, we sought to identify if patients with IBD have a higher incidence of suicide through a systematic review/meta-analysis.
**Aims:** To determine the incidence of suicide in IBD and to determine if patients with IBD were more likely to die from suicide compared to control.
**Methods:** Systematic literature search for articles using EMBASE and MEDLINE was conducted to identify studies investigating suicide in IBD. We included studies reporting expected number of death or standarized mortality ratio (SMR) for suicide in IBD. Meta-analysis for Crohns disease and ulcerative colitis was conducted separately, as well as combined.
**Results:** Seven cohort studies were identified through our search strategy and were included in our systematic review/meta-analysis. In our analysis, the SMR for suicide in patients with IBD for all studies included was 1.20 (95% CI 0.94-1.54). The overall pooled SMR for CD and UC were 1.36 (95% CI 0.98-1.88) and 1.16 (95% CI 0.8-1.69) respectively.
**Conclusions:** Patients with Crohn's disease and ulcerative colitis may have an increased risk of suicide. These results highlight the importance physicians must place on ensuring the mental health of patients with IBD is both assessed and treated appropriately.

Descriptive Statistic for Characteristics of Included Studies

| Author | Year | Country | Condition | Gender | Cohort size | Number of overall death | Number of suicide death |
|---|---|---|---|---|---|---|---|
| Winther et al | 2003 | Denmark | UC | M | 541 | 145 | 4 |
| Winther et al | 2003 | Denmark | UC | F | 619 | 116 | 6 |
| Jess et al | 2006 | USA | UC | M | 212 | 36 | 1 |
| Jess et al | 2006 | USA | UC | F | 166 | 26 | 0 |
| Jess et al | 2006 | USA | CD | M | 155 | 30 | 0 |
| Jess et al | 2006 | USA | CD | F | 159 | 26 | 0 |
| Persson et al | 1996 | Sweden | UC | M&F | 1547 | 255 | 5 |
| Persson et al | 1996 | Sweden | CD | M&F | 1251 | 174 | 9 |
| Jess et al | 2002 | Denmark | CD | M | 157 | 39 | 0 |
| Jess et al | 2002 | Denmark | CD | F | 217 | 45 | 1 |
| Ekbom et al | 1992 | USA | UC | M&F | 2509 | 505 | 9 |
| Ekbom et al | 1992 | USA | CD | M&F | 1469 | 179 | 3 |
| Jussila et al | 2014 | Finland | UC | M&F | 16649 | 1805 | 55 |
| Jussila et al | 2014 | Finland | CD | M&F | 5315 | 439 | 20 |
| Palli et al | 1998 | Italy | UC | M&F | 689 | 47 | 3 |
| Palli et al | 1998 | Italy | CD | M&F | 231 | 23 | 1 |



Standardized mortality ratio (SMR) with 95% confidence intervals for all study population, together with the random effects pooled SMR.

**Funding Agencies:** None

A136

**PREDICTING THE NEED FOR MEDICAL RESCUE IN PATIENT ADMITTED WITH ACUTE SEVERE ULCERATIVE COLITIS**

B. Al Ibrahim[2], B. Markandey[2], V. Jairath[1], B. Yan[2]

1. Medicine, Gastroenterology, Epidemiology and biostatistics, Western University., London, ON, Canada; 2. Western University, London, ON, Canada

**Background:** High dose corticosteroids(CS) are the mainstay of treatment for hospitalized patients with acute severe ulcerative Colitis (ASUC), and up to 40% of these cases require further salvage biological therapy or colectomy.
**Aims:** To identify clinical features at the time of hospital admission which predict the need for inpatient medical rescue therapy and to measure quality of in-patient care.
**Methods:** Retrospective chart review of consecutive adult patients with UC admitted to London Health Sciences Center between January 1, 2010 and June 30, 2016. ASUC was defined as exacerbation of symptoms with the need for hospitalization and intravenous CS. Baseline predictors of rescue therapy assessed were the Seo Index, Truelove and Witts Severity Index, White Blood Count, CRP, Pulse, Temperature, and number of bloody bowel movements. Care quality metrics were use of thromboprophlyaxis, stool culture, AXR, sigmoidoscopy within 48 hours and surgical discussion.
**Results:** Eighty-eight patients met inclusion criteria (57% male; mean age 38,5 years). The majority had pancolitis (63%) and were receiving oral steroids (56%) and 5-ASAs (67%) on admission. With just 22% receiving immunosuppressives and 13% anti-TNFs. The mean CRP (74.5), pulse (94.2) and number of bloody bowel movements (11.2) was consistent with ASUC. 51% received salvage rescue therapy with infliximab. The only factor associated with rescue therapy was the baseline Mayo endoscopic score. 68% received thromboprophylaxis, 70% sigmoidoscopy within 48 hours and 82% stool/C.diff culture.
**Conclusions:** The Mayo Endoscopic score was strongly associated with the need for inpatient infliximab salvage therapy. There is room for improvement in the quality of care for inpatients with ASUC.

The results of the univariable associations between the independent variables in both subsets of patients.

| Baseline Evaluation | CS (n=43) | IFX (n = 45) | OR (95% CI) | P Value |
|---|---|---|---|---|
| Seo {mean (SD)} | 214.6 (33.4) | 220.7 (30.4) | 1.01 (0.99, 1.02) | .371 |
| Truelove and Witts – Severe {n (%)} | 34 (81.0%) | 37 (86.1%) | 1.45 (0.46, 4.61) | .528 |
| CRP {mean (SD)} | 70.7 (79.7) | 78.8 (72.8) | 1.00 (1.00, 1.01) | .629 |
| WBC {mean (SD)} | 13.3 (6.6) | 11.4 (5.0) | 0.94 (0.88, 1.02) | .138 |
| Pulse {mean (SD)} | 96.3 (18.3) | 94.9 (23.3) | 1.00 (0.98, 1.02) | .764 |
| Temperature {mean (SD)} | 37.0 (0.8) | 37.1 (0.7) | 1.13 (0.61, 2.07) | .706 |
| Number of bloody BM {mean (SD)} | 10.7 (6.4) | 13.2 (8.6) | 1.05 (0.98, 1.12) | .162 |
| Mayo Endoscopic score {mean (SD)} | 2.23 (0.80) | 2.69 (0.47) | 2.8 (1.1-7.4) | .007 |

**Funding Agencies:** None

A137

**THERAPEUTIC DRUG MONITORING WITH INFLIXIMAB TROUGH LEVELS LEAD TO INCREASED INTERVENTION**

N.C. Stern[2], R. Fedorak[2], K. Wong[2], B.P. Halloran[1], L.A. Dieleman[3], V. Huang[2], F. Peerani[2], K.I. Kroeker[3]

1. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Therapeutic drug monitoring (TDM) of infliximab (IFX) as indicated in patients with loss of response (LOR) (known as reactive strategy) is a widely accepted strategy in the management of patients with inflammatory bowel disease (IBD). Proactive drug monitoring of IFX trough levels has been proposed as a way to pre-empt LOR and hopefully preserve IFX as a therapeutic options. The impact of proactive TDM at week 14, following induction therapy is not well studied.
**Aims:** To compare week 30 remission rates in IFX IBD patients with week 14 TDM to those without TDM, as well as determine the proportion of patients with week 14 TDM that were dose escalated.
**Methods:** This retrospective chart review in which ulcerative colitis (UC) and Crohn's disease (CD) patients 17 years of age or older that were on IFX for at least 30 weeks. Charts were reviewed for objective and subjective assessments of clinical remission, concomitant immunosuppressants and dose changes. Parameters of ± 1 week were allowed for trough level inclusion and ± 1 month for all other markers. Categorical and quantitative data were presented as proportions through a Chi-squared test and the t-test, respectively. All significance is assessed at $p < 0.05$.
**Results:** In total, 240 patients initiated on IFX between January 2015 - June 2017 were identified and 156

patients were included in the final analysis. Eighty-four patients were excluded due to: clinical LOR at week 14 (*n*=1) and patients not on IFX at week 30 (*n* = 83). Clinical remission with TDM was not greater than those without TDM (69.4% - 84.8%; *p* = 0.049). Furthermore, dose escalation in patients was more common in patients with TDM than without TDM (77.3% - 30.4%; *p* < 0.001).
**Conclusions:** In conclusion, proactive TDM was associated with more frequent dose escalation.

| | Therapeutic drug monitoring | No therapeutic drug monitoring | P-value |
|---|---|---|---|
| Age (Mean ± SD) | 29.9 (13.3) | 30.2 (15.5) | 0.919 ‡ |
| Type of IBD (Crohn's) | 26 (59.1) | 76 (67.9) | 0.300 † |
| Dose escalated prior to week 30 (n %) | 34 (77.3) | 34 (30.4) | < 0.001 † |
| Remission at week 30 (n %) | 25 (69.4) | 78 (85.7) | 0.049 † |

† Chi-square; ‡ T-Test

**Funding Agencies:** None

A138
**LONG-TERM OUTCOMES AFTER PRIMARY BOWEL RESECTION IN PEDIATRIC-ONSET CROHN'S DISEASE**
F. Rinawi[1], R. Shamir[2], A. Assa[2]

1. Gastroenterology, hepatology and nutrition, Hospital for sick children, Toronto, ON, Canada; 2. Schneider children's hospital, Petach-Tikva, Israel

**Background:** There is limited evidence on the long-term outcome of intestinal resection in pediatric-onset Crohn's disease (POCD) with no established predictors of adverse outcomes.
**Aims:** We aimed to investigate clinical outcomes and predictors for adverse outcome following intestinal resection in POCD.
**Methods:** The medical records of patients with POCD who underwent at least one intestinal resection between 1990 and 2014 were reviewed retrospectively. Main outcome measures included time to first flare, hospitalization, second intestinal resection and to non-prophylactic biologic therapy.
**Results:** Overall, 121 patients were included. Median follow-up was 6 years (range 1-23.6). One hundred and seven (88%) patients experienced at least one post-surgical exacerbation, 52 (43%) were hospitalized and 17 (14%) underwent second intestinal resection. Of 91 patients who underwent surgery after the year 2000, 37 (41%) were treated with anti-tumor necrosis factor α (anti-TNFα) (not prophylactic) following intestinal resection. Time to hospitalization and to second intestinal resection were shorter among patients with extra-intestinal manifestations (EIMs) (HR 2.7, P=0.006 and HR=3.1, P= 0.03, respectively). Time to initiation of biologic treatment was shorter in patients with granulomas (HR 2.1, P=0.038), while being naïve to anti-TNFα treatment prior to surgery was a protective factor for biologic treatment following surgery (HR 0.3, P=0.005). Undergoing intestinal resection beyond the year 2000 was associated with shorter time to first flare (HR 1.9, P=0.019) and hospitalization (HR 2.6, P=0.028).
**Conclusions:** Long term risk for flares, hospitalization or biologic treatment is significant in POCD following bowel resection. EIMs increase the risk for hospitalization and second intestinal resection

**Funding Agencies:** None

A139
**AGREEMENT OF IB*DOC®* AND *QUANTON CAL®* RAPID LATERAL FLOW-BASED FECAL CALPROTECTIN TESTS WITH ACCEPTED LAB-BASED ASSAYS FOR MONITORING INFLAMMATORY BOWEL DISEASE**
R.T. Sutton[1], C. Prosser[2], N. Dhami[1], D. Sadowski[1], S. van Zanten[1], K.I. Kroeker[1], K. Wong[1], B.P. Halloran[1], R. Fedorak[1], V. Huang[1]

1. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 2. Department of Laboratory Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Fecal calprotectin (FCP) is a useful biomarker for monitoring inflammatory bowel disease, showing good correlation to endoscopic disease activity. Currently used lab tests take 2-4 weeks to return a result, limiting their usefulness. Recently, lateral flow-based rapid tests have been combined with smartphone applications to allow patients to complete FCP testing at home, with their physician receiving the result the same day.
**Aims:** We aim to compare FCP results from two point-of-care test (POCT) devices (IB*Doc*; Buhlmann, *Quanton Cal*; Preventis) in real world use, to two widely accepted lab based methods.
**Methods:** Patients brought first morning stool to the University of Alberta IBD clinic, completed partial Mayo (pMayo) and Harvey-Bradshaw index (mHBI) scores, received training, and performed the IB*Doc* test. A portion of their raw sample was sent to the hospital lab, stored at -20°C, thawed and then analyzed using *Quanton Cal* POCT kits (performed by laboratory staff) and two weight-based lab tests: Immunodiagnostik (ELISA) and Buhlmann Turbo (immunoturbidimetric) assays. Numerical FCP values were tabulated and dichotomized by ≥250 µg/ml (active) or <250 µg/ml (remission). Clinical scores were dichotomized as symptomatic if mHBI≥5 or pMayo≥2.
**Results:** Twenty patients provided raw stool and completed the IB*Doc* test, including 12 (60.0%) females and 9 (45.0%) with Crohn's disease. The median age is 33.5 years (IQR: 29.5 to 37.5). Maintenance medications: 3

(15.0%) taking no medications, 4 (20.0%) on 5-ASA, 4 (20.0%) on immunomodulators, 9 (45.0%) on biologics, of whom 3 (15.0%) were on biologic combotherapy. Median FCP values and IQRs for all four tests are shown in Figure 1. Spearman's correlation with results from Immunodiagnostik was 0.93 for IB*Doc,* 0.89 for *Quanton Cal*, and 0.97 for Buhlmann Turbo. Upon dichotomizing FCP as active or inactive, 18/20 (90%) of results were in agreement between IB*Doc* and Immunodiagnostik, 19/20 (95%) between *Quanton Cal* and Immunodiagnostik, and 19/20 (95%) between IB*Doc* and *Quanton Cal*. However; pMayo/mHBI and FCP were not as agreeable with 12/20 (60%) reaching the same conclusion (symptomatic or asymptomatic) for IB*Doc*, 13/20 (65%) for *Quanton Cal*, and 14/20 (70%) for Immunodiagnostik.

**Conclusions:** There is good correlation between POCTs and lab tests at <250 µg/ml, although correlation was better between the two lab tests. POCTs can *differentiate* disease activity from remission and can be performed remotely, an advantage for rural patients. The quantitative values >250 µg/ml are not reproducible and would be misleading if used to monitor disease *progression*. FCP close to cutoffs should be repeated and does not correlate very well with patient reported symptoms.

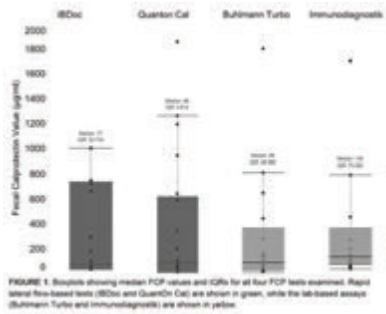



FIGURE 1. Boxplots showing median FCP values and IQRs for all four FCP tests examined. Rapid lateral flow-based tests (IBDoc and QuantOn Cal) are shown in green, while the lab-based assays (Buhlmann Turbo and Immunodiagnostik) are shown in yellow.

**Funding Agencies:** None

A140

**IBD DASHBOARD: AN INNOVATIVE E-HEALTH PROGRAM FOR PROVIDING EQUAL ACCESS TO QUALITY CARE FOR ALL INFLAMMATORY BOWEL DISEASE PATIENTS**

R.T. Sutton[1], E. Wishart[1], N. Dhami[1], D. Sadowski[1], J. Siffledeen[2], M. Sauve[3], R. Hundal[4], K. Ismond[1], S. van Zanten[1], V. Huang[1]

1. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 2. Grey Nuns Hospital, Edmonton, AB, Canada; 3. River City Centre, Fort Mcmurray, AB, Canada; 4. Mortimer Medical, Lethbridge, AB, Canada

**Background:** Individuals with inflammatory bowel diseases (IBD) often live remote to specialized tertiary care centers. In traditional practices, this impedes the close surveillance of symptoms, objective markers of disease (C-reactive protein (CRP), fecal calprotectin (FCP), and optimization of therapies recommended to achieve the best health outcomes. Emerging self-management and e-Health strategies have improved medication adherence and reduced duration and severity of disease flares. Our center developed an innovative eHealth platform, the "IBD Dashboard", a secure, online portal where patients can upload their self-collected data at regular intervals to provide a cross-sectional and longitudinal assessment of disease state. The IBD clinician can modify therapy accordingly in near real-time to prevent disease relapse.

**Aims:** To test the feasibility and impact of the IBD Dashboard for providing optimized care in a virtual environment to IBD patients based upon patient self-reported data.

**Methods:** Physicians across Alberta invited their adult IBD patients to enroll into the study. Patients were instructed to submit clinical scores every month on the IBD dashboard, and complete a home FCP (Buhlmann IBDoc FCP test) at baseline, 3 and 6 months. Those who had elevated FCP repeated FCP 1 and 2 months later. Feasibility questions included ease of use, impact on management decisions of the physician, patient medication adherence, and patient acceptance.

**Results:** A total of 29 patients have consented to the study thus far, including 12 (41.4%) females and 14 (48.3%) with Crohn's disease. The median age is 37.0 years (IQR: 32.0 to 50.0). Medication snapshot: 9 (31.0%) on 5-ASA, 2 (6.9%) on steroids, 6 (20.7%) on immunomodulators, 19 (65.5%) on biologics, and 4 (13.8%) taking no medications. A total of 21 (65.5%) have completed baseline FCP. The median FCP was 276.0 mcg/g (IQR: 64.0 to 956.0), with 11 (52.4%) having an FCP $\geq$250 mcg/g. Of these patients with elevated FCP, 5 (45.5%) self-report symptoms consistent with disease remission (<5 modified Harvey Bradshaw or <2 partial Mayo).

**Conclusions:** Our feasibility pilot study on the use of IBD dashboard, an innovative eHealth platform, is showing near seamless integration in the routine clinical management of remote patients. It is accessible and easy to use for both physicians and patients. The high proportion of patients with elevated FCP, half of which were asymptomatic, suggests a need for close surveillance irrespective of clinical disease symptoms.

**Funding Agencies:** Alberta Health Services Digestive Health Strategic Clinical Network (DC SCN)

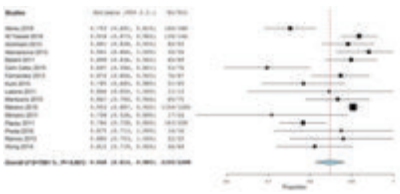
A141

**CONCORDANCE BETWEEN TUBERCULIN SKIN TEST AND INTERFERON GAMMA RELEASE ASSAY FOR LATENT TUBERCULOSIS SCREENING IN INFLAMMATORY BOWEL DISEASE (META-ANALYSIS).**

S. Alrajhi[1], P. Germain[1], M. Martel[1], P.L. Lakatos[1], W. Afif[2]

1. McGill University, Montreal, QC, Canada; 2. Gastroenterology, McGill University, Montreal, QC, Canada

**Background:** Screening for latent tuberculosis infection (LTBI) is mandatory prior to initiating anti-tumor necrosis factor (anti-TNF) medications. New guidelines recommend interferon-gamma release assays as first line screening method for the general population. Studies have provided conflicting evidence on the performance of interferon-gamma release assays (IGRAs), compared to tuberculin skin test (TST) in inflammatory bowel disease (IBD) patients. We assessed the concordance of these two tests in IBD patients and the effect of immunosuppression on their performance.
**Aims:** We performed a systematic search of MEDLINE, EMBASE and Cochrane Library databases, from 2011 to 2016, for relevant studies testing both TST and IGRA in IBD patients. The primary outcome was concordance between TST and IGRA. Secondary outcomes were effects of immunosuppressive therapy on both TST and IGRA. Immunosuppression was defined as either steroids more than 5 mg for at least two weeks, thiopurine, methotrexate or cyclosporine.
**Methods:** We used the Mantel-Haenszel method for a pooled random effects model, given heterogeneity of studies included. We also compared the fixed effects model to exclude any effect of smaller studies. Heterogeneity between studies was analysed using the statistical $I^2$, Q and Tau 2 tests. The quality of included studies was evaluated using a modified QUADAS-2 method.
**Results:** Sixteen studies, including 2488 patients with IBD, were included for the analysis. The pooled concordance between the TST and IGRA was 85% (95% confidence interval [CI] 81%-88%, p=0.01). Effects of immunosuppression on both tests were reported in eight studies including 814 patients with IBD. The odds ratio of testing positive by IGRA decreased to 0.57 if immunosuppressed (95% confidence interval [CI] 0.31-1.03, p=0.06). The odds ratio of testing positive by TST if immunosuppressed was 1.14 (95% confidence interval [CI] 0.61-2.12, p=0.69). Using the fixed effect model yielded similar results, however the negative effect of immunosuppression on IGRA reached statistical significance (p=0.06 to 0.01).
**Conclusions:** While concordance was 85% between TST and IGRA, the performance of IGRA seems to be negatively affected by immunosuppression. Given the importance of detecting latent TB prior to anti-TNF initiation, using only IGRA should be avoided in immunosuppressed IBD patients.



Pooled concordance of TST and IGRA in all IBD patients.

**Funding Agencies:** None

A142

## CLINICAL AND RADIOLOGIC PREDICTORS OF RESPONSE TO ANTI-TNF ALPHA THERAPY IN PATIENTS WITH PERIANAL CROHN'S DISEASE.

S. Parlow[1], B. Macdonald[2], I. Abdul-Kareem[2], E. Sabri[3], J. McCurdy[1]

1. University of Ottawa Department of Medicine, Ottawa, ON, Canada; 2. University of Ottawa Department of Radiology, Ottawa, ON, Canada; 3. Ottawa Hospital Research Institute, Ottawa, ON, Canada

**Background:** Perianal fistulas are a frequent manifestation of Crohn's Disease (CD) and often result in substantial morbidity. Pelvic magnetic resonance imaging (MRI) is commonly performed prior to initiating therapy to evaluate fistula anatomy, and the presence of complications. These factors are critical for determining if therapy can be safely initiated. Although anti Tumor Necrosis Factor alpha (anti-TNF) therapy has emerged as the most effective treatment for perianal CD (PCD), a substantial proportion of patients who receive this therapy will not achieve clinical remission.
**Aims:** The aim of this study is to determine clinical and radiologic factors associated with clinical remission in patients with PCD.
**Methods:** A retrospective, observational study was performed between 2005-2016. Patients with PCD who underwent a pelvic MRI were identified by a search of our institutional electronic picture archiving and communication system (WEB PACS). Study inclusion criteria included: patients over the age of 18 with PCD who underwent a pelvic MRI within 12 months of starting anti-TNF therapy. Clinical remission, defined as a lack of fistula drainage without clinical evidence of abscess, was assessed at 3 months after initiating therapy. A single, experienced radiologist reinterpreted each MRI study using a standardized template. Clinical and radiologic factors were selected a priori and were compared among patients with and without clinical remission. Chi square, Wilcoxon Score and Fisher exact tests were used to compare variables where appropriate.
**Results:** Seventy-seven patients met our inclusion criteria. Twenty-five (32.5%) patients achieved clinical remission at 3 months and fifty-two (67.5%) did not. Age, gender, and smoking status were similar between both groups of patients, as were age of diagnosis, Montreal Classification of disease characteristics, and duration of disease. Patients who did not achieve remission required more examinations under anesthesia (OR 2.4; p=0.076), and received a higher number of setons (p=0.063) prior to initiation of anti-TNF therapy. Patients who did not achieve remission were also more likely to have multiple primary fistula tracts (OR 4.8; p=0.035), multiple liquid containing tracts (OR 2.57; p=0.06), and a greater number of primary enhancing tracts (p=0.047) seen on MRI.
**Conclusions:** Multiple radiologic features are

associated with a lack of clinical remission in patients with PCD and may help in patient counselling, and to determine which patients should be treated aggressively.

**Funding Agencies:** None

A143

**THE CANADIAN LANDSCAPE OF IBD CARE: ARE WE KEEPING PACE? PRELIMINARY RESULTS FROM A NATIONWIDE SURVEY**

M. Miles[1], J. Pena-Sanchez[4], C. Heisler[3], J. Jones[2]

1. Internal Medicine, Dalhousie University, Halifax, NS, Canada; 2. Medicine, Dalhousie University, Halifax, NS, Canada; 3. Gastroenterology, Research Services, QEII Health Sciences Centre, Halifax, NS, Canada; 4. University of Saskatchewan, Saskatoon, SK, Canada

**Background:** Patients with inflammatory bowel disease (IBD) require lifelong medical and surgical management of their disease. Globally, many institutions have adopted integrated collaborative care models to improve patient care. Studies of these dedicated IBD services have shown they improve patient outcomes and quality of life. Little is known, however, what models of care for the management of patients with IBD are currently used across Canada.
**Aims:** The objectives of this study are to 1) determine the structure and processes used in clinics providing care for patients with IBD across Canada, 2) understand how IBD patients access IBD clinics across Canada, 3) identify the IBD practitioners and allied health professionals working with IBD clinics across Canada, and 4) determine the process and structure of referral pathways and clinical visits for IBD patients.
**Methods:** Evidence-based survey development methods were used to develop a peer-reviewed and piloted, web-based questionnaire to survey Canadian gastroenterologists who provide care for IBD patients. The questionnaire was developed using Novi Survey software. The contact information for each gastroenterologist in Canada was acquired using a database provided by Scott's Directories. Participants' lists were finalized after cross-referencing the Scott's database with gastroenterologists listed by the Royal College of Physicians and Surgeons. In October 2017, the entire target population was invited to participate in the survey using the Dillman's Tailored Design methodology.
**Results:** This work is in progress. To date, 14/583 (3%) survey questionnaires have been received from 7 provinces. Nine (65%) respondents are male and the mean age is 45 (SD=10) years. Working in or affiliated with most respondent IBD clinics are gastroenterologists specializing in IBD (71%), medical residents (71%), medical students (64%), gastroenterology residents (64%), IBD nurse non-practitioners (64%), research nurses (64%) general gastroenterologists (57%), IBD nurse practitioners (57%), dieticians (57%) and radiologists (57%). Few respondent IBD clinics have nurse educators (36%), general surgeons (36%), colorectal surgeons (36%), ophthalmologists (36%), social workers (36%), nurse navigators (29%) or psychiatrists (21%) working in or affiliated with them.
**Conclusions:** IBD in Canada represents a significant burden of illness. Most of the respondents to date work in IBD clinics comprised of gastroenterologists, trainees, IBD nurses, research nurses and dieticians while few work with nurse educators or navigators, surgeons, social workers or psychiatrists. Given the limited number of responses to date the sample thus far is likely not representative and the final results of this survey will be presented once the survey distribution process is complete.

**Funding Agencies:** None

A144

**AN EXPLORATORY PROSPECTIVE LONGITUDINAL STUDY INTO THE BREASTFEEDING PRACTICES OF WOMEN WITH INFLAMMATORY BOWEL DISEASE**

V.V. Nguyen[1], C. Baker[2], S.R. Andrishak[1], L. Ambrosio[1], K. Berga[1], L.A. Dieleman[1], B.P. Halloran[1], K.I. Kroeker[1], F. Peerani[1], K. Wong[1], R. Fedorak[1], V. Huang[1]

1. University of Alberta, Edmonton, AB, Canada; 2. Grant Macewan University , Edmonton , AB, Canada

**Background:** Breastfeeding is important for infant health, with recommendations to exclusively breastfeed until 6 months postpartum. Women with inflammatory bowel disease (IBD) have been reported in retrospective and survey studies to avoid initiating or cease breastfeeding early, with rates that differ between countries, and decades.

**Aims:** We aimed to explore breastfeeding practices among a cohort of women with IBD and healthy volunteer mothers through a prospective longitudinal survey study.
**Methods:** Adult women with and without IBD were invited to complete surveys regarding breastfeeding status at delivery, postpartum 3, 6, 9, and 12 months. Sociodemographic data on education and income level were obtained. Women with IBD were assessed for clinical disease activity using the Harvey Bradshaw Index for Crohn's disease (CD) or partial Mayo score for ulcerative colitis (UC). Rates of breastfeeding were calculated at each time point and compared between maternal groups.
**Results:** A total of 80 IBD (25 CD and 43 UC) mothers and 12 healthy mothers completed surveys. Similar proportions of IBD mothers and healthy mothers initiated breastfeeding (95.6% vs 100.0%, p=0.458) and continued until 3 months postpartum (75.0% vs 91.7%, p=0.202). Fewer IBD mothers breastfed at 6 months compared to healthy mothers (54.4% vs 90.9%, p=0.023). There was no significant difference in breastfeeding based on delivery method, or IBD disease activity (for IBD mothers). Lower income mothers were less likely to breastfeed than those with higher income brackets.The main reasons reported for cessation of breastfeeding were insufficient milk production,

initiation of new medications, and baby was sick/ unwilling to breastfeed.
**Conclusions:** Breastfeeding practices differ among mothers with IBD and healthy mothers, with a large proportion of IBD mothers ceasing to breastfeed earlier than the recommended 6 months postpartum. Future research into these reasons may contribute towards a better understanding of the complex interaction between maternal IBD and milk production, IBD medications and breast milk composition, and impact of maternal IBD and breast feeding on infant health.

**Funding Agencies:** CEGIIR University of Alberta

A145
**BREASTFEEDING INCREASES COLONIC INFLAMMATION IN INFANTS BORN FROM HEALTHY MOMS, WHICH EFFECT IS LACKING IN INFANTS BORN FROM MOMS WITH IBD**
V.V. Nguyen, L. Ambrosio, G. Dunsmore, A. Agrawal, N. Hotte, L.A. Dieleman, B.P. Halloran, K.I. Kroeker, R. Fedorak, S. elahi, K. Madsen, V. Huang

Faculty of Medicine, University of Alberta , Edmonton, AB, Canada

**Background:** Breastfeeding (BF) is recommended for at least 6 months postpartum because of the beneficial components of breast milk. Studies show that there is a healthy inflammatory response (measured by fecal calprotectin (FCP)) in healthy full term breastfed infants. Whether this effect of breastfeeding on infant intestinal inflammation is affected by maternal IBD and IBD therapies is unknown.
**Aims:** In this study, we compared the FCP levels in infants born to and breastfed by healthy mothers with those born to and breastfed by IBD mothers.
**Methods:** Mothers with IBD (CD or UC) and healthy mothers (HC) were consented to collect their infant's stool at delivery, post-partum 3 months, and 6 months. FCP was extracted and measured by ELISA. Breastfeeding status was documented as exclusively (EBF) or not exclusively breastfed (non-EBF). IBD medications (no medications, 5-ASA only, thiopurine, biologics) was documented.
**Results:** There were 21 (5 CD, 12 UC, 4 HC) PP3 months stools and 22 (5 CD, 10 UC, 6 HC) PP 6 months stools. Only 11 infants (4 CD, 4 UC, 3 HC) were exclusively breastfed until 6 months. As shown in Figure 1, at 3 months post-partum breastfed non-IBD infants have higher FCP than non-EBF infants or infants from IBD moms, the latter category irrespectively of BF or not. This effect of breastfeeding on infant FCP seems to disappear at 6 months post-partum. At PP 3, this lack of increased FCP in breastfed infants from IBD moms was not affected by oral 5-ASA or biologics, although the numbers are too small to draw definitive conclusions.
**Conclusions:** Infant intestinal inflammation is increased by breastfeeding among healthy infants, but not in IBD infants. Further investigation into the infant's intestinal inflammation by maternal clinical disease activity, and IBD medications through breast milk are currently in progress.

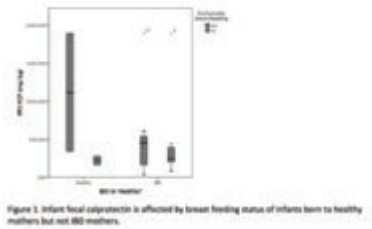


Figure 1. Infant fecal calprotectin is affected by breast feeding status of infants born to healthy mothers but not IBD mothers.

**Funding Agencies:** CEGIIR University of Alberta

A146
**DIETARY INTAKE OF PATIENTS WITH CROHN'S DISEASE IN REMISSION: A CROSS-SECTIONAL STUDY**
L. Taylor[1], A. Almutairdi[1], R. Reimer[5], K. Madsen[2], S. Ghosh[4], R. Panaccione[1], N. Shommu[6], R. Fedorak[3], M. Raman[1]

1. University of Calgary, Calgary, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Los Alamos National Laboratory, Edmonton, AB, Canada; 4. Gastrointestinal Section, Imperial College london, London, United Kingdom; 5. University of Calgary, Calgary, AB, Canada; 6. University of Calgary, Calgary, AB, Canada

**Background:** Many patients with inflammatory bowel disease (IBD), particularly Crohn's disease (CD) suffer from macro- and micronutrient deficiencies and do not meet current evidence-based guidelines for dietary intake. The intake patterns of these patients have not been well documented.

**Aims:** To describe the (a) macro- and micronutrient intake and (b) dietary servings of red meat, poultry, fish, fruits, vegetables and probiotic containing foods in a cohort of patients with CD in remission from a single tertiary care center.
**Methods:** Adult CD patients in endoscopic and clinical remission with ileal or ileocolonic disease were recruited prospectively at the University of Calgary. Patients completed a detailed 3-day food diary, which was reviewed with the patient by a registered dietitian (RD). Nutrient analysis was completed using ESHA, a nutrition analysis program. Research ethics board approval was obtained.

**Results:** Fifty-nine patients meeting inclusion and exclusion criteria were consecutively recruited (27 males and 32 females). The mean intake of nutrients, servings of meat, fruit and vegetables, and probiotics were calculated for each gender and compared to dietary reference intakes (DRI) and Canada's Food Guidelines (CFG) for healthy populations. The mean total calories, carbohydrates, fat, and fiber intake did


To view enlarged images and tables, please refer to Abstract Library.

not meet DRI (68%, 58%, 85% and 50%) respectively. Protein mean intake was high with males and females consuming 168% and 150% of their DRI respectively. Apart from the micronutrients, vitamins D, E, K, calcium, magnesium, potassium, and folate, the mean intake of the remaining vitamins was close to the DRI for both genders. Vitamin D mean intake was the lowest among the vitamins, with patients consuming less than 20% of the DRI in both genders. Servings of fruits and vegetables per day was low, 50% of the recommended daily servings as per the CFG in our study population. Mean weekly red meat servings were six, (600grams/week). No study patients ingested probiotic-containing foods.

**Conclusions:** Even among patients in clinical and endoscopic remission, patients with Crohn's disease have inadequate dietary intake and decreased dietary diversity. The impact on the natural history of disease is unknown. However, patient-centered dietary counseling would likely be beneficial in this patient population.

**Funding Agencies:** Broad Foundation

A147

**RESPONSE AND REMISSION AFTER 16 WEEKS OF USTEKINUMAB– AN ALL PATIENTS ANALYSIS FROM THE UNITI CROHN'S STUDIES**

J.F. Colombel[1], S. Sloan[2], C. Gasink[3], L. Gao[4], D. Jacobstein[5], S.D. Lee[6], S. Targan[7]

1. School Of Medicine, Mount Sinai Medical Center, New York, NY; 2. Janssen Scientific Affairs, LLC, Horsham, PA; 3. Janssen Scientific Affairs, LLC, Horsham, PA; 4. Janssen Scientific Affairs, LLC, Horsham, PA; 5. Janssen Research & Development, LLC, Spring House, PA; 6. University of Washington Medical Center, Seattle, WA; 7. Cedars-Sinai Medical Center, Los Angeles, CA

**Background:** Ustekinumab(UST) has been shown to induce & maintain clinical response & remission in moderate-severe Crohn's disease(CD) in 2 induction[(UNITI-1(anti-TNF failures) & UNITI-2(anti-TNF non-failures) & 1 maintenance(IM-UNITI)] randomized, PBO-controlled Ph3 trials.
**Aims:** We evaluated efficacy (response & remission) for all pts who received an IV induction dose of approximately 6mg/kg, including responders(CDAI decrease ≥100) & non-responders, 8wks after first UST maintenance dose of 90mg SC, i.e. 16wks from the IV induction dose.
**Methods:** Pts achieving clinical response 8wks after a single IV induction dose were randomized to SC PBO, UST 90mg q12wks or q8wks. UST pts not in clinical response 8wks after IV induction dose were given UST90mg SC & if in clinical response 8wks later were continued on 90mg SC q8w dosing. A total of 458pts were exposed to an IV induction dose of 6mg/kg(UNITI-1,N=249 & in UNITI-2 N=209) with a response rate at wk8 of 37.8% & 57.9% vs. PBO response rate of 20.2% & 32.1% respectively. The remission rate at wk8 in UNITI-1 & UNITI-2 was 20.9% & 40.7 vs. PBO of 7.3% & 19.6% respectively. For this evaluation, response & remission status of the entire population exposed to an IV induction dose of 6mg/kg of UST was evaluated 8wks after the first SC maintenance dose of UST. All pts who received 6mg/kg IV UST induction were included, including responders randomized to SC PBO (who did not receive SC UST at wk8).
**Results:** Of the 219 pts not in clinical response to a single UST IV induction dose in UNITI 1&2, 37.6% & 60.5% respectively were in clinical response 8wks after the first maintenance UST dose (90 mg SC). Evaluating all pts exposed to 6mg/kg IV UST induction, response rates 8wks after the first SC injection (16wks after the IV induction dose) for UNITI1&2 were 47.4% & 73.7% respectively. In the sub-population who were anti-TNF naïve upon enrolment into UNITI-2 (n=144), at 8 weeks after the first SC injection, 72.9% were in clinical response and 60.4% were in clinical remission.
**Conclusions:** These numbers at wk16 are expected to reflect real world experience in pts who receive the induction dose & one additional maintenance dose 8wks later. The resulting rates of response & remission are higher than previously reported in induction studies across all populations (anti-TNF non-failures & anti-TNF failures). About 73% of anti-TNF non-failures attain clinical response & over half are in remission. The data support the clinical rationale for providing at least one SC maintenance dose of UST irrespective of clinical response 8wks after IV induction to assess UST benefit.

**Funding Agencies:** Janssen Research & Development, LLC funded this study

A148

**EBV STATUS AND IMMUNOSUPPRESSANT USE IN IBD PATIENTS WHO SUBSEQUENTLY DEVELOP LYMPHOMA: A RETROSPECTIVE AND PROSPECTIVE STUDY**

M. Reeson[3], L. Ambrosio[4], G.Y. Lam[6], R. Fedorak[1], L.A. Dieleman[2], K.I. Kroeker[5], V. Huang[4], A. Peters[1], B.P. Halloran[1]

1. University Of Alberta , Edmonton, AB, Canada; 2. Medicine, University of Alberta, Edmonton, AB, Canada; 3. Medicine and Dentistry , University of Alberta, Edmonton, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada; 5. University of Alberta, Edmonton, AB, Canada; 6. University of Alberta, Edmonton, AB, Canada

**Background:** Immunosuppressive agents have revolutionized the treatment of inflammatory bowel disease (IBD). However, a number of studies over the last decade have identified a concerning link between immunosuppression and lymphoproliferative disorders (LPDs). These LPDs have been associated with Epstein-Barr virus (EBV) infection in which the virus provides the impetus for malignant transformation while immunosuppression hampers the immune

system's ability to detect and clear these malignant cells. There is limited knowledge on LPD risk in individuals with IBD.
**Aims:** This study is conducted to determine if immunosuppressive therapy in the IBD population increases the risk of LPDs.
**Methods:** This study is divided into two arms: a retrospective and a prospective study. A retrospective chart review was conducted on IBD patients in Alberta from 2005-2015. Alberta Cancer Registry (ACR) and Electronic Medical Records (EMRs) used by the IBD team at the University of Alberta Hospital were searched with keywords "lymphoma" and "IBD". Patient age, gender, year of IBD diagnosis, year of lymphoma diagnosis, and type of lymphoma data were obtained. An ongoing prospective study has followed patients from the IBD Clinic and the University of Alberta Hospital from 2016 to present. Initial EBV serologies were completed at baseline. Patients are to be followed-up for 3 years to determine if seroconversion and immunosuppression confer increased risk of LPD development.
**Results:** In total, 209 patients have been enrolled in this study; 176 (84.2%) have been screened, while 33 (15.8%) are pending results. Of the 176 screened, 108 (61.4%) are female. Ninety (51.1%) patients are diagnosed with Crohn's disease, 79 (44.9%) with Ulcerative Colitis, and 7 (4.0%) with Indeterminate Colitis. The EBV serology results showed 9.1% (16) of patients with negative exposure, 72.7% (128) with past exposure, 9.7% (17) with indeterminate IgM, while 1.1% (2) had a positive viral load. Of the 16 patients with negative exposure, 10 (62.5%) were on biologics, 8 (50%) on an immunomodulatory, and 6 (37.5%) were on both. Retrospectively, 14 patients (9 male) had developed lymphoma. Positive EBV histology was found in 3 (21.4%) patients.
**Conclusions:** These interim results suggest that LPD remains a small but possible risk of immunosuppressant use in IBD patients. The utilization of an EBV serologic monitoring protocol may help to identify those at the highest risk of LPD development.

Type of immunosuppressant therapy in the seronegative population

| | EBV Serology Results | Medication | | |
|---|---|---|---|---|
| Age | Negative Exposure | Immunomodulator | Biologic | Immunomodulator + Biologic |
| < or = 30 | 8 | 6 | 7 (2 new starts) | 5 |
| >30 | 8 | 2 (1 new start) | 3 (1 new start) | 1 |
| Total | 16 | 8 | 10 | 6 |

**Funding Agencies:** CEGIIR (The Center of Excellence for Gastrointestinal Inflammation and Immunity Research)

A149
**ENDOSCOPIC BALLOON DILATION IS A SAFE AND EFFECTIVE THERAPEUTIC INTERVENTION FOR PATIENTS WITH SMALL BOWEL CROHN'S DISEASE**
M. Reeson[3], R. Fedorak[3], C.W. Teshima[4], S. Zepeda-Gomez[2], B.P. Halloran[1]

1. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 2. Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Medicine and Dentistry , University of Alberta, Edmonton, AB, Canada; 4. Gastroenterology, University of Toronto, Toronto, ON, Canada

**Background:** Crohn's disease (CD) is an inflammatory bowel disease that is characterized by chronic transmural inflammation of the gastrointestinal (GI) tract which can become complicated by the formation of strictures. CD can affect any part of the GI tract with 30-40% of patients having isolated small bowel CD. Complicated CD carries with it significant risk factors for the patient that can often only be alleviated through surgery or medication. However, the advent of Endoscopic Balloon Dilation (EBD) has allowed for temporary relief of obstructive symptoms and could potentially be an alternative therapy that prolongs the need for surgical intervention.
**Aims:** This study is conducted to assess the safety and efficacy of EBD in patients with small bowel CD.
**Methods:** A retrospective chart review was undertaken to examine all patients with small bowel CD who underwent BAE between July 2013 and August 2017. The data collection included patient demographics, disease characteristics, procedural characteristics, and stricture dilation data.
**Results:** 152 BAEs (84 DBE, 68 SBE) were performed on 82 patients (45 female). The mean age at the time of the BAE was 53.4 ± 15.7 years. The mean disease duration was 17.4 ± 14.0 years. Fifty (61.0%) patients had undergone a previous gastrointestinal surgery. Of the 152 procedures, 84 (55.3%) required EBD, constituting 58.5% (48) of the total patients. In total, 191 strictures were dilated; 75.9% (145) were native strictures, 24.1% (46) were anastomotic strictures. There were a total of 3 (2.0%) complications, and there were no perforations or deaths. Thirty-five procedures (23.1%) involved a non-traversable stricture; in 25 (71.4%) of these procedures, the non-traversable stricture prevented the endoscopist from EBD.
**Conclusions:** Endoscopic Balloon Dilation is a safe and effective intervention for the treatment of small bowel Crohn's disease and is likely under-utilized as an en-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doscopic tool. EBD can alleviate obstructive symptoms for both patients who have had previous resections or those with primary stenosis. In some patients, EBD may be effective enough to prolong or prevent the need for surgical resection.

Procedural data for patients with small bowel Crohn's disease undergoing Endoscopic Balloon Dilation

| Outcome | Total Procedures (n=152) | %/SD |
|---|---|---|
| Endoscopic Ballon Dilation Procedures | 84 | 55.3% |
| Successful Stricture Dilations | 191 | |
| Native | 145 | 75.9% |
| Anastomotic | 46 | 24.1% |
| Non-Traversable | 34 | 22.4% |
| Failed Dilations | 2 | 1.3% |
| Mean Minimum Dilation Diameter (mm) | 15.5 | ±2.4 |
| Complications | 3 | 2.0% |
| | | |

**Funding Agencies:** CEGIIR (The Center of Excellence for Gastrointestinal Inflammation and Immunity Research)

A150

**IS FOCAL ACTIVE COLITIS OF GREATER SIGNIFICANCE IN PEDIATRIC PATIENTS? A RETROSPECTIVE REVIEW OF 68 CASES WITH CLINICAL CORRELATION.**

D. Ashok[1], A. Osmond[1], C. Francouer[2], M. Miller[2], J. Walsh[3]

1. Pediatrics, Western University, London, ON, Canada; 2. Children' Hospital of Western Ontario, London, ON, Canada; 3. Western University, London, ON, Canada

**Background:** Focal active colitis (FAC) is a histopathologic finding of uncertain clinical significance in individual patients. In adult cases, infection accounts for approx. 50%, Crohn's disease (CD) for 0-13%, and 20-30% are idiopathic (likely related to bowel preparation). One previous study of 29 cases of pediatric FAC showed a 28% rate of CD. Histologic features to distinguish between idiopathic FAC and inflammatory bowel disease (IBD) related FAC have not been determined.
**Aims:** Our study aimed to review a large cohort of pediatric patients with FAC to determine what proportion of them had IBD, and whether there was an amount or pattern of inflammation that predicted IBD.
**Methods:** Sixty eight biopsy sets from 68 patients aged ≤18 years with FAC were identified and reviewed retrospectively. Patients with a prior diagnosis of IBD or chronic colitis in the index biopsies were excluded. Original slides were assessed for a number of inflammatory criteria. Clinical data including presenting symptoms, medication history and final diagnoses were recorded. Data were analysed using Pearson correlations and Fisher's exact chi-square analyses.
**Results:** Sixteen patients (24%) had a final diagnosis of IBD. When cases with terminal ileal inflammation and / or granulomas were excluded 6 of 54 remaining patients had a final diagnosis of IBD (11%). A final diagnosis of IBD was significantly associated with the presence of crypt abscesses in patients with and without terminal ileal inflammation (Fisher's exact=5.67, p=0.027 and Fisher's exact=7.99, p=0.025) and the presence of one or more elevated serum inflammatory markers (Fisher's exact=11.44, p=0.001 and Fisher's exact=15.02, p=0.001). IBD was significantly associated with TI inflammation (Fisher's exact=20.27, p<0.001). An amount or pattern of inflammation that could be used to predict IBD was not determined.
**Conclusions:** In keeping with the previous pediatric study, this study demonstrated a 24% rate of IBD in pediatric patients with FAC; however, when patients with associated terminal ileal inflammation and / or granulomas were excluded, the rate was 11%, similar to the reported rates in adults. When TI inflammation is present in association with FAC there is a high probability of IBD (10/14 cases, 71%). In all patients, the presence of crypt abscesses or increased serum inflammatory markers is associated with a higher likelihood of IBD. In pediatric patients whose biopsies show FAC without terminal ileal inflammation, the clinical implications appear to be the same as those in the adult population and do not warrant more aggressive follow up.

| Final clinical diagnosis | N (%) |
|---|---|
| IBD (CD=14, UC=2) | 16 (24%) |
| Infectious colitis | 2 (3%) |
| Allergic colitis | 6 (9%) |
| Other definitive diagnosis accounting for FAC | 11 (16%) |
| Idiopathic FAC | 33 (49%) |

Final Clinical Diagnosis

**Funding Agencies:** None

A151

**FECAL CALPROTECTIN RETURN RATE IN IBD PATIENTS ON INFLIXIMAB**

M. Altuwaijri[1], Y. Leung[2], S. Whittaker[2], B. Bressler[2], G. Rosenfeld[2]

1. University of British Columbia and King Saud University, Vanouver, BC, Canada; 2. University of British Columbia, Vancouver, BC, Canada

**Background:** Fecal calprotectin (FC) is a simple, non-invasive test that has been previously considered a

reliable marker of inflammatory bowel disease activity (IBD) and closely correlates with endoscopic evidence of mucosal inflammation. Multiple studies have utilized FC to monitor response to therapy, to assess for mucosal healing and to predict flares during remission. However, the utility of FC may be limited by a low completion rate of the test.
**Aims:** To evaluate the return rate of FC stool samples in IBD patients and assess factors associated with completion rate.
**Methods:** We conducted a retrospective study of all IBD patients at Pacific Gastroenterology Associates, a tertiary ambulatory care clinic in Vancouver, BC, who are receiving infliximab for IBD and received a requisition for FC testing. Patients received a stool collection kit through the patient support program over the period between March 2016 and July 2017. Demographic data and FC results were obtained through a review of the electronic medical record. Multivariable logistic regression was employed to examine what factors (e.g., age, gender, duration of treatment, and disease indication) were associated with a successfully completed FC test.
**Results:** Data was collected from 120 patients with a median age was 32.5 years, 51% were males and 75% had Crohn's disease. The median duration time on infliximab was 3.5 years. A FC test was successfully completed by 88 patients (73%). A further 12% of patients (14) have been mailed collection kits but have yet to return them. For 9 patients, the allotted number of samples was exceeded and the samples were not processed and the samples were expired for another 9. Both Univariable and multivariate logistic regression analyses showed that a completed FC was significantly associated with older age (p = 0.03).
**Conclusions:** Despite the usefulness of FC for diagnosing and monitoring IBD activity, the test completion rate is lower than anticipated limiting its value as a clinical tool. The present study suggest that older patients are more likely to complete testing. Measures to improve patient compliance with FC testing in the future could improve the utility of this test in clinical practice.

**Funding Agencies:** None

A152

**RISK OF VENOUS THROMBOEMBOLIC EVENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN THE POST-DISCHARGE PERIOD**

A. Israel[2], M. Hasan[2], R. Weng[2], J. McCurdy[1], M. Carrier[1], T. Ramsay[3], R. Mallick[4]

1. TOH, Ottawa, ON, Canada; 2. University of Ottawa, Ottawa, ON, Canada; 3. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 4. Ottawa Hospital Research Institute, Ottawa, ON, Canada

**Background:** Patients with inflammatory bowel disease (IBD) are at increased risk of venous thromboembolism (VTE), particularly in the hospital setting. A number of factors which place these patients at increased risk of VTE, may persist after discharge. Although guidelines recommend thromboprophylaxis for all admitted patients with IBD, it remains unclear if prophylaxis should be extended after hospital discharge.
**Aims:** To determine the incidence and timing of VTE in patients with IBD in the post discharge setting, and to identify which patients are at highest risk.
**Methods:** A retrospective, single center, observational cohort study was conducted between January 1, 2009 and December 31, 2016. Patients with IBD admitted to our institution were identified by our institutional database. A manual chart review was conducted to confirm a diagnosis of IBD, and VTE events during hospitalization and within 6 months of discharge. Patients with a VTE event during hospitalization and those with inadequate follow-up were excluded. Risk factors associated with developing VTE were determined by univariate logistic regression accounting for repeated observations from a single patient using a random effects model.
**Results:** Our search identified 1175 eligible patients with a total of 2161 encounters; 1453 (67%) Crohn's disease (CD) encounters and 688 (32%) ulcerative colitis (UC) encounters. Overall 1370 (63%) were admissions for an IBD flare, and 679 (31.4%) involved inpatient surgery. Fifty-nine encounters (2.7%) were diagnosed with a VTE within 6 months of discharge; 43 (3.0%) of all CD encounters, and 16 (2.3%) of all UC encounters. Of the patients who underwent surgery, 12(1.8%) were diagnosed with a VTE event. Overall the median time to event was 60 days (range 3-182 days). Age (OR, 1.02; 95% CI, 1.01–1.04), length of hospitalization (OR, 1.01; 95% CI, 1.00–1.03), and prior VTE event (OR, 31.73; 95% CI, 14.14–71.22) were significantly associated with risk of VTE following discharge.
**Conclusions:** A minority of patients with IBD develop VTE events after discharge from hospital. Age, length of hospitalization, and prior VTE events may predict patients at highest risk that would benefit from extended thromboprophylaxis. Further studies are required to confirm these findings and to determine if extended prophylaxis can reduce the risk of VTE in the post discharge setting.

**Funding Agencies:** None

A153

**QUALITY OF CARE AND OUTCOMES IN A TERTIARY HOSPITAL INFLAMMATORY BOWEL (IBD) CENTER: MONITORING AND TREATMENT ALGORITHMS DURING FOLLOW-UP**

S. Restellini[1], L. Gonczi[2], Z. Kurti[2], T. Bessissow[1], W. Afif[1], G. Wild[1], R. Kohen[1], E.G. Seidman[1], A. Bitton[1], P.L. Lakatos[1]

1. Division of Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 2. Semmelweis University, Budapest, Hungary

**Background:** Optimal management of IBD requires harmonized monitoring processes and treatment

pathways.
**Aims:** We aimed to retrospectively analyze quality of care indicators (QIs) during follow-up including patient monitoring, treatment decisions and outcomes in the McGill University Health Center (MUHC) IBD Center.
**Methods:** We retrospectively analyzed out- and inpatient records of all consecutive patient at the MUHC IBD center between June and December 2016. Demographic variables, outpatient visits, inpatient stays, laboratory, imaging and endoscopy data, current medications and/or changes in medications, and vaccination profile were captured.
**Results:** 653 patients (46.2% men, 66.6% Crohn's disease (CD), age at index follow-up visit: 44.7 years, duration of follow-up: 4.2 years) were included. Complicated behavior and perianal disease were found at index visit in respectively 47% and 24% of CD patients, while extensive UC in 41%. 44% of patients received biologics among which 11% non-anti TNF-biologics. Patient re-evaluation was common: ileocolonoscopy was performed in 34 %, MRI in 11 % and CT in 23 % within 6 months after index visit. Biomarkers were measured frequently (CRP: 67%, FCAL: 33%). New or repeated HBV/HCV testing was performed in 20%, C.difficile in 28%, stool culture in 24%, TB in 10%, therapeutic drug monitoring was performed in 26% of patients on biologics. Treatment was changed in 18%. Need for surgery (4%) and hospitalization (8%) were relatively low within 6 months after index visit. Waiting time for ileocolonoscopy (35 vs 60 days, $p<0.001$), but not for cross sectional imaging (45-48 days for MRI, 25-30 days for CT), was shorter in active disease.
**Conclusions:** Our data support that tight monitoring strategy is applied in the MUHC IBD center during follow-up with objective patient reassessment and accelerated medical strategy in patients with and without flares.

**Funding Agencies:** McGill University Health Center (MUHC) Department of Medicine CAS Research Award

A154

**BENEFITS OF IMPLEMENTING A RAPID ACCESS CLINIC IN A HIGH VOLUME INFLAMMATORY BOWEL DISEASE CENTER: ACCESSIBILITY, RESOURCE UTILIZATION AND OUTCOMES**

S. Restellini, I. Morin, T. Bessissow, W. Afif, G. Wild, E.G. Seidman, A. Bitton, P.L. Lakatos

Division of Gastroenterology, McGill University Health Center, Montreal, QC, Canada

**Background:** IBD impacts on patient's physical health, social functioning and quality of life, contributing to the health-economic burden associated with the disease, especially in emergency situations.
**Aims:** We aimed to prospectively measure indicators of quality-of-care, after implementation of a new rapid access clinic (RAC) at a tertiatry care IBD center.
**Methods:** Consecutive patients from the McGill University Health Center who accessed the RAC via email were prospectively included, between June and September 2017. Time to medical appointment, utilization of imaging, endoscopy, laboratory, treatment decisions and need for unplanned emergency room (ER) visits or admissions 30 to 90 days after consulting the RAC was assessed.
**Results:** 74 patients (35% men, mean age: 35 years, CD:72%, L3:59%, B2-3:39%, UCE3: 48%, biological therapy:76%, previous surgery:23%) were included. 75% of requests were considered appropriate for a RAC appointment. Outpatient visits were a median 2 days (mean 3.3) after the email request. 5 patients required an ER visit within 30 days after the RAC appointment, out of which 3 were initiated during the rapid appointment. Two of these 3 patients required admission and underwent urgent IBD- related surgery. No patients required an ER visit within 90 days. Treatment was modified in 40 patients (72%). Laboratory assessment including FCAL (65%) and therapeutic drug monitoring (30%) was performed as appropriate. The need for subsequent accelerated assessment was infrequent. Fast-track endoscopy was performed in 4 patients, and 2 patients had an abdominal/pelvic CT for assessment.
**Conclusions:** Implementation of a RAC improved healthcare delivery by avoiding unnecessary ER visits and patient care by increasing access to an IBD center.

**Funding Agencies:** McGill University Health Center CAS Departement of Medicine Research Award

A155

**QUALITY OF CARE IN THE INFLAMMATORY BOWEL DISEASES (IBD) CENTER FROM A TERTIARY REFERRAL HOSPITAL: PATIENT ASSESSMENT STRATEGY AT REFERRAL**

S. Restellini[1], L. Gonczi[2], Z. Kurti[2], W. Afif[1], T. Bessissow[1], G. Wild[1], E.G. Seidman[1], R. Kohen[1], A. Bitton[1], P.L. Lakatos[1]

1. Division of Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 2. Semmelweis University, Budapest, Hungary

**Background:** IBD impacts substantially on patient's physical health, social functioning and quality of life.
**Aims:** We aimed to analyze quality of care indicators (QIs) including structural and process QIs at referral in the McGill University Health Center (MUHC) IBD Center that includes 6 IBD specialists, 2 IBD nurses, 2 research nurses, and 2 IBD fellows with rapid access to colorectal surgeons and imaging.
**Methods:** We retrospectively analyzed out- and inpatient records of all consecutive patient at the MUHC IBD clinic between June and December 2016. Demographic variables, outpatient visits, inpatient stays, laboratory, imaging and endoscopy data, medications history, and vaccination profile were captured.
**Results:** 653 patients (46.2% men, 66.6% Crohn's disease (CD), age at referral: 41.3 years) were included. At referral 38% of CD patients had L3 classification,

46% complicated behaviors (B2 or B3) and 22% perianal disease.31% and 40% of UC patients had extensive and moderate-to severe disease, respectively. 60% of patients had a documented previous ileocolonoscopy at referral, 10% MRI and 28% CT. 16% of patients were on biologics. 66% had an ER visit, 45% required hospitalization, while 30% of CD patients had IBD-related surgery in the past. 78% of patients were employed. Patients were objectively re-evaluated at referral: 81% underwent ileocolonoscopy, 13% upper GI endoscopy, 31% of CD patients had abdomino-pelvic MRI or CT and 15% abdominal US. CBC, CRP and FCAL were measured in 85%, 75% and 24%, respectively. Medical therapy was changed in 55% (active disease: 78%, remission: 22%) with a maximum therapeutic step of biologics in 32%. 10% of patients required hospitalization while 5% surgery at referral.

**Conclusions:** Our data support that a tight monitoring was applied at the MUHC IBD center including a high emphasis on objective patient (re)evaluation, and accelerated treatment strategy already at referral.

**Funding Agencies:** NoneMcGill University Healtch Center (MUHC) Department of Medicine CAS Research Grant

A156

**CONTRASTING THE USE OF 5-ASA IN PATIENTS WITH ULCERATIVE COLITIS AND CROHN'S DISEASE: A CROSS-SECTIONAL ANALYSIS AT A TERTIARY CARE IBD CLINIC**

**ALKHATTABI M[1,2], JAIRATH V[1,3], CHANDE N[1], WALTON-MENNILL P[1], GREGOR J[1]**

1 DEPARTMENT OF MEDICINE, WESTERN UNIVERSITY.
2 DEPARTMENT OF MEDICINE, KING ABDULAZIZ UNIVERSITY, RABIGH CAMPUS.
3 DEPARTMENT OF EPIDEMIOLOGY AND BIOSTATISTICS, WESTERN UNIVERSITY.

M. Alkhattabi, V. Jairath, N. Chande, P. Walton-Mennill, J.C. Gregor

Western University, London, ON, Canada

**Background:** 5-ASA is a mainstay of initial induction and maintenance therapy in patients with ulcerative colitis (UC). Although often used in patients with Crohn's disease (CD), its clinical efficacy in this condition is uncertain. An upcoming Canadian multi centre randomized controlled trial will assess the non-inferiority of 5-ASA withdrawal versus continuation in CD (STATIC Trial NCT03261206)
**Aims:** To determine the prevalence of 5-ASA use in patients with CD and contrast it with its use in UC in a tertiary care setting.
**Methods:** All patients seen at a single site IBD clinic at London Health Sciences Centre, Victoria Hospital, between January and June 2016 were reviewed. Patients were only included if they had a definite diagnosis of UC or CD. Patients with indeterminate colitis were excluded. If patients were seen on multiple occasions during the study period, characterization of their medication profile was derived from their last visit. Chi squared analysis was used for comparison of proportions.
**Results:** 575 patients were included in the analysis. Of these, 389 (67.7%) had a diagnosis of CD and 186 (32.3%) had a diagnosis of UC. 274/575 (47.6%) patients were on biologics (36.3% on anti-TNF, 7.1% on vedolizumab, 4.2% on ustekinumab). 189/575 (32.9%) patients were on immunomodulators (12.9% on methotrexate, 20% on azathioprine). 50/575 (8.7%) patients were on corticosteroids at their last visit. 5/575 (0.9%) patients were on investigational agents. 175/575 (30.4%) patients were on 5-ASA. When broken down according to diagnosis, 134/186 (72.0%) of patients with UC were taking oral and/or rectal 5-ASA while 41/389 (10.5%) of CD patients were taking this class of medication ($p < 0.001$). When used as monotherapy, 77/134 (57.5%) of UC patients were using 5-ASA as monotherapy while 23/41 (56.1%) of CD patients were using 5-ASA as their only treatment ($p = 0.877$).
**Conclusions:** 5-ASA is much more commonly used in UC than CD. However, when used as monotherapy the proportion of patients on 5-ASA alone does not appear to vary between the two conditions. The upcoming STATIC trial will add new evidence to determine whether this ongoing use of 5-ASA in CD is efficacious.

**Funding Agencies:** None

A157

**THE THRESHOLD FOR INFLIXIMAB TROUGH LEVELS LEADING TO DOSE ESCALATION DIFFERS BETWEEN CROHN'S DISEASE AND ULCERATIVE COLITIS**

T.A. Cookson[3], R. Fedorak[1], B.P. Halloran[1], L.A. Dieleman[4], K. Wong[1], V. Huang[2], F. Peerani[2], K.I. Kroeker[4]

1. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Department of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 4. Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Therapeutic drug monitoring (TDM) of infliximab (IFX) provides an objective measure that allows physicians to optimize the dose for patients on biologic therapies and potentially reduce loss of response (LOR). The currently accepted therapeutic range is 3 – 7 µg/mL. With the potential for LOR with low drug levels and the high cost of IFX, it is important to manage medications efficiently. To better understand how physicians at the University of Alberta Hospital are using TDM, we conducted a retrospective chart review to see the clinical decisions made in response to TDM. Major clinical decisions include: no change, dose escalate (increase in dose or shorten interval), reload (2 extra doses 2 weeks apart), or dose de-escalate (decrease in dose or lengthen interval).

**Aims:** To measure the proportion of IFX trough levels that lead to a clinical change in therapy and compare how the cut-offs used to change therapy vary by disease type.
**Methods:** This is a retrospective chart review of all IBD patients (17+ years) on IFX at the University of Alberta IBD Clinic who had at least one trough level measured between 2015 and 2017. Charts were reviewed for demographic data, TDM drug levels, and any clinical decisions relating to the drug levels. Numerical data and categorical data are presented as a mean (standard deviation) and proportions, respectively, using t-tests and Chi-squared tests. Statistical significance is assessed at $p<0.05$.
**Results:** The information of 758 drug levels was collected from 402 patients. Demographic data for the drug levels included: 51.7% male; 72.1% Crohn's disease; mean age of 38.9 (±14.8). 54.5% of all levels had the patient on concomitant immunosuppressants. Of all trough levels, 344 (45.4%) led to a clinical change in therapy. A majority (52.7%) of trough levels that had an elevated fecal calprotectin (FCP) of >250µg/g led to a dose escalation ($p<0.001$). Drug levels with positive IFX antibodies (ATIs) correlate to switching to a new biologic ($p=0.042$) where the mean ATI level was 3.00 (3.39). **Table 1** shows the mean IFX level for clinical changes made by disease type.
**Conclusions:** Physicians at the University of Alberta IBD Clinic use FCP, a therapeutic range of ~3 – 14 µg/mL, and the presence of antibodies as major factors in making clinical changes in IFX therapy for patients with IBD. Cut-offs used to reload and dose escalate are significantly higher in UC patients compared to CD patients.

Table 1. Mean infliximab level for each clinical change and how they vary by CD and UC

| Clinical Decision | n (CD) | Mean Infliximab Level (CD) | n (UC) | Mean Infliximab Level (UC) | p-value |
|---|---|---|---|---|---|
| Dose Escalate | 296 | 2.50 (2.58) | 71 | 3.03 (3.53) | 0.005 |
| Reload | 95 | 1.37 (1.23) | 40 | 2.02 (2.56) | < 0.001 |
| No Change | 298 | 9. 14 (6.06) | 115 | 9.42 (6.10) | 0.460 |
| Dose De-escalate | 16 | 18.01 (7.32) | 2 | 17.35 (14.78) | 0.168 |

**Funding Agencies:** Department of Medicine Clinical Research and Projects Studentship Grant

A158

## COST-EFFECTIVENESS OF FECAL CALPROTECTIN AS A DIAGNOSTIC OR MONITORING TOOL FOR IBD: A SINGLE CENTER EXPERIENCE

A. Alahmadi[1], M. Al Khalaf[1], M. Elnenaei[1], J. Jones[2]

1. Gasrtoenterology, Dalhousie University, Halifax, NS, Canada; 2. Medicine, Dalhousie University, Halifax, NS, Canada

**Background:** Fecal calprotectin (FC) is a protein that is produced by neutrophils and monocytes. It can be detected in tissues, body fluids and stool which makes it valuable marker for neutrophil activity. FC concentrations increase in intestinal inflammation which makes it a valuable tool to distinguish inflammatory from non-inflammatory gastrointestinal conditions. We conducted a retrospective quality assurance audit on the use and cost-effectiveness of fecal Calprotectin assay at the Outpatient Gastroenterology Clinic at the Queen Elizabeth II Health Sciences Center in Halifax, NS.
**Aims:** To assess our use of Feacal Caloprotectin and the cost-effectiveness of it in our practice
**Methods:** Patients being followed through the gastroenterology clinic at the QE II Health Sciences Center who underwent FC testing were identified through lab services at the NSHA central zone. Inclusion criteria included any adult patient being followed through the GI ambulatory clinic at the QE II Health Sciences Center (HSC). A retrospective chart review was conducted for any FC testing performed between September 28, 2017 and March 29, 2017. Clinical visits before and after FC testing were reviewed for indication and to determine the clinical impact of FC testing. We considered FC testing to have had a "positive clinical impact" if it lead to dose escalation or change of medication (IBD management) or aided in endoscopic decision making. FC testing was considered to be cost-effective if supplanted endoscopic investigation for purposes of monitoring or screening patients.
**Results:** One hundred and five FC tests were ordered over a period of 6 months (28th September 2017 to 29 March 2017). Eighty-one FC tests had clinical information which allowed for evaluation of test indications and outcomes. Seventy percent of the patients were female. FC testing was ordered as a screening test for bowel inflammation (21%) or as an IBD disease monitoring tool (77%). The most common clinical symptoms prompting FC testing in IBD patients were diarrhea and abdominal pain (53% and 32%, respectively). The test aided in clinical decision making in 50 patients (61.7%). In some cases, FC results didn't change the clinical decision making process (23%), were not followed-up after the test (13%), or the indication wasn't clear (1%). In 28 patients, the decision to perform endoscopic investigation was prompted by the FC results. Colonoscopy was averted in almost 40 percent of the patients as a result of normal FC concentrations.
**Conclusions:** FC was demonstrated to have significant clinical impact when used to diagnose or monitor patients with IBD. The results of this study suggest that FC-enhanced diagnosis and monitoring may be more cost-effective than non-FC enhanced clinical decision making. Larger, long-term studies that consider the impact on health economics are needed.

**Funding Agencies:** None

A159

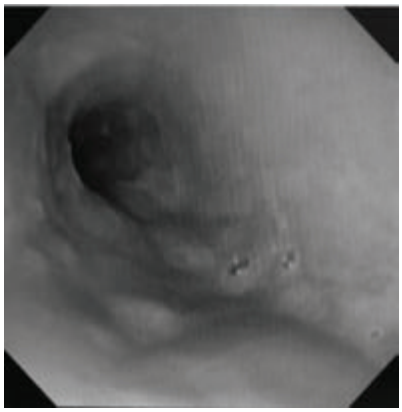
**VERY EARLY-ONSET INFLAMMATORY BOWEL DISEASE (VEO-IBD): CASE REPORT AND REVIEW OF THE LITERATURE**

A.A. Alahmari, V. Nguyen, V.D. Morinville, N. Ahmed, A. Sant'Anna

Montreal Children's Hospital - McGill University, Montreal, QC, Canada

**Background:** Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract, and its pathogenesis involves genetic and environmental factors. Very early-onset IBD (VEO-IBD) is a designation given to disease diagnosed before 6 years of age. This subgroup is often characterized by higher severity, aggressive progression, strong family history of IBD, predilection for colon-only involvement, and poorer response to conventional treatments. Immunodeficiencies are identified in up to 25% of cases, which may impact response, safety, and indication to different therapies.
**Aims:** To describe a case of VEO-IBD and review of the literature.
**Methods:** Case report and literature review.
**Results:**

We report a 6 month-old female that presented at 2 months with a history of fever, lethargy and bloody diarrhea after receiving standard 2 month-vaccinations (including rotavirus). Laboratory results demonstrated neutropenia (ANC 0.13), elevated inflammatory markers (CRP: 103-330 mg/L) and low albumin (16g/L), with a negative infectious work-up, including blood culture, stool culture, Clostridium difficile toxin, and viral serology (CMV). There was no improvement of bloody diarrhea on initial intravenous (IV) broad spectrum antibiotic coverage nor on exclusive elemental diet. Abdominal ultrasound showed mild circumferential wall thickening of transverse and descending colon with hyperemia compatible with colitis. An upper endoscopy and rectosigmoidoscopy revealed mild to moderate patchy chronic gastritis with several giant cells, a normal duodenum, and moderate to severe chronic patchy active colitis, suggestive of IBD. Due to early age of onset, a partial immunologic investigation was undertaken: chronic granulomatous disease, IL-10 and IL-10R pathway activity, were normal. A genetic panel to try to identify whether one of the genes identified in cases of VEO-IBD is planned.
Sulfasalazine was attempted but, led to worsened abdominal pain, distention, and bleeding; IV methylprednisolone was started (1.0 and then 1.5mg/kg/day), with partial response (decrease blood in stools, but inability to progress enteral feeds). Upper and lower endoscopies were repeated after one month of steroid, showing decreased colonic inflammation and normalized gastric biopsies. However, due to only partial response, enteral vancomycin and tobramycin were added, as well as hydrocortisone enemas, which led to improved symptoms and feeding tolerance.
**Conclusions:** VEO-IBD must be considered in infants with non-infectious bloody diarrhea unresponsive to hypoallergenic formula. More than 50 monogenic defects in innate and adaptive immune system have been associated with VEO-IBD and this is likely to grow with advances in genome sequencing. These disorders should be sought in VEO-IBD as positive findings may help guide more appropriate treatment.



**Funding Agencies:** None

A160

**IBD PATIENTS' ACCESS TO TELEPHONE / EMAIL SERVICE PROVIDED BY IBD NURSES IN CANADA**

U. Chauhan[2], I. Nistor[1], B. Currie[3], J. Nicholl[4], W. McCaw[5], M. Watson[6], L. Westin[7], A. Fernandes[8], C. Norton[9]

1. Halton Heathcare, Oakville, ON, Canada; 2. Digestive Disease, McMaster Uiversity Medical Centre , HAMILTON, NU, Canada; 3. QEII Health Sciences Centre, Halifax, NS, Canada; 4. Inomar Strategies , Oakville, ON, Canada; 5. Robarts Clinical Trials, London, ON, Canada; 6. London Health Sciences Centre, London, ON, Canada; 7. Red Deer Regional Hospital, Red Deer, AB, Canada; 8. McMaster University, Hamilton, ON, Canada; 9. King's College London, Waterloo, United Kingdom

**Background:** IBD is characterized by intermittent exacerbations of disease, known as 'flares', with activity free periods of 'remission'. The course of disease is unpredictable and it has a substantial negative impact on patients' quality of life and healthcare resources. The care of IBD patients extends beyond routine medical provider office visits as the disease activity is unpredictable and it does not coincide with the scheduled appointments. Nurses play an integral part in ensuring access to care during and between office visits.
**Aims:** The primary objective of this study was to examine the utilization of IBD nursing telephone/email service provided to IBD patients during a 14 day period in Canada.
**Methods:** Using a mixed method approach, data was

collected by CANIBD Nurses conducting an audit of telephone / email services provided by nurses working with IBD patients over a 2-weeks period. The nurses' interactions with IBD patients were compared using paired and independent t-tests.
**Results:** 84 IBD nurses across Canada were invited to participate in the study. 21 nurses participated in the study, including 4 research nurses, 7 adult and 2 pediatric RNs, 2 Clinical Nurse Specialists, 6 Nurse Practitioners ( 4 adult and 2 pediatric) with good representation from across the country. 431 encounters were reported: 78 (14%) via email, 327 (57%) via telephone and 26 (5%) telephone conversation following email interaction. The reasons for the telephone/email contact were divided into 9 themes: disease flare, other GI symptoms, medication related concerns, follow up with investigation results, scheduling appointments, questions related to insurance coverage, psychosocial concerns, financial concerns and other. Based on their interaction with the IBD patients, IBD nurse(s) were able to provide nurse managed interventions 343(60%), schedule an appointment in the IBD Clinic 112 (20%), consult the primary healthcare practitioner 109 (19%), consult an allied health practitioner such a dietician or ostomy nurse 13 (2%), instructed the patient to go to the Emergency Department 10 (2%), contact a patient support program 48 (8%), schedule a follow up telephone call to reassess 66 (12%), adjust medications 6 (1%) and other 111 (20%).
**Conclusions:** A few IBD nurses in Canada offer telephone/email access to care for IBD patients. Although 84 IBD nurses were invited to participate in this outpatient IBD nursing practice audit, only 21 completed the survey. IBD nurses are a critical point of contact for patients and our study identified and compared common reason for call in the adult and pediatric settings. Nurses were able to manage the "reason for call" 60% of the time. Further research would be valuable to explore the impact IBD nurses have on the wellbeing of patients with IBD and their healthcare utilization.

**Funding Agencies:** None

A161
**EVALUATING THE DIFFERENCES IN PERCEIVED STRESS AMONG NON-INFLAMMATORY AND INFLAMMATORY IBD FLARES**
T. Hansen[2], L. Targownik[2], J.R. Walker[4], M.T. Bernstein[2], K. Sexton[3], C.N. Bernstein[1]

1. Uiversity of Manitoba, Winnipeg, MB, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. University of Manitoba, Winnipeg, MB, Canada; 4. University of Manitoba, Winnipeg, MB, Canada

**Background:** The presence and severity of symptoms in IBD correlate poorly with the degree of inflammatory activity, especially in Crohn's disease (CD). Psychological factors, including perceived stress and mood disruption are associated with symptom activity. This relationship is bidirectional with increased symptoms predicting later increased perceived stress and vice versa. It is unclear whether the association between high perceived stress and active symptoms is weighted more towards high perceived stress being associated with symptomatic activity in individuals and no concurrent active inflammation than it would be in persons with increased symptoms and evidence of intestinal inflammation.
**Aims:** To evaluate whether perceived stress is associated with increased symptoms in non-inflammatory versus inflammatory IBD flares.
**Methods:** We recruited 487 persons from the University of Manitoba IBD registry to assess the relationship between intestinal inflammation, symptomatic disease activity, and psychologic factors. Disease activity was assessed using the Harvey Bradshaw Index (HBI) for CD and the Powell Tuck Index (PTI) for UC. Perceived stress was measured using the Cohen Perceived Stress (CPSS) scale with high scores defined as $\geq$ 20. A fecal calprotectin (FCAL) level >250ug/g was the cut point for active inflammation. An inflammatory flare was defined as a FCAL > 250ug/g and disease index >4. A non-inflammatory flare was defined as FCAL $\leq$250 and disease activity index >4. Completed surveys and stool samples were submitted at baseline, 3 months and 6 months.
**Results:** For CD (n=265), 31 (11.7%) were in an inflammatory flare at baseline while 55 (20.8%) were in a non-inflammatory flare. For UC (n=222) 32 (14.4%) were in an inflammatory flare while 39 (17.6%) were in a non-inflammatory flare. There was no significant difference in the likelihood of having a high CPSS score between those with inflammatory vs non-inflammatory flares either at baseline or at 6 months(Table 1). There were no differences in the scores on individual items in the CPSS score between persons in inflammatory flares versus those in non-inflammatory flares.
**Conclusions:** Increased perceived stress is equally associated with increased symptoms with persons with IBD regardless of the presence of inflammatory activity.

Table 1. Clinical Scores

| | Crohn's Disease Inflammatory Flare (n=31) | Crohn's Disease Non-Inflammatory Flare (n=55) |
|---|---|---|
| % with high CPSS Score at baseline | 70.97 | 80.00 |
| Average HBI Score at baseline | 8.03 | 9.67 |
| | | |
| | Ulcerative Colitis Inflammatory Flare (n=32) | Ulcerative Colitis Non-Inflammatory Flare (n=39) |
| % with high CPSS Score at baseline | 40.63 | 66.67 |

| | | |
|---|---|---|
| Average PT Score at baseline | 7.72 | 7.77 |

**Funding Agencies:** None

## INTESTINAL DISORDERS

A162

**PHYSICIAN DIAGNOSES AND SELF-DIAGNOSIS OF PATIENTS WITH CELIAC DISEASE IN THE INTERNET ERA**

T. Hansen[2], J. Silvester[2], L. Rigaux[5], L.A. Graff[3], C.N. Bernstein[1], J.R. Walker[4], D. Duerksen[2]

1. Uiversity of Manitoba, Winnipeg, MB, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. Clinical Health Psychology, University of Manitoba, Winnipeg, MB, Canada; 4. University of Manitoba, Winnipeg, MB, Canada; 5. University of Manitoba, Winnipeg, MB, Canada

**Background:** Celiac disease (CD) is an immune condition defined by intestinal inflammation in response to gluten. Manifestations of CD are variable and diagnostic delays are common. With growing public awareness of CD, many individuals are turning to resources such as the Internet, family and friends for health information.

**Aims:** In a population of newly diagnosed CD subjects, identify:

1. Alternate diagnoses prior to CD diagnosis
2. Resources used to self-diagnose CD
3. The role of the Internet in directing the diagnosis of CD

**Methods:** Between July 2014 and February 2017, adults with positive TTG and/or EMA antibodies and Marsh III histology were prospectively enrolled in the Manitoba CD Cohort. The initial study visit (within 6 weeks of initiating a gluten-free diet) included an optional online survey with items related to symptoms, use of health information sources and diagnoses given prior to CD.

**Results:** Among 99 subjects who completed the survey, median symptom duration was 3 years (IQR 1-10) prediagnosis and 1 year (IQR 0.25-3) prior to seeking health care evaluation. The most common symptoms at diagnosis were gas (58%), urgency (45%) and difficulty concentrating (35%). Many subjects (35%) were given a diagnosis other than CD for their symptoms, most commonly IBS or a psychological diagnosis (Table 1). The Internet and family doctor were considered the most important sources used to identify a diagnosis. About 80% of subjects who were Internet users (n=93) used the Internet to research their symptoms. The most accessed Internet sites were the Canadian Celiac Association (n=55), Mayo clinic (n=52) and WebMD (n=39). One quarter (n=18) made a self-diagnosis based on their search, with 7 concluding that CD was the most likely diagnosis. As a result of their Internet search, 66% talked to a friend, 54% saw their family doctor, and 43% changed their diet. Doctors visits were used to ask for a TTG (31%), discuss what was found on the Internet (27%) and/or ask for a gastroenterology referral (24%).

**Conclusions:** Many doctors and patients attribute symptoms of CD to alternate conditions, which may contribute to diagnostic delays. Many individuals diagnosed with CD used the Internet to research their symptoms thereby initiating the CD evaluation. More work is needed to raise awareness about CD screening.

Diagnoses for CD symptoms

| | MD diagnosis (n=35) | Self-diagnosis (n=18) | |
|---|---|---|---|
| | | Possible | Most likely |
| CD | n/a | 12 | 7 |
| Psychologic | 49% | 15 | 1 |
| IBS | 46% | 10 | 3 |
| Iron deficiency | 29% | 0 | 0 |
| Lactose intolerance | 23% | 5 | 1 |
| Menstrual issues | 20% | 4 | 0 |
| Gallbladder disease | 11% | 3 | 1 |
| Diverticular disease | 9% | 1 | 1 |
| Other | 31% | 4 | 2 |

**Funding Agencies:** None

## Poster of Distinction

A163

**THE ROLE OF ANTIBIOTICS IN ACUTE UNCOMPLICATED DIVERTICULITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

V. Mocanu, J. Dang, N. Switzer, I. Tavakoli, C. Tian, C. de Gara, D.W. Birch, S. Karmali

Department of Surgery, University of Alberta, Edmonton, AB, Canada

**Background:** Diverticular disease is the most common disease of the large bowel and poses a significant burden on healthcare resources. In the United States alone, the cost of diverticular disease has been estimated to be over $3 billion making it the fifth most important gastrointestinal disease economically. The use of antibiotics in the management of acute uncomplicated diverticulitis (AUD), however, is primarily based on expert opinion as current high-quality evidence is lacking. Recent studies have not only questioned the optimal type and duration of antibiotic regimens, but whether

antibiotics provide any benefit in the treatment of AUD.
**Aims:** The aim of the present study was to perform a systematic review of the literature to determine the role of antibiotics in the management of AUD.
**Methods:** A comprehensive literature search for both published and unpublished studies of "diverticulitis AND antibiotics" from 1946 to June 2017 was performed using Medline, EMBASE, Scopus, the Cochrane Library, and Web of Science databases. Included studies were assessed for methodological quality and bias. Abstracts and titles were screened for inclusion by two independent reviewers as per PRISMA guidelines. Outcomes assessed in the meta-analysis included treatment failure, recurrence, abscess, perforation, bleeding, stenosis, hospital length of stay, need for elective surgery or emergent surgery and overall morbidity using the Revman 5.3 software.
**Results:** Eight studies with 2469 patients were included for review. Overall complication rates (Figure 1) were not statistically significant between groups (OR 0.72; CI 0.45 to 1.16; P = 0.18), but antibiotic use was associated with a longer length of stay in hospital (MD -1.13; CI -1.77-to -0.48; P = 0.0006). Subgroup analysis revealed no difference in readmission rates (OR 0.77; CI 0.55 to 1.09; P = 0.14), treatment failure rates (OR 0.43; CI 0.15 to 1.27; P = 0.13), progression to complicated diverticulitis, or increased need for elective (OR 0.66; CI 0.24 to 1.79; P = 0.80) or emergent surgery (OR 0.69; CI 0.24 to 1.79; P = 0.80) between study groups.
**Conclusions:** Antibiotic use in patients with acute uncomplicated diverticulitis is not associated with a reduction in major complications, readmissions, treatment failure, progression to complicated diverticulitis, or need for elective and emergent surgery. However, it increases the length of hospital stay. Antibiotics may not be warranted, but given the risk of selection bias in included studies, further randomized trials are needed to clarify the need for antibiotics in uncomplicated diverticulitis.

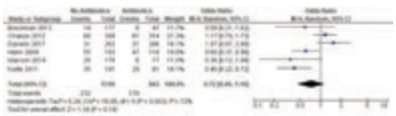


Figure 1. Major complications for antibiotics vs no antibiotics

**Funding Agencies:** None

## Poster of Distinction

A164
**HIGHLY EFFICIENT DIFFERENTIATION OF HUMAN PLURIPOTENT STEM CELLS INTO LONG-TERM EXPANDABLE "MINI-GUT" ORGANOIDS**
P. Kramer, P. Soriano, R. Conder, T.E. Thomas, A.C. Eaves, S.A. Louis
STEMCELL Technologies, Vancouver, BC, Canada

**Background:** The differentiation of human pluripotent stem cells (hPSC) into intestinal organoids represent an attractive mechanism for generating cells for disease modelling, drug screening and cell-replacement therapy. Although it is possible to generate intestinal organoids from adult stem cells, the derivation of organoids from hPSCs has been shown to result in a broader variety of cells as the starting material.
**Aims:** Introduce novel PSC to intestinal differentiation kit and protocols.
**Methods:** We developed the STEMdiff™ Intestinal Organoid Kit, a specialized serum-free and fully-defined medium formulation that efficiently and reproducibly promotes differentiation of human embryonic stem (ES) and induced pluripotent stem (iPS) cells through developmental stages of 1) definitive endoderm, 2) mid-/hindgut, and 3) small intestine.
**Results:** Here we demonstrate that monolayers generated with multiple human ES (WA01, WA07, WA09) and iPS (WLS-1C, STiPS-FO16, STiPS-MOO1) lines maintained in mTeSR™ with Corning Matrigel™, differentiate into FOXA2$^+$/SOX17$^+$ endoderm cultures with an efficiency of 81.6% ± 8.6% (n=21). Further differentiation into posterior endoderm to promote the formation of mid-/hindgut resulted in 71.4 ± 8.5% (n=13) of cells expressing the hindgut marker CDX2, but none of the cells expressing the anterior gut tube marker SOX2. Twenty-four hours after the emergence of CDX2$^+$ cells, clusters in the flat cell sheet monolayers changed their morphology to tightly packed epithelial tubes that generated budding spheroids which detached from the monolayer. These detached hindgut spheroids are composed of CDX2$^+$/E-cadherin$^+$ epithelia and adjacent CDX2$^+$/VIM$^+$ mesenchyme. When these spheroids were collected, embedded in Corning™ Matrigel™ and cultured in fully defined IntestiCult™-hPSC Organoid Growth Medium (OGM), they generated intestinal organoids composed of a polarized intestinal epithelium patterned into villus-like structures, and a surrounding niche factor-producing mesenchyme. Organoids cultured for > 25 days *in vitro* and analyzed by immunohistochemistry and/or qRT-PCR demonstrate the presence of enterocytes (villin), goblet cells (MUC2), paneth cells (lysozyme), and intestinal stem cells (LGR5). These organoids can be further dissociated and passaged every 7 to 10 days for multiple passages in IntestiCult™-hPSC OGM. Our results demonstrated that a starting population of approximately 200,000 hPSCs seeded in a single well of a 24-well plate gave rise to 216 ± 19.7% (n=10) intestinal organoids, which could be passaged and expanded long-term (> 8 months, n=3) using IntestiCult™-hPSC OGM.
**Conclusions:** In summary, STEMdiff™ Intestinal Organoid Kit is an easy to use kit for the derivation of large quantities of human intestinal organoids from hPSC in a highly efficient and reproducible manner.

**Funding Agencies:** None

## Poster of Distinction

A165

### GENETIC DELETION OF *HDAC1* AND *HDAC2* DISRUPTS MURINE ENTEROID DEVELOPMENT AND METABOLIC PROGRAM

A. Gonneaud, N. Turgeon, C. Jones, C. Couture, F. Boisvert, F. Boudreau, C. Asselin

Department of Anatomy and Cell Biology, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** Histone deacetylases HDAC1 and HDAC2 are homologous enzymes removing acetyl groups from histones and non-histone proteins. This epigenetic mark regulates many biological processes including cell proliferation and differentiation. We have shown that HDAC1 and HDAC2 drive intestinal epithelial cell (IEC) development and that *Hdac1* and *Hdac2* deletion in murine IEC disrupts intestinal architecture and IEC differentiation, leading to chronic colonic inflammation.
**Aims:** We hypothesize that HDAC1 and HDAC2 display similar as well as distinct functions in IEC and that IEC-specific HDAC activity alterations modify basal IEC behavior and the intrinsic IEC response to environmental inflammatory signals.
**Methods:** Jejunal villin-Cre *Hdac1* or *Hdac2* enteroids were established and grown in medium with or without SILAC, for proteome quantification by mass spectrometry. The transcriptome was assessed by RNA-Seq. Pathways were identified by bioinformatics approaches (DAVID, IPA). Villin-Cre$^{ER}$ *Hdac1* and *Hdac2* enteroids were treated with hydroxytamoxifen to induce gene deletion. The phenotype of Villin-Cre$^{ER}$ *Hdac1* and *Hdac2* as well as Villin-Cre *Hdac1* and *Hdac2* enteroids was observed by microscopy. To evaluate inflammatory response, enteroids were treated with TNF-α for 16h. Expression of selected targets was assessed by qPCR and Western blot
**Results:** Embryonic or inducible deletion of *Hdac1* and *Hdac2* led to reduced enteroid growth and increased degeneration. Proteomic analysis of *Hdac1* or *Hdac2* deleted enteroids revealed shared enrichment of ontology terms, including metabolic and lipid metabolic processes or cell-cell adhesion. Transcriptomic analysis uncovered inflammatory response, immune system, retinol metabolic and oxydo-reduction processes and development ontology terms as being shared between HDAC1 and HDAC2. Transcriptomic analysis also revealed distinct pathways, namely response to virus and response to IFNγ upon *Hdac2* deletion, and cholesterol homeostasis, ion transport and negative regulation of cell migration, upon *Hdac1* deletion, among others, while proteomic analysis exposed many metabolic processes and ATP-dependent chromatin remodeling as distinct enriched ontology terms for *Hdac1* deleted enteroids, and cellular responses to many environmental signals for *Hdac2* deleted enteroids. TNF-α treatment induced apoptosis, as determined by Caspase 3 cleavage, in both mutated enteroids, while decreased NF-kB p65 phosphorylation was observed in *Hdac2* deleted enteroids.
**Conclusions:** HDAC1 and HDAC2 are necessary for intrinsic IEC growth. HDAC1 and HDAC2 regulate similar as well as distinct gene and protein expression programs, thereby indicating specific molecular functions in IEC. Selective inhibition of HDAC1 or HDAC2 in IEC by pharmacological agents could affect the mucosal response to inflammation.

**Funding Agencies:** CCC, CIHR

A166

### THE LONG-LIVED ANTI-COLITIC EFFECT OF ADOPTIVE TRANSFER OF INTERLEUKIN-4 EDUCATED MACROPHAGES

A. Wang[3], G. Leung[1], A.J. Shute[4], D.M. McKay[2]

1. The Hospital for Sick Children, Toronto, ON, Canada; 2. Physiology & Pharmacology, Uni. Calgary, Calgary, AB, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. Phisiology and Pharmacology, University of Calgary , Calgary, AB, Canada

**Background:** Postulating that cellular immunotherapy could be used to treat IBD, we showed that intraperitoneal (ip) injection of murine bone-marrow derived macrophages (BMDM) treated with IL-4 (M(IL4), i.e. alternatively activated macrophages), reduced the severity of dinitrobenzene sulphonic acid (DNBS)-induced colitis.
**Aims:** Here we investigated the longevity of this response and queried a role for the microbiota in the inhibition of colitis evoked by the adoptive transfer of M(IL4)s.
**Methods:** BMDM were treated with IL-4 (20 ng/mL, 48h) and $10^6$ M(IL4)s were given to Balb/c mice (n=5-21, 1-3 experiments) by ip. injection 2, 5, 8 or 14 days prior to intra-rectal (ir) delivery of 3 mg of DNBS. Three days post-DNBS, mice were necropsied and disease severity assessed by macroscopic and histological disease scores. Other mice received a 1-week broad spectrum antibiotic (Abx) regimen in their drinking water and DNBS ± M(IL4)s 2 days prior to the DNBS.

**Results:** DNBS-treated mice consistently displayed loss of body weight, shortening of the colon, significant histopathology and disease activity scores (DAS) of 3.6±0.9 (mean±SD, n=21; max. score is 5). M(IL4)s given 2 days prior to DNBS suppressed colitis, and remarkably mice treated with M(IL4)s 14 days before ir. DNBS were equally protected (DAS=1.5±0.9, n=7), although some mice still displayed significant histopathology. In addition, M(IL4)s (2-day pretreatment) failed to ameliorate DNBS-induced colitis in mice concomitantly treated with antibiotics (DAS: control = 0±8; DNBS = 3.6±1.3; DNBS+M(IL4) = 0.9±1.2; DBNS+M(IL4)+Abx = 3.3±1.2; n=8-12, 3 experiments).
**Conclusions:** These data provide proof-of-concept support for M(IL4) immunotherapy to treat colitis and

suggest that each treatment could protect the individual for a considerable period of time. There are caveats with the use of antibiotics, nevertheless, these preliminary findings suggest that consideration of the gut microbiota may be needed in the translation of M(IL4) therapy for a targeted cohort of patients with IBD.

**Funding Agencies:** CCC, CIHR

A167

**EVALUATING THE DIAGNOSTIC YIELD OF COMPUTED TOMOGRAPHIC ENTEROGRAPHY FOR PATIENTS WITH IRON DEFICIENCY ANEMIA**

J. Buttar, Z. Hirji, K. Atkinson

University of British Columbia, Vancouver, BC, Canada

**Background:** Although several etiologies exist, gastrointestinal bleeding is widely considered to be responsible for Iron Deficiency Anemia (IDA). Currently, there is debate regarding the most appropriate course of investigation following negative bidirectional endoscopy. Computed Tomographic Enterography (CTE) has emerged as a prospective diagnostic tool but limited studies have outlined its role, specifically for investigation of IDA.
**Aims:** To evaluate the efficacy of CTE through diagnostic yield for patients with IDA. Furthermore, to outline etiologies of gastrointestinal bleeding, predictive symptoms, and changes in management for true positive cases.
**Methods:** Patients were identified by CTE requisition orders at the Royal Columbian Hospital Centre consecutively between Jan 1, 2013 and June 1, 2017. Only patients diagnosed with Iron Deficiency Anemia, or who had experienced obscure occult gastrointestinal bleeding were included. To determine the diagnostic yield of CTE, patients' charts were retrospectively studied. Negative endoscopy or lack of further small bowel investigation following a negative CTE was defined as a True Negative. Positive endoscopy for small bowel carcinomas matching the description of a prior CTE was defined as a True Positive.
**Results:** 937 CTE results were reviewed and 223 patients matched our inclusion criteria. 7 positive CTE results were identified, 3 of which were false positives. 216 negative CTE results were identified, none of which were false negatives. Follow-up Capsule Endoscopy (CE) was used in 13 negative cases, of which 3 identified non-malignant sources of GI bleeding. The diagnostic yield of CTE was 1.8%, with 100% sensitivity and 98.6% specificity. The etiologies of the 4 positive cases included a GIST tumor, a small bowel spindle cell neoplasm, and two moderately differentiated adenocarcinomas. Further investigation included an imaging technique (Colonoscopy or Laparoscopy) followed by surgical small bowel resection. In one case, CE was used to localize the tumor within the small bowel following positive CTE. None of the symptoms exhibited by the patients of the four positive cases were atypical of diagnostic symptoms of IDA.
**Conclusions:** CTE has high sensitivity and specificity in investigating IDA. Only 1.8% of patients had a change in management based on CTE but all were significant. The four lesions identified by CTE required further imaging, including CE, before surgical resection. Given that CE has a higher diagnostic yield than CTE, it may be a better choice for IDA if no contraindication to CE exists, as opposed to CTE followed by CE.

**Funding Agencies:** None

A168

**KAISO-INDUCED INTESTINAL INFLAMMATION IS ACCOMPANIED BY FAULTY CELL ADHESION AND ABERRANT INTESTINAL REPAIR.**

S. Robinson[1], R. Chaudhary[2], R. Jimenez-Saiz[2], L. Rayner[3], M. Jodana[2], J. Daniel[3]

1. Cell Biology Program, The Hospital for Sick Children Research Institute, Toronto, ON, Canada; 2. McMaster Immunology Research Centre, McMaster University, Hamilton, ON, Canada; 3. Dept. of Biology, McMaster University, Hamilton, ON, Canada

**Background:** Kaiso is a member of the POZ-ZF family of transcription factors that play key roles in vertebrate development and disease. We previously reported that intestinal-specific overexpression of Kaiso (*Kaiso$^{Tg}$*) potentiates Wnt-induced colon cancer and results in chronic inflammation in 1-year old mice. Notably, the intestines of *Kaiso$^{Tg}$* mice exhibit phenotypes reminiscent of human IBD, including leukocyte infiltration, expanded crypts, and blunted villi. However the mechanism underlying Kaiso-induced inflammation was unknown.
**Aims:** In this work, we seek to identify the factors/mechanisms predisposing Kaiso transgenic mice to subsequent intestinal inflammation.
**Methods:** To assess morphological differences relative to non-transgenic (nonTg) mice, histological comparisons were performed using two independent *Kaiso$^{Tg}$* mouse lines at 8-months of age. Flow cytometry was performed to ascertain differences in immune cell populations. We also performed myeloperoxidase (MPO) activity assays to assess neutrophil activity in *Kaiso$^{Tg}$* mice. Immunohistochemistry (IHC) of cell adhesion proteins was used to determine differences in subcellular location, and western blot was used to quantify differences in their expression. IHC of Ki67 and western blot of Cyclin D1 were used to compare differences in proliferation. To assay *in vivo* collective cell migration, mice were given a single injection of BrdU and sacrificed 24- and 48-hours post injection. The distance migrated of BrdU-retaining cells was then quantified.
**Results:** In this work, we show that Kaiso overexpression elicits a neutrophil-specific inflammatory response, as indicated by increased MPO activity, elevated mRNA expression of the neutrophil chemokine, MIP-2, and formation of crypt abscesses. To identify the factor(s) predisposing *Kaiso$^{Tg}$* mice to subsequent inflammatory disease, subclinical

(12-week old) mice were examined prior to the onset of inflammation. Notably, E-cadherin localization and expression were reduced in subclinical *Kaiso*$^{Tg}$ mice, thus weakening the intestinal barrier and predisposing the mice to subsequent inflammation. Subclinical *Kaiso*$^{Tg}$ mice also displayed abnormal intestinal renewal mechanisms, such as delayed proliferation and accelerated cell migration.
**Conclusions:** Together, these findings demonstrate that a weakened intestinal barrier and irregular intestinal renewal mechanisms may play a role in the development of subsequent intestinal inflammation caused by Kaiso overexpression. Importantly, our findings may hold clinical significance, since Kaiso expression is elevated in colon cancer and some cases of Crohn's disease.

**Funding Agencies:** CIHRNSERC

A169

## EFFICACY AND SAFETY OF ELUXADOLINE IN ELDERLY PATIENTS WITH IRRITABLE BOWEL SYNDROME WITH DIARRHEA

B. Lacy[1], L. Harris[2], L. Chang[3], S. Lucak[4], C. Gutman[5], L. Dove[6], P. Covington[6], A. Lembo[7]

1. Dartmouth-Hitchcock Medical Center, Lebanon, NH; 2. Mayo Clinic, Phoenix, AZ; 3. University of California, Los Angeles, CA; 4. Weill Cornell Medical Center, New York, NY; 5. Allergan plc, Parsippany, NJ; 6. Former employee of Furiex Pharmaceuticals, Inc., an affiliate of Allergan plc, Parsippany, NJ; 7. Beth Israel Deaconess Medical Center, Boston, MA

**Background:** Irritable bowel syndrome with diarrhea (IBS-D) is characterized by abdominal pain and diarrhea and can affect people of all ages. Eluxadoline (ELX) is approved for the treatment of IBS-D in Canada, the U.S., and the E.U., based on Phase 3 trials in which it simultaneously improved abdominal pain and stool consistency.
**Aims:** To examine the efficacy and safety of ELX in patients aged <65 and ≥65 years in a post hoc analysis of Phase 3 clinical trials.
**Methods:** Two Phase 3 clinical trials randomized patients meeting Rome III criteria for IBS-D to twice-daily (BID) treatment with ELX (75 or 100 mg) or placebo for 26 weeks. Patients rated worst abdominal pain (0–10), stool consistency (Bristol Stool Form Scale [BSFS]; 1–7), and global symptom score (GSS; 0–4) daily. Patients with a decrease in abdominal pain (≥30%) and improvement in stool consistency (BSFS <5) on the same day for ≥50% of days were considered composite responders. A GSS score of 0 or 1 or an improvement of ≥2.0 indicated a GSS response.
**Results:** Overall, 9.9% of patients were aged ≥65 years. Significantly more patients aged <65 and ≥65 years were composite responders at both ELX doses compared to placebo (Table). The proportion of abdominal pain responders was significant only for patients <65 years, while the proportion of stool consistency responders was significantly greater than placebo at both ELX doses in both age groups (Table). In patients ≥65 years, only ELX 75 mg was associated with a significantly higher proportion of GSS responders vs. placebo. Among patients aged ≥65 years, the responder rate for each of these endpoints was greater with ELX 75 mg compared to ELX 100 mg. The proportion of patients with ≥1 adverse event was slightly higher among patients aged ≥65 years compared to younger patients (66.2% vs. 59.7% and 65.3% vs. 57.5% of patients receiving ELX 75 or 100 mg, respectively). In patients <65 years, constipation occurred in 7.3% and 8.4% of patients receiving ELX 75 or 100 mg, respectively, compared to 9.2% and 10.7% in patients ≥65. Of six total cases of pancreatitis, one occurred in a patient aged ≥65 years.
**Conclusions:** ELX improved IBS-D symptoms in patients aged <65 and ≥65 years. While the data are limited by sample size, in patients aged ≥65 years, the lower approved ELX dose of 75 mg BID was associated with a greater response rate than the 100 mg BID dose. Hence, the lower approved dose is recommended for this population.

| | <65 years | | | ≥65 years | | |
|---|---|---|---|---|---|---|
| n (%) | Placebo (n=707) | ELX 75 mg BID (n=743) | ELX 100 mg BID (n=732) | Placebo (n=102) | ELX 75 mg BID (n=65) | ELX 100 mg BID (n=74) |
| Composite responders† | 138 (19.5) | 183 (24.6)* | 220 (30.1)*** | 20 (19.6) | 33 (50.8)*** | 30 (40.5)** |
| Abdominal pain responders | 300 (42.4) | 331 (44.5) | 349 (47.7)* | 56 (54.9) | 43 (66.2) | 40 (54.1) |
| Stool consistency responders | 169 (23.9) | 217 (29.2)* | 263 (35.9)*** | 24 (23.5) | 34 (52.3)*** | 34 (45.9)** |
| GSS responders | 232 (32.8) | 292 (39.3)* | 289 (39.5)* | 37 (36.3) | 35 (53.8)* | 34 (45.9) |

†Patients with simultaneous abdominal pain and stool consistency response on ≥50% of days
*p<0.05 vs. placebo; **p<0.005 vs. placebo; ***p<0.001 vs. placebo

**Funding Agencies:** Allergan plc

A170

**CANADIANS WITH CELIAC DISEASE MISINTERPRET PRODUCT LABEL INFORMATION WHICH MAY LEAD TO UNSAFE FOOD CHOICES DESPITE ALLERGEN LABELLING LAWS**

E. Gutowski[2], J. Silvester[2], L. Rigaux[5], K. Green[5], D. Weiten[6], C.N. Bernstein[1], J.R. Walker[3], L.A. Graff[4], D. Duerksen[3]

1. University of Manitoba, Winnipeg, MB, Canada; 2. Harvard Celiac Disease Program, Boston, MA; 3. University of Manitoba, Boston, MA; 4. Clinical Health Psychology, University of Manitoba, Winnipeg, MB, Canada; 5. St Boniface Hospital, Winnipeg, MB, Canada; 6. Grace General Hospital, Winnipeg, MB, Canada

**Background:** Patients with celiac disease (CD) often report challenges reading labels as well as inadvertent gluten exposures and the most common cause of non-responsive CD is gluten exposure.
**Aims:** To assess whether patients with CD can proficiently assess product labelling to determine if a product is gluten-free.
**Methods:** The Manitoba Celiac Disease Cohort includes newly diagnosed adults with elevated TTG and/or EMA antibodies and Marsh III histology. At each follow-up visit (6, 12 and 24 months), participants were presented with 25 grocery items purchased at a local supermarket (different items at each time point) and asked to determine whether each was gluten-free based upon labeling information. The Celiac Diet Assessment Tool (CDAT) and Gluten-Free Eating Assessment Tool (GF-EAT) were used to assess GFD adherence.

**Results:** There were 78 participants (62% female, mean age 40 years) who completed the 24 month study visit, of whom 70 also completed the 6 month assessment and 62 the 12 month assessment. Participants generally reported good gluten-free diet adherence (median CDAT score < 13 at each time point, which is associated with adequate adherence); however, at 24 months 73% reported rare gluten exposure less than once per month on the GF-EAT. Grocery Quiz scores were [median (IQR)]: 6 months, 22/25 correct (21-23); 12 months, 21 (20-22); 24 months, 18 (18-19). Participants were more likely to make errors with gluten-containing items and least likely to make errors with gluten-free products with explicit “gluten-free" labelling claims. There were no significant correlations between quiz scores and either TTG antibody levels or standardized gluten-free diet adherence assessment tools.
**Conclusions:** Patients who are trying to follow a gluten-free diet may not be able to consistently choose appropriate gluten-free foods based upon product labeling information. The ability to correctly read food labels does not appear to improve with time. Further studies are needed to evaluate whether insufficient label reading skills are associated with persistent villous atrophy.

**Funding Agencies:** CAG, CIHRNational Institutes of Health (United States)

A171

**DEVELOPMENT AND VALIDATION OF THE DIETITIAN INTEGRATED EVALUATION TOOL FOR GLUTEN-FREE DIETS (DIET-GFD)**

A. Atsawarungruangkit[1], J. Silvester[2], D. Weiten[3], K. Green[4], K. Wilkey[2], L. Rigaux[4], C.N. Bernstein[5], L.A. Graff[5], J.R. Walker[5], D. Duerksen[5]

1. MetroWest Medical Center, Framingham, MA; 2. Harvard Center for Celiac Disease Research, Boston, MA, Boston, MA; 3. Grace General Hospital, Winnipeg, MB, Canada; 4. St. Boniface Hospital, Winnipeg, MB, Canada; 5. Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, MB, Canada

**Background:** Celiac disease (CD) is a chronic autoimmune disease characterized by small intestinal villous damage that recovers with a gluten-free diet (GFD). A consultation with a skilled dietitian is the clinical gold standard for monitoring GFD adherence. Yet, there is no standardized tool for dietitians to objectively grade GFD adherence.
**Aims:** To develop a standardized tool to evaluate GFD adherence that can be used by dietitians.
**Methods:** Participants were recruited from the Manitoba Celiac Disease Cohort, a prospective inception cohort of confirmed CD based on elevated TTG and/or EMA antibodies and Marsh III histology. Using a consensus process, an expert panel of gastroenterologists, dietitians with expertise in GFDs, clinical health psychologists and persons with CD developed the DIET-GFD. Two dietitians then performed duplicate assessments of 27 newly diagnosed participants who had been advised to follow a GFD. The global adherence scale was further revised following panel discussions of the cases where the dietitian ratings were discordant or they were uncertain which rating to apply. The scoring system was then validated using duplicate assessments of additional 37 CD participants. Interrater agreement between the two dietitians was assessed using square-weight Cohen's kappa.
**Results:** The DIET-GFD includes features related to frequency and quantity of gluten ingestion based upon self-report and food frequency evaluation, shopping and dining habits, how and where food is prepared and consumed, eating behaviors, and label reading skills. The DIET-GFD global assessment is reported using a 10-point ordinal descriptive scale ranging from 1 (takes few precautions and regularly eats gluten) to 10 (no gluten in kitchen and rarely eats food prepared outside the home). The validation study included 38 study visits (n = 38) involving 37 participants. The kappa of DIET-GFD global assessment was 0.845 (almost perfect agreement).
**Conclusions:** DIET-GFD is a useful tool for dietitians to evaluate GFD adherence. Given a high level of agreement between two expert dietitians, further

studies are needed to confirm that the score from DIET-GFD is reliable across institutions and cultures as well as dietitians who do not have GFD expertise.

**Funding Agencies:** CAG, CIHRNational Institutes of Health (NIH)

A172

**ATTITUDES TOWARDS MEDICAL TREATMENT AND MEDICATION ADHERENCE IN IBD PATIENTS TAKING CONVENTIONAL, ANTI-TNF, OR COMBINATION THERAPY**

C. Evans[2], M.A. MacMillan[1], G. Stoica[3]

1. Gastroenterology, Dalhousie University, Halifax, NS, Canada; 2. Medicine , Dalhousie University , Sackville, NB, Canada; 3. Horizon Health Network, Saint John, NB, Canada

**Background:** Inflammatory bowel disease (IBD) is a chronic, progressive, immune-mediated disease for which Canada has among the highest incidence and prevalence in the world. Adherence to medical therapy is paramount in reaching management goals of symptom reduction and ultimately disease remission.
**Aims:** Our aim is to illustrate the perceived necessity and concerns (attitudinal score) of IBD patients towards their medical treatment plan and patient-reported medication adherence. We hypothesize that patients' who report 'ambivalent' attitudes towards their IBD treatment are less adherent to their medical therapy compared to 'accepting' patients which could hinder treatment efficacy.
**Methods:** We used the internationally validated 2014 ALIGN questionnaire with eligible voluntary participants from a single Canadian gastroenterology practice. Inclusion criteria was a diagnosis of IBD, current therapy of Imuran or Methotrexate, anti-TNF, or combination anti-TNF with Imuran or Methotrexate, and age ≥18 years.
**Results:** The majority (55%) of patients were *accepting* of their treatment plan, 34% *ambivalent*, 8% *skeptical,* and 3% *indifferent.* The majority of patients were also either moderately or highly adherent to their therapy (48%, 46%), with only 6% reporting low adherence. As hypothesized, *accepting* patients reported higher medication adherence in comparison to *ambivalent* patients (49%, 39%).
**Conclusions:** More than half of the IBD patients in our sample did not report high medication adherence, therefore their IBD is not receiving essential disease modifying therapy. Untreated IBD leaves patients at higher risk of hospitalizations, surgeries, colon cancer and reduced quality of life. Although most participants were *accepting* towards their current therapy, 45% felt otherwise. Patients' concerns and beliefs about their medical therapy warrant better exploration during consults as to address the effect of attitude on medication adherence and subsequent disease course.

**Funding Agencies:** None

A173

**HOME BASED FECAL CALPROTECTIN TESTING: A CANADIAN USER PERFORMANCE EVALUATION STUDY OF IB*DOC*®**

A. Wong[5], B. Bressler[1], V. Huang[4], R. Bourdages[6], Y. Leung[3], G. Rosenfeld[2]

1. Pacific Gastroenterology Associates, Vancouver, BC, Canada; 2. Medicine, UBC, Vancouver, BC, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada; 5. Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 6. Hôtel-Dieu de Lévis, Lévis, QC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

**Funding Agencies:** BÜHLMANN Laboratories AG

A174

**ASSESSMENT OF DISTRIBUTED EDUCATION ON GLUTEN-FREE DIET TO FAMILIES OF CHILDREN WITH NEWLY DIAGNOSED CELIAC DISEASE**

M. Rashid[1], J. Haskett[1], L. Parkinson-McGraw[1], A. Noble[1], J. Van Limbergen[2], A. Otley[1]

1. IWK Health Centre, Halifax, NS, Canada; 2. Pediatric Gastroenterology and Nutrition, IWK Health Centre, Halifax, NS, Canada

**Background:** Treatment of celiac disease (CD) is a strict life-long gluten-free diet (GFD). The GFD is complex and counselling by an expert dietitian is essential. Number of new CD diagnoses is increasing, leading to significant impact on dietitian resources. Distributed education is a means of providing GFD teaching to groups of families off site instead of one-to-one sessions.
**Aims:** To assess the feasibility and effectiveness of GFD education using distributed teaching.
**Methods:** The IWK Health Centre in Halifax, Nova Scotia is the only tertiary care paediatric institution in the three Maritime Provinces of Canada. It has two paediatric dietitians with expertise in GFD who provide teaching to families of children with newly diagnosed CD. Families often have to travel long distances to come to the institution, sometimes in excess of 4 hours driving. Patients outside Halifax area were offered to participate in teaching sessions via live videoconference link at their regional hospitals free of charge. All family members of the patient were encouraged to attend. Sessions were held once a month at noon and were 2-2.5 hours in duration. They were interactive, with a gastroenterologist giving a brief overview of CD, a social worker or psychologist providing information on finances/coping and dietitian providing details of GFD. All families who attended the sessions were surveyed by mail with a 10-item questionnaire to assess Content/Delivery and Usefulness of Information received on a five-point Likert scale.
**Results:** From January to June 2017, a total of 39 families attended the GFD teaching sessions. Of these, 21 (54%) were in Halifax (local) and 18 (46%) at



To view enlarged images and tables, please refer to Abstract Library.

distributed sites including 8 at various places in Nova Scotia, 6 in New Brunswick and 4 in Prince Edward Island. Number of families at each session ranged from 3-9 with all sessions having participants from both local and distributed sites. All sessions were completed successfully.
Feedback survey was completed by 26 (67%) families, 12 local and 14 from distributed sites. All participants at both sites Strongly Agreed/Agreed that the physical setting (e.g. sound, visuals) was good for learning and information provided was easy to understand. At the distributed sites 86% and at local site 92% of participants Strongly Agreed/Agreed that the learning environment was interactive. There were no significant differences in responses between the two groups to other questions asked. Three participants wished there was more time, while two felt that session was too long.
**Conclusions:** Distributed education on gluten-free diet using videoconferencing is feasible and effective. It affords convenience for families and savings on dietitian resources. Challenges include organization of teaching sessions for multiple sites and determining their appropriate duration.

**Funding Agencies:** None

A175
**LINACLOTIDE AND PRUCALOPRIDE FOR MANAGEMENT OF CONSTIPATION IN PATIENTS WITH PARKINSONISM.**
M. Freitas[1], A. Alqaraawi[3], A. Lang[1], L.W. Liu[2]

1. Division of Gastroenterology, Department of Medicine, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada; 2. Medicine, University Health Network, Toronto, ON, Canada; 3. King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

**Background:** Constipation is a common condition in patients with neurodegenerative parkinsonism, including Parkinson's disease (PD), multiple system atrophy (MSA), and progressive supranuclear palsy (PSP). Chronic constipation negatively impacts quality of life and decrease the absorption of antiparkinsonian drugs. Linaclotide (guanylate cyclase C agonist) and prucalopride (selective 5-$HT_4$ receptor agonist) are emerging effective drugs for the management of chronic idiopathic constipation (CIC). To date, neither of these drugs has been tested in controlled trials in parkinsonism patients and their efficacy is unknown in this population.
**Aims:** We aimed to identify patients who received linaclotide or prucalopride in our clinic database and to review the change in bowel movement frequency and the patient perception of drug effect.
**Methods:** We searched our patient database for patients diagnosed with neurodegenerative parkinsonism and constipation who had received linaclotide or prucalopride. Constipation was defined by Rome III criteria. Demographics, treatment characteristics, BM frequency, side effects were captured from medical records. Objective improvement was defined as post-treatment BM frequency of 3 or more per week. Subjective improvement was assessed by clinical or telephone interview and defined as agreement or strong agreement in a 5-point Likert scale. Continuous variables were expressed as median[range] or mean±SD (Wilcoxon signed-rank or Fisher's exact test).
**Results:** Among the 31 patients identified, 13 patients received linaclotide, 11 received prucalopride, and 7 individuals initially received prucalopride, which was switched to linaclotide. The number of BM per week significantly increased after treatment with either linaclotide (1[1-3] vs. 3.5[2-7]; $p<0.05$) or prucalopride (1[1-2] vs. 5[1-7]; $p<0.05$). In patients who did not respond to prucalopride, 71.4% reported improvement after switching to linaclotide.
**Conclusions:** Both drugs improved the BM frequency in our patients with neurodegenerative parkinsonism who had failed initial constipation management. Interestingly, a higher proportion of patients reported subjective satisfaction in controlling their constipation symptoms with the use of linaclotide as compared with prucalopride. Our preliminary results suggested potential benefits of these medications, thus should encourage further well-designed controlled trials to advance the standard of care of constipation in patients with parkinsonism.

**Funding Agencies:** None

A176
**SMALL GASTROINTESTINAL STROMAL TUMORS (GISTS): A RETROSPECTIVE ANALYSIS OF EUS SURVEILLANCE**
C. MacDonnell, C. Galorport, J.J. Telford, E. Lam, R.A. Enns

Department of Medicine, Division of Gastroenterology, St. Paul's Hospital, UBC, Vancouver, BC, Canada

**Background:** Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the GI tract. They are often noted incidentally at endoscopy or cross sectional imaging. Following the identification of such lesions, further investigation via endoscopic ultrasound, often with fine needle aspiration (EUS-FNA) is used to confirm diagnosis. The natural history and appropriate management of small (< 2 cm) GISTs is not well understood and in 2010 the National Comprehensive Cancer Network (NCCN) guidelines recommended surveillance EUS every 6-12 months.
**Aims:** To determine if our management strategy for small GISTs was consistent with present guidelines. Secondary outcomes were to identify any barriers to surveillance and determine the natural history of GISTs.
**Methods:** A retrospective chart review of all EUS procedures at St. Paul's Hospital, Vancouver, Canada from 01/05-06/17 was completed. Individuals with small (< 2 cm) GISTs were identified. GIST was defined as a hypoechoic lesion arising from the 2nd or 4th layer of the gastrointestinal wall +/- cytological or histologic diagnosis. Data collected included patient demograph-

ics, clinical presentation, initial and subsequent EUS findings, interval between EUS, reasons for not undergoing surveillance EUS, and any pathology. Candidates were then collated based on the presence of GISTs and whether appropriate follow-up occurred based on the National Comprehensive Cancer Network (NCCN) guidelines. This study was approved by the IRB at St. Paul's Hospital.
**Results:** GISTs were identified by EUS in 143 patients, 69 (48%) had lesions <2 cm in size. Mean age of diagnosis was 64 years (SD: 12.5), with 52% being female. 80% were referred due to incidental findings at initial endoscopy and 20% were referred based on CT imaging. All GISTs identified were located in the stomach. Out of the 69 patients identified with <2cm GISTs, surveillance was recommended in 63 (91%) and 49 (71%) had at least one surveillance EUS completed. Of the 14 patients in which surveillance was recommended but not completed, the barrier to surveillance was not identified. Over the time period of the review, there was an improvement in adherence to surveillance, reaching 100%. During a median follow-up of 12 months (range 12-24 months), all 49 GISTs remained unchanged in size and none were referred for surgery.
**Conclusions:** St. Paul's endosonographers recommendations for surveillance of small GISTs agreed with current guidelines in 91% of patients and improved over the time period of the study to 100%. There was no progression of GISTs in this cohort but a larger study is required to determine whether surveillance intervals can be increased for patients with small GISTs that have been stable over serial examinations.

**Funding Agencies:** None

A177
**CHYLOMICRON RETENTION DISEASE: A CASE OF INFANT PRESENTING WITH VOMITING AND FAILURE TO THRIVE WITHOUT DIARRHEA**
M. Woods, S. Parkash, S. Chowdhury, M. Rashid

Dalhousie University, Halifax, NS, Canada

**Background:** Chylomicron retention disease (Anderson's disease) is a rare autosomal recessive disorder due to mutation of SAR1B gene causing accumulation of lipoproteins in enterocytes and hypocholesterolemia. This leads to malabsorption and deficiencies of fat soluble vitamins with serious clinical sequelae. Patients most commonly present in infancy with nonspecific symptoms such as vomiting, diarrhea and failure to thrive. Diarrhea is reported to be universally present in all cases.
**Aims:** We report an infant with chylomicron retention disease presenting without diarrhea.
**Methods:** A 5-month-old term male of French Canadian descent was referred from community hospital with vomiting and severe failure to thrive. By 2 months of age, he had grown to only 4.8kg and then length and head circumference plateaued. He was exclusively breastfed for first 3 months and transitioned to formula due to poor growth. The spitting starting in first few weeks of life progressed to frequent non-bilious vomiting. There was no diarrhea. An upper GI series showed minimal reflux. A barium enema done for Hirschsprung's disease was negative. Sweat test was normal. Treatment with PEG3350 for presumed constipation and lansoprazole had been started along with formula NG feeds. Upon transfer to Paediatric unit, the infant was emaciated with distended abdomen and poor muscle strength.
**Results:** Investigations revealed normal urine, blood gas, electrolytes, glucose, renal function, bilirubin, ammonia, and organic acids. Serum albumin was low and transaminases mildly elevated. Stool microscopy showed fat globules. Upper GI endoscopy showed milky white appearance of duodenal mucosa. Biopsies showed normal villous height and architecture with significant steatosis of the enterocytes. Electron microscopy confirmed large amount of lipid droplets in the cytoplasm of enterocytes. Further workup revealed markedly reduced LDL-cholesterol, borderline low HDL-cholesterol and normal triglycerides. Vitamin A, D and E levels were decreased. Genetic testing revealed two different heterozygous variants in SAR1B gene; c.537T>A and c.409G>A. Parents were both carriers of the variants in SAR1B, confirming that each variant was on a separate copy of the SAR1B gene.
The infant was started on a partially hydrolyzed formula with higher medium chain triglyceride content orally and by NG tube. Supplementation with vitamin A, D, E and K was initiated. In follow-up at 10 months of age, he was doing very well, thriving with normal fat soluble vitamin levels.
**Conclusions:** Chylomicron retention disease can present without diarrhea. A high index of suspicion for a disorder of hypocholesterolemia and early endoscopy is recommended in infants with persistent vomiting and failure to thrive. A timely diagnosis and treatment is essential to avoid serious clinical sequelae, especially neurological impairment.

**Funding Agencies:** None

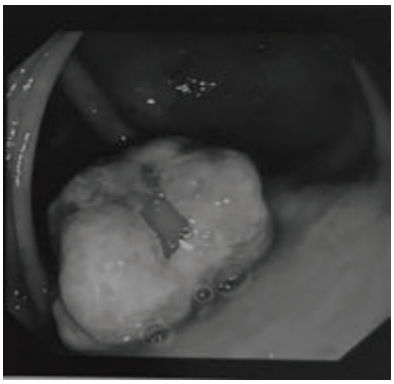
A178
**RARE BENIGN LYMPHOID COLONIC POLYP**
Y. Alshamali[2], A. Al Taleb[3], T. Al-Taweel[1]

1. Haya Al-Habeeb Gastroenterology Center Mubarak Al-Kabeer Hospital, Jabrya, Kuwait; 2. Gastroenterology, UBC, Vancouver, BC, Canada; 3. Mubarak Al-Kabeer Hospital, Jabriya, Kuwait

**Background:** Benign Lymphoid polyps are uncommon lesions that were mostly described in the small bowel and in children. Those lesions were occasionally found in the colon. There are only few reported cases in adults in which the lesions were mostly polypoid and described as lymphonodular hyperplasia. We are presenting a case of a large benign lymphoid polyp in the transverse colon of a 64 year-old lady referred to our care for alteration in bowel habit and anemia. Colonoscopy showed a 3 cm (Paris 1p) friable Polyp which was excised in its entity. Histopathology

examination revealed prominent lymphoid follicle formation with prominent germinal centers and no signs of malignancy. Benign lymphoid polyp is a rare condition posing a diagnostic challenge as it can be misinterpreted for a malignant lesion.
**Aims:** The aim is to highlight Benign lymphoid polyp as a rare condition posing a diagnostic challenge as it can be misinterpreted for a malignant lesion.
**Methods:** Previous case reports for this uncommon condition were reviewed.
**Results:** Intestinal lymphoid hyperplasia is a localised or widespread benign proliferation of lymphoid tissue within the intestinal wall, producing single or multiple lesions. Histopathological examination is required to role out malignancy.

we are describing a Large benign lymphoid polyp in the transverse colon of a 64 year-old lady referred to our care for alteration in bowel habit and anemia. Colonoscopy showed a 3 cm (Paris 1p) friable Polyp which was excised in its entity. Histopathology examination revealed prominent lymphoid follicle formation with prominent germinal centers and no signs of malignancy.
**Conclusions:** Benign lymphoid polyp is a rare condition posing a diagnostic challenge as it can be misinterpreted for a malignant lesion.



**Funding Agencies:** CCC, None

A179
**PREVALENCE OF CHRONIC DIARRHEA AMONGST PATIENTS FOLLOWED IN GASTROENTEROLOGY**
D. Daoud[2], M. Bouin[3], L. Bellemare[1], M. Nemer[2]

1. Gastroenterology, CHUM, Montréal, QC, Canada; 2. Centre Hospitalier de l'Université de Montréal - CHUM, Montréal, QC, Canada; 3. Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada

**Background:** The prevalence of chronic diarrhea in patients followed in gastroenterology is unknown.
**Aims:** To measure the prevalence of chronic diarrhea and assess the clinical characteristics that are associated with chronic diarrhea.
**Methods:** Prospective study (October 2016 to February 2017) conducted at the CHUM's gastroenterology clinic (Centre Hospitalier de l'Université de Montréal ). All patients 18 years old or older and capable of giving consent filled an anonymous questionnaire (10 minutes) on demographic characteristics, clinical symptoms and objective criteria of chronic diarrhea. Answers were computerized to facilitate analysis.
**Results:** 268 patients were included in the study (mean age: 48.6 ± 14.4 years old, 62% women, 92% Caucasians). The overall prevalence of chronic diarrhea was 29,5%, but variations were observed between groups of patients with different underlying pathologies. The prevalence was 43% in indeterminate colitis, 41% in irritable bowel syndrome, 38% in Crohn's disease and 23% in ulcerative colitis. In patients with active inflammatory bowel disease, the prevalence was higher than in inactive disease (43,7 vs 12,3%: $p<0.05$). Compared to the group without chronic diarrhea, the group with chronic diarrhea had more: 1) fecal incontinence (63 vs 48%; $p<0.05$), 2) Crohn's disease (52 vs 35%; $p<0.05$), 3) ileal resection (29 vs 13%; $p<0.05$) and 4) partial colectomy (25 vs 8%; $p<0.001$).
**Conclusions:** The study demonstrates a high prevalence of chronic diarrhea (29%) amongst patients consulting in our gastroenterology clinic. This prevalence remains high in patients with inactive inflammatory bowel disease (12,3%) and is associated with a high prevalence of fecal incontinence (63%).

**Funding Agencies:** None

A180
**GLUTEN SENSITIVITY IS COMMON AMONG PATIENTS WITH IBS-D:CASE CONTROL STUDY FROM A LOW PREVALENCE AREA.**
Y.M. Khayyat

Umm AlQura University, Makkah, Saudi Arabia

**Background:** Irritable bowel syndrome (IBS) is a common clinical problem in several age groups in Saudi Arabia ,reached about 9 % in adult students and up to 40 % in teachers .Effort is needed to correctly manage IBS and identify any coexistent condition that mimic the symptoms especially gluten sensitivity (GS). It is considered of low prevalence in Asian and Middle Eastern countries compared to high prevalent regions in Europe and North America.
**Aims:** This prospective study aims to estimate the prevalence of different subtypes of IBS, celiac disease positive serology and possible association that may exist, in an area of high IBS diagnosis and relatively low prevalence of celiac disease.
**Methods:** A Prospective study at a tertiary care private hospital at the western region of Saudi Arabia over the period of August 2013 to August 2016. Adults above the age of 15 year invited to participate in the study. ROME 3 criteria was used to identify and diagnose different subtypes of IBS as IBS- Pain ,IBS- constipation ,IBS –Diarrhea and IBS – Mixed. Basic demographic

data collected. The patients filled questionnaire that outline questions related to these subtypes. Laboratory work included CBC, Electrolytes, urea, creatinine, TSH, Tissue transglutaminase antibody (TTG) Ig A and Ig G collected. Patients with Positive serology for TTG invited to undergo upper endoscopy and duodenal biopsies to verify features of Gluten sensitivity according to Modified Marsh classification.A Control group done as a healthy blood donors who are symptom free of irritable bowel syndrome . Serum TTG IgA and IgA levels measured .

**Results:** A 305 patients with IBS of mixed subtypes according to ROME 3 criteria recruited. Predominantly IBS with mixed features 293 patients (96 %), Demographic data to be presented in ( table 1). There is 17 patients (5.6%) with positive TTG serology. Duodenal biopsies obtained for only 4 patients (2 patients of Marsh 0 and 2 patients of Marsh 3b classification respectively). There is statistically significant correlation between IBS with diarrhea predominant subtype,Age of the patient population and positive TTG-IgA . There is no significant association between the level of TTG IgA of the GS patients in the study and their modified marsh histological stage.Control group is 204 individuals , Males are 122 (24%).There is no statistically significant difference between the age and gender of the cases and control groups.Three Positive cases detected among the control group ( Blood donors ) 1.47 %.No IgA deficiencies detected.

**Conclusions:** Gluten sensitivity is prevalent in IBS patients especially diarrhea predominant subtype in the area of the study as compared to the healthy control. Performing serological tests and duodenal biopsies for positive cases will aid in detecting a large group of undiagnosed celiac patients and hence would improve the overall management of irritable bowel syndrome.

**Funding Agencies:** Umm ALQura University Research Institute.

## POSTER SESSION 2
## SUNDAY, FEBRUARY 11, 18H00-19H30

## CHRONIC LIVER DISEASE INCLUDING ALCOHOLIC, CHOLESTATIC, AND METABOLIC DISEASE

### Poster of Distinction

A181

**BIRTH COHORT EFFECTS ON CIRRHOSIS INCIDENCE FROM 1997-2015**

J.A. Flemming[1], C.M. Booth[2], Y. DeWit[3], P. Groome[4]

1. Queen's University, Kingston, ON, Canada; 2. Queen's University, Kingston, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Kingston, ON, Canada; 4. Queen's University, Kingston, ON, Canada

**Background:** The incidence of cirrhosis in North America has not been described using population-level data.
**Aims:** The aim of this study was to describe the epidemiology of cirrhosis using an Age-Period-Cohort (APC) approach to explore how changes in environmental exposures over time are influencing cirrhosis incidence.
**Methods:** Retrospective population-based cohort study from Ontario, Canada using linked administrative health data-sets. All patients ≥ 18 years with cirrhosis diagnosed during 1997-2015 were identified using a validated case definition. Adjusted annual standardized incidence rates (ASIR) and prevalence rates (ASPR) were calculated and stratified by age, birth-cohort, and sex. An Age-Period-Cohort (APC) approach was used to calculate incidence rate ratios (IRR) to describe the effect of birth cohort on cirrhosis incidence over the study period.
**Results:** 196,342 individuals with cirrhosis were identified; median age at diagnosis was 57 years (IQR 46-67); 62% were male. The ASIR overall increased over the study period (63/100,000 person-years [py] 1997 vs. 107.9/100,000py 2015) as did the prevalence (ASPR: 0.37% in 1997 vs. 0.92% in 2015). Age-specific ASIRs by birth cohort showed that the incidence of cirrhosis at age 60 was higher in 'Baby-boomers' (born 1945-1965) compared to those born 1925-1944 (154/100,000py vs. 123/100,000py respectively). However, the incidence of cirrhosis at age 32 was higher in the 'Millennial' (born >1980: 38.4/100,000py) and 'Gen X' (born 1966-1979: 29.6/100,000py) generations compared to 'Baby-boomers' (24.6/100,000py). Using APC modeling and mid-birth cohort reference years, cirrhosis incidence if born in 1980 was 63% higher (IRR 1.63: 95% CI 1.58-1.69, P <.001); and 142% higher if born in 1990 (IRR 2.42: 95% CI 2.28-2.58, P <.001) compared to being born in 1951. The cirrhosis incidence increase was stronger in women than men. (table).
**Conclusions:** The incidence of cirrhosis has increased over two decades more so in more recent birth cohorts and in women. Given that the majority of chronic liver diseases are related to lifestyle choices and environmental exposures, public health initiatives to reduce the burden of non-alcoholic fatty liver disease, hepatitis C, and alcohol-related liver disease are needed in order to reverse these trends for future generations.

Age-Period-Cohort analysis describing birth-cohort effects on cirrhosis incidence.

| Birth Year | | | |
|---|---|---|---|
| | All | Males | Females |
| 1925 | 0.75 (0.73-0.77) | 0.81 (0.78-0.84) | 0.66 (0.63-0.68) |
| 1945 | 0.87 (0.87-0.88) | 0.87 (0.86-0.88) | 0.85 (0.84-0.86) |
| 1966 | 1.30 (1.28-1.33) | 1.15 (1.13-1.18) | 1.52 (1.48-1.56) |
| 1980 | 1.63 (1.58-1.69) | 1.37 (1.32-1.44) | 2.11 (2.00-2.22) |
| 1990 | 2.42 (2.28-2.58) | 2.12 (1.96-2.30) | 2.96 (2.71-3.24) |

Incidence rate ratios and 95% CI compared to the 1951 birth year

**Funding Agencies:** Southeastern Ontario Academic Medical Association New Clinician Scientist Award

### Poster of Distinction

A182

**SIX-MINUTE WALK TEST AND SARCOPENIA IN PREDICTING MORTALITY IN PATIENTS WITH CIRRHOSIS**

T. Dang[3], M. Ebadi[3], A.J. Montano-Loza[2], P. Tandon[1]

1. University of Alberta, Edmonton, AB, Canada; 2. Division of Gastroenterology & Liver Unit , University of Alberta , Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Low muscle mass (sarcopenia) is associated with increased mortality in patients with cirrhosis. The association of functional performance with sarcopenia and its impact on mortality has not been well established in cirrhosis.
**Aims:** 1) Determine the association of functional performance assessed by the six-minute walk test (6MWT) and sarcopenia
2) Assess the prognostic value of the 6MWT in patients with cirrhosis
**Methods:** Patients who were assessed for liver transplant (LT) at the University of Alberta hospital were retrospectively enrolled in the study. Cross-sectional imaging within 1 year of assessment was used to determine sarcopenia. The third lumbar vertebra was used to quantify skeletal muscle cross sectional areas,

which was then normalized to height to calculate the skeletal muscle index (SMI; $cm^2/m^2$). Sarcopenia was defined using pre-established cut-offs in patients with cirrhosis. Cut-offs for 6MWT to predict mortality (death or delisting for being too sick for LT) were determined using receiver-operating characteristic (ROC) curves. Cox proportional hazard models were conducted to assess associations between sarcopenia, functional performance assessed by the 6MWT, and mortality.
**Results:** There were a total of 180 cirrhotic patients who were evaluated for liver transplant who had a 6MWT test at the time of assessment and corresponding CT imaging (Table 1). There was a weak association between SMI and 6MWT observed as dimensional variables (r=0.022; P=0.003). A 6MWT < 489 m was independently associated with mortality, with AUC of 0.61 (95% CI, 0.51-0.71, P=0.03) and subsequently defined as "poor physical performance." By univariate Cox analysis, both sarcopenia (HR 3.27; 95% CI 1.82-5.89; P<0.001) and low 6MWT (HR 2.72; 95% CI 1.45-5.13; P<0.001) were predictors of mortality. In a multivariate model, adjusted for MELD, sarcopenia (HR 2.96; 95% CI 1.59-5.51; P=0.001) and low 6MWT (HR 2.33; 95% CI 1.21-4.51; P=0.01) were independently associated with mortality. Poor physical performance was observed in 31 (60%) out of 52 sarcopenic patients. Sarcopenic patients with poor physical performance experienced a 6 times higher risk (HR 6.24; 95% CI 2.65-14.68; P<0.001) of death. Sarcopenic patients with low 6MWT survived for 25 months (95%CI, 12-38) compared to 69 months (95%CI, 27-112) in sarcopenic patients with normal 6MWT (Log Rank=0.04).
**Conclusions:** Sarcopenia and poor physical performance independently associate with mortality in patients with cirrhosis. Although poor physical performance was observed in more than half of the sarcopenic patients, its ability to discriminate mortality requires further investigation.

**Funding Agencies:** None

A183

**ANXIETY IMPACTS HEALTH-RELATED QUALITY OF LIFE AND HOSPITALIZATIONS IN PATIENTS WITH CIRRHOSIS**

T. Dang[3], N. Mitchell[3], K. Farhat[2], J. Abraldes[2], M. Ma[2], R. Bailey[1], P. Tandon[2]

1. Royal Alexandra Hospital, Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Psychological distress is common in patients with cirrhosis. Depression has a significant effect on health-related quality of life (HRQoL), adaptive coping, functional status and mortality. The effect of anxiety on HRQoL and clinical outcomes is not as well understood.
**Aims:** 1. Determine the prevalence of anxiety in cirrhosis and its association with clinical outcomes
2. Inform a rapid cirrhosis-specific anxiety screening tool by identifying multivariate predictors of anxiety using relevant clinical variables and subcomponents of the Hospital Anxiety and Depression Scale (HADS)
**Methods:** Patients 18-80 years old with a diagnosis of cirrhosis were recruited consecutively from liver clinics at three tertiary care hospital sites in Alberta. Individuals were excluded if they: were disoriented to person, place, or time orhad overt hepatic encephalopathy; active malignancy or hepatocellular carcinoma outside of the Alberta liver transplant criteria; end-stage renal disease on dialysis; or were on antidepressants. Patient sociodemographic and cirrhosis characteristics were collected. Patients were identified as having anxiety using the Mini Neuropsychiatric Interview (MINI) modules for panic disorder, agoraphobia, social phobia, and generalized anxiety disorder. The HADS was also completed to assess anxiety. The chronic liver disease questionnaire (CLDQ) and EQ-VAS score were used to determine HRQoL and participants were followed up to 6 months to determine whether they had unplanned hospitalizations or deaths during that time.
**Results:** Of the 369 patients, 65 patients were excluded for being on anti-depressants, leaving a total of 304 patients. Of those, 17.1% had anxiety by the MINI. Multivariate analysis revealed active smoking and 3 HADS subcomponents as independent predictors of anxiety (Table 1). Anxious patients had lower HRQoL as assessed by CLDQ (P < 0.001) and EQ-VAS (P < 0.001) and were more frail by the Clinical Frailty score (P = 0.004). Although numerically higher, there were no statistically significant difference between anxious and non-anxious patients for hospitalizations or death within 6 months of testing (P = 0.14). The 8.2% of patients meeting diagnostic criteria for both anxiety and depression had worse CLDQ, EQ-VAS and Clinical Frailty scores than anxious-only or depressed-only patients.
**Conclusions:** Anxiety is common in patients with cirrhosis and not routinely screened for. Anxiety has a significant impact on HRQoL and functional status, most pronounced in those patients with anxiety-depression overlap. Active smoking and three HADS subcomponents were identified as being independent predictors of anxiety. Multidisciplinary approaches targeting psychosocial and lifestyle factors as well as pharmacological therapies should be explored to treat anxiety in patients with cirrhosis.



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**Funding Agencies:** None

A184

**ASSOCIATION BETWEEN INDICATION FOR TIPS AND SURVIVAL IN PATIENTS WITH CIRRHOSIS: A POPULATION-BASED STUDY**

J.M. Mah[3], Y. DeWit[2], A. Menard[1], C.M. Booth[1], J.A. Flemming[1]

1. Queen's University, Kingston, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Kingston, ON, Canada; 3. Queen's University, Kingston, ON, Canada

**Background:** The transjugular intrahepatic portosystemic shunt (TIPS) procedure is designed to reduce portal pressure in patients with cirrhosis, thereby treating complications of portal hypertension. While several clinical trials have described the short-term outcomes following TIPS, long-term outcomes remain unclear.
**Aims:** The aim of this study was to determine the association between indication for TIPS and long-term survival in the general population of patients with cirrhosis.
**Methods:** We conducted a retrospective cohort study utilizing administrative health care data from Ontario, Canada accessed through the Institute of Comparative Evaluative Sciences. All patients with cirrhosis who received TIPS between January 1998 and December 2015 were included and were categorized into the following groups based on their indication for TIPS: refractory ascites and/or hepatic hydrothorax (RA/HH), variceal haemorrhage (VH), both, and other. Liver transplant-free (LTF) survival was described using Kaplan-Meier curves and the log-rank test. The association between the indication for TIPS and LTF survival was evaluated using multivariate Cox proportional hazards regression.
**Results:** 837 unique patients were included and the indication for TIPS was RA/HH in 52.6%, VH in 34.5%, both in 3.5% and other in 9.4%. 1-year LTF survival post-TIPS was lowest in those with both VH and RA/HH (44.0%), followed by those with only VH (54.4%), 59.0% with only RA/HH, and 63.6% for other indications (P=0.08). Using multivariate Cox regression, patients had a higher hazard of death if the indication for TIPS was both VH and RA/HH (HR 1.67, 95% CI 1.09-2.58, P=0.02) or only VH (HR 1.33, 95% CI 1.11-1.61, P=0.002) compared to patients with only RA/HH. Other factors independently associated with increased mortality included older age (HR 1.03 per year increase, 95% CI 1.02-1.04, P<0.001), Charlson-Deyo Comorbidity Index ≥4 (HR 1.32, 95% CI 1.08-1.63, P=0.008), and community hospital type (HR 1.36, 95% CI 1.09-1.69, P=0.006).
**Conclusions:** Patients with an indication for TIPS related to VH are at increased risk of death following the procedure. These results can be used to target interventions towards this subset of patients following TIPS. Future studies should focus on identifying modifiable risk factors that may decrease the risk of death in this group.

**Funding Agencies:** Southeastern Ontario Academic Medical Association New Clinician Scientist Award

A185

**ASSOCIATION BETWEEN SHORT-TERM HOSPITAL READMISSION AND OVERALL SURVIVAL IN PATIENTS WITH CIRRHOSIS: A POPULATION-BASED STUDY**

J.M. Mah[1], Y. DeWit[2], P. Groome[3], C.M. Booth[1], J.A. Flemming[1]

1. Queen's University, Kingston, ON, Canada; 2. Institute for Clinical Evaluative Sciences, Kingston, ON, Canada; 3. Queen's University, Kingston, ON, Canada

**Background:** Readmissions in patients with cirrhosis is common. Whether early readmission is related to long-term survival at the population level is unknown.
**Aims:** We aimed to determine the association between early hospital readmission and long-term survival in the general population of patients with cirrhosis.
**Methods:** We conducted a retrospective cohort study utilizing routinely collected health care data from Ontario, Canada accessed through the Institute for Clinical Evaluative Sciences. Adults with cirrhosis were identified using a validated coding algorithm and those with at least one hospital admission resulting in discharge between January 1992 and March 2016 were included, with follow-up until December 2016. Patients were classified into three readmission groups: 1) ≤30 days, 2) 31-90 days and 3) >90 days or never readmitted. Overall survival (OS) after index discharge was described using Kaplan-Meier curves and the log-rank test. The association between hospital readmission and OS was evaluated using multivariate Cox proportional hazards regression.
**Results:** 134,610 patients met inclusion criteria. The 30 and 90 day readmission rates were 15.6% and 27.1%, respectively. The median OS post-discharge was considerably shorter in patients readmitted in ≤30 days (2.1 years, IQR 0.2-10.9 years) or 31-90 days (2.9 years, IQR 0.5-11.4 years) compared to those >90 days/never readmitted (10.3 years, IQR 3.3-23.7 years, P<0.001). After adjusting for potential confounders,

those readmitted in ≤30 or 31-90 days had a higher hazard of death than those who were not (HR 2.05, 95% CI 2.01-2.09, P<0.001; HR 1.80, 95% CI 1.77-1.85, P<0.001, respectively). Other factors associated with decreased OS were older age (HR 1.05 per year increase, 95% CI 1.05-1.05, P<0.001), male sex (HR 1.34, 95% CI 1.32-1.36, P<0.001), Charlson-Deyo Comorbidity Index score ≥4 (HR 1.85, 95% CI 1.80-1.91, P<0.001), liver-related index admission (HR 1.46, 95% CI 1.42-1.50, P<0.001), paracentesis at index admission (HR 1.71, 95% CI 1.67-1.75, P<0.001), and index admission to a community hospital (HR 1.09, 95% CI 1.07-1.11, P<0.001).
**Conclusions:** Early readmission in patients with cirrhosis is a strong predictor of decreased OS. These results can be used when counselling patients and families regarding prognosis after a short-term readmission.

**Funding Agencies:** Southeastern Ontario Academic Medical Association New Clinician Scientist Award

A186
**LOWER HOSPITAL READMISSION RATES IN PATIENTS RECEIVING TIPS FOR ESOPHAGEAL VARICEAL BLEEDING: A NATIONWIDE LINKED ANALYSIS**
N. Deol[2], M. Brahmania[1], B. Rush[3]

1. University of Western , London, ON, Canada; 2. Gastroenterology , Western University, London, ON, Canada; 3. University of British Columbia, Vancouver, BC, Canada

**Aims:** Readmission to hospital following a Transjugular Intrahepatic Portosystemic Shunt (TIPS) procedure after an episode of esophageal variceal bleeding (EVB) has not been assessed. We aimed to address this gap in knowledge.
**Methods:** The Nationwide Readmission Database (NRD) was used to study the readmission rates for patients with decompensated cirrhosis who had a TIPS procedure performed for EVB. The NRD is a national database powered to track patients longitudinally for hospital readmissions. A propensity score matching model was created to match patients who received TIPS to those who did not.
**Results:** A total of 42,679,001 hospital admissions from the 2012-2014 NRD sample were analyzed. There were 33,934 patients with EVB who met inclusion criteria for the study, of which, 1,527 (4.5%) received TIPS after EVB. After propensity score matching, 1,527 patients without TIPS were matched to 1,527 patients who received TIPS. After a uniform follow-up of 3 months, patients with TIPS were less likely to be readmitted to hospital with a recurrent EVB (3.0%, 95% CI: 2.0%-3.9% vs. 9.3%, 95% CI: 7.6%-11.0%, p=0.01). Furthermore, at 3 months there was no difference in all cause hospital readmission between the two groups (38.8%, 95% CI: 38.1%-44.9% TIPS vs. 41.5%, 95% CI: 34.1%-43.3% no TIPS, p=0.17).
**Conclusions:** In this large nationally represented analysis we showed that patients with EVB who underwent TIPS have a significantly lower risk of 3-month readmission for recurrent EVB. Further randomized controlled trials are warranted to confirm these findings.

**Funding Agencies:** None

A187
**META-ANALYSIS AND SYSTEMATIC REVIEW OF NUTRITIONAL SCREENING AND ASSESSMENT TOOLS IN CIRRHOSIS**
M. Ney[3], S. Li[2], M. Raman[3], P. Tandon[1]

1. University of Alberta, Edmonton, AB, Canada; 2. Intermal Medicine, University of Alberta, Edmonton, AB, Canada; 3. University of Calgary, Calgary, AB, Canada

**Background:** Malnutrition is prevalent in patients with cirrhosis and has been shown to predict morbidity and mortality in this population. Many nutritional assessment and screening tools have been described in the literature, which have been studied to varying degrees in patients with cirrhosis.
**Aims:** In order to inform practice and facilitate the development of an effective nutritional screening tool (NST) in patients with cirrhosis, we aimed to provide an up-to-date meta-analysis and systematic review of the existing literature.
**Methods:** Pubmed, Embase and Web of Science were searched for articles meeting criteria for inclusion. Inclusion criteria were: 1) Full-text English language articles, 2) Patients with cirrhosis ≥16 years of age, 3) Studies assessing clinical outcomes as predicted by NSTs or nutritional assessment tools (NATs), and 4) Studies measuring validity of NSTs for diagnosing malnutrition. Exclusion criteria were: 1) <75 percent cirrhotic patients, and 2) hepatocellular carcinoma >25%.
**Results:** After the search, 2831 titles and abstracts were found for review. Of these, 92 articles were identified for full-text examination. After full review, 35 articles were included. Five articles were discovered through the references of included studies, for a total of 40 total studies for analysis. Three studies examined NSTs while 38 of 40 studied NATs. The 2 NSTs investigated were the Royal Free Hospital Nutritional Prioritizing Tool (n=1) and the Nutritional Risk Screening 2002 (n=2). The most prevalent NATs studied were sarcopenia (n=12), BMI (n=6), mid-arm muscle circumference (MAMC) (n=6), phase angle (n=5) and triceps skinfold thickness (TSF) (n=5). In preliminary meta-analysis, MAMC had an odds ratio (OR) for predicting mortality of 4.42 (95% confidence interval (CI) 2.76-7.06, heterogeneity 64%) from 3 studies with a total of 442 patients (figure 1). The mortality OR for TSF (3 studies and 432 patients) was 4.16 (95% CI 2.49-6.95, heterogeneity 3%). For HGS, the ORs for mortality and complications of liver disease (2 studies and 130 patients) were 7.05 (95% CI 1.27-38.97, heterogeneity 0%) and 6.29 (95% CI 2.55-15.53, heterogeneity 29%) respectively. For sarcopenia, the OR for mortality (5 studies and 661


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patients) was 2.64 (95% CI 1.82-3.81, 68% heterogeneity) and the OR for post-liver transplant mortality (2 studies and 276 patients) was 6.02 (95% CI 2.43-14.93, 0% heterogeneity).
**Conclusions:** A large number of studies have been published on NATs in cirrhosis while published data on NSTs is lacking. Although limited studies have meta-analyzable data, preliminary analysis has found MAMC, TSF, HGS and sarcopenia to predict mortality, HGS to predict complications from liver disease and sarcopenia to predict post-liver transplant mortality. Sarcopenia and MAMC had heterogenous results for non-transplant mortality.

Figure 1: Forest plot of MAMC as a predictor of mortality in patients with cirrhosis

**Funding Agencies:** None

A188
**LOW INCIDENCE OF SPONTANEOUS BACTERIAL PERITONITIS IN ASYMPTOMATIC OUTPATIENTS WITH CIRRHOSIS UNDERGOING PARACENTESIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**
O. Ahmed[1], D.M. Rodrigues[3], M. Brahmania[2], K. Patel[2]

1. University of Toronto, Toronto, ON, Canada; 2. Gastroenterology, University of Toronto, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada

**Background:** Spontaneous bacterial peritonitis (SBP) is a common sequelae of ascites in patients with decompensated cirrhosis and is associated with significant morbidity and mortality. Current literature suggests SBP rates of 30% in hospitalized patients with decompensated cirrhosis. However, the incidence of SBP in asymptomatic outpatients undergoing large volume paracentesis is thought to be low, though there is a paucity of literature. Nevertheless, current AASLD guidelines recommend that all patients undergoing routine paracentesis have ascitic fluid analysis.
**Aims:** The primary aim of our study was to perform a systematic review and meta-analysis to determine the incidence of SBP in asymptomatic patients undergoing routine large volume outpatient paracentesis.
**Methods:** A systematic search of Medline and EMBASE was performed (to September 2017) along with a manual search of reference lists of retrieved articles. Two authors (OA, DR) independently reviewed articles retrieved. All studies looking at asymptomatic outpatients with decompensated cirrhosis were included. Data was extracted to determine the incidence of SBP (SBP; positive culture and polymorphonuclear cells (PMNs) greater than 250 PMNs/mm$^3$), the incidence of culture-negative neutrocytic ascites (CNNA; PMN count greater than 250 PMNs/mm$^3$), and the incidence of mononuclear bacterascites (MNB; positive ascitic culture but no elevation in PMNs). Pooled analysis was performed on studies when possible.
**Results:** A total of 309 articles were retrieved with 12 studies being included in the review. 7 were peer-reviewed publications while 5 were in abstract form. A total of 1307 patients were included and a total of 3684 paracentesis were performed. 9 studies provided information on SBP, CNNA or MNB while 3 studies did not specifically differentiate in their diagnostic parameters for SBP. The total incidence of any suspected infection (SBP, CNNA or MNB) was 3% (116/3684) of paracentesis. However, the incidence of definite SBP only was 0.5% (9/1728), while the incidence of SBP or CNNA was evident in 1% (24/1728) of paracentesis. The post-diagnosis management was variable between studies (either no treatment, outpatient antibiotics, or hospitalization).
**Conclusions:** There is a low incidence of SBP and CNNA in asymptomatic outpatients with cirrhosis that require LVP. The utility of analyzing routine analysis of all samples in this population is debatable and likely not beneficial. Further studies are required to determine the cost-effectiveness of routine analysis and to determine whether certain subgroups are at higher risk of SBP.

**Funding Agencies:** None

A189
**A RETROSPECTIVE ANALYSIS OF OUTCOMES ASSOCIATED WITH PEGYLATED-INTERFERON (PEG-IFN) TREATMENT IN CHRONIC HEPATITIS B (CHB)**
A. Syed, S. Lee, H. Israelson, J. Pinto, C.S. Coffin

Liver Unit, Division of Gastroenterology, Department of Medicine, University of Calgary, Calgary, AB, Canada

Background: PEG-IFN is first-line therapy for CHB offering the advantage of a finite treatment, but is rarely used due to concerns about tolerability and efficacy. Nucleot(s)ide analogues (NUC) therapy are well tolerated but require prolonged therapy, with significant cost as well as potential for long-term adverse effects.
Aims: We aim to assess tolerability and long term outcomes in treatment-naive patients who received PEG-IFN for CHB. The primary outcome assessed was durability of off-treatment response (i.e. HBV DNA<2000 IU/mL, normal ALT). Secondary outcomes assessed included the proportion of those who required subsequent NUC therapy, quantitative HBV surface antigen (qHBsAg) levels, and the proportion with side effects.
Methods: In this retrospective cohort study, CHB patients who received antiviral therapy from January 1st, 2007 - July 1st, 2017 were identified via the Calgary Liver Unit Hepatitis B database. Data collected included age, sex, ethnicity, FibroScan® results, labs (HBV DNA, genotype, qHBsAg, ALT), total treatment duration, on treatment virological response (HBV DNA and qHBsAg if available) and reported side effects.

Patients co-infected with hepatitis D treated with Peg-IFN (n=4) were excluded.
Results: In total, 893 patients were started on a NUC, of which 50 (5.6%) patients received PEG-IFN therapy, including 3 currently on treatment who were excluded. The patients' had the following demographics: median age 43±9.3 years, 72.3% male, 80.8% East Asian, and 57% with unknown genotype. 70.2% (33/47) completed the 48 week course of PEG-IFN therapy. From the 29.2% (14/47) who discontinued interferon early, 64.2% did so due to treatment failure and 21.4% due to side effects. 21/47 (44.7%) who received PEG-IFN did not require subsequent NUC treatment during median follow-up of 33.9 months (±27.5,range 0.9-82.1). 85.7% had normal ALT and 61.9% had DNA levels <2000 IU/mL on most recent follow-up. 55% (26/47) of patients treated with PEG-IFN had a virological and biochemical rebound requiring initiation of a NUC within a median of 18.7 months (±15.6, range 3.2-55.4) post PEG-IFN treatment. In those with sustained response to Peg-IFN, 16/21 had available end of treatment qHBsAg that showed that 8/16 (50%) had levels <1000 IU/mL (median 986.5±1973.3, range 1.2-6384). 24/26 patients who failed PEG-IFN had end of treatment qHBsAg that showed 5/24 (20.8%) had levels <1000 IU/ml (median 3449.5±13661.5, range 3.9-63511). Difference between the two groups was not statistically significant.
Conclusions: A significant proportion (44.7%) of patients treated with Peg-IFN showed a SVR, including low qHBsAg levels (<1000 IU/mL), indicating robust immune control of HBV. Careful patient selection and adherence to treatment discontinuation rules based on qHBsAg levels will optimize management usage of PEG-IFN therapy for CHB.

**Funding Agencies:** None

A190

**A PROSPECTIVE EVALUATION OF SYMPTOM BURDEN, OPIOID RISK, AND PERCEIVED BENEFITS OF NON-PHARMACOLOGICAL THERAPY IN CIRRHOSIS PATIENTS**

M. Niazi, S. Chavda, E. Hjartarson, R.J. Bailey, P. Tandon, a.j. brisebois

University of Alberta, Edmonton, AB, Canada

**Background:** Cirrhosis is associated with magnitude of symptoms leading to disability and poor quality of life. Although opioids are effective in many cases, opioid use has been associated with increased frequency of hepatic encephalopathy, cost related to hospital admission and longer hospital stay. In other chronic disease population including cancer, non-pharmacological therapies including yoga, group therapy, and mindfulness-based stress reduction have been shown to be efficacious for reducing pain, emotional distress, and fatigue. Patient interest, current use as well as perceived benefit and barriers for utilization of non-pharmacological therapies are unclear in cirrhosis patients.
**Aims:** Within a population of patients with cirrhosis, we aimed to: 1) assess symptom burden; 2) risk of opioid dependency; 3) willingness to consider non-pharmacological therapy for symptom management.
**Methods:** In a prospective study, we recruited 135 patients with chronic liver disease attending Cirrhosis Care Clinic at the University of Alberta Hospital and Royal Alexandra Hospital. Our inclusion criterion for the study was documented cirrhosis on imaging in individuals 18 years of age and older. We collected data on patient demographics, symptom burden using the Edmonton Symptoms Assessment Scale (ESAS-r), perceived overall wellbeing using EuroQuol Visual Analogue Scale (EQ-VAS), and risk of opioid dependency using Opioid Risk Tool Calculator. We also assessed patients' familiarity with non-pharmacological therapy, willingness to try these therapies and any barriers preventing them from utilizing non-pharmacological modalities.
**Results:** 135 patients were recruited, mean age of 60 years with 62% being male patients, Child Pugh Class: A (58%), B (36%), and C (6%). Overall health status using EQ-VAS (EQ-VAS 0-100 Scale) was rated at 63.9± 22. Most commonly reported symptoms included: tiredness (52%), mood disorder (40%), drowsiness (36%), and pain (22%). In our study, 57% had moderate to severe opioid risk score, with higher scores being correlated with increased risk for opioid dependency and future abuse. Majority (85%) of patients were willing to learn about non-pharmacological approaches for their symptoms with the majority preferring an in person one-on-one delivery modality. The top three perceived barriers were expense, discomfort and concerns about privacy in a group setting.
**Conclusions:** Despite the relatively well-compensated status of our cirrhosis cohort, symptom burden was significant and quality of life was low. In our study, we observed significant risk of opioid dependency. Patients have a high willingness to proceed with non-pharmacological therapy, with only few noted barriers. Therefore, more research is needed surrounding non-pharmacological therapeutic options in cirrhosis patients.

**Funding Agencies:** None

A191

**THE SAFETY AND FEASIBILITY OF ENDOSCOPIC ULTRASOUND-GUIDED PARENCHYMAL LIVER BIOPSY AT A LARGE COMMUNITY HOSPITAL**

C. Rombaoa, A. Chen

Internal Medicine, Santa Clara Valley Medical Center, Mountain View, CA

**Background:** Parenchymal liver biopsy is important for diagnosis and management for many liver disease patients. Percutaneous image-guided liver biopsy is currently the most widely used method; however, endoscopic ultrasound (EUS)-guided liver biopsy with newer flexible large-bore core needles represents an

emerging approach for sampling. EUS-guided liver biopsy (EUS-LB) offers certain advantages over traditional methods such as doppler assistance to avoid intervening vessels and the ability to image both hepatic lobes to minimize sampling error.
**Aims:** Our aim is to evaluate the feasibility and safety of EUS-LB in obtaining adequate tissue samples for diagnosis of unexplained liver disease and to compare our results to percutaneous liver biopsy at our institution.
**Methods:** We conducted a retrospective chart review of patients who underwent EUS-LB at Santa Clara Valley Medical Center in San Jose, California between January 1 and September 30, 2017. All patients who underwent EUS-LB had 2 passes taken. For comparative purposes, we also identified patients who underwent a percutaneous liver biopsy for similar indications. We collected data on procedure duration, adverse events, complete portal tracts (CPTs), inflammation grade, and fibrosis grade.
**Results:** To date, there have been 8 patients who have undergone EUS-LB with a 19-gauge Acquire needle (Boston Scientific) at our institution. The indications for EUS-LB included unexplained abnormal LFTs (n=6), staging of hepatitis B (n=1), and cirrhosis of unclear etiology (n=1). The average procedure duration for EUS-LB and percutaneous liver biopsy was 19 minutes and 28 minutes, respectively. The average number of CPTs was 9.4 (range 6-13) and 9.1 (range 6-14), respectively. Three-quarters of patients in the EUS-LB group were determined to have mild inflammation (6/8, 75%). Most patients had 0 stage of fibrosis (7/8, 87.5%). Recovery time for EUS-LB patients averaged 30 minutes while percutaneous liver biopsy patients were all placed in observation for 240 minutes prior to discharge. No patients experienced any adverse events.
**Conclusions:** EUS-LB is feasible, safe, and produces a comparable sample adequacy for histologic examination compared to percutaneous liver biopsy at our community hospital. In addition, EUS-LB requires less time to complete, both in procedure time and recovery time. Further study regarding EUS-LB is warranted for optimal technique (e.g. the use and amount of suction) as well as direct comparison to percutaneous approach in terms of possible cost reduction and improved patient satisfaction.

**Funding Agencies:** None

A192

**CHARACTERISTICS AND OUTCOMES OF PATIENTS REFERRED TO THE HEPATOLOGY TRIAGE CLINIC: A QUALITY IMPROVEMENT INITIATIVE TO ASSESS AND OPTIMIZE SCREENING PROTOCOLS AND RESOURCE ALLOCATION STRATEGIES FOR MANAGEMENT OF PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE**

C.F. Rueda-Clausen, T. Davyduke, M. Ma

University of Alberta, Edmonton, AB, Canada

**Background:** Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in adults. Remarkably, its natural history and course is highly variable and poorly understood. It is anticipated that the number of referrals for assessment and management of suspected NAFLD will overwhelm the current installed capacity of the health care system. Therefore, strategies for screening and management of these patients are in demand.

**Aims:** To describe a cohort of subjects referred to the Hepatology Triage Clinic (HepTriC) for assessment of abnormal liver function tests and the outcomes of a pilot program for initial screening and management of these patients.

**Methods:** Descriptive cross-sectional examination and description of relevant clinical outcomes + cohort assembly. Criteria for referrals to the HepTriC include: Age 16 to 50 y, abnormal ALT (>50 IU/mL), no history of existing chronic liver disease other than NAFLD, no evidence of cirrhosis or acute liver ilnes.

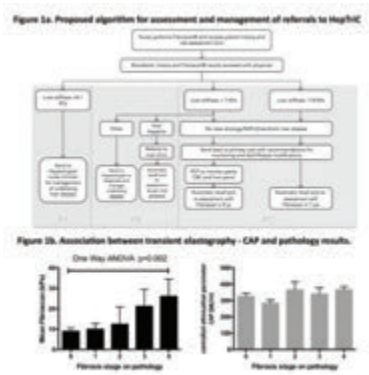
Referred patients underwent an Initial assessment that included extended labwork and a transient elastography (Fibroscan) plus controlled attenuation parameter (CAP) performed by a registered nurse. Depending on the results of this assessment, patients were booked for further evaluation by an hepatologist +/- liver biopsy or to be followed in 1 or 2 years (Fig 1a).

**Results:** From Nov-16 to Jun-17, 156 referrals were seen at the HepTriC (mean waiting time= 21d). Cohort baseline characteristics included: 74% Male, 42±10 yrs., BMI 31±6 m/Kg$^2$, diabetes 20.5%, dyslipidemia 30.7%, hypertension 29.5%, AST 40±22 IU/L, ALT 66±34 IU/L, Bilirubin 13±7mM Albumin 44± 2 g/L, $FIB_4$ 0.99±0.79, APRI 0.46±0.11, NFS -2.3±1.23.

Transient elastography assessment was accomplished in 150 (96%) subjects 43% of those required the XL probe. Mean stiffness 7.1±4.5 kPa, (range 3.2 to 36.3 kPa). Mean CAP 318±48 dB/m (range 204 to 400 dB/m). Significant Alcohol use was documented in 28 (18%) patients, from those, 9 (32%) had advance liver fibrosis. NAFLD transient elastography results). Liver stiffness assessed by internal acoustic radiation force (ARFI) was available in 23 patients. The correlation between Fibroscan and ARFI was very poor 5.9%, p=0.8.

In total 14 Liver biopsies were performed in patient in whom there was diagnostic uncertainty. Fibroscan but not CAP results have a proportional correlation with the pathology fibrosis scoring. (Fig1b)

**Conclusions:** NAFLD is the most common cause of otherwise unexplained abnormal LFTs. However, alcohol intake and uncommon metabolic conditions need to be explore in this population. Fibroscan seems to have strong correlation with liver pathology results. Fibroscan and ARFI elastography have very poor correlation.



**Funding Agencies:** Public Health Agency or Canada (PHAC), Digestive Health Strategic Clinical Network (DH-SCN)

A193

**LOW UTILIZATION OF PALLIATIVE CARE AT THE END OF LIFE WITH DECOMPENSATED LIVER DISEASE**

T. Kulai, M. McLeod, D. Leddin

Dalhousie University, Halifax, NS, Canada

**Aims:** Liver cirrhosis is often progressive and proceeds to decompensation. In patients who are not candidates for transplantation, complications often necessitate recurrent hospital admission. We sought to characterize the patient population with end-stage chronic liver disease served by our centre and detail their health care utilization, including palliative care services.
**Methods:** Retrospective review was conducted on adult patients with known cirrhosis who were admitted with decompensated cirrhosis to Queen Elizabeth II Health Sciences Centre in Halifax, NS, from May 2015 – May 2017, and died during their admission. Patients were identified using International Classification of Diseases-10 codes for most responsible diagnosis. Information on length of stay, etiology of underlying liver disease, decompensations, co-morbidites, complications, goals of care discussions, transplant candidacy and Model for End Stage Liver Disease Sodium (MELD-Na) score was collected. Consultations, procedures, diagnostic imaging tests, use of palliative care, admission to intensive care (ICU) and need for intubation or dialysis were detailed. Previous visits to emergency departments, clinics and endoscopy and admissions were reported for previous 6 and 12 months before death. Basic descriptive statistics and qualitative analysis were performed.
**Results:** A total of 28 patients with known liver cirrhosis were admitted with decompensated disease and died during study time period. Patients were aged 44 to 79 (mean 59) and 61% male with a 22-day average length of stay and mean MELD-Na score 26. Most patients (26/28; 93%) had at least one previous decompensation documented prior to admission. Stays were intensive with the following utilization: 24/28 (86%) antibiotics, 11/28 (40%) at least one endoscopy, 22/28 (79%) at least one specialist consultation, 20/28 (71%) at least three diagnostic images, 7/28 (25%) ICU admission and 4/28 (14%) new dialysis. Most patients did not have eligibility for liver transplantation detailed anywhere within their chart during hospitalization (19/28; 68%) nor documented previously (21/28; 75%). Patients had mean 3.2 emergency department visits and 2.3 clinic visits 6 months before admission, although only 13/28 (46%) saw hepatology during that time. About half of patients (15/28; 54%) were noted as "do not resuscitate" on admission and 36% (10/28) had an advanced directive, whereas only 4/28 (14%) saw palliative care prior to their death and 2/28 (7%) had documented outpatient goals of care discussions within 2 years prior to death.
**Conclusions:** Patients who die in hospital with decompensated liver disease have high MELD-Na scores and prolonged admissions; however, very few have goals of care discussions in the last years of life or documentation of their eligibility for liver transplantation.

**Funding Agencies:** CAG

A194

**PERSISTENT NAFLD AT 12 MONTHS POST-ROUX-EN-Y GASTRIC BYPASS SURGERY IS ASSOCIATED WITH LOWER IMPROVEMENTS IN WAIST CIRCUMFERENCE AND WORSE GLYCEMIC CONTROL**

K. Schwenger[1], S. Fischer[2], T.D. Jackson[1], A. okrainec[3], J. Allard[2]

1. University of Toronto, Hamilton, ON, Canada; 2. Toronto General Hospital, Toronto, ON, Canada; 3. University Health Network, Toronto, ON, Canada

**Background:** In obese individuals undergoing Roux-en-Y Gastric Bypass (RYGB), non-alcoholic fatty liver disease (NAFLD) is seen in 75 to 100% of cases. This improves post-surgery but some patients continue to have persistent NAFLD.
**Aims:** The purpose of this study was to determine the factors associated with persistent NAFLD at 12-months post-RYGB.
**Methods:** This is a prospective cohort study of 42 patients who underwent RYGB. Biochemical and clinical parameters were collected pre- and 12-months post-RYGB. All patients underwent a liver biopsy for histology during the RYGB (wedged) and at 12-months post-RYGB (ultrasound guided needle biopsy). Based on histology at 12 months, patients were separated in 2 groups: those with normal liver (NL) and those with persistent NAFLD.
**Results:** At baseline NAFLD was diagnosed in 85.7% of patients and at 12-months post-RYGB, NAFLD was present in 19.1% of patients. Patients who had a NL at baseline, remained with NL. RYGB resulted in significant decreases in BMI, waist circumference,

blood pressure, AST, ALT, fasting glucose and insulin, HbA1c and triglycerides, and significant increases in HDL cholesterol. Changes were similar in both groups except for waist circumference, which showed lower changes in those with persistent NAFLD compared to NL. In addition, those with persistent NAFLD had significantly higher (P<0.05) fasting glucose and insulin at 12-months with a higher proportion of these patients having insulin resistance compared to those with NL.
**Conclusions:** RYGB resulted in significant improvements in biochemical and clinical parameters including liver histology. However, despite similar weight loss, those with persistent NAFLD had less improvement in waist circumference and worse glycemic control suggesting that, other than weight loss, these factors may influence the liver response to RYGB.

**Funding Agencies:** CIHR

A195
**TRIPLE OVERLAP SYNDROME? A RARE CASE OF AIH, PBC AND PSC OVERLAP**
W. Alghamdi, K. Qumosani

Gastroenterology Devision/Department of Medicine, London Health Sciences Centre, Western University, London, ON, Canada

**Background:** Autoimmune liver diseases share the principle of immune-mediated damage directed towards either hepatocytes or bile ducts. They are classified into Autoimmune Hepatitis and Primary Biliary Cholangitis (AIH-PBC), AIH and Primary Sclerosing Cholangitis (AIH-PSC) and AIH and undefined cholestatic syndrome. AIH-PBS and AIH-PSC are recognized in the literature. Few case reports presented PBC-PSC overlap. The occurrence of all three entities together is extremely rare.
**Aims:** To describe a rare presentation of immune-mediated liver disease with features of AIH, PBC and PSC.
**Methods:** Case report and literature review.
**Results:** A 61-year-old Caucasian lady was referred to our hepatology clinic with a diagnosis of PBC for 10 years and subtle features of AIH on liver biopsy. She was on ursodeoxycholic acid (UDCA) dose of 1.5 g/day which was reduced due to weight loss and anorexia. She had no features of cirrhosis. A year after, she experienced severe itching with an increase in her ALT to 150 U/L, AST to 134 U/L and AP to 367 U/L. Her total bilirubin (TBIL) was 12.3 umol/L and direct bilirubin (DBIL) was 6.9 umol/L. Her ANA and SMA levels were negative. Her AMA titre was > 1:320 with IgG level of 17.3, normal IgA and IgM. Her IgG subtypes, p-ANCA and c-ANCA levels were normal along with CA19-9. She, subsequently, underwent a liver biopsy which showed loose granulomas, Batts/Ludwig fibrosis grade of 2 /4 with activity of 1 /4, positive AMA, periportal lymphoplasmacytic infiltrates and patchy interface hepatitis. There was no definite ductopenia. Based on these findings, we increased her UDCA dose back and started her on budesonide 9 mg/day with azathioprine. Her itching along with ALT, AST and AP levels improved with this regimen at 3 months follow up. We then started weaning off her budesonide. Her pancreatic enzymes, TBIL and DBIL increased which led to stopping azathioprine and increasing her budesonide dose. Abdominal imaging showed normal pancreas, splenomegaly with heterogenous liver parenchyma and dilated intrahepatic bile ducts. Gastroscopy showed small esophageal varices and portal hypertensive gastropathy. She remained asymptomatic with no itching. Her TBIL and DBIL levels improved. Her ALT, AST and AP levels were 76, 96, 266 U/L, respectively. MRCP showed moderate intra and extra-hepatic biliary dilatations with multifocal strictures, and extrahepatic duct wall thickening and stenosis with stones and sludge can't be ruled out. ERCP confirmed MRCP findings and intrahepatic PSC. She is currently maintained on budesonide and UDCA. Her MELD-Na score was 6 at her last clinic visit.
**Conclusions:** To the best of our knowledge, this is only the third reported case presenting with overlapping features of AIH-PBC-PSC together. Treatment of similar rare presentations is usually challenging and individualized with variable responses given the lack of randomized controlled trials (RCTs).

**Funding Agencies:** None

A196
**AN EXTRA BENEFIT TO USING STATINS: A CLINICAL OBSERVATIONAL STUDY ON NAFLD PATIENTS (PILOT STUDY)**
J. Zhou[1], S.M. Gauthier[2]

1. Health Sciences, University of Ottawa, North Bay, ON, Canada; 2. North Bay Regional Health Centre, North Bay, ON, Canada

**Background:** Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide – with an estimated 25% of Canadians affected. NAFLD has the potential to progress to nonalcoholic steatohepatitis (NASH), cirrhosis and fibrosis of the liver, and ultimately, liver failure. Globally, cirrhosis affects 1.6% people. NAFLD is often asymptomatic and found in people with metabolic syndrome. Both conditions can progress to an adverse event which relies on antidyslipidemic agents for treatment. The first-line of treatment for patients with dyslipidemia are statins. Recently, the use of statins has been suggested to be safe in NAFLD patients, but there is a lack in certainty of its effectivity in treating liver disease.
**Aims:** To determine if statins are effective for NAFLD treatment.
**Methods:** An observational study was conducted at the NorthGate Clinic, by searching for patients undergoing statin treatment with NAFLD suppression. A FibroScore was obtained for the patients to establish the severity of liver damage and NAFLD. Patients were then retested to obtain a post-stain use FibroScore. Alanine transaminase (ALT) and aspartate transaminase (AST) levels, another measure of liver condition, were also assessed with the continued usage of statins. After

determining the cases with NAFLD, these cases were then included based on their improvement post-statin usage.
**Results:** A total of 27 patients from the NorthGate Clinic met the inclusion criteria. These NAFLD patients were on statins to treat some form of dyslipidemia, and found an additional benefit of the drug – suppression of the symptoms of and treatment of NAFLD. However, only 21 patients had pre- and post-FibroScore data. Overall, patients found a decrease in FibroScore, ALT and AST levels with the continued usage of statins.
**Conclusions:** Evidence from the observational study indicated that the use of statins was associated with the suppression of NAFLD symptoms and a lower FibroScore, and ALT and AST levels. In general, this study suggests that the usage of statins was beneficial and safe in a particular sub-segment of the Canadian population with NAFLD. Therefore, suggesting that NAFLD patients are a population of interest. Limitations of the observational study included insufficient statistical power, uncontrolled selection bias and confounding factors. Moreover, since the data was obtained retrospectively, some data was missing. Thus, this study cannot assert that usage of statins induced an improvement to the liver (lower AST and ALT levels, and FibroScore).
Currently, available studies indicate that the benefits of statins outweigh the adverse effects of these drugs in NAFLD patients. Additional research needs to be provided on the long-term side effects associated with the use of statins in this population. Future studies should focus on providing more evidence to support the effect of statins in NAFLD patients.

**Funding Agencies:** None

## CLINICAL PRACTICE

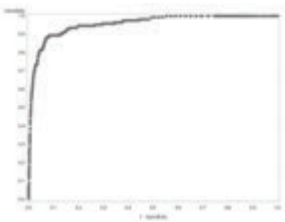
### Poster of Distinction

A197
**A PREDICTION MODEL OF RISK OF HARBOURING ADVANCED COLORECTAL NEOPLASMS IN LOW TO MODERATE RISK PERSONS OVER AGE 50**

S. Murthy[2], G. Le Gal[2], E.I. Benchimol[1], R. Hae[2], S. Burke[2], A. Rostom[2], C. Dube[2]

1. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada

**Background:** Colonoscopy decreases the incidence of colorectal cancer (CRC) and CRC-related death, primarily through timely detection and treatment of advanced colorectal neoplasms (ACNs), including CRC and high-risk adenomas (HRA). Unfortunately, risk stratification methods for colonoscopy are poor, and less than 20% of persons over age 50 who undergo colonoscopy are diagnosed with ACNs. Current guidelines do not adequately account for the simultaneous contribution of multiple major and minor risk factors and protective factors for developing ACNs. Combined with increasing demands for colonoscopy, Canadians now faces wait times that greatly exceed recommended targets, escalating colonoscopy-related costs and poor value for the money spent on these procedures. Widespread implementation of population-based FIT screening in average-risk patients in coming years will compound these problems.
**Aims:** To derive prediction models that discriminate between individuals who are likely or unlikely to harbour ACNs.
**Methods:** We studied 11,719 consecutive persons aged 50 years or older who underwent outpatient colonoscopy at The Ottawa Hospital between 2008 and 2012 for low-to-moderate risk indications, including non-life-threatening signs or symptoms, personal history of adenomas, family history of CRC and average-risk screening. We excluded individuals who had high risk or rare indications, as well as those who had incomplete colonoscopy, poor bowel preparation, or important missing information. We obtained model variables through chart review and linkage to Ontario health administrative databases. We tested 22 candidate predictors, encompassing colonoscopy indication, age, sex, residential setting, household income, co-morbidity burden, cancer history, and prior colonoscopy and polypectomy exposure. We used multivariable logistic regression with stepwise selection to derive our final models. We tested the performance of our primary models in multiple subgroups.
**Results:** Our final models retained eight variables that are easily ascertainable in an office setting. The models showed excellent discriminatory capacity (c-statistic > 0.95) and calibration (p-value > 0.5 for goodness-of-fit test) for CRC in the main cohort and all subgroups, and improved the specificity of colonoscopy for detecting ACNs without significantly impacting sensitivity. Applying the models to our derivation cohort would have allowed for a 25% reduction in colonoscopy volume with a CRC miss rate of < 1% and a HRA miss rate of < 10%.
**Conclusions:** We have derived predictive models with high discriminatory capacity for ACNs that could help optimize the use of colonoscopy resources in clinical practice. If successfully validated, these models have the potential to improve the clinical utility and cost-effectiveness of colonoscopy.




To view enlarged images and tables, please refer to Abstract Library.

Figure 1. Receiver operating curve for model of colorectal cancer (area under curve = 0.96)

**Funding Agencies:** Academic Health Sciences Centres Alternate Funding Plan Innovation Fund (administered by The Ottawa Hospital Academic Medical Association)

## Poster of Distinction

A198

**PERSONALIZING THE AGE TO STOP COLORECTAL CANCER SCREENING IN CANADA BASED ON COMORBIDITY AND PRIOR SCREENING HISTORY: MODEL ESTIMATES OF HARMS AND BENEFITS**

D. Cenin[2], J. Tinmouth[3], C. Dube[1], B. McCurdy[4], L. Paszat[3], L. Rabeneck[4], I. Lansdorp-Vogelaar[2]

1. The Ottawa Hospital, Ottawa, ON, Canada; 2. Erasmus MC, Rotterdam, Netherlands; 3. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 4. Cancer Care Ontario, Toronto, ON, Canada

**Background:** The Canadian Task Force on Preventive Health Care recommends against screening individuals at average risk of colorectal cancer (CRC) after age 74. However, harms and benefits of screening may depend on age, sex, comorbidities and prior screening history.
**Aims:** To determine stop ages for CRC screening with faecal immunochemical testing (FIT) based on sex, comorbidity and prior screening history.
**Methods:** We used the Microsimulation Screening Analysis-Colon (MISCAN-Colon) model to simulate a cohort of Canadian citizens born in 1960. The model was used to estimate the harms and benefits of undergoing one more CRC screen in males and females, aged 66 to 90 years by comorbidity status (no, low, moderate or severe) and previous screening history (no, 50% (adequate) and 100% (perfect) adherence). Screening was assumed to occur in an organized CRC screening program using biennial FIT. In order to determine the stop age that results in an acceptable balance between harms and benefits, we compared the harms and benefits for each cohort to that of an average health Canadian population, who had perfect prior screening, undergoing one more screening event at 74 years of age.
We present the incremental number needed to screen to gain one additional life year per 1,000 screened individuals compared to the threshold, defined by stopping screening at 74 years and 76 years in the healthy, average risk population with a history of perfect prior screening.
**Results:** Using the threshold described above, previously unscreened men and women with no comorbidity can be screened up until the age of 88 years. As comorbidity increased, the age to stop screening decreased for both males and females. For those with no or low comorbidity, as prior screening compliance improved, the age to stop screening decreased. For example, those with no comorbidity and adequate or perfect prior screening should stop screening at 80 and 76 years of age, respectively. Participants with severe comorbidity had the lowest age to stop screening (age 66 or lower) which did not vary by prior screening history (see Table).
**Conclusions:** The stopping age for CRC screening using biennial FIT can be personalized based on the participant's comorbidities and prior screening history; sex appears to have limited impact on screening stop age. Patients and providers can use these findings for decision-making regarding screening. Policy makers may wish to consider them in the design of organized CRC screening programs.

Suggested stop ages by prior screening & comorbidity

| | Female | | | | Male | | | |
|---|---|---|---|---|---|---|---|---|
| | No CM | Low CM | Mod CM | Sev CM | No CM | Low CM | Mod CM | Sev CM |
| No screening | 88 | 86 | 86 | <66 | 88 | 88 | 86 | 66 |
| 50% screening | 80 | 78 | 78 | <66 | 80 | 80 | 76 | 66 |
| 100% screening | 76 | 74 | 74 | <66 | 76 | 76 | 72 | 66 |

CM=comorbidity

**Funding Agencies:** Cancer Care Ontario

A199

**EFFICACY OF TOFACITINIB RETREATMENT FOR ULCERATIVE COLITIS AFTER TREATMENT INTERRUPTION: RESULTS FROM THE OCTAVE CLINICAL TRIALS**

J. Panés[1], B. Bressler[2], J.F. Colombel[3], N. Lawendy[4], E. Maller[4], H. Zhang[4], D. Woodworth[4], G. Chan[4], C. Su[4]

1. Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain; 2. Division of Gastroenterology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada; 3. Division of Gastroenterology, Icahn School of Medicine at Mount Sinai Hospital, New York, NY; 4. Pfizer Inc, Collegeville, PA

**Background:** Tofacitinib is an oral, small molecule JAK inhibitor that is being investigated for ulcerative colitis (UC). It is not expected to elicit formation of neutralizing anti-drug antibodies that may limit successful retreatment after treatment interruption.
**Aims:** To evaluate the efficacy of tofacitinib retreatment following treatment interruption in patients (pts) with UC participating in an ongoing Phase 3, open-label,

long-term extension (LTE) study (OCTAVE Open, NCT01470612; data as of July 2016).
**Methods:** The OCTAVE clinical trial program included induction (OCTAVE Induction 1 & 2),[1] maintenance (OCTAVE Sustain)[1] and LTE (OCTAVE Open) studies. OCTAVE Open included non-responders from OCTAVE Induction 1 & 2 and pts who completed or experienced treatment failure in OCTAVE Sustain. This analysis included the subpopulation of pts in OCTAVE Open who achieved clinical response (≥3-point and 30% reduction from induction baseline total Mayo score plus decrease ≥1 point in rectal bleeding subscore [RBS] or absolute RBS ≤1) following 8 weeks (wks) of induction therapy with tofacitinib 10 mg twice daily (BID), entered OCTAVE Sustain and experienced treatment failure while receiving placebo for up to 52 weeks and subsequently entered OCTAVE Open and received tofacitinib 10 mg BID. Treatment failure was defined by increase ≥3 points from maintenance study baseline total Mayo score plus increase in both RBS and endoscopic subscore (ES) ≥1 point; ≥8 wks of maintenance therapy. We evaluated rates of clinical response, mucosal healing (ES ≤1) and remission (total Mayo score ≤2, no individual subscore >1 and RBS=0) at Months (M) 2 and 12 of the LTE study using non-responder imputation (NRI).
**Results:** Of 914 pts enrolled in OCTAVE Open and treated for ≥2 M at data cut-off, 101 entered OCTAVE Open with clinical response to tofacitinib 10 mg BID in OCTAVE Induction 1 or 2 and treatment failure with PBO during OCTAVE Sustain. Clinical response, mucosal healing and remission rates were, respectively, 75.8%, 55.4% and 40.4% at M2, and 67.5%, 53.6% and 43.4% at M12 (Table).
**Conclusions:** For pts who responded to induction therapy with tofacitinib 10 mg BID and subsequently experienced treatment failure while receiving PBO maintenance therapy, efficacy responses were recaptured by a majority of pts by M2 and generally sustained at M12 after reinitiating tofacitinib 10 mg BID. Safety data were not presented for the retreatment subpopulation, limiting assessment of whether tofacitinib can be re-introduced safely in these pts.
1. Sandborn WJ et al. N Engl J Med 2017;376:1723-36.

| | Tofacitinib retreatment subpopulation[a] N=101 |
|---|---|
| **Efficacy, based on local endoscopic subscore, NRI** | |
| **Clinical response,[b] n/N (%)** | |
| Baseline | 5/101 (5.0) |
| M2 | 75/99 (75.8) |
| M12 | 56/83 (67.5) |
| **Mucosal healing, n/N (%)** | |
| Baseline | 3/101 (3.0) |
| M2 | 56/101 (55.4) |
| M12 | 45/84 (53.6) |
| **Remission,[c] n/N (%)** | |
| Baseline | 0/101 (0.0) |
| M2 | 40/99 (40.4) |
| M12 | 36/83 (43.4) |

[a]The retreatment subpopulation comprised pts who had clinical response at Week 8 with tofacitinib 10 mg BID in OCTAVE Induction 1 or 2 and subsequent treatment failure with PBO during OCTAVE Sustain. Per protocol, these pts received tofacitinib 10 mg BID in OCTAVE Open. [b]Clinical response was defined as ≥3-point and 30% reduction from induction study baseline total Mayo score plus decrease ≥1 point in RBS or absolute RBS ≤1. [c]Remission in the OCTAVE trials was defined as total Mayo score ≤2, no individual subscore >1 and RBS =0
Efficacy data are FAS, NRI, based on local read of endoscopy
BID, twice daily; FAS, full analysis set; M, Month; N, number of evaluable pts; n, number of pts with response in the given category; NRI, non-responder imputation; PBO, placebo; pts, patients; RBS, rectal bleeding subscore

A200
**THE USE OF CAPSULE ENDOSCOPY FOR DIAGNOSIS OF IRON DEFICIENCY ANEMIA- A RETROSPECTIVE ANALYSIS**
J. Stone, K. Grover, C.N. Bernstein

University of Manitoba, Winnipeg, MB, Canada

**Background:** Many patients who present with undiagnosed iron deficiency anemia (IDA) are presumed to have occult gastrointestinal (GI) bleeding as the cause. When investigations include a negative upper endoscopy and colonoscopy, a negative celiac antibody screen and there is no obvious GI source of blood loss, occult GI bleeding from a small bowel source is considered and capsule endoscopy (CE) is pursued. Recent Canadian Association of Gastroenterology guidelines on the use of CE suggested that CE is indicated in only selected cases of iron deficiency anemia; however, evidence on the yield of CE in IDA and how to optimally select cases is limited.
**Aims:** We aimed to examine the yield of CE in diagnosing the cause of IDA and to define clinical parameters that predict higher diagnostic yields
**Methods:** 1351 individuals underwent CE in Manitoba between the years of 2005-2016. All studies were reported by one reading physician and all requisitions included demographics and requested information on medication use, prior imaging studies, and hemoglobin and ferritin levels. 620 (46%) CE was indicated for occult GI bleeding or IDA. Positive findings on CE were separated into 'definite' and 'possible'. Descriptive statistics are reported and multinomial regression analysis was used to determine the variables correlated with definite CE findings.
**Results:** Of the 620 included subjects, mean age was 62.9 years, and mean hemoglobin was 89 g/L and mean ferritin was 32 uMol/L. 210 (33.9%) had positive findings (definite; 23%, possible;10.8%). 107 (17.2%) of all patients were taking ASA, 31 (5%) were on an antiplatelet agent, and 33 (5.3%) on an anticoagulant. Vascular ectasias were the majority of definite findings (47.5%). Predictors of definite findings were age (relative risk (RR) 1.04; 95% CI 1.02-1.06) and male sex (RR 1.88; 95%CI 1.25-2.83). None of serum Hg or ferritin, rural vs urban residence, number of prior upper or lower endoscopies, prior small bowel enteroscopy, use of ASA, antiplatelet, anticoagulant or PPI medications predicted a positive CE.
**Conclusions:** To our knowledge, this is the largest study examining the use of CE in iron deficiency anemia and occult GI bleeding. The diagnostic yield of 33.9% and more importantly 23% for definite lesions is within the range of previously reported yields. Within this cohort, age and male sex are predictors of definite findings on CE. Antiplatelet agents and anticoagulants did not predict positive findings in our study. Further research is needed to determine which findings lead to interventions that positively impact on patient outcomes

**Funding Agencies:** Pfizer Inc

**Funding Agencies:** None

A201

**EFFICACY OF PROTON PUMP INHIBITOR PLUS MUCOPROTECTIVE AGENT FOR ENDOSCOPIC SUBMUCOSAL DISSECTION-DERIVED ULCER; A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROL TRIAL**

R. Pittayanon[1], M. Martel[2], A.N. Barkun[3]

1. Medicine, McGill University, Montreal, QC, Canada; 2. McGill University Health Center, Montreal, QC, Canada; 3. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada

**Background:** Currently, it is still unclear whether adding a mucoprotective agent to a Proton Pump Inhibitor (PPI) (combination treatment) results in better outcomes compared to using a PPI alone, in term of both ulcer healing and delayed bleeding in patients with post gastric-endoscopic submucosal dissection (ESD) ulcers.
**Aims:** We conducted a meta-analysis of randomized control trials examining the efficacy of PPI alone versus combination treatment in post gastric-ESD ulcer healing as well as delayed bleeding.
**Methods:** We performed a systematic search of MEDLINE, EMBASE, Cochrane, and ISI Web of knowledge databases, up until May 2017, for randomized trials (RCTs) comparing PPI alone versus PPI plus a mucoprotective drug in achieving ulcer healing in patients undergoing gastric ESD. Medical subject headings and keywords included PPI (omeprazole, esomeprazole, lansoprazole, dexlansoprazole, pantoprazole and rabeprazole) and mucoprotective agents (rebamipide and sucralfate). Pediatrics trials, non human subjects, not fully published articles or non-English publications were excluded. The primary outcome is scaring stage (S1 or S2) on endoscopic assessment at 4 weeks or 8 weeks after gastric ESD. Preplanned subgroup and sensitivity analyses were performed. A meta-analysis was conducted using random effect models with results reported as risk-ratios (RR) with 95% confidence intervals. Heterogeneity and publication bias were assessed and quantified.
**Results:** From an initial 2250 citations, seven articles with 897 patients were analysed. Various PPI molecules were studied, but rebamipide was the only mucoprotective agent used in all studies. Up to 4 or 8 weeks after ESD, patients receiving combination treatment achieved a greater scaring stage significantly more often than PPIs alone (RR=1.4, 95% CI; 1.02-1.94 with heterogeneity: $I^2$ = 76%). There were no significant between treatment-group differences in term of delayed bleeding (RR= 0.64, 95% CI; 0.17-2.44). In sub-group analysis, no differences were noted in scaring stage between combination treatment and PPI alone at either 4 (RR=1.51, 95% CI; 1.00-2.27) or 8 weeks (RR=1.12, 95% CI; 0.78-1.62) follow-up when analyzing separately. Neither location of ulcer nor *H. pylori* infection were related to ulcer scaring stage whether the patients received combination treatment or PPI alone. Combination therapy was more effective than PPI alone in achieving rapid post–ESD ulcer healing amongst studies published before 2014 (RR=1.74, 95% CI; 1.39- 2.20). In contrast, no differences were noted amongst more recent studies (RR=0.92, 95% CI; 0.77-1.09).
**Conclusions:** Combination treatment may be more effective in accelerating the process of ulcer healing in patients undergoing gastric ESD than the use of PPI alone, but does not alter delayed bleeding risk.

**Funding Agencies:** None

A202

**EFFECT OF A SINGLE DOSE OF LORAZEPAM ON SALIVARY CORTISOL RESPONSE IN CHILDREN UNDERGOING DIGESTIVE ENDOSCOPY: A RANDOMIZED DOUBLE BLINDED STUDY**

F. Chennou[2], A. Verreault[2], A. Bonneau Fortin[2], A. Broz[2], O. Portolese[2], L. Belmesk[2], M. Jean-Pierre[1], G. Côté[1], M.H. Dirks[1], P. Jantchou[1]

1. Sainte Justine Univerity Hospital , Montreal, QC, Canada; 2. CHU Sainte Justine Research Center, Montreal, QC, Canada

**Background:** Children undergoing digestive endoscopies express a high level of procedural anxiety. We have shown that salivary Cortisol (sCortisol) is a reliable biomarker of stress in children undergoing endoscopy. It was recently suggested that preoperative psychological status can impact procedural comfort.
**Aims:** This randomized trial was designed to investigate the impact of an oral benzodiazepine on the levels of sCortisol and pain score during digestive endoscopies under intravenous sedation.
The primary aim was to assess the effect of Lorazepam as compared to placebo on the changes of sCortisol between baseline (C1) and one hour after administration (C2).
The secondary aims were to assess the percentage of children experiencing procedural pain and procedure duration.
**Methods:** Subjects were prospectively randomized in one of the following groups: Group A (oral Lorazepam, 0.5 mg (body weight < 40 kg) or 1 mg (body weight > 40 kg); Group B (placebo). Randomization was done by blocks of 6 and stratification was performed on sex and previous endoscopy experience. Before the procedure, 2 saliva samples (C1 and C2) were taken with cortisol Salivette tubes. A visual anxiety scale (VAS) and the State Trait Anxiety Inventory for Children (STAIC) were completed at baseline. Sedation protocol was done with intravenous administration of Fentanyl and Midazolam +/- Ketamine. Pain assessment was performed by recording the Nurse-Assessed Patient Comfort Score (NAPCOMS) during each procedure.
**Results:** Ninety children were included in the study. In this interim analysis of 44 children (22 females), sCortisol baseline mean (SD) was 75.3 ± 32.4 nmol/L in Group A and 66.7± 34.6 nmol/L in Group B (p=0.47).

For children having a colonoscopy, there was a decrease in sCortisol in the Lorazepam arm whereas it increased in the placebo arm. The mean (min-max) change in sCortisol between C1 and C2 was -4.8 (-43.8; + 94.5) nmol/L in Group A and +31.4 nmol/L (-35.2; +267.5) in Group B. For the NAPCOMS, the median (IQR) was lower in Group A than in Group B: [2 (0.0 – 5.0) and 5.0 (2.5 – 6.0) respectively (p=0.185)]. In Group B, 27% of children felt pain (NAPCOMS ≥ 6) compared to 18.2 % in Group A (p=0.47). For children undergoing colonoscopy, 37.5 % felt pain in the placebo arm as compared to 20 % in the Lorazepam arm (absolute difference of 17.5%). No difference was found between groups for adverse events rate.
**Conclusions:** Oral Lorazepam was associated with a decrease of sCortisol and a lower pain score in patients having a colonoscopy. This pilot study had a decent inclusion rate (61% of eligible participants). A large randomized trial assessing the impact of Lorazepam on pain score in children before colonoscopy is therefore feasible.

**Funding Agencies:** FRQS

A203
**PEDIATRIC VALIDATION OF THE NURSE-ASSESSED PATIENT COMFORT SCORE (NAPCOMS) IN CHILDREN UNDERGOING COLONOSCOPY**
F. Chennou[2], A. Bonneau Fortin[3], P. Jantchou[1]

1. Sainte Justine Univerity Hospital , Montreal, QC, Canada; 2. CHU Sainte Justine Research Center, Montreal, QC, Canada; 3. CHU Sainte Justine Research Center, Montreal, QC, Canada

**Background:** Given the subjective nature of pain, it is difficult to assess the level of pain and discomfort felt by patients during medical procedures. Several tools have been developed in order to objectively evaluate the level of pain, such as the Nurse-Assessed Patient Comfort Score (NAPCOMS). This scale was designed and prospectively validated in a cohort of 300 adults undergoing colonoscopy (Rostom et al). It includes three domains: a) pain (intensity- frequency-duration), the sum of the three items gives a total pain score between 0 and 9 (0 being no pain, and 9 the highest level); b) sedation level (0-3); and c) a global tolerability rating (0-3). In children, no reliable tool exists to assess pain and comfort during colonoscopy.
**Aims:** As part of our quality assurance program in pediatric digestive endoscopy, sedation, pain and comfort were considered as main quality indicators. We conducted this study to validate the NAPCOMS in a pediatric setting with patients undergoing colonoscopy under intravenous (IV) sedation.
**Methods:** NAPCOMS validation was carried out in two steps. In the first step, two research assistants simultaneously and independently recorded the NAPCOMS during endoscopic procedures in the operating room (N=34 patients). The results were compared using the Spearman correlation. For the second analysis, a research assistant and an endoscopy nurse completed the score (N=33 patients). The results of the research assistant and the endoscopy nurse were compared with the Spearman correlation. One hour after the procedure, patients reported two different outcomes: a global evaluation of procedural pain (Yes/No) and a comfort assessment on a 3-point Likert (no discomfort, mild discomfort severe discomfort).
**Results:** For the first step, the intraclass correlation was 0.90 between the two research assistants for the pain score (p<0.0010). As for the second step, the intraclass correlation was 0.94 between the nurse and the research assistant for the pain score (p<0.0010). There was a modest correlation between the NAPCOMS and pain perception as expressed by the patients partly due to a high percentage of children expressing amnesia of procedure (20%). The Spearman correlation between NAPCOMS and patients experience of pain and comfort were 0.42 (p< 0.002) and 0.031 (p=0.02) respectively.
**Conclusions:** The NAPCOMS can be considered as a reliable pain assessment tool for pediatric colonoscopy. There was a high agreement between the two investigators and the endoscopy nurse.

**Funding Agencies:** FRQS

A204
**IMPACT OF A SIMULATION-BASED TRAINING CURRICULUM USING GAMIFICATION FOR COLONOSCOPY: A RANDOMIZED CONTROLLED TRIAL**
M.A. Scaffidi[2], C.M. Walsh[1], M. Pearl[2], R. Khan[2], R. Kalaichandran[2], E. Lui[2], K. Winger[2], A. Almazroui[2], M.J. Abunassar[2], S.C. Grover[2]

1. Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children and The Wilson Centre, Toronto, ON, Canada; 2. Gastroenterology, University of Toronto, Toronto, ON, Canada

**Background:** Simulation-based training (SBT) curricula for training novices in gastrointestinal (GI) endoscopy have been shown to be effective. Gamification, the application of principles from games such as competition and rewards, has been used to enhance procedural learning in healthcare. There are no known applications of gamification for training of GI endoscopy, however.
**Aims:** To evaluate a SBT curriculum using gamification for novice endoscopists on the performance of simulated colonoscopies, compared to a conventional SBT curriculum.
**Methods:** Twenty-one novice endoscopists (completed <20 previous colonoscopies) from the general surgery and gastroenterology programs at the University of Toronto participated. Participants were randomized into the *Conventional Training Curriculum (CTC)* or *the Gamified Integrated Curriculum (GIC) Group*. Both groups received the same SBT curriculum on two simulator models, a benchtop and EndoVR® model. The GIC included a game-board, game narrative, badges for training landmarks, and rewards for top

performance. Performance was assessed at three points: prior to training, immediately after training, and 4 to 6 weeks after training. Assessments took place on the EndoVR® simulator. The primary outcome measure was the difference in colonoscopic performance between the two groups, assessed using the Joint Advisory Group for GI Endoscopy Direct Observation of Procedural Skills (JAG DOPS). The secondary outcome was the difference in cognitive load, as rated by participants themselves using the Cognitive Load Index for Colonoscopy (CLIC), which measures intrinsic, extrinsic, and germane cognitive load.
**Results:** For the JAG DOPS scores, there was no significant difference between the two groups with respect to performance of simulated colonoscopies (P>0.05). For the CLIC, there was a significant difference between the two groups immediately after training for intrinsic load, as the GIC demonstrated a significantly lower load (P=0.04). There were no other significant differences between the two groups for cognitive load.
**Conclusions:** We found that a SBT curriculum using gamification for colonoscopy was associated with a significantly lower intrinsic load after training. A lower instrinsic load indicates that participants in the GIC group found that the task of colonoscopy was not as difficult as their counterparts in the CTC group. Although we did not find a difference with respect to colonoscopic performance, these findings represent an interim analysis. The completion of this study will likely yield important insight into further improvements of endoscopic training.

**Funding Agencies:** None

A205
**A PROSPECTIVE ASSESSMENT OF INSERTION VERSUS WITHDRAWAL AS A COMPONENT OF A COLONOSCOPY TECHNICAL SKILLS ACQUISITION CIRRICULUM**
M. Lemke[1], A. Banwell[1], N. Rubinger[1], M. Wiepjes[2], M. Ropeleski[1], S. Vanner[1], L. Hookey[1]

1. Queen's University, Kingston, ON, Canada; 2. Medicine, Queen's University, Kingston, ON, Canada

**Background:** Colonoscopy technical skills curricula should include methods that reduce trainee anxiety and optimize success. One variable factor in training programs is whether trainees begin learning with colonoscope withdrawal that focuses on scope tip control and luminal view, or insertion that requires additional skills in navigation.
**Aims:** The aim of this project was to determine whether colonoscopy training focussing on colonoscope withdrawal leads to lower stress levels, cognitive workload, and increased perceived helpfulness in skills acquisition.
**Methods:** Participants were internal medicine trainees with no prior endoscopy experience. After initial simulation lab teaching with models, trainees were randomized to start with insertion or withdrawal phase of a colonoscopy, with one of two gastroenterologists as trainers. Salivary cortisol levels and State-Trait Anxiety Inventory (STAI) surveys from participants were compared at baseline and following each procedure to assess stress level. NASA Task Load Index (TLX) survey was used to assess cognitive workload. A visual analogue scale was used to assess perceived helpfulness of the training program on specific colonoscopy technical skills. Paired t-tests were used to compare the results between withdrawal and insertion, and between first and second procedure.
**Results:** 11 trainees were randomized. No significant differences in cortisol, STAI levels, workload, or reported helpfulness were detected between withdrawal or insertion (Table 1). Of the trainees, 70.0% reported insertion teaching to be of greater value, 20.0% reported withdrawal, and 10.0% found both equally valuable. Of the trainers, only 22.2% found insertion more valuable and 77.8% found withdrawal more valuable.
**Conclusions:** Training of insertion or withdrawal colonoscopy technical skills did not result in differences in trainee stress, cognitive workload, nor perceived helpfulness in skills acquisition. Residents reported higher perceived value in learning the more complicated insertion method; whereas their trainers reported higher value in withdrawal. With neither insertion nor withdrawal identified as a superior method for teaching, gastroenterologists and residents could utilize the method they are most comfortable with. Longitudinal data collection on skill acquisition rates could possibly clarify which approach is optimal.

Table 1. Changes in stress level, workload, and perceived helpfulness of procedure compared between withdrawal and insertion procedures

| | Withdrawal Mean ±SD | Insertion Mean ±(SD) | P-value |
|---|---|---|---|
| Difference between cortisol before and after procedure (nmol/L), n=10 | -3.28 ±3.46 | -1.71 ±2.21 | 0.152 |
| Difference between STAI score before and after procedure, n=11 | 0.00 ±1.67 | -0.09 ±1.38 | 0.867 |
| NASA-TLX score after procedure, n=11 | 239.73 ±54.18 | 272.45 ±55.72 | 0.065 |
| Helpfulness score after procedure, n=11 | 33.27 ±10.95 | 36.64 ±10.12 | 0.065 |

SD: standard deviation

**Funding Agencies:** SEAMO Clinician Scientist Award

A206

## STATE OF THE NATION: ADULT GASTROENTEROLOGY TRAINING IN CANADA

B.P. Chan[1], M. Fine[1], S. Shaffer[2]

1. Gastroenterology, McMaster University, Hamilton, ON, Canada; 2. University of Manitoba , Winnipeg, MB, Canada

**Background:** The Royal College of Physicians and Surgeons of Canada provides objectives in procedural skills, medical knowledge, and CanMEDS roles required for certification in gastroenterology. The means by which this is achieved is at the discretion of the training programs.
**Aims:** The aim of this study was to evaluate the Canadian adult gastroenterology training experience from a resident perspective in light of the upcoming transition to competency based medical education (CBME) and need for more standardization in training.
**Methods:** A survey consisting of seven sections and 35 questions was distributed to Chief Residents (CR) at all 14 adult training programs. Continuous variables were analyzed with mean, median, and range.
**Results:** Eleven out of 14 CR responded to the survey. Median number of trainees per site was 6, with an average of 3 hospital sites. Majority of programs (8/11) were admitting, with a median (range) of 8 admitted patients (0-45). Median inpatient exposure was 36 weeks (10-104) and outpatient exposure 15 weeks (2-70). Mean number of call shifts per block was 7, including on average, one weekend. Residents were called into hospital on average 50% of the time, with a mean of 5 hours of sleep per call shift. Most CR felt they were unable to take a post-call day but all respondents felt supported by staff on call. Staff were available for the resident call rota at 5/11 programs. Mandatory rotations were highly variable, with the one constant across all programs being inpatient consults. All but one program provided core training in percutaneous endoscopic gastrostomy tubes, while only 4 provided training in endoscopic manometry, despite it being a Royal College requirement. The majority of programs provided accommodation for residents writing the Internal Medicine Royal College Exam. Only 6/11 programs provided specific gastroenterology Royal College Exam preparation and 6/11 CR did not feel they received adequate career counselling. Despite this, nearly all residents (10/11) were satisfied with their program. The most common area of suggested improvement was increased access to outpatient endoscopy lists.
**Conclusions:** Each gastroenterology training program in Canada is unique and provides a slightly different training experience. Mandatory rotations are heterogeneous and core procedures vary widely. Despite this, the vast majority of residents were satisfied with their program. The incoming transition to CBME provides an ideal juncture to re-evaluate and standardize aspects of gastroenterology training in Canada.

**Funding Agencies:** None

A207

## POST-COLONOSCOPY COLORECTAL CANCERS IN ALBERTA: ROOM FOR QUALITY IMPROVEMENT

M.S. Mohamed[1], D. Sadowski[1], D. Johnson[2], C. Wong[1]

1. University of Alberta, Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada

**Background:** Post-colonoscopy colorectal cancer (PCCRC) is an indicator of colonoscopy quality and can happen as a result of technical factors surrounding the procedure such as inadequate bowel preparation, incomplete examination, missed or partly resected early lesions and failure to adhere to follow-up guidelines. There is a gap in our knowledge of the prevalence and root causes of PCCRC in Alberta, which are essential for quality improvement interventions
**Aims:** The aim of this study was to find out the prevalence and the factors associated with the development of PCCRC from a population based perspective.
**Methods:** This study was carried out in Alberta, which has a population of 1.8 million people older than age 39. 100,000 colonoscopies are done in the province annually. Centralized population-based data is available through the Alberta Cancer Registry (ACR), National Ambulatory Care Reporting System (NACRS), Discharge Abstract Database (DAD), and the Alberta Ambulatory Care Reporting System (AACRS).
All initial cases of CRC appearing in the ACR during 2013 were linked to the NACRS, DAD and AACRS databases to determine dates and characteristics of all antecedent colonoscopies. Health record of the retrieved cases were reviewed. The study authors according to a structured algorithm reviewed an abstract of each case. Cases were classified according to a set of predetermined root causes
**Results:** 1278 patients > 39 years of age were diagnosed with CRC in 2013 and had a colonoscopy identified by the database linkage. 146 CRC cases were diagnosed based on colonoscopy that was performed > 6 months but < 60 months after index colonoscopy. Cases were classified to root causes (See Table 1).
A total of 71 colonoscopists had at least one missed cancer with one colonoscopist missed 5 cancers
**Conclusions:** This study provides a rational basis for case exclusion as well as systematic categorization of PCCRC root causes. This approach can be used to obtain PCCRC data over longer periods of time and to get a more accurate estimate of its prevalence. The root causes identified in this study indicate that there is room for improvement in colonoscopy quality as well as for enhancement of clinical care pathways

Table1

| Root Cause | Number (%) |
|---|---|
| PCCRC diagnosed > 6 < 36 months | 48 (33) |
| PCCRC diagnosed > 36 < 60 months | 29 (19) |
| Inadequate follow-up | 15 (10) |



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| | |
|---|---|
| Patient related factors (e.g. refusal, inter-current illness) | 24 (17) |
| High risk (e.g. IBD, genetic syndromes) | 21 (14) |
| Path to care issues (Healthcare access) | 9 (6) |
| Total | 146 |
| Total Number Colonoscopists in Database | 245 |
| Colonoscopists with any missed cancer | 71 |
| Colonoscopists with 1 missed cancer | 58 |
| Colonoscopists with 2 missed cancer | 7 |
| Colonoscopists with 3 missed cancer | 5 |
| Colonoscopists with 5 missed cancer | 1 |

**Funding Agencies:** None

A208

**OPTIMIZING THE UTILITY OF CT ENTEROGRAPHY FOR THE EVALUATION OF OBSCURE GASTROINTESTINAL BLEEDING: A NOVEL HIGHLY SENSITIVE CLINICAL PREDICTION TOOL**

K. Leung[1], U. Khan[1], J. McCurdy[1], P.D. James[2]

1. Internal Medicine, The Ottawa Hospital, University of Ottawa, Ottawa, ON, Canada; 2. Department of Medicine, University Health Network, University of Toronto, Toronto, ON, Canada

**Background:** Computed tomography (CTE) and capsule endoscopy (CE) are common modalities used to investigate obscure GI bleeds (OGIB). Although recent guidelines recommend CE before CTE as the first modality to evaluate OGIB, CTE offers multiple advantages including lower cost, greater availability, and the ability to detect strictures, masses, and extraluminal pathology. It is not yet clear which OGIB patients would most benefit from CTE before CE.
**Aims:** Our study sought to determine patient factors associated with positive CTE in OGIB patients to develop a novel clinical decision tool to predict which patients are more likely versus less likely to have a diagnostic CTE.
**Methods:** This was a retrospective study using patients who underwent CTE for OGIB defined as a suspected gastrointestinal (GI) bleed with no cause identified on gastroscope or colonoscopy at The Ottawa Hospital between 2005- 2015. Factors (symptoms, history, investigations, interventions, outcomes) selected a priori from literature review were collected by chart review. Logistic regression with univariate and multivariate analysis were performed to identify factors associated with a positive CTE study.
**Results:** Of 147 patients with OGIB, CTE was positive in 1 in 5 cases (n=31, 21%). 22 (71%) of the CTE positive cases had at least one of intestinal wall thickening, angiodysplasias, suspected bowel mass, or concerning stricture. The presence of overt GI bleeding (OR 12.4, 95% CI 1.6-95.0), abdominal or constitutional symptoms (OR 2.9, 95% CI 1.2-7.0), or a personal history of GI cancer (OR 17.5, 95% CI 1.9-163.5) were factors that predicted a positive CTE study with univariate analysis. This was also seen in multivariate analysis (OR 13.3, 95% CI 1.5–121.9; OR 2.5, 95% CI 1.0-6.6; OR 30.3, 95% CI 1.4-634.2 respectively). Absence of these 3 factors was associated with zero likelihood of having a positive CTE, while presence of any of these factors was associated with a 1 in 4 likelihood of having a positive CTE. A rule based on the absence of these factors for predicting a positive CTE would have a sensitivity, specificity, negative predictive value, and positive predictive value of 100% (95% CI 80-100%), 16% (95% CI 10-24%), 100%, and 24% (95% CI 23-26%) respectively.
**Conclusions:** CTE can be diagnostic in 1 in 5 cases of OGIB. Diagnostic yield may be greater for patients with overt GI bleeding, abdominal and/or constitutional symptoms, or a personal history of GI malignancy. Absence of these 3 factors was associated with zero likelihood of a positive CTE. Together, these factors can function as a highly sensitive tool to predict which OGIB patients are unlikely to have a diagnostic CTE. This can potentially reduce non-diagnostic CTE and avoid the need for CE. Future research to validate this tool in other populations with OGIB are needed.

**Funding Agencies:** None

A209

**ENDOSCOPY BLEEDING RISK IN PATIENTS WITH INHERITED COAGULATION DISORDERS, A RETROSPECTIVE STUDY**

M. Tomaszewski[1], B. Marc[1], O. Kherad[2], S. Restellini-Kherad[3], A.N. Barkun[3], W. Margaret[4], T. Bessissow[3]

1. Internal Medicine, McGill University, Montreal, QC, Canada; 2. Internal Medicine, Hôpital de la Tour and University of Geneva, Meyrin, Switzerland; 3. Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 4. Hematology, McGill University Health Centre, Montreal, QC, Canada

**Background:** Hemophilia A and B and Von Willebrand Disease (VWD) are congenital bleeding disorders which respectively lead to factor VIII (F8) and factor IX (F9) deficiency and Von Willebrand Factor defects. Rarer bleeding disorders include factor VII (F7) and factor XI (F11) deficiency. These diseases predispose to bleeding adverse events, especially during medical interventions. The bleeding risk of these patients when undergoing a gastrointestinal endoscopy is unknown and has only been estimated in small case series. To mitigate the bleeding risk, peri-procedure treatment with factor concentrates, DDAVP and tranexamic acid is advocated.
**Aims:** The primary outcome of this study is to determine the point estimate of bleeding events within 72 hours of gastrointestinal endoscopy on a cohort of patients with inherited bleeding diatheses. The secondary outcome aims to establish predictors of

bleeding in this cohort and to evaluate whether peri-procedure treatments helps prevent such complications.
**Methods:** Data on 131 endoscopies performed on patients with hemophilia A or B, VWD, F7 or F11 deficiency was retrospectively collected. Demographic parameters, biochemical markers of disease severity and bleeding risk, peri-endoscopic treatments received and complications of the procedure were collected. Endoscopies were excluded from analysis if indication for procedure was bleeding. Point estimate of 72-hour bleeding rate was calculated and a univariate analysis was performed to assess for predictors of bleeding risk.
**Results:** 104 endoscopies were eligible for analyses and another 27 were excluded given bleeding as indication for procedure. Endoscopy was performed on 62 patients with 21 female and 41 male patients. Hemophilia A comprised the majority of patients at 44%, followed by VWD at 40%, F11 deficiency at 11%, hemophilia B at 5% and F7 deficiency at 4%. The point estimate of 72-hour bleeding rate was 0.96% (95% confidence interval 0.92-1.00%). 50% of endoscopies were accompanied by use of factor concentrates, DDAVP or tranexamic acid. 24% of endoscopies included a higher risk procedure such as polypectomy. Inferential testing via univariate analyses between bleeding risk and demographic parameters, coagulation parameters, type of endoscopic procedure and medications were non-significant.
**Conclusions:** This is the largest cohort to show that gastrointestinal endoscopy can be performed safely in patients with inherited coagulation disorders if peri-procedure treatment to enhance hemostasis is provided. The very low incidence of bleeding complications limited further inferential statistical analysis. Larger studies are required to assess for predictors of bleed and to evaluate the role of peri-procedure treatment with factor concentrates, DDAVP or tranexamic acid.

**Funding Agencies:** None

A210
**THE IMPACT OF IBD REFERRAL QUALITY ON WAIT TIMES**
H. Mathias, C. Heisler, J.B. Morrison, J. Jones

Gastroenterology, Research Services, QEII Health Sciences Centre, Halifax, NS, Canada

**Background:** Due to health and socioeconomic burdens associated with Inflammatory Bowel Disease (IBD), timely access to specialist care is important. In Canada, speciality gastroenterology (GI) care is accessed only by referral. To receive timely care, referrals must include a high quantity/quality of information. In 2012, 2 in 3 Canadian specialist physicians surveyed reported a lack of basic information on referrals. Referrals are often returned to referring physicians for more information, which is costly to patients and physicians. Some studies have examined referral quality, but not how the quality of referrals influences patient outcomes.
**Aims:** The objectives of this study are to determine if referrals to the Nova Scotia Collaborative IBD (NSCIBD) program contain enough information to allow accurate triage for timely access to care, and how the quality of initial referrals to the NSCIBD program inform patient outcomes (e.g. disease flare, hospitalization) while waiting for specialist consultation.
**Methods:** This is an ongoing retrospective cohort study of patients referred for appointments in the NSCIBD program between August 2016-2017. A sample size of 200 was required to have a power of 0.80 (p=0.50). Patients were included if they were referred for a first visit to the NSCIBD program for confirmed or suspected IBD. Referrals were excluded if they were for a non-IBD-related concern, an endoscopic test, or a follow up. Referrals were evaluated using a data abstraction form developed with an IBD specialist and two GI nurse practitioners. Based on the information included, referrals were classified as either low, moderate, or high quality. Descriptive statistics were used for a preliminary analysis of the baseline, cross-sectional data.
**Results:** To date, 150 records have been reviewed. There were 9 high quality referrals (6.0%), 32 moderate (21.0%), and 109 low quality referrals (72.7%). The majority of referrals were from family doctors (49.3%) with 81.1% of those being low quality. On average, patients with low quality referrals had a mean wait time of 48.0 days (SD=173.3, range=0-873 days) until triage and a mean wait time of 29.9 weeks (SD=37.3, range=0-160 weeks) to be seen by a GI. Patients with moderate-high quality referrals had a mean wait time of 16.6 days (SD=21.9, range=0-81 days) for triage and a mean of 16.7 weeks (SD=14.9, range=1-65 weeks) to be seen by a GI.
**Conclusions:** The majority of referrals analyzed to date are low quality and have longer average wait times. Prolonged wait time is concerning given its documented impact on patient satisfaction, quality of life and administrative resources. Further analysis will focus on whether there are significant differences in patient outcomes between the qualities of referrals, and factors informing referral quality. Moving forward, higher levels of referrer education, as well as patient awareness and advocacy are needed.

**Funding Agencies:** CIHRNova Scotia Health Authority Fund

A211
**OUTCOME OF CAPSULE ENDOSCOPY IN THE SETTING OF IRON DEFICIENCY ANEMIA IN PATIENTS ABOVE AGE 65.**
J.G. Lee[1], C. Galorport[2], R.A. Enns[2]

1. Department of Medicine, University of British Columbia, Vancouver, BC, Canada; 2. Department of Medicine, Division of Gastroenterology, St Paul's Hospital, University of British Columbia, Vancouver, BC, Canada

**Background:** Iron deficiency anemia (IDA) is a common indication for a capsule endoscopy (CE), which is often offered after a negative bidirectional endoscopy. Since malignancy is a concern in the older population with IDA, upper and lower endoscopic exams are typically performed. If these tests are negative, a CE study may be offered to evaluate the small intestine. However, choosing the ideal candidates who will benefit from a CE study is challenging.
**Aims:** To assess the outcomes for CE in patients with IDA over age 65 and which factors are more likely to contribute to a positive result.
**Methods:** A retrospective review of all CE studies at St. Paul's Hospital from 01/10-06/16 was conducted after ethics approval. Inclusion: age>65, hemoglobin<120 g/dL, serum ferritin<70 mg/L, minimum 12 month follow up and at least one high quality complete EGD/colonoscopy performed prior to CE. Variables to assess factors that are more likely to contribute to a positive capsule yield included: use of anticoagulation, NSAIDs, and cardiac disease.

Chi-Square test was used to determine clinical predictive factors of a positive and negative study.
**Results:** 1149 CE studies were reviewed of which 106 CE studies met inclusion criteria. 43 studies (40.6%) had positive findings and from this group, 26 (60.5%) recommended active intervention (i.e. EGD n=7, colonoscopy n=9, enteroscopy n=5, small bowel resection n=3, escalation of Crohn's therapy n=2), while 17 (39.5%) were managed supportively, typically with Fe supplementation. Most negative studies (57 of 63) recommended supportive therapy (others: hematological workup n=3, hiatal hernia repair n=1, PPI initiation n=1, stop donating blood n=1).

History of cardiac disease had a significant association with positive findings (0.54 vs. 0.33, p=0.039). Conversely, a known history of hiatal hernia was associated with a negative study (0.22 vs. 0.07, p=0.036).
**Conclusions:** These findings suggest that the diagnostic yield of CE in IDA in patients above age 65 is relatively low. The majority of all CE studies recommended supportive therapy and/or repeat endoscopic exams (EGD/Colonoscopy) of areas previously assessed. Clinical history of cardiac disease was associated with more positive findings on CE, whereas the presence of a hiatal hernia was associated with a negative study. Emphasis on these data may help select more appropriate patients for CE.

Positive CE Findings by Location (N=43)

| Finding (N)<br>- Location (N) |
|---|
| Ulceration (9)<br>- Proximal SB (1)<br>- Mid-Distal SB (5)<br>- ICV/TI (3) |
| Vascular Lesion (14)<br>- Gastric (3)<br>- Proximal SB (7)<br>- Mid-distal SB (2)<br>- Colon (2) |
| Polyp (2)<br>- Gastric (1)<br>- Mid-distal SB (1) |
| Erosion (4)<br>- Gastric (3)<br>- ICV/TI (1) |
| Blood (12)<br>- Gastric (1)<br>- Proximal SB (2)<br>- Mid-distal SB (6)<br>- ICV/TI (1)<br>- Colon (2) |
| Other (2)<br>- Abnormal Mucosa at Mid-distal SB (1)<br>- Loss of Villi at ICV/TI (1) |

SB=Small Bowel, ICV= Ileocecal Valve, TI= Terminal Ileum

**Funding Agencies:** St. Paul's Hospital GI Research Institute

A212
**ENDOSCOPIST-DIRECTED PROPOFOL AS AN ADJUNCT TO STANDARD SEDATION: A CANADIAN EXPERIENCE**
V. Heron[1], C. Golden[2], R. Battat[3], P. Galiatsatos[2], B.L. Stein[4], J. Wyse[5], A. Cohen[6]

1. McGill University, Montréal, QC, Canada; 2. Medicine, Division of Gastroenterology, SMBD Jewish General Hospital, Montrreal, QC, Canada; 3. Gastroenterology, McGill University , Montreal, QC, Canada; 4. McGill University Health Centre, Montreal, QC, Canada; 5. SMBD Jewish General Hospital, Montreal, QC, Canada; 6. SMBD Jewish General Hospital, Montreal, QC, Canada

**Background:** Sedation practices vary widely by region. In Canada, endoscopist-directed administration of a combination of fentanyl and midazolam is standard practice, with only a minority of cases performed with propofol.

**Aims:** To demonstrate the safety of non-anesthetist administered propofol for endoscopic sedation.
**Methods:** This was a single-centre retrospective cohort study of patients having undergone endoscopic procedures with propofol sedation between 2004 and 2012 in an academic hospital in Montreal. Procedures were performed by gastroenterologists trained in Advanced Cardiovascular Life Support. Sedation was administered by IV bolus by a registered nurse, under the direction of the endoscopist. Outcomes of procedures were collected using the hospital's endoscopy database.
**Results:** 4955 patients were included. Cecal intubation rate for colonoscopies (n=2920) was 90.0%. Gastroscopies (n=1625), flexible sigmoidoscopies (n=28), ERCP (n=341) and PEG insertion (n=41) had success rates of 98.4%, 96.4%, 94.4% and 92.7% respectively. The average dose of propofol used for each procedure was 34.6 mg. Fentanyl was used in 68% of procedures at an average dose of 94.4 mcg. Versed was used in 92.9% of cases at an average dose of 3.0 mg. Reversal agents (naloxone or flumazenil) were used in 0.4% of cases (n=21). Patients having received reversal agents were discharged uneventfully within the usual post-procedure recovery time. One patient required transfer to the ER. Most patients having received propofol in addition to standard sedation agents experienced no adverse events (99.6%). There were no deaths.
**Conclusions:** The use of propofol administered by a registered nurse under the direction of the endoscopist as an adjunct to fentanyl and versed is safe and effective.

**Funding Agencies:** None

A213
**DETERMINING TRANSITION READINESS IN INFLAMMATORY BOWEL DISEASE (TREAD-IBD): A MULTI-CENTRE CROSS SECTIONAL STUDY**
A. Foster[1], B. Bressler[6], M.W. Carroll[7], J. deBruyn[9], W. El-Matary[5], Y. Fu[8], H.Q. Huynh[4], K.I. Kroeker[7], S. Lawrence[1], C. Seow[3], E. Wine[2], K. Jacobson[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Pediatrics, University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Calgary, Calgary, AB, Canada; 4. Pediatrics, University of alberta, Edmonton, AB, Canada; 5. University of Manitoba, Winnipeg, MB, Canada; 6. Pacific Gastroenterology Associates, Vancouver, BC, Canada; 7. Pediatric Gastroenterology, Univeristy of Alberta, Edmonton, AB, Canada; 8. University of British Columbia, Vancouver, BC, Canada; 9. Paediatrics , University of Calgary, Calgary, AB, Canada

**Background:** Transitioning inflammatory bowel disease (IBD) patients from pediatric to adult care is a challenging and complex process. Knowledge of the potential factors influencing transition readiness is limited, especially in this unique population.
**Aims:** To evaluate potential factors including patient and parent psychosocial wellbeing, self-management, self-advocacy skills and geographical location of medical care, and to explore their effects on transition readiness in patients with IBD.
**Methods:** An ongoing cross-sectional multicentre study evaluating transition readiness in IBD patients 16 to 19 years of age who have been enrolled from pediatric and adult gastroenterology clinics in Western Canada (Vancouver, Calgary, Edmonton and Winnipeg). Questionnaires include the OnTRAC Readiness Assessment Questionnaire, the Screen for Child Anxiety Related Disorders (SCARED), the Patient Health Questionnaire (PHQ-8) to screen for depression and the Generalized Anxiety Disorder (GAD-7) to screen for parental anxiety. The patient, parent and physician also score the child and parent's readiness to transition on a scale of 1-10 (1=not ready and 10=completely ready).
**Results:** To date, 31 patients have been enrolled from participating Vancouver sites, 24 with Crohn's disease, 4 with ulcerative colitis and 3 with indeterminate colitis. Questionnaires indicated scores consistent with an anxiety disorder in 38% of those with IBD (only 20% of parents suggested anxiety in their child), and mild to severe depression in 23% of those with IBD. In addition, 24% of the parents themselves had GAD-7 scores consistent with mild to severe anxiety.

Patients reported a mean readiness to transition score of 7.4. The physicians' evaluations of readiness to transition was similar to the patient group (mean 7), while the parent group gave a lower score (mean 5.8).

Indeed, 77% of patients never or rarely saw the physician on their own at visits, 59% of parents indicated that they call the healthcare team with disease-related questions or concerns for their child and 46% of patients need reminders from parents to take medications.
**Conclusions:** Survey data from initial recruited patients suggest that a large proportion of transitioning youth continue to have behaviours that reflect a lack of self-advocacy and independence. In addition, depression and anxiety scores are high in this population which could impact the level of preparation for transition to adult care. Further data will be collected in this ongoing multi-centre study to assess the impact of youth and parental factors on transition readiness and to evaluate possible site to site variability.

**Funding Agencies:** Janssen Pharmaceuticals

A214
**A COMPARISON OF REAL-WORLD UTILIZATION PATTERNS OF INNOVATOR AND BIOSIMILAR INFLIXIMAB: A PRESCRIPTION CLAIMS DATA SUBGROUP ANALYSIS OF GERMAN GASTROENTEROLOGISTS**
E. Ewara[1], V. Jairath[2], M. Marrache[1], X. Baraliakos[3]

1. Janssen Inc., Toronto, ON, Canada; 2. Western University & London Health Sciences Centre, London,

ON, Canada; 3. Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne, Germany

**Background:** Data on utilization patterns for innovator infliximab (IFX) and biosimilar infliximab (CT-P13) in IBD are scarce. Given low uptake of biosimilars in Canada, evaluation of treatment initiation and discontinuation was undertaken in a proxy country, Germany, which has a similar healthcare environment.
**Aims:** To compare utilization patterns of patients prescribed IFX and CT-P13 by a gastroenterologist (GI) in a treatment naïve population at 12 months and in patients who continued IFX vs those who switched to CT-P13 at 6 months.
**Methods:** Quintiles IMS™ longitudinal health insurance prescription data captured patients with an initial claim of IFX or CT-P13 prescribed by a GI between Feb 2015-Oct 2016. Patients in each analysis had a minimum of either 6 or 12 months of claims history post-index or post-switch and ≥ 2 total claims of IFX or CT-P13. Six-month analyses included a matched and unmatched analysis for IFX exposure prior to switch. Log-binomial regression analyses were conducted to determine the relative risk (RR) of being retained on treatment at 6 or 12 months adjusted for age, sex, biologic status and prescriber.
**Results:** 636 and 655 patients had follow up time for inclusion in the 12-month treatment naïve and 6-month post-switch analyses, respectively. Only IFX to CT-P13 switch utilization was investigated (n=42). The risk adjusted probability of being retained on treatment after 12 months was 19% greater in the IFX group than in the CT-P13 group (RR IFX=1.19, 95%CI: 1.03-1.38, p= 0.0171) (Table 1). In the matched 6 months post-switch analysis the risk adjusted probability of being retained on treatment was 48% greater in the IFX maintenance group than in the CT-P13 switch group (RR IFX=1.48, 95%CI: 1.19-1.85, p=0.0005) (Table 1). Similar results were found in the unmatched analysis (RR IFX =1.56, 95%CI: 1.25-1.94, p<0.0001) (Table 1).
**Conclusions:** Findings from Germany demonstrate significant differences in real-world utilization patterns of patients prescribed IFX or CT-P13 by a GI. Limitations include no distinction between Crohn's disease or ulcerative colitis, disease severity and the reasons for staying on treatment or switching could not be determined. Although the sample size of the 6 months analysis of patients who switched from IFX to CT-P13 was small, the analysis provides comparative information on utilization patterns – data that is currently scarce. Future analyses should capture clinical outcomes to better understand observed utilization patterns.

Table 1: Multivariable Models Results

| Variable | Relative Risk | 95% Lower Limit | 95% Upper Limit | p-Value |
|---|---|---|---|---|
| 12-Month Treatment Naïve Analysis | | | | |
| IFX | 1.19 | 1.03 | 1.38 | 0.0171 |
| 6-Month Post-Switch Analysis (Matched to Prior IFX Exposure) | | | | |
| IFX | 1.48 | 1.19 | 1.85 | 0.0005 |
| 6-Month Post-Switch Analysis (Unmatched to Prior IFX Exposure) | | | | |
| IFX | 1.56 | 1.25 | 1.94 | 0.0001 |

Only reporting variables that are statistically significant (p<0.05)

**Funding Agencies:** Janssen Inc.

A215

## QUALITY INDICATORS OF UPPER AND LOWER DIGESTIVE ENDOSCOPY IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS

A. Bicamumpaka Shema[1], A. Groleau[1], P. Jantchou[2]

1. Université de Montréal, Montreal, QC, Canada; 2. Centre de recherche du CHU Sainte-Justine, Montreal, QC, Canada

**Background:** Digestive endoscopy is a useful diagnostic and therapeutic tool for children with intestinal diseases. However, unlike litterature on adult population, little data exist in the pediatric litterature regarding quality indicators in digestive endoscopy. Many adult quality indicators are not applicable to children.
**Aims:** The aims of review of the literature and meta-analysis were: 1) to synthesize published data on the practice of pediatric digestive endoscopy 2) to identify potential quality indicators specific to children.
**Methods:** A systematic search of the literature in English and French, from 1980 to 2016, was performed via the EMBASE, Medline and PubMed databases. The data extracted related to indications, bowel preparation, sedation, wait times, completion of the procedure, complications and outcomes (macroscopic and microscopic).
**Results:** Of the 301 articles identified, 23 articles were selected. Among these articles, most used general anesthesia and sedation. The choice mainly depended on the patient's condition, the endoscopist's preference or the habits of the team. The quality of bowel preparation was insufficient in 17,3% ± 7,6% of the cases (n = 2 studies). Caecum and ileum intubation rates were respectively 88.7% ± 2.3% and 83.9% ± 0.2% (n = 3 studies). Oesogastroduodenoscopies (OGDs) were macroscopically normal in, 51.8% ± 4.3% of cases (n = 6 studies) and 47,8% ±11,8%, microscopically normal (n = 2 studies). Regarding colosnoscopies, 41,6% ± 1,7% (n = 4 studies) and 40,0% ± 10,0% (n = 2 studies) were respectively macroscopically and microscopically normal. The mean rate of complications was 3.4% ± 1.1% (n = 4 studies) for OGD and 2.5% ± 0.7% (n = 5 studies) for colonoscopies. It was also noted that 74.0% to 99.7% of endoscopies had an appropriate indication (n = 3 studies).

**Conclusions:** The rate of complications in pediatric digestive endoscopy is similar between studies and most of them are benign complications (eg. desaturations). The outcomes between macroscopic and microscopic analysis were similar and high, suggesting either an inappropriate application of the current indications or a need for revision of these indicators. A success rate of colonoscopy reaching the caecum greater than 80% could be an objective to be achieved. The quality of the bowel preparation and the rate of cancellations are an other important criteria but few studies reported these outcomes. Likewise, there was few studies on wait times and the results were significantly different.

**Funding Agencies:** None

A216

**PREDICTING DIFFICULT CASES IN POEM (PER-ORAL ENDOSCOPIC MYOTOMY) PROCEDURES.**

F. Jowhari[1], H. Inoue[2], H. Ikeda[2], M. Onimaru[2], R. Bechara[1]

1. Queen's University, Kingston, ON, Canada; 2. Showa University Koto-Toyosu Hospital, Tokyo, Japan

**Background:** POEM (per-oral endoscopic myotomy) is emerging as the new endoscopic standard for treating patients with achalasia. Originating from Japan, POEM is now performed at many tertiary care centers in North America. Hitherto, data from institutions regarding the safety & efficacy of the procedure has shown promising results. To ensure that the procedure is seamless, identifying challenging cases ahead of time would allow for better resource allocation & to plan accordingly.
**Aims:** To identify if certain pre-procedural factors are associated with intra-procedural factors or post-procedural complications, to ultimately formulate a POEM difficulty score to allow endoscopists to predict difficult cases ahead of time.
**Methods:** 51 POEM procedures performed for achalasia at a tertiary care centre in Japan were analyzed in the study. Most procedures were performed by advanced-therapeutics trainees with close proctoring by experienced endoscopists. Various pre-determined pre-procedural factors (age, sex, achalasia type, duration of symptoms, Eckardt score, morphology & prior treatments); intra-procedural factors (tunnel distention, submucosal fibrosis, abnormal contractions, submucosal oozing, orientation, length of myotomy, procedure time, number of clips used & intra-procedural adverse events) & post-procedural data points were collected & analyzed. A preliminary POEM difficulty score (out of 10) was formulated with each component worth 2 points (tunnel distention, submucosal fibrosis, abnormal contractions, submucosal oozing, orientation). Analyses were performed using chi-square tests for categorical data & T-tests/ANOVAs/Spearmans correlations for continuous data.
**Results:** The mean age was 44.3 ±15.5 yrs & mean duration of symptoms 8.1 ± 9.9 yrs. Mean Eckardt score was 6.7 ± 2.2. Six patients (11.8%) had an intra-procedural event & 3 (5.9%) had an in-hospital adverse event. In the univariate analyses, the POEM difficulty score did not correlate with the occurrence of an intra-procedural event (p=0.203) or post procedure complications (p=0.80). Factors that correlated with the POEM difficulty score included morphology (S1/S2 vs. NS-D or NS-ND, p=0.006), prior treatments (pneumatic dilation vs. none, p=0.028) & age (p=0.030). A multivariate regression analysis was also conducted with variables removed sequentially, and even though trends were seen with some variables, type of achalasia was the only variable that maintained significance (p=0.048).
**Conclusions:** Based on this study, there are indications that procedures involving older patients; S1/S2 morphology; type of achalasia (Type 1); and those with prior treatments may be more difficult overall. Further validation of these results as well as the POEM difficulty score is needed as our study was limited by smaller numbers, minimal adverse events, more trainee involvement, and less challenging procedures overall.

**Funding Agencies:** None

A217

**EXTERNAL VALIDATION OF THE PARK SCORE FOR BOWEL PREPARATION CLEANLINESS DURING CAPSULE ENDOSCOPY**

M.H. Alageeli[1], B. Yan[10], S. Zepeda-Gomez[5], S. Alshankiti[3], L. Stitt[1], B.S. Thomas[9], Z. Bahreini[8], R. Homenauth[4], T. Dang[6], R. ROFAIEL[1], M. Al-Zahrani[1], C.M. Townsend[2], D. Yoo[1], J. Jarosh[11], M. Kloc[11], A. Smith[11], C. Singh[11], J. Luhoway[1], L. Merotto[1], O. Gilani[1], J. Friedland[1], M. Sey[7]

1. UWO, London , ON, Canada; 2. Medicine, University of Western Ontario, London, ON, Canada; 3. Provincial Health Services Authority, Vancouver, BC, Canada; 4. Adult Gastroenterology, University of Alberta, Edmonton, AB, Canada; 5. Gastroenterology, University of Alberta, Edmonton, AB, Canada; 6. Medicine, University of Alberta, Edmonton, AB, Canada; 7. Western University, London, ON, Canada; 8. Gastroenterology, Western University, London, ON, Canada; 9. Medicine, Western University, London, ON, Canada; 10. Medicine, Gastroenterology, Western University, London, ON, Canada; 11. LHSC, LONDON, ON, Canada

**Background:** Capsule endoscopy is the test of choice for small intestinal diseases although it can be limited by poor bowel preparation. The Park score measures small intestinal cleanliness based on the % of mucosa visualized and % of view obstructed and is a promising tool for assessing small bowel preparation although further validation is required before it can be routinely used.
**Aims:** The objective of this study was to externally validate the Park score among a large number of readers with varying levels of expertise in capsule endoscopy.
**Methods:** A total of 20 readers consisting of 4 capsule



To view enlarged images and tables, please refer to Abstract Library.

endoscopists, 4 GI fellows, 4 internal medicine residents, 4 medical students, and 4 nurses were invited to participate in the study. All readers completed a web-based Training Module on the Park score followed by an Assessment Module which was repeated 4 weeks later. The Assessment Module consisted of 1,233 images derived from 25 randomly selected capsule videos. Images were selected at 5 minute intervals between the first duodenal and first cecal images of each video and readers rated the % of the mucosa visualized and the % of view obstructed as defined by the Park score. The primary outcome was inter-observer and intra-observer agreement for the total score and secondary outcomes included stratification by subscores and reader group. Agreement was determined based on intraclass correlation coefficients.
**Results:** The mean inter-observer and intra-observer agreement for the total Park score between all readers was 0.81 (95% CI 0.70-0.87) and 0.92 (0.87-0.94). Stratified by sub-scores, the mean inter and intra-observer agreement for % visualized mucosa was 0.79 (0.67-0.85) and 0.91 (0.86-0.93) and for % of view obstructed was 0.77 (0.64-0.84) and 0.91 (0.87-0.94). The agreement between capsule endoscopists and GI fellows, internal medicine residents, medical students, and nurses were 0.93 (0.88-0.97), 0.90 (0.82-0.95), 0.90 (0.82-0.95), 0.85 (0.74-0.92), respectively.
**Conclusions:** The Park score is a simple and reliable scoring system to measure small intestinal cleanliness with excellent agreement between a wide range of readers with varying levels of experience with capsule endoscopy.

**Funding Agencies:** None

A218
**EVALUATION OF IBD SPECIALTY CARE IN NOVA SCOTIA: THE REFERRING PHYSICIAN PERSPECTIVE**
E.E. Burns[1], C. Heisler[2], O. Kits[1], S. Veldhuyzen van Zanten[3], J. Jones[1]

1. Faculty of Medicine, Dalhousie University , Halifax, NS, Canada; 2. Gastroenterology, Research Services, QEII Health Sciences Centre, Halifax, NS, Canada; 3. University of Alberta, Edmonton, AB, Canada

**Background:** The incidence and prevalence rates of Inflammatory Bowel Disease (IBD) in Canada have been observed to be amongst the highest globally, with the highest observed estimates in Nova Scotia (NS). Excessive wait times for outpatient consultations is a well-documented problem. As increased wait times lead to negative outcomes for IBD patients, it is crucial that a thorough understanding of access to care is obtained by engaging multiple stakeholders including patients, referring physicians, specialist physicians, and administrative personnel.
**Aims:** The study aim was to identify barriers in access to IBD care for referring physicians and their patients.
**Methods:** This was a mail-out survey between July and October 2017 of a representative sample of general practitioners (GPs) referring to GI IBD specialty care in NS. Stratified sampling was done to ensure geographic representativeness of the sample. The survey incorporated social exchange theory and included a non-conditional incentive to maximize response rates. The questionnaire consisted of five sections: 1) demographic information (e.g. sex, age, patient load); 2) geographic information (e.g. urban versus rural); 3) referral processes (e.g. number of referrals sent to GI, communication between GP and GI offices); 4) patient wait times (e.g. how many patients on wait list); 5) referral process satisfaction. Descriptive analyses were carried out using Stata software. The project was approved by the NS Health Authority Research Ethics board.
**Results:** This survey is still in progress. A total of 634 surveys were mailed out, and thus far 145 were returned (23%). Mean age was 48 years (29 to 77 years), mean number of years in practice was 18 (1 to 50 years). Sixty-eight percent (n=99) worked in a private practice setting, and 46 (44%) in an urban setting. Thirty-one percent of respondents did not have access to IBD specialty care in their community, but the majority (84%) had access in their health zone. Over half (57%) of respondents were either dissatisfied or very dissatisfied at the current referral process. Forty-one percent felt the current referral process was either inefficient or very efficient. Respondents identified the following as being access barriers: 1) perceived inequity in access to GI for rural compared to urban areas, 2) need to increase number of GIs, and 3) need to create a centralized referral and triage process for the whole province.
**Conclusions:** The results show wait times for IBD patients are a significant problem and there is major dissatisfaction among GPs about the referral process. Identification of barriers to IBD specialty care can lead to informed system redesign with goals of improving access to GI specialist IBD care, improving access efficiency, overcoming access inequities for patients and referring physicians and ultimately improving health outcomes.

**Funding Agencies:** CIHRNova Scotia Health Authority Research Fund

A219
**A RETROSPECTIVE ANALYSIS COMPARING THE OUTCOMES OF INFLAMMATORY BOWEL DISEASE PATIENTS WHO ARE POSITIVE FOR C DIFFICILE TOXIN BY EIA VERSUS C DIFFICILE PCR**
N. Winczura[4], D.H. Kao[1], B. McSweeney[3], V. Huang[3], L.A. Dieleman[4], B.P. Halloran[2], K.I. Kroeker[4], F. Peerani[3], R. Fedorak[1], K. Wong[4]

1. University of Alberta, Edmonton, AB, Canada; 2. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. Medicine, University of Alberta, Edmonton, AB, Canada

**Background:** Clostridium difficile infection (CDI) is

defined by the presence of diarrhea with either positive C. difficile toxin test or pseudomembranes at colonoscopy. The diagnosis of CDI in Inflammatory Bowel Disease (IBD) is challenging due to diarrhea from underlying disease, lack of pseudomembranes and higher C. difficile carriage rates. Molecular testing (toxin gene PCR) has been shown to lead to over-diagnosis of CDI in one study that demonstrated worse clinical outcomes in patients who are C. difficile toxin positive versus PCR positive.

**Aims:** In this study, we analyze data from IBD patients to determine if worse clinical outcomes of C. Difficile are in those who test positive by toxin (EIA) or PCR.

**Methods:** We preformed a retrospective chart analysis of IBD patients who tested positive for C. difficile by either toxin or PCR. Data collection included baseline characteristics (demographics, IBD type and location, antibiotic exposure) and CDI and IBD outcomes (colectomy, hospitalization, death or need for escalation of IBD therapy).

**Results:** 3119 C. difficile tests were completed in IBD patients at University of Alberta IBD clinic from 2014-2017. 129 patients tested positive for C. difficile with 49% (63/129) by toxin EIA and 51% (66/129) by PCR. No differences were identified in outcomes when comparing toxin positive to PCR positive patients with similar rates of IBD/C. difficile-related hospitalizations, surgery or death found. There were also no differences found in IBD-related outcomes of need for escalation of therapy or flare-ups.

**Conclusions:** In contrast to non-IBD patients, we found no difference in clinical outcomes for IBD patients who are C. difficile toxin (by EIA) or PCR positive. C. difficile PCR positivity may not represent innocent colonization in IBD patients.

| | Toxin N=63 | PCR N=66 | p-value |
|---|---|---|---|
| Hospitalization | 13 | 14 | 0.935 |
| Surgery | 4 | 5 | 0.785 |
| Death | 0 | 1 | |
| Medication Escalation | 31 | 38 | 0.341 |
| Flare up (documented) | 38 | 46 | 0.264 |

**Funding Agencies:** UAH Foundation

A220

**TIME TO DIAGNOSIS OF COLORECTAL CANCER FROM FINDING OF IRON DEFICIENCY ANEMIA**

N. Zhou[1], J. Costello[2]

1. Gastroenterology, University of Ottawa, Ottawa, ON, Canada; 2. Memorial University, St John's, , Canada

**Background:** Colorectal cancer (CRC) is the 3rd most commonly diagnosed cancer within Canada. Newfoundland has the highest CRC incidence rates per capita and mortality rates in the country. There have been several well documented signs and symptoms of CRC, including microcytic anemia/iron deficiency anemia (IDA). Current practice is to have those with IDA be considered for upper or lower GI investigations. Delays in referral for appropriate investigations can lead to a delay in diagnosis. It has been demonstrated that early detection of CRC can improve survival. Referral to those who are able to perform endoscopy of the GI tract or other methods of accessing the GI tract can decrease the amount of time from documentation of IDA to diagnosis of CRC. The cornerstone of CRC treatment remains early diagnosis and early treatment.

**Aims:** Determine the amount of time between documentation of either iron deficiency anemia, microcytosis, or hypoferritinemia and subsequent diagnosis of colorectal cancer

**Methods:** This is a retrospective study on all patients in Newfoundland with a new diagnosis of colorectal cancer in the year 2009. Records were obtained from the Dr. H Bliss Murphy Cancer Care center. A chart review was completed to determine how many patients had either pre-existing iron deficiency anemia (IDA) - defined as a hemoglobin below 120 g/L for women, or a hemoglobin below 140 g/L for men; a microcytosis – defined as an MCV below 80 $\mu m^3$; or a ferritin below 50 ng/ml . Time from laboratory finding to diagnosis was calculated. The date of diagnosis was determined by the date of submission of the pathology sample confirming histologic evidence of colorectal cancer.

**Results:** 500 patients were diagnosed with colorectal cancer in 2009 in Newfoundland. Of the 500 patients, we were able to obtain laboratory data prior to the diagnosis of CRC on 1 or more of our parameters on 213 patients. Of the 213 patients 120 had anemia, 46 had microcytosis and 72 had hypoferritinemia prior to their diagnosis of colorectal cancer. The median time from documentation of anemia to diagnosis of colorectal cancer was 92 days while the mean time was 377 days. The median time from documentation of microcytosis to colorectal cancer was 19 days while the mean time was 130 days. The median time from documentation of hypoferritinemia to colorectal cancer was 145.5 days while the mean time was 480 days.

**Conclusions:** In 2009, the median time from documentation of IDA to CRC was longer than the recommended standard for wait times for investigation of IDA (Recommended standard wait times are within 60 days). In a province that has high rates and high mortality from CRC, our aim should be to improve timely investigation of IDA as early detection can improve outcomes

**Funding Agencies:** None

A221

**IMPACT OF A SPECIALIZED CLINIC IN IMPROVING IBD-RELATED PREGNANCY KNOWLEDGE**

N. Rodriguez[4], V.V. Nguyen[2], L. Ambrosio[5], L.A. Dieleman[3], B.P. Halloran[1], K.I. Kroeker[3], F. Peerani[6], K. Wong[2], R. Fedorak[2], V. Huang[5]

1. Medicine, Divison of Gastroenterology, University Of

Alberta , Edmonton, AB, Canada; 2. Faculty of Medicine, University of Alberta , Edmonton, AB, Canada; 3. Medicine, University of Alberta, Edmonton, AB, Canada; 4. Science, University of Alberta, Edmonton, AB, Canada; 5. University of Alberta, Edmonton, AB, Canada; 6. University of Alberta, Edmonton, AB, Canada

**Background:** Inflammatory bowel disease affects women during their reproductive ages. IBD-related pregnancy knowledge has been reported to be low among women with IBD. We developed a specialized consultation clinic to educate and optimize the management of IBD.
**Aims:** We aimed to assess IBD-related pregnancy knowledge among the patients referred to the clinic, and whether this clinic improves IBD-related pregnancy knowledge.
**Methods:** Adult women with IBD who were seen in the Preconception and Pregnancy in IBD clinic, University of Alberta, were invited to participate. Demographics, reproductive history, IBD history, CCPKnow (Crohn's Colitis Pregnancy Knowledge) survey were obtained. The clinic offers protocolled education, clinical and objective disease monitoring throughout pregnancy and postpartum. Upon completion of follow up (postpartum 3 to 12 months), CCPKnow was reassessed. Pre and post CCPKnow scores were compared using student t-test for raw scores and chi-square test for rank.
**Results:** A total of 99 (47 CD, 52 UC) mothers completed baseline surveys, CCPKnow 10 (IQR: 8 - 13); 22.2% poor, 36.4% adequate, 21.2% good, 20.2% very good. Of these, 37 (13CD and 24 UC) completed postpartum CCPKnow surveys: 13.5% poor, 35.1% adequate, 16.2% good, 35.1% very good. Analysis showed that 21.6% had no change in score, 62.2% improved by at least 1 point, 62.2% remained in the same level, 29.7% improved their level. Of the 7 patients with poor baseline knowledge, all 7 improved CCPKnow score, 3 (42.9%) improved at least 1 level. Of the 14 patients with adequate baseline knowledge, 8 (57.1%) improved CCPKnow score, 4 (28.6%) improved at least 1 level.
**Conclusions:** A specialized consultation clinic improves IBD-related pregnancy knowledge among women with IBD. Further investigation into whether this protocolled clinic improves maternal and fetal clinical outcomes is currently in progress.

**Funding Agencies:** CAGWCHRI, CEGIIR, University of Alberta Faculty of Medicine

A222
**TRAINEE INVOLVEMENT IN EUS PROCEDURES MAY INITIALLY BE ASSOCIATED WITH GREATER RISK AND LOWER DIAGNOSTIC YIELD: A LARGE SINGLE CENTRE STUDY**
U. Khan[1], M.J. Abunassar[2], A. Chatterjee[3], P.D. James[2]

1. Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada; 2. Department of Medicine, University Health Network, University of Toronto, Toronto, ON, Canada; 3. Department of Medicine and The Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, ON, Canada

**Background:** Limited data exists on the quality of advanced endoscopic procedures completed by trainees.
**Aims:** The aim of this study was to describe the quality of endoscopic ultrasound (EUS) procedures performed by advanced endoscopy trainees with staff supervision (TS), using diagnostic yield (DY) and adverse event risk (AE) as quality indicators.
**Methods:** We performed a retrospective chart review of patients who underwent EUS at The Ottawa Hospital between September 2009 and May 2015. Data was collected regarding patient demographics, procedure details, and DYs. AEs were identified by reviewing all emergency room visits and hospitalizations within 30 days of the patient's EUS procedure. Relation of the hospital encounter (definitely, possibly and not) to the EUS procedure was established by consensus using pre-defined criteria.
**Results:** 1647 EUS cases were analyzed. The median patient age was 64 (IQR, 53-73) years and 50% of the patients were male. The EUS DY was 78% and the risk of an AE was 3.5% (58 cases). 27% (450) of all EUS procedures were performed by TS. Overall, TS procedures were not associated with a reduction in DY (80%, p = 0.2) or excess AE risk (4.9%, p = 0.06) in comparison to procedures performed by a staff alone (SA). However, TS DY improved every 4 months (Table 1; 76%, 79%, 84%) and TS AE risk was highest in the first and last 4 months of training (Table 1; 6.8%, 2.1%, 5.9%). This trend was not seen for procedures performed by SA (see Table 1).
**Conclusions:** In the first four months of training, EUS procedures performed by trainees may be associated with lower DY and increased risk of AEs. This warrants further evaluation to determine how to avoid compromising service quality during advanced endoscopy training.

Table 1. Adverse event risk and diagnostic yield during the training period.

| Training Period | Adverse Event Risk (n = 1647) | | | Diagnostic Yield (n = 878) | | |
|---|---|---|---|---|---|---|
| | SA (%; n = 1197) | TS (%; n = 450) | P-value* | SA (n = 614) | TS (n = 264) | P-value* |
| 1 | 13 (2.9) | 8 (6.8) | 0.06 | 76% | 76% | 0.86 |
| 2 | 9 (2.6) | 3 (2.1) | 1.00 | 79% | 79% | 0.93 |
| 3 | 14 (3.5) | 11 (5.9) | 0.17 | 74% | 84% | 0.04 |

*Chi-square or Fisher exact test as required comparing the SA and TS groups. SA= staff alone; TS = trainee with staff

**Funding Agencies:** None

A223

**FACTORS ASSOCIATED WITH EUS DIAGNOSTIC YIELD AND ADVERSE EVENT RISK: A LARGE RETROSPECTIVE SINGLE CENTRE STUDY**

U. Khan[1], M.J. Abunassar[2], A. Chatterjee[3], P.D. James[2]

1. Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada; 2. Department of Medicine, University Health Network, University of Toronto, Toronto, ON, Canada; 3. Department of Medicine and The Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, ON, Canada

**Background:** Maximizing endoscopic ultrasound (EUS) diagnostic yield (DY) and safety is key to providing high quality care, yet the influence of patient and procedure factors on both these outcomes have only been examined using limited sample sizes.
**Aims:** We aim to examine factors associated with EUS diagnostic yield and adverse event (AE) risk using a large cohort of patients who underwent a EUS procedure at our centre.
**Methods:** A retrospective chart review of EUS procedures performed between 2009 and 2015 at The Ottawa Hospital was conducted. Data regarding patient demographics and details of the lesion, procedure, medications, and DY were collected. All patient ER visits or hospitalizations within 30 days of the EUS procedure were also collected and reviewed. Relation of the hospital encounter (definitely, possibly, and not) to the EUS procedure was established by consensus using pre-defined criteria.
**Results:** 1647 EUS procedures were examined. The median patient age was 64 (IQR, 53-73) years and 50% were female. Of all EUS cases, 105 (6.4%) presented to the ER or were hospitalized; however, only 58 (3.5%) were related to EUS. DY was 78% for EUS-FNA cases only. Rapid on-site evaluation impacted DY (73% vs. 80%, p = 0.02) but not AE risk (p = 0.53). Multivariate analysis of all cases demonstrated performing a FNA (OR 2.1, 95% CI 1.0–4.4) and having anesthesia-guided sedation (OR 3.9, 95% CI 1.8–8.5) was associated with an increased AE risk. DY was associated being a smoker (OR 0.7, 95% CI 0.5–0.9).

Upon separating out EUS-FNA procedures only, we found on multivariate analysis that lesions > 3 cm (OR 2.4, 95% CI 1.1–5.3), using anesthesia-guided sedation (OR 3.9, 95% CI 1.3–12.0), and using a $P_2Y_{12}$ inhibitor (OR 7.9, 95% CI 2.5–25.1) was associated with an increased AE risk. Solid lesions (OR 2.0, 95% CI 1.1–3.6) and lesions > 3 cm (OR 1.9, 95% CI 1.2–3.2) were associated with an increased DY.
**Conclusions:** Lesions > 3 cm should be subject to fewer FNA passes to decrease AE risk. EUS procedures on patients who expect to receive anesthesia-guided sedation should be reconsidered. Finally, patients receiving $P_2Y_{12}$ inhibitors should not be subject to FNA, unless their medication is stopped.

Table 1. Factors associated with adverse events within 30 days of EUS procedure diagnostic and yield, multivariate analysis.

| Risk Factor | | | Multivariate, OR (95% CI) | P-value |
|---|---|---|---|---|
| Adverse Event Risk | All EUS | FNA performed | 2.08 (1.00 – 4.36) | 0.05 |
| | | Anesthesia-guided sedation | 3.90 (1.79 – 8.49) | <0.01 |
| | EUS-FNA only | Size of lesion (any dimension > 3 cm) | 2.35 (1.05 – 5.27) | 0.04 |
| | | Anesthesia-guided sedation | 3.93 (1.29 – 12.00) | 0.02 |
| | | P2Y12 inhibitor | 7.89 (2.48 – 25.09) | <0.01 |
| Diagnostic Yield | All EUS | Smoker | 0.68 (0.49 – 0.93) | 0.02 |
| | EUS-FNA only | Lesion type: solid | 1.96 (1.07 – 3.59) | 0.03 |
| | | Size of lesion (any dimension > 3 cm) | 1.94 (1.17 – 3.22) | 0.01 |

**Funding Agencies:** None

A224

**COST-EFFECTIVENESS ANALYSIS OF FECAL CALPROTECTIN USED IN PRIMARY CARE IN THE DIAGNOSIS OF INFLAMMATORY BOWEL DISEASE**

M. Chavannes[1], C. Wong[2], T. Mohammadi[2], W. Zhang[2], G. Rosenfeld[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. CHEOS, Vancouver, BC, Canada

**Background:** Inflammatory bowel diseases (IBD) are chronic conditions with a relapsing and remitting course. The presenting symptoms are heterogeneous and may overlap with other gastrointestinal conditions such as irritable bowel syndrome (IBS), which can lead to delays in diagnosis. Fecal calprotectin (FCP) is a protein excreted from granulocytes and is an accurate marker of intestinal inflammation. When done at the primary care level, it could be a cost-effective method to prioritize and expedite referrals at the specialist level.
**Aims:** Assessment of the cost-effectiveness of introducing FCP testing at the primary care level in the diagnosis of IBD.

**Methods:** A decision analytic tree with a one- year time horizon was constructed to estimate the cost-effectiveness of FCP test versus standard practice of blood test at primary care level, in adult patients presenting symptoms suggestive of IBS or IBD, from a health system perspective in Canada. Outcomes were incremental cost-effectiveness ratio (ICER) of FCP test versus standard of care, the additional cost to avert one false negative (FN) result by FCP test, and time to diagnosis.
**Results:** The ICER of FCP test was $102,669.32 per quality-adjusted life year (QALY). The ICER was sensitive towards prevalence of IBD, monthly utility decrement of IBD, and cost of FCP test. Probabilistic analysis demonstrated that at a willingness- to- pay threshold of $50,000 per QALY, there was only 3.28% chance of FCP test being cost- effective. It would cost an additional $1,180.57 to avert one FN result with FCP test, as compared to standard of care. The use of FCP test at primary care shortened the time to IBD diagnosis by 19.10 days.
**Conclusions:** The result of the analysis suggested that FCP test was not cost- effective in the diagnosis of adult IBD in Canada. However, this analysis was not without limitations. The limitations were mainly due to the lack of key data such as prevalence, as well as cost and utility decrement due to complications associated with endoscopy. Further threshold analysis will identify at which prevalence level, e.g., FCP test can be cost effective.

**Funding Agencies:** Janssen, Future Leaders in IBD Grant

A225
**A NEW STANDARD: AN OPEN-LABEL TRIAL EXAMINING THE EFFECTIVENESS OF INDIVIDUALIZED WEB BASED COLONOSCOPY PREPARATION INSTRUCTION**
E. Nap-Hill, M. Suzuki, C. Galorport, J. Yonge, J. Amar, B. Bressler, H. Ko, E. Lam, A. Ramji, G. Rosenfeld, J.J. Telford, S. Whittaker, R.A. Enns

Department of Medicine, Division of Gastroenterology, St. Paul's Hospital, UBC, Vancouver, BC, Canada

**Background:** Non-pharmalogical factors such as patient education have been shown to significantly improve bowel preparation quality for colonoscopy. For the endoscopist, optimal bowel cleaning increases cecal intubation rates, increases adenoma detection rates, and minimizes necessity for repeat procedures. Following a randomized study demonstrating that the web based patient education tool was superior to traditional paper instructions, this study aims to implement the program at a larger scale; a real life scenario.
**Aims:** To determine the effectiveness of web-based pre-colonoscopy instructions for patients, as measured by the percentage of patients achieving an excellent level of colon cleanliness, equivalent to Boston Bowel Preparation Score (BBPS) ≥ 8. Secondary goals were to assess the patient satisfaction and practicality of this means of education being used by the entire GI clinic for all outpatient colonoscopies.
**Methods:** Prospective, single center, open label study. Adult outpatients scheduled for non-urgent colonoscopy, aged 19 or greater with English proficiency or an available family member/friend who can translate the instructions for them who have a functioning email account were recruited for this study. Patient demographics, cancellations, and quality of bowel preparation (assessed using Boston and Ottawa Bowel preparation scales) were collected. Patient satisfaction surveys were completed the day of their colonoscopy before their procedure to assess clarity and usefulness of the standardized online instructions.
**Results:** Finalized data analysis (n = 900) shows that 84.5% of patients have achieved a score demonstrating adequacy on the BBPS (mean 7.0; adequate score considered ≥ 6 and 90.1 % have scored adequately on the OBPS (mean 3.4; adequate considered ≤ 7). 94.2% of patients scored the web education tool as "Very Helpful" (8 or higher out of 10 on our usefulness scale), and 92.1% scored as "Very Clear" (8 or higher in terms of the clarity of information presented to them).
**Conclusions:** Our analysis suggests that the online instruction pathway is a sufficient alternative to paper instruction, and can be effectively utilized as a standard of care in a real life scenario. Although we did not attain the excellent score (BBPS) ≥ 8, the majority of our preparations were adequately prepared. Our instruction methodology also presents advantages compared to paper because it is uniquely modified for each patient and limits the instruction required by an assistant. Patient satisfaction scales have demonstrated an overwhelming majority of patients who are very satisfied with the clarity and helpfulness of the program.

**Funding Agencies:** None

A226
**PERCEPTION OF PPI PRESCRIBING AMONGST RESIDENTS AND FELLOWS TRAINING IN PRIMARY AND SPECIALTY CARE**
M. Taheri Tanjani[1], A. Al Khoury[2], B. Hari[1], M. Martel[2], A.N. Barkun[2]

1. Queen's University, Kingston, ON, Canada; 2. McGill University Health Center, Montreal, QC, Canada

**Background:** Proton pump inhibitors (PPI) are widely prescribed in North America. Several adverse events linked to their use, most probably not causal, have been reported. Yet no prescribing guidelines have addressed how to balance PPI efficacy in light of such possible side effects.
**Aims:** To acquire knowledge on the varying perceptions of outpatient PPI long-term prescribing (≥8 wks) amongst primary and specialty care residents/fellows in 2 Canadian Universities.
**Methods:** A web-based survey was completed by Family Medicine (FM), Internal Medicine (IM), and Gastroenterology (GI) residents/fellows. A knowledge assessment component examined the participants'

understanding of pertinent efficacy data in the literature and approved indications, as well as literature on PPI-related possible side effects. 20 case scenarios with related targeted management questions were created. Demographics are expressed as proportions; inferential testing compared prescribing decisions between juniors (PGY1/2 FM and 1/2/3 IM) vs senior trainees, and across specialties.
**Results:** Between April and July 2017, 163 trainees participated in the survey (FM 51%, IM 44%, and GI 5%). 83% were junior trainees,17% senior, 59% female; 53% practicing in Ontario, 85% were aged 26-35 yrs. Only 42% had received formal education on prescribing long-term PPI, while 93% believed they would benefit from such teaching. 98% would follow detailed prescribing guidelines. No between-group differences were observed in the appropriate identification of recommended indications, nor of presumed associated side-effects when comparing juniors to seniors, or different specialties. Significant differences were noted in deprescribing PPIs appropriately or inappropriately given established indications in the presence of possible side-effects. 13 clinical stems described an absolute indication for long-term PPI use that should have overshadowed concerns about various possible PPI side effects. Inappropriate discontinuation of the PPI was suggested by 26%-76% of respondents. Amongst 7 clinical stems that described a poor indication for long-term PPI use, despite the introduction of various possible PPI side effects, respondents still elected to continue PPIs inappropriately in 15-44%. Proportions of possible inappropriate prescribing were significantly different according to training seniority in 4 of 20 scenarios, and differed by specialty in 7.
**Conclusions:** There exist significant differences in prescribing attitudes according to level of training and in primary care versus specialty programs, leading to varying levels of inappropriate PPI de/prescribing practices. These findings highlight the need for the creation and wide diffusion of multidisciplinary guidelines to better assist young practitioners in learning optimal management strategies for patients being considered for long-term PPI use

**Funding Agencies:** CAG

A227
**UNDERSTANDING ACCESS TO IBD SPECIALTY CARE IN NOVA SCOTIA THROUGH THE PATIENT LENSE**
C. Heisler[2], H. Mathias[2], J.B. Morrison[2], O. Kits[1], S. Veldhuyzen van Zanten[3], J. Jones[1]

1. Medicine, Dalhousie University, Halifax, NS, Canada; 2. Digestive Care and Endoscopy, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; 3. University of Alberta, Edmonton, AB, Canada

**Background:** Inflammatory Bowel Disease (IBD) is a chronic immune-mediated disease with significant societal burden. The highest age and sex-adjusted standardized incidence and prevalence estimates of IBD have been observed in Canada, with Nova Scotia exhibiting the highest rates in the country. Despite this burden, Canadians living with IBD often face access barriers when seeking gastroenterology specialty care.
**Aims:** To examine IBD care access through the patient perspective in order to identify barriers and facilitators for equitable and efficient access to gastroenterology specialty care in Nova Scotia.
**Methods:** A peer-reviewed and patient-piloted questionnaire was developed through extensive consultation with clinicians, epidemiologists, nurse practitioners (NP), and patients. Questionnaires were developed using evidence-based principles and included demographic, disease, referral structure, and referral process-related questions. The survey was administered using a stratified, random sampling approach to ensure geographic representation. Questionnaires were completed by patients presenting to the Nova Scotia Collaborative IBD Program following their appointment with a luminal GI clinician or IBD NP.
**Results:** As of October 2017, 33 respondents completed questionnaires (sample target: 372). Twenty patients were female (20/33, 61%), mean age of 44 years (SD=16.7, range 19-76 years). Crohn's disease was the most common diagnosis (20/33, 61%), with patients experiencing symptoms between 1 month and 8 years before being seen by a specialist. The majority of patients (25/33, 76%) reported using healthcare services to manage their IBD while waiting to see a specialist, including emergency room services and walk-in clinics. Approximately 20% (7/33) of patients reported that most or all of their appointments were located outside of their community, with a mean wait time of 3-6 months for a specialist appointment. Patients identified long wait times (17/33, 52%), limited resources (e.g. lack of a GI specialist in their community) (10/33, 30%), and poor communication (e.g. lack of communication between patient, referring physician, and specialist) (7/33, 21%) as major access barriers. The top three recommendations by patients for improved access to care were being able to contact the specialists' office to notify them of worsening symptoms (15/33, 46%), receiving direct communication about wait times and appointments (14/33, 42%), and ability to self-refer (9/33, 27%).
**Conclusions:** This is one of the first studies conducted which examines access to gastroenterology IBD specialty care from the patient perspective. Our findings show clear patient-perceived barriers to accessing IBD specialist care in Nova Scotia with long wait times despite a high medical need. Survey administration is ongoing.

**Funding Agencies:** CIHRNova Scotia Health Authority Research Fund

A228
**GASTROENTEROLOGISTS DIFFER IN THEIR PREFERRED MODE OF DELIVERY FOR PREGNANT WOMEN WITH ILEAL ANAL-POUCH ANASTOMOSIS**
E. Kuenzig[1], M. Mathivanan[2], C. Seow[3], E.I. Benchimol[1], R. Panaccione[2], A. MacLean[2], M. Raman[2], Y. Leung[4]


To view enlarged images and tables, please refer to Abstract Library.

1. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. Medicine, University of Calgary, Calgary, AB, Canada; 4. University of British Columbia, Vancouver, BC, Canada

**Background:** Ileal pouch-anal anastomosis (IPAA) is common among individuals with medically-refractory ulcerative colitis and familial adenomatous polyposis syndrome and is often performed during patients' reproductive years. Female infertility is common after IPAA but is decreased with laparoscopic procedures. Clinical practice guidelines recommend caesarean(C-) section but are based on little evidence.
**Aims:** Determine recommendations given to pregnant women with IPAA by their gastroenterologist with regard to mode of delivery.
**Methods:** Canadian gastroenterologists (GIs) were surveyed through the Canadian Association of Gastroenterology in May 2014. The questionnaire included demographic and clinical practice characteristics, and queried GIs on recommendations made to women with IPAA using a clinical vignette. We assessed physician characteristics associated with providing recommendations using a Fisher's exact test (categorical variables) and Wilcoxon rank-sum test (duration of clinical practice).
**Results:** 57 gastroenterologists responded and had practiced for a median of 9 years (IQR 15). Two-thirds (38/56; 68%) of GIs practiced in an academic centre. Most GIs regularly (29/54; 54%) or sometimes (14/54; 20%) recommended a mode of delivery to women with IPAA of childbearing age. Physicians with ≥200 IBD patients in their practice and ≥10 patients with an IPAA were more likely to provide recommendations ($p<0.05$ for both; Table). Among gastroenterologists providing recommendations, 14/40 (35%) would recommend a trial of labour with a low threshold for C-section; 5/40 (13%), elective C-section; and 4/40 (10%), spontaneous vaginal delivery. The remaining physicians would defer to another specialty or patient preference.
**Conclusions:** While the majority of gastroenterologists recommend a specific mode of delivery to their female patients of childbearing age with an IPAA, their recommendations are heterogeneous. This differs from the clinical practice guidelines on IBD in pregnancy, which recommend C-section in women with IPAA. Additional research is needed to identify the safest mode of delivery for these women and to assess uptake of these guidelines.

Characteristics of GIs recommending a mode of delivery to women with IPAA

| | GIs Providing Recommendations (n=43) | GIs Not Providing Recommendations (n=11) |
|---|---|---|
| Duration of clinical practice, median (IQR) | 9 (14) years | 6 (19) years |
| Academic affiliation Academic Non-academic | 32 (74%)<br>11 (26%) | 5 (45%)<br>6 (55%) |
| Proportion of time spent in clinical practice ≤ 75% > 75% | 25 (58%)<br>18 (42%) | 4 (36%)<br>7 (64%) |
| Gender Male Female | 30 (70%)<br>13 (30%) | 10 (91%)<br>1 (9%) |
| Number of IBD patients in practice* ≤ 200 > 200 | 20 (47%)<br>23 (53%) | 6 (55%)<br>5 (45%) |
| Number of patients with IPAA in practice* < 10 ≥ 10 | 14 (33%)<br>29 (67%) | 8 (73%)<br>3 (27%) |

*$p<0.05$

**Funding Agencies:** CAG, CCC, CIHR

A229
**QUALITY ASSESSMENT OF SURVEILLANCE PATTERNS OF PATIENTS WITH BRANCH DUCT TYPE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (BD-IPMN)**
C. Enns, C. Galorport, J.J. Telford, E. Lam, R.A. Enns

Department of Medicine, Division of Gastroenterology, St. Paul's Hospital, UBC, Vancouver, BC, Canada

**Background:** BD-IPMN are typically small neoplastic tumors that are located on the side branches of the main pancreatic duct. These cysts are usually found incidentally with cross-sectional imaging. Although main duct IPMN have high malignant potential, BD-IPMNs are low risk for progression to malignancy therefore surveillance is often appropriate. The 2015 AGA guidelines recommend imaging in one year and then every two years for a total of five years and if the cyst is unchanged, the patient can be discharged from further surveillance.
**Aims:** To assess the surveillance pattern of patients diagnosed with BD-IPMN by EUS and compare to AGA

guidelines. Secondary objectives included analyzing the proportion of BD-IPMN that progressed and if surveillance methods have changed over the time.
**Methods:** A retrospective chart review from 01/11-02/17 of endoscopic ultrasound (EUS) procedures at St. Paul's Hospital, Vancouver, Canada was performed to identify patients with BD-IPMN. Information acquired included patient demographics, patient co-morbidities, BD-IPMN anatomic location, presence of high-risk features, and surveillance imaging (EUS, CT, MRI) findings. Patient follow up was compared to the recommendations implemented in the AGA guidelines to determine if appropriate surveillance was performed.
**Results:** Acquired data included 324 branch type IPMN patients (out of 1250 EUS procedures) with 30% containing high risk features: 21.6% containing a cyst ≥ 3 cm, 10.5% mural nodularity, and 12.7% having a dilated main pancreatic duct > 5mm. In those undergoing surveillance, recommended follow up was in 98% of patients. From 2011 – 2016, there was a gradual increase in the percentage of patients returning for follow up at our institution with 2016 displaying the highest degree of efficient 1 year follow up at 40%. Despite this, mean percentage of patients undergoing surveillance at year 1, 3 and 5 was 33.4%, 20.2% and 15.7% respectively. No patients developed malignancy during follow up.
**Conclusions:** Although endoscopists recommended follow up routinely in patients with BD-IPMN, only a small proportion of patients adhered to recommendations. The follow up is much better at year one than year 5 and also demonstrates improvement in all parameters over time suggesting increasing compliance. Additionally, the follow up has not demonstrated development of cancer suggesting that these guidelines are reasonable. Other measures to ensure appropriate follow up need to be instituted to ensure compliance with recommended guidelines.

**Funding Agencies:** None

A230

**NOT ALL PATIENTS WITH GASTROINTESTINAL COMPLAINTS REQUIRE SPECIALIST CARE: TWO YEAR OUTCOMES FROM AN ENHANCED PRIMARY CARE PATHWAY**

M.S. Mazurek[1], P.J. Belletrutti[1], J. Halasz[1], G.S. Heather[2], M. Swain[1], K.L. Novak[1]

1. Gastroenterology, University of Calgary, Calgary, AB, Canada; 2. Alberta Healther Services, Calgary, AB, Canada

**Background:** High referral volumes to digestive disease specialists in Canada highlight the ubiquity of gastrointestinal disorders. Yet, due to demand-supply mismatch, wait times for specialist consultation continue to grow, exceeding consensus targets. At our institution, a single point of entry model is used to centralize intake. Recently, an Enhanced Primary Care (EPC) pathway was created to identify certain low-risk patients who do not require immediate specialist consultation. These patients are managed by their primary care physician with support from co-developed best practice guidelines.
**Aims:** This study aims to evaluate the overall safety and outcomes for patients declined by our central triage referral system.
**Methods:** All patients triaged to the EPC pathway from January 1, 2015–January 31, 2017 were identified. The subset that re-entered the system through an emergency room (ER) visit and/or re-referral to a specialist was determined. Anonymized patient data, including demographics, referral indication, and referral closure date were abstracted and correlated with endoscopic and histopathologic findings. Clinically significant findings were defined as those imparting significant morbidity or need for further specialist management.
**Results:** During the 25-month study period, a total of 1266 unique closed referrals were captured. 136 patients (10.7%) had a subsequent gastrointestinal-related ER visit, of which, 45 (33%) went on to endoscopy. Overall, 192 patients (15.2%) re-entered the referral system and had assessment with esophagogastroduodenoscopy (67%), colonoscopy (17%), sigmoidoscopy (2%), or bidirectional endoscopy (14%). The median time from referral closure to endoscopy was 186 days (range 6–804). The majority of patients were female (60.9%) with an overall median age of 43 years (range 18–87). The most common indications for re-referral were dyspepsia (42%), gastroesophageal reflux (28%), and suspected irritable bowel syndrome (20%). Overall, clinically significant findings were identified in only 4 of 214 procedures (2%). These included 2 patients with esophagitis, 1 advanced adenoma, and 1 benign peptic stricture. No patients were found have malignancy, inflammatory bowel disease, microscopic colitis, or celiac disease. Fully 148 of 214 procedures (69%) were completely normal.
**Conclusions:** Not all patients referred for gastrointestinal consultation require specialist care or endoscopy. Through careful patient selection, the use of the EPC pathway is both safe and effective in identifying low risk patients who are most appropriately managed within primary care. This facilitates optimization of consultative and endoscopic resources for higher risk patients.

**Funding Agencies:** Division of Gastroenterology, University of Calgary

A231

**URGENT PRIORITY ENDOSCOPY PATHWAY IN A HIGH VOLUME CENTRAL ACCESS MODEL: OPTIMIZING GASTROENTEROLGY CARE FOR THE SICKEST PATIENTS**

M.S. Mazurek[1], K.L. Novak[1], V.C. Heather[2], G.S. Heather[2], M. Swain[1], P.J. Belletrutti[1]

1. Gastroenterology, University of Calgary, Calgary, AB, Canada; 2. Alberta Health Services, Calgary, AB, Canada

**Background:** Increasing demand for endoscopic

evaluation of digestive diseases in Canada challenges the capacity of gastroenterologists to provide timely access to care. Hence, the accurate identification of high risk patients requiring expedited care because of significant morbidity is essential. Yet, predicting significant pathology based on the referral history alone is limited. At our institution, a single point of entry model is used to centralize intake and improve referral management. Recently, due to increased demand, an Urgent-Priority Endoscopy (UPE) pathway was created to enhance access for patients requiring the most urgent diagnostic endoscopies.
**Aims:** This study aims to assess the effectiveness of the UPE pathway in providing appropriate patient triage and timely access to endoscopic assessment.
**Methods:** All patients triaged to the UPE pathway from December 1, 2016–May 31, 2017 were identified. Anonymized patient data, including demographics, initial referral date and indication were abstracted and correlated with endoscopic and histopathologic findings.
**Results:** During the six-month study period, from a total referral volume of 11 116 cases, 131 were triaged directly to endoscopy through the UPE pathway. Patients underwent esophagogastroduodenoscopy (101), colonoscopy (27), both (1), or sigmoidoscopy alone (1). The median wait time from referral to procedure was 4.1 weeks (range 1-55.1). Median age was 60 years (range 19-92) with 69 (52.7%) male patients. The most common indication was dysphagia (n=50, 38.1%), of which 40 patients (80%) had an attributable cause identified: gastroesophageal reflux-related (38%), benign structural causes (24%), motility disorders (6%) or malignancy (6%). Other reasons for referral included abnormal imaging findings (26%), suspected upper gastrointestinal bleeding (19%), anemia (3.8%), mass on digital rectal exam (2.3%), and weight loss (2.3%). Overall, an attributable cause for the referring indication was found in 87/131 patients for a diagnostic yield of 66%. A malignant cause was found in 10 patients (7.6%), namely adenocarcinoma of the colon (4), stomach (4), esophagus (1), and 1 gastric lymphoma.
**Conclusions:** Triage to the UPE pathway via a single point of entry model provided expedited assessment for alarming gastrointestinal symptoms and identified significant pathology in the majority of patients. Yet, one third of patients had a normal endoscopy. Improved referral quality—through access to electronic medical records, for example, or mandated objective measures of significant disease upon referral—could further improve the triage accuracy and facilitate timelier access to care.

**Funding Agencies:** Division of Gastroenterology, University of Calgary

A232
**AUTOMATED TELEPHONE REMINDER TO IMPROVE BOWEL PREPARATION QUALITY FOR COLONOSCOPY**
M. Church, L. Hookey, N. Rubinger
Queen's University, Kingston, ON, Canada

**Background:** Colonoscopy preparation is challenging, involving the consumption of a large volume of prep solution in the day leading up to procedure. Adequate preparation is vital for the endoscopist to visualize the full colon. Upwards of 20% of outpatient colonoscopies have inadequate bowel prep, often requiring a repeat procedure and accompanying costs and risks.

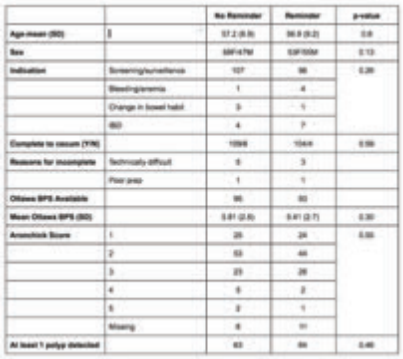
Prior research has examined the impact of educational tools such as booklets and visual aids to improve bowel prep quality. The best success thus far has been with time-intensive physician or nurse delivered educational sessions (in person or by phone). No studies to date have quantified the impact of an automated telephone reminder system on bowel prep quality.
**Aims:** This study aims to determine the impact of an automated telephone reminder system on measured quality of bowel preparation in patients undergoing outpatient colonoscopy.
**Methods:** This study is a prospective trial, using a randomized consent structure. Adult patients were consented to a receive telephone reminder at their initial booking visit. Those who consented were randomized into either the intervention group that received a reminder in addition to written instructions, or a control group that received written instructions alone. The automated reminder was a 30 second recorded message that reminded patients of the upcoming colonoscopy and emphasized the importance of fluid intake and following the bowel prep instructions.

Upon arrival for colonoscopy, subjects were informed of the study, asked for consent to participate in the full study, and completed a questionnaire regarding their fluid consumption and recollection of receiving a telephone reminder.

Each colonoscopy was scored by the endoscopist performing the procedure. They were blinded to the group allocation. The primary outcome was the numeric score of bowel preparation quality using the Ottawa bowel preparation scale.
**Results:** 298 patients agreed to receive a telephone reminder, with 260 randomized to intervention and control groups. The randomized consent protocol meant that participants had to consent again prior to colonoscopy. Ultimately, 108 patients were included in the intervention group and 115 in the control group.

Analysis of the endoscopist-scored bowel preparation quality showed no significant difference in the primary outcome of mean Ottawa Bowel Preparation Score between the two groups. The reminder group had a score of 5.41 versus a score of 5.81 in the no reminder group (the score is from 0 to 14, where a lower score indicates better prep).
**Conclusions:** This study did not show any significant difference in measured bowel preparation quality between those who had received an automated

telephone reminder and those who did not. Despite this, patients subjectively reported satisfaction with the reminder phone call.



| | | No Reminder | Reminder | p-value |
|---|---|---|---|---|
| Age-mean (SD) | | 57.2 (9.9) | 56.9 (9.2) | 0.8 |
| Sex | | 68F/47M | 53F/50M | 0.13 |
| Indication | Screening/surveillance | 107 | 98 | 0.29 |
| | Bleeding/anemia | 1 | 4 | |
| | Change in bowel habit | 3 | 1 | |
| | IBD | 4 | 7 | |
| Complete to cecum (Y/N) | | 103/9 | 104/4 | 0.09 |
| Reasons for incomplete | Technically difficult | 5 | 3 | |
| | Poor prep | 1 | 1 | |
| Ottawa BPS Available | | 95 | 93 | |
| Mean Ottawa BPS (SD) | | 5.81 (2.5) | 5.41 (2.7) | 0.30 |
| Arendrick Score | 1 | 25 | 24 | 0.55 |
| | 2 | 53 | 44 | |
| | 3 | 23 | 28 | |
| | 4 | 5 | 2 | |
| | 5 | 2 | 1 | |
| | Missing | 6 | 11 | |
| At least 1 polyp detected | | 63 | 64 | 0.40 |

**Figure 1**: Study results

**Funding Agencies:** Ferring Pharmaceuticals

A233

**IMPLEMENTING RESOURCE STEWARDSHIP INTO UNDERGRADUATE MEDIAL EDUCATION: CHOOSING WISELY CANADA**

E. Wishart, C. Pendrith, K. Eppler, E.J. Cheng

University of Calgary, Calgary, AB, Canada

**Background:** It is estimated that up to 30% of medical services in Canada are potentially unnecessary, not supported by evidence, and may even result in preventable harm. This type of practicing negatively impacts patients and the health care system and ultimately, leads to suboptimal quality of care. In order to promote resource stewardship (RS) and improve patients' health, Choosing Wisely Canada (CWC) was launched in 2014. One CWC initiative involved the development of specialty-specific lists of recommendations, and a gastroenterology list has been endorsed by the Canadian Association of Gastroenterology. Studies suggest that medical education strongly impacts resource utilization in future practice; therefore it is imperative that RS efforts be implemented early in medical training.
**Aims:** Using the recommendations of CWC we set out to incorporate RS into the undergraduate medical education (UME) curriculum during the gastrointestinal (GI) course. We implemented this change in an iterative manner to enable us to adapt to feedback.
**Methods:** Using a Plan-Do-Study-Act cycle CWC was introduced into the GI course at the University of Calgary Cumming School of Medicine in an iterative manner. In the first iteration, CWC was incorporated by adding relevant recommendations into the case-based small group sessions' learning objectives and content. Qualitative analysis was performed on the narrative data collected via course end surveys from the first iteration of the curriculum. From this analysis, themes were identified and used to influence future iterations of the RS curriculum.
**Results:** The student post-course survey was completed by 143 students. Sixty percent of students reported the inclusion of CWC improved their ability to develop a management plan. Content analysis identified that the students found RS valuable. However, students found inconsistencies in the teaching of RS between seminars, exams and small group sessions. Many students felt that not enough consistent emphasis was placed on RS and the concept was not clear to them. Lastly, many students felt they were too early into their medical training for them to fully grasp the concept of resource restraint while simultaneously tasked with learning thoroughness of care.
**Conclusions:** RS in UME is felt by students to be an important concept. However, content analysis identified numerous areas for improvement. In the next iteration of the GI course, we added an introductory lecture regarding RS to draw attention to the concept. To further address the inconsistencies, we expanded CWC content into large-group lectures and piloted associated exam questions. Next steps to this study include evaluating feedback from these changes, incorporating new additional GI content recently added to the CWC list of recommendations, and obtaining faculty feedback to help inform additional changes for the subsequent iteration.

**Funding Agencies:** None

A234

**LUMEN APPOSING METAL STENTS VERSUS PLASTIC STENTS IN THE MANAGEMENT OF PANCREATIC PSEUDOCYST: A COST-EFFECTIVENESS ANALYSIS**

Y. Chen[1], M. Khashab[3], V. Adam[1], G. Bai[3], V. Singh[3], A.N. Barkun[2]

1. Divison of Gastroenterology and Hepatology, McGill University Health Centre, Outremont, QC, Canada; 2. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 3. Johns Hopkins Medicine, Baltimore, MD

**Background:** EUS-guided drainage is an effective and accepted primary modality for the management of PP. A lumen apposing metal stent (LAMS) has recently been developed specifically for drainage of pancreatic fluid collections, which may be superior to using traditional plastic stents (PS).

**Aims:** Comparing the cost-effectiveness of LAMS to PS.

**Methods:** A decision tree is developed assessing both endoscopic drainage strategies for patients with PP. LAMS and PS over a 6 months time horizon. For each strategy, in-patients received a stent and are followed for subsequent need for direct further interventions or adverse events leading to unplanned endoscopy,

percutaneous drainage (PCD), surgery, or successful endoscopic drainage using probabilities obtained from the literature. The unit of effectiveness is successful endoscopic drainage without need for PCD or surgery. Costs in 2016 US$ are based on inpatient institutional costs. Physician fees are obtained from the American Medical Association. A third-party payer perspective is adopted and sensitivity analyses performed.
**Results:** The success rate is 93.9% for LAMS and 96.96% for PS. Respective costs per successful drainage are US$18,129 (LAMS) and US$10,403 (PS). Being both more costly and less effective, the LAMS strategy is thus characterized as dominated (in the economic sense) by the PS approach. Both deterministic and probabilistic sensitivity analyses confirm the robustness of these findings. .

**Conclusions:** The use of LAMS is not more effective and more costly than PS in the management of patients with PP. As such, PS should be preferred over LAMS as initial management of these patients.

**Funding Agencies:** None

A235
**EXPLORING PATIENT FACTORS FOR CANCELLED OR MISSED APPOINTMENTS TO AN URGENT GASTROENTEROLOGY OUTPATIENT CLINIC.**
K. Khan, W. KABIR, H. Fergani, S. Ganguli, S. Jalali, R. Spaziani, D. Morgan, K. Tsoi

McMaster University, Hamilton, ON, Canada

**Background:** The Canadian Association of Gastroenterology reports that wait times to see a gastroenterologist are too long, even for urgent problems. Cancellations and no-shows compound this problem and lead to poor services utilization. A weekly urgent GI clinic started at St Joseph's Healthcare Hamilton in March 2014 to improve timely access for patients. The clinic accepted referrals from the emergency room (ER) and urgent care with a capacity of 6 patients per week booked within 3 weeks of referral. The cancellation and absence rate from the clinic was 25% in the first 6 months despite patients receiving mail and phone reminder. Studies in no-show predictors focus on primary care, pediatric population and routine outpatient appointments. Published studies on absence rate in urgent clinic settings are very limited.
**Aims:** The present study explores patient factors for the high absence rate at our urgent GI clinic.
**Methods:** Retrospective review of patients booked to the urgent GI clinic between March and September 2014 that were absent at their appointment. The patient demographics, reasons for referrals, duration of symptoms were reviewed from the chart. The patients were contacted to explain why they missed their appointment and were offered to be rebooked.
**Results:** Between March and October 2014, 37 patients (25%) were absent for their appointment to the urgent GI clinic. The average age of patients was 51 years, and 43% were females. The mean duration of symptoms was 28.2 weeks, but 56% of patients had more acute symptoms for 1 week or less when presenting to ER or urgent care. The reasons for referrals included lower GI bleeding (24%), upper GI bleeding (22%), abdominal pain (16%), dysphagia (8%), anemia (5%) and inflammatory bowel disease (5%). Several attempts were made to contact patients, and 22/37 (59%) were reached. Of the 22 patients, 10 elected to cancel without rebooking, 3 were seen as inpatients, and 3 were seen by another outpatient gastroenterologist. Only 6/22 (27%) were rebooked to another urgent clinic appointment.
**Conclusions:** The urgent GI clinic is a useful means for seeing patients with subacute GI illness but has an unacceptably high rate of missed appointments. Of the patients we contacted, only 27% were rebooked back to the urgent clinic. Almost half elected not to rebook suggesting that an urgent referral may not have been appropriate. On the other hand, 3 patients were admitted, suggesting that outpatient management may not have been suitable either, and 3 patients decided to follow up with their established gastroenterologist. The urgent GI clinic now screens all referrals for appropriateness, and does not see patients seen within the past year by another gastroenterologist. Follow-up data will hopefully demonstrate reduction in absence rate with this new strategy.

**Funding Agencies:** None

A236
**UTILIZATION OF AN URGENT GASTROENTEROLOGY CLINIC FOR PATIENTS SEEN IN THE EMERGENCY ROOM OR URGENT CARE CENTRE**
K. Khan, W. KABIR, H. Fergani, S. Ganguli, S. Jalali, R. Spaziani, K. Tsoi, D. Morgan

McMaster University, Hamilton, ON, Canada

**Background:** The Canadian Association of Gastroenterology reports that wait times to see a gastroenterologist are too long, even for urgent problems. To improve timely access for patients, a dedicated urgent GI clinic started at St Joseph's Healthcare Hamilton in March 2014. The clinic accepted referrals from the emergency room (ER) and urgent care clinic with a capacity of 6 patients per week booked within 3 weeks of referral. Suggested referral criteria included a) subacute GI bleeding b) progressive dysphagia c) suspected diagnosis of IBD based on imaging/results and other reasons including liver diseases.
**Aims:** To review the utility of the clinic, appropriateness of referrals, and utilization of endoscopy resources to guide any necessary changes to the clinic.
**Methods:** Retrospective review of all cases that were seen in the urgent GI clinic to identify demographic factors, reasons for referrals, duration of symptoms, whether they had previously seen a gastroenterologist, utilization of endoscopy resources and requirement for ongoing follow up.

**Results:** Between March and October 2014, 119

patients were seen in the urgent GI clinic and 118 were reviewed. An average of 4.5 patients was seen per clinic out of 6 allocated spots giving a missed appointment rate of 25%. The average age of the patient was 52.9 years, and 57% were females. The mean duration of symptoms was 23.4 weeks, but 59% of patients had more acute symptoms for 1 week or less when presenting to ER or urgent care. The most common reasons for referrals included lower GI bleeding (31%), abdominal pain (25%), upper GI bleeding (13%), anemia (5%), and dysphagia (3%). Of the 119 patients, 42% had previously seen a gastroenterologist, and 46% had recently visited the ER or urgent care. A high proportion (71%) was booked for endoscopic tests after the consultation, and 52% were booked for a follow-up appointment.
**Conclusions:** The urgent clinic provides a useful mechanism to see subacute GI illnesses in a timely fashion. However, further optimization is needed to reduce incidence of missed appointments, seeing patients already under care of a gastroenterologist, and referrals for chronic GI illness. There are challenges in high endoscopy utilization and clinic follow-up associated with this strategy. Longer studies may help illustrate further benefits of healthcare utilization by examining reduction in recurrent visits to ER or urgent care.

**Funding Agencies:** None

A237
**COLONOSCOPY PREPARATION OPTIMIZATION FOR INPATIENTS (COIN STUDY). A RANDOMIZED CONTROLLED TRIAL COMPARING 4L PEGLYTE TO REGULAR DOSE PICO SALAX AND SPLIT DOSE PICO SALAX FOR COLONOSCOPY BOWEL PREPARATION IN HOSPITALIZED PATIENTS.**
K. Khan, A. Merali, N. Forbes, H. Fergani, S. Ganguli, S. Jalali, R. Spaziani, K. Tsoi, D. Morgan

McMaster University, Hamilton, ON, Canada

**Background:** Colonoscopy is routinely performed in hospitalized patients (HP) for investigation and treatment. Being a HP is a risk factor for a poor bowel preparation but there are limited studies examining bowel cleansing in this population.
**Aims:** Our goal was to determine whether a low volume prep (PicoSalax) taken the day before or as a split prep is superior to a 4L of PegLyte taken the day before colonoscopy.
**Methods:** This single-centre, endoscopist-blinded, three armed randomized controlled trial compared 4L PEG-Lyte to regular dose Pico Salax and to split dose Pico-Salax for colonoscopy preparation in HP's. In addition, all patients were given Bisacodyl before starting the preparation. Inclusion criteria: Adult in-patients requiring colonoscopy. Exclusion criteria: renal insufficiency, severe congestive heart failure, recent myocardial infarction, ileus, ascites, severe colitis, megacolon, gastrointestinal obstruction, presence feeding tube, bowel resection, pregnancy, or allergy to study drugs. The primary outcome was overall cleansing efficacy using the Ottawa Bowel Preparation Scale (OBPS) as determined by the endoscopist. Secondary outcomes were components of the OBPS, canceled or repeated procedure due to poor cleansing, and safety and tolerability. The study sample size was calculated to be 126 patients.
**Results:** From October 2012 to November 2016, 44 patients were recruited and randomized. One patient refused to take the preparation. One patient's procedure was canceled, and one patient was un-blinded due to poor response. The average patient age was 65.7 year's with 22 females (50%). Indications for colonoscopy include investigation of bleeding (18), anemia (13), change in bowels (6), and abnormal imaging (2). There were 16 patients in the Pico Salax day before group, with mean OBPS of 6.5 (standard deviation (SD) 3.4), 13 patients in the Pico Salax split dose group, with mean OBPS of 4.3 (SD 2.6) , and 15 patients in the PEGLyte group, with mean OBPS of 4.9 (SD 2.9) with ANOVA showing no difference between groups (p=0.15). Four patients reported severe adverse effects while taking the prep. Bowel preparation did not result in any cancelation or repeat procedure. The study was terminated early due to poor recruitment.
**Conclusions:** Preparing hospitalized patients for colonoscopy is a challenging task. The optimal bowel preparation for these patients remains unknown. This study did not show any meaningful difference between groups taking PicoSalax the day before colonoscopy, or Pico Salax as a split preparation, or PEG Lyte the day before colonoscopy but was limited in power because of poor recruitment. Further research is needed in this population.

**Funding Agencies:** Resident Research Grant, Department of Medicine, McMaster University.

A238
**COMPARISON OF ADENOMA DETECTION RATES IN COLONOSCOPIES PERFORMED IN-HOSPITAL VERSUS AN OUT OF HOSPITAL FACILITY IN A SINGLE PRACTICE**
S. Hussain, A. Nguyen

Tri-City Colonoscopy Clinic, Kitchener, ON, Canada

**Background:** Colonoscopy is considered the gold standard for colorectal cancer screening. Adenoma detection rate is considered an important quality indicator for any endoscopists who perform colonoscopies in patients for the purpose of colon cancer screening. Endoscopists may have specialties in different areas of medicine, including gastroenterology, general surgery, and internal medicine. Depending on individual practice and setting, a significant proportion of colonoscopies may not be for colon cancer screening. In Ontario, a significant proportion of colonoscopies are performed in out of hospital setting, or “private" clinics. To date there has been very limited data on the quality of procedures performed in out of hospital clinics in Ontario compared to the in-hospital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setting.
**Aims:** To determine whether location of colonoscopy (in-hospital versus out of hospital facility) affects adenoma detection rate.
**Methods:** In this retrospective study, we analyzed colonoscopy data from a single general community gastroenterologist, who performs colonoscopies in both hospital and out of hospital facilities in approximately equal volumes. For each setting, the Polyp Detection Rate (PDR) and Adenoma Detection Rate (ADR) were determined as a gross rate and "true" rate. Gross rate is based on total number of colonoscopies performed for all indications. The eligibility criteria for "true" rate included symptomatic patients over the age of 50, surveillance at appropriate interval based on guidelines, family history of colon cancer, and positive fecal occult blood test fitting screening criteria based on Cancer Care Ontario ColonCancerCheck program guidelines.
**Results:** While total volumes in each setting is similar (approximately 500 annually in each setting), qualifying cases for true screening cases were lower in hospital setting (234 versus 466), but patients in hospital tended to be older (63.65 years compared to 58.94 years). Patients undergoing colonoscopy in hospital were more likely female (52.14%) and primarily for symptomatic reasons (46.15%). Patients undergoing colonoscopy in out of hospital clinic were more likely male (53.65%), and primarily for surveillance purposes (43.8%). In these population of patients, we report PDR rates of 70.94% in hospital colonoscopies and 75.32% in out of hospital clinic colonoscopies. The corresponding ADR rate in hospital colonoscopies was 54.70% and in out of hospital clinic was 59.01%.
**Conclusions:** While this is retrospective data that is not controlled for many variables, adenoma detection rate for colonoscopies in an out of hospital clinic appears to be at least comparable, if not superior, to in hospital colonoscopies. As such, the quality of colonoscopies, as measured by ADR, performed in an out of hospital facility are comparable to those performed in an in-hospital setting.

**Funding Agencies:** None

A239
**BRISK GASTROINTESTINAL BLEED: AN ATYPICAL CULPRIT**
J. LeBlanc[1], K. Waschke[2]

1. Internal Medicine, McGill University, Lachine, QC, Canada; 2. Montreal General Hospital, Montreal, QC, Canada

**Background:** A 68 year-old female is referred to the Gastroenterology consultation service from the Emergency Department (ED) for brisk gastrointestinal bleeding. Five months prior, she was admitted for multiple intra-abdominal abscesses from perforated appendix, requiring right hemicolectomy and small bowel resection. She was also known for deep vein thrombosis on low-molecular-weight heparin and ovarian cancer considered in remission.
**Aims:** Case report and review of the literature
**Methods:** See above
**Results:** She presented to the Royal Victoria Hospital for witnessed syncope and significant hematochezia of acute onset. She was profoundly hypotensive, requiring aggressive fluid resuscitation. Her physical exam showed mild epigastric and right lower quadrant pain, as well as bright red blood on the digital rectal examination. Her initial hemoglobin of 80 dropped to 32, with ongoing hematochezia. Nasogastric tube insertion was unsuccessful. A gastroscopy showed normal mucosa with no blood seen up to the distal duodenum. Overnight, she suffered from a recurrent episode of brisk hematochezia, requiring the activation of a massive transfusion protocol. Given her ongoing blood loss, she was sent for a mesenteric angiogram which identified an actively-bleeding fistula from the right external iliac artery to the transverse colon. The interventional radiologist decided to deploy a balloon-assisted covered stent to close off the fistula. Immediately after deployment, the patient's hemodynamics improved. The vascular surgery team decided against operative management in view of a suspected low operative success from multiple prior surgeries and radiation therapy. Asymptomatic, she was discharged eleven days after her presentation.
**Conclusions:** This rare case highlights the importance of early recognition of life-threatening conditions, such as arterioenteric fistulas (AEF). It also illustrates a rare mechanism of fistula formation. Most cases of AEFs are described as secondary, namely as a complication of prior aortic reconstruction. Approximately 250 cases of primary AEF have been reported in the published literature, of which only 15% affected the colon. In our patient's case, the main risk factors for primary AEF were encasing peri-iliac abscesses, subsequent bowel manipulation and prior radiation therapy.

Prompt investigation is a key component of AEF prognosis. Angiography permits direct AEF visualization and potential placement of a covered stent graft, either as a bridge to open surgery or as a definitive therapy for patients with high operative risk. However, stent placement harbours significant rebleeding rates and infectious complications. Optimal management in these cases remains controversial, such as the use of prophylactic antibiotics or serial imaging. Even though high-quality evidence is scarce, angiography with endovascular intervention is considered first-line treatment in patients with hemodynamic instability.

**Funding Agencies:** None

A240
**BOWEL PREPARATION INDUCED MONOCULAR BLINDNESS**
N. Bollegala[1], M. Bernstein[2]

1. GI, Women's College Hospital, Toronto, ON, Canada; 2. Sunnybrook Health Sciences Center, Toronto, ON, Canada

**Aims:** The authors present an association between bowel preparation induced dehydration and acute cataract worsening.
**Methods:** This association was identified through a clinical case encountered during routine practice.
**Results:** A 63 year old man was seen for average risk colorectal cancer (CRC) screening. His past medical history was significant for coronary artery disease, dyslipidemia, hypertension, type 2 diabetes, benign prostatic hyperplasia, degenerative disc disease, right cataract surgery. Medications included ASA, atorvastatin, gliclazide, janumet, ramipril, indapamide, ezetimibe, insulin glargine. He had no allergies to medications. He was married, had 2 adult children, was born in Sri Lanka, worked as an auditor and was functionally independent. He was an ex-smoker, and drank 2 alcoholic beverages per night. Family history was unremarkable for gastrointestinal conditions. Colonoscopy was performed for routine CRC screening. Bowel preparation consisted of 4 liters of Go-Lytely the day prior to the procedure. His procedure was conducted as an out-patient within a tertiary care teaching hospital. The colonoscopy was uncomplicated and the examination was normal. He was discharged home and resumed his normal diet and normal medications. Shortly after the colonoscopy, the patient experienced a rapid loss of visual acuity in the left eye, which worsened over the following 48 hours. He presented to the emergency department for evaluation. A CT head was performed showing only scattered white matter changes secondary to mild microangiopathic changes, mild right maxillary fluid but no obvious cerebrovascular accident (CVA). He was referred to ophthalmology who confirmed the acuity loss (the patient was only able to count fingers) and performed fundoscopy after pupillary dilation identifying a dense white cataract. There was low clinical suspicion for giant cell arteritis, no relative afferent pupillary defect to suggest central retinal artery occlusion or central retinal vein occlusion (although fundoscopy was limited due to the cataract itself). The patient was told that that acute worsening of cataracts can occur due to dehydrationand this was likely induced by the bowel preparation. He was also seen by the general internal medicine service who felt the likelihood of CVA, given the absence of focal neurological deficits (aside from the visual acuity loss), was low. The patient underwent successful cataract excision and lens replacement 6 weeks later, with a return to normal left eye vision.
**Conclusions:** While acute dehydration is a known risk factor for worsening of cataracts, a review of the literature did not demonstrate any reported association between colonoscopy bowel preparation, dehydration and acute cataract worsening. The product monograph for GoLytely does not list this as a potential adverse effect. This is the first case report documenting such an association.

**Funding Agencies:** None

A241

## MASSIVE OBSCURE GI BLEEDING FROM IDIOPATHIC JEJUNAL VARICES IDENTIFIED USING SINGLE BALLOON ENTEROSCOPY

N. Harris, H. Moloo, A. Rostom

University of Ottawa, Ottawa, ON, Canada

**Background:** Obscure GI bleeding from idiopathic small bowel varices is both a diagnostic and management challenge for physicians. There are very few cases reported in the literature and there is no consensus on management recommendations.
**Aims:** To present the case of a 34-year-old male with bleeding from idiopathic jejunal varices and to review the literature.
**Methods:** A case of idiopathic jejunal varices is reported. A literature review was conducted which identified 24 articles describing idiopathic small bowel varices.
**Results:** A 34-year-old male was referred for obscure GI bleeding and anemia requiring >20 pRBC transfusions over one month. The patient reported intermittent melena and anemia over the last year. He had no risk factors for portal hypertension. Upper and lower endoscopies were non-diagnostic.

Anterograde single balloon enteroscopy revealed petechial like lesions that were not classic for angiodysplasia. They were treated with argon plasma coagulation and clipped. Distal to these lesions, in the mid to distal jejunum, small bowel varices were suspected but not treated pending further evaluation. No venous abnormalities were identified on CTA.

The patient returned to emergency three weeks later with anemia (Hgb 69g/L). He received 2 u pRBC. The single balloon enteroscopy was repeated. There was no evidence of bleeding and the varices were tattooed (fig. 1). The patient underwent an endoscopically assisted exploratory laparoscopy that was converted to a laparotomy upon finding a grossly abnormal distal jejunum. Dilated and tortuous varicosities were identified involving approximately 150cm of small bowel. It was decided to resect the 40cm segment in which varices were visible endoscopically (fig 1).

There was no evidence of thrombosis in the resected specimen. Post operatively the patient convalesced well except for a pulmonary embolism that was treated with warfarin. This event was believed to be provoked by the surgery. The patient has had no re-bleeding 12 months post-resection.

Literature Review: Both familial and non-familial accounts of small bowel varices in the absence of a primary cause have been reported in the literature. When supportive therapy is insufficient, the most common treatment modality chosen is surgical resection. Select cases have also demonstrated that sclerotherapy and varix dissection can be used for to treat these lesions.
**Conclusions:** Idiopathic small bowel varices pose both


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diagnostic and therapeutic challenges for physicians. In the literature, several treatment modalities have been shown to be successful; these include surgical resection, varix dissection and sclerotherapy. There is no consensus on the preferred treatment strategy. This report demonstrates that endoscopically assisted surgical resection is a viable management strategy for bleeding of idiopathic small bowel varices, an uncommon cause of occult GI bleeding.

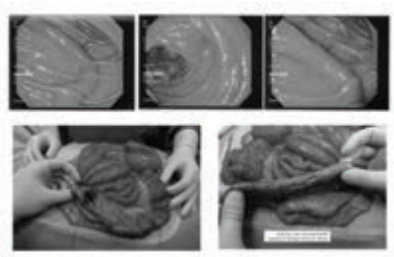

Fig. 1 – Top: varices viewed endoscopically. Bottom: varices visible on the exterior of the bowel wall

**Funding Agencies:** None

A242

**SIGMOID PERFORTATION: A RARE CASE OF REFRACTORY CELIAC DISEASE TYPE II**

R. Chibbar[2], j. Nostedt[1], D. Mihalicz[1], R. Mclean[3], j. deschenes[1], L.A. Dieleman[1]

1. Medicine, University of Alberta, Edmonton, AB, Canada; 2. Gastroenterology, University of British Columbia, Kamloops, BC, Canada; 3. Royal Alexandra Hospital, Edmonton, AB, Canada

**Background:** Celiac disease is an autoimmune enteropathy caused by gluten ingestion in genetically susceptible individuals. Treatment consists of a gluten-free diet (GFD). Non-responders typically have an incidental source of gluten ingestion; however, 1% develops refractory celiac disease (RCD). RCD is defined as persistent or recurrent malabsorption, villous atrophy despite a strict GFD for 6-12 months. It is further classified as type I (RCD I) and type II (RCD II) by immunophenotyping. RCD I has a normal population of intraepithelial lymphocytes (IELs), while RCD II has aberrant IELs, which have T-cell clonality. RCD II is associated with EATL and is considered a pre-malignant condition, and more difficult to treat.
**Aims:** -
**Methods:** A 68-year old gentleman with a background including hypothyroidism, small bowel obstruction with lysis of adhesions, and family history of CD presented with acute-onset abdominal pain. CT abdomen showed free air and stranding in the proximal jejunum. Exploratory laparotomy found a spontaneous jejunal perforation and proximal stricturing. 20 cm of small bowel was resected. Histology review showed monoclonal T-cell receptor arrangement. He presented 2 months later with weight loss, diarrhea, and hypoalbuminemia. Gastroscopy showed scalloping of the duodenal mucosa and flattened villi; colonoscopy was normal. Biopsies showed villous atrophy with intraepithelial lymphocytosis, lymphocytic gastritis, and lymphocytic colitis. He was given supplemental nutrition and intravenous corticosteroids, but did not improve. Small bowel enteroscopy demonstrated a purulent-appearing anastomosis with fistulous opening; biopsies showed severe villous atrophy, and the anastomosis demonstrated mucosal ulceration with inflammatory exudate. Following repeat colonoscopy, he had a perforation and underwent exploratory laparotomy, lysis of adhesions, and small bowel and sigmoid resection. Biopsies confirmed ulcerative jejunoileitis consistent with RCD II. He continued to be non-responsive to corticosteroid therapy. Though there was no histologic evidence of malignancy, he continued to do poorly, and died. This patient's serum sample was collected for antigen analysis, versus patients with classic celiac disease.
**Results:** -
**Conclusions:** RCD II is a rare entity, emphasizing the importance of immunophenotyping in diagnosis; this has significant prognostic implications. Treatment data relies primarily on case reports; there is a paucity of randomized control trials. Therapy typically results in clinical and histological improvement, but does not prevent progression to EATL. This case highlights the difficulty of diagnosis of RCD II. It is one of the first cases to present with sigmoid perforation and to demonstrate both lymphocytic gastritis and lymphocytic colitis in RCD II. In addition, it is a pilot study of the serum analysis in RCD II patients.

**Funding Agencies:** None

A243

**AN UNCONVENTIONAL CASE OF OLMESARTAN ASSOCIATED ENTEROPATHY**

j. ghaith[2], A. Szilagyi[1]

1. Medicine, Gastroenterology, Jewish General Hospital, Montreal, QC, Canada; 2. Medicine, McGill, Montreal, QC, Canada

**Background:** While chronic diarrhea is costly, drug-induced enteropathy is a treatable etiology if identified. Olmesartan has been reported to cause chronic diarrhea since 2012. There are approximately 200 cases reports/series linking Olmesartan with observed villous atrophy on duodenal biopsies. It is essential to recognize that OAE is a differential diagnosis in cases of refectory celiac disease and it's severity ranges through a spectrum of clinical and histolpatholigcal findings. In our report, we identify a case of OAE based on clinical symptom with preserved villous architecture on small bowel biopsy.
**Aims:** - To report a clinical case of OAE with preserved villous architecture on duodenal biopsy and modestly elevated serologic markers of Celiac Sprue.
- To increase awareness among clinician of OAE; a new missed differential of sprue-like enteropathy.

**Methods:** We present a clinical case of chronic worsening severe diarrhea encountered in gastrointestinal outpatient clinic followed up from January 2017 to September 2017.
**Results:** A 62- years-old female patient known for hypertension and Irritable Bowel Syndrome-D for 8 years presented in late 2016 with worsening persistent diarrhea. Work up including colonoscopy with biopsies and MRI Enterography was negative. Serologically, carcinoid and infectious etiology were also negative. However, transglutaminase antibody (IgA TTG) levels were modestly elevated (45U/ml - April 2017 then 19 U/ml- May 2017 , N < 9U/ml). An earlier IgA TTG was negative in 2010. On the contrary, small bowel biopsies exhibited preservation of villous architecture with increased CD3+ intraepithelial lymphocyte (MARSH 1A). Therapeutic trials including gluten free diet (GFD) for 3 weeks, antibiotics, and corticosteroids failed. Supportive medications loperamide had modest benefit. Finally, on review of medication, patient was noted to be on Olmitec$^{R}$ (Olmesartan), and soon upon the cessation of the medication, patient reported improved bowel habits.
**Conclusions:** Drug-induced enteropathy is a frequently missed differential for chronic diarrhea. Almost all previously reported cases depicted histological evidence of villous atrophy along with mucosal inflammation with recovery upon cessation of Olmesartan or other offending ARBs. Our case report has identified OAE presenting as celiac mimicker but without clinical response to GFD. OAE can be a difficult entity to diagnose in the setting of equivocal histological findings. Olmesartan can inflict a spectrum of intestinal injury ranging from mild lymphocyte infiltration to severe villous atrophy. Clinical judgment and careful medication review should be applied to distinguish celiac from drug-associated enteropathy.

**Funding Agencies:** None

## GASTRO INTESTINAL ONCOLOGY

### Poster of Distinction

A244
**ROLE OF THE NUCLEAR RECEPTOR HNF4α AND ITS MANY ISOFORMS IN COLORECTAL CANCER**
E. Lambert[4], J. Babeu[1], D. Levesque[1], F. Boisvert[3], F. Boudreau[2]

1. Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Anatomie et biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 3. Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada; 4. Cell biology and anatomy, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** Hepatocyte nuclear factor 4 alpha (HNF4α) is a transcription factor regulating the expression of intestinal epithelial genes. Up to 12 HNF4α isoforms can be produced by the use of promoters P1 and P2, and alternative splicing. HNF4α has recently been associated with colorectal cancer, and the variable expression of the P1 and P2 classes could explain the contradictory roles of HNF4α in this disease. However, little is known on the specific functions for each HNF4α isoform during colorectal cancer.
**Aims:** The overall aim of this study was to elucidate how HNF4α, through the expression of its many isoforms in the colon, may contribute to the progression of colorectal cancer. More specifically, the twelve HNF4α isoforms were functionally characterized by evaluating their DNA binding and transactivation capabilities, and identifying distinct protein interaction networks using quantitative proteomics.
**Methods:** Expression of the HNF4α isoforms was evaluated by RT-PCR in different cell lines and in different human gastrointestinal tissues. Stable cell lines expressing each of the twelve isoforms tagged with either GFP or BioID2 proteins were generated in the HCT116 human colorectal cancer cell line. EMSA, luciferase and qPCR assays were performed to characterize every single isoform. Protein interaction networks for specific isoforms expressed in the colon were characterized by quantitative mass spectrometry.
**Results:** Important variations in the expression of HNF4α isoforms were first observed by RT-PCR in different colorectal cancer cell lines as well as in several healthy human gastrointestinal tissues. Stable HCT116 cell lines expressing each of the HNF4α isoforms in an inducible manner were generated. Although each isoform was expressed and localized in the nucleus with a similar pattern, EMSA assays revealed differences in DNA binding capabilities for a subset of isoforms. This correlated with differences observed in the transactivation potential of these isoforms, as determined by luciferase assays and qPCR. Finally, important variations in the protein interactomes for these different isoforms were detected by quantitative mass spectrometry. The nature of these differences was related to proteins involved in transcription and chromatin assembly regulation.
**Conclusions:** Our data identified differential transcriptional properties among the various HNF4α isoforms. Specific transcriptional partners were identified to differently interact with these isoforms. It is expected that the future characterization of these specific interactions will provide insight as to why HNF4α could have both oncogenic and tumor suppressive properties during colorectal cancer.

**Funding Agencies:** CIHRNSERC

### Poster of Distinction

A245
**THE ROLE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN COLITIS-ASSOCIATED CANCER**
H. Good, A. Shin, E. Fazio, L. Zhang, S. Asfaha

University of Western Ontario, London, ON, Canada

**Background:** Colorectal cancer (CRC) is the 2nd leading cause of cancer death in Canada. A major risk factor for this disease is chronic inflammation. For this reason, patients with inflammatory bowel disease (IBD), such as Crohn's disease or Ulcerative colitis, require frequent colon cancer screening. Despite the clear link between inflammation and cancer, the exact mechanism by which colitis leads to cancer is unknown. Our group has focused on a rare and ill-defined cell type in the gut known as a tuft cell that uniquely expresses doublecortin-like kinase-1 (Dclk1). Using a novel transgenic mouse model, we have previously shown that Dclk1+ tuft cells are quiescent and long-lived, and remain resistant to proliferation even upon mutation of the tumor suppressor *APC*. Interestingly, these cells become powerful cancer-initiating cells upon exposure to inflammation, but the mechanism by which inflammation leads to colonic tumors is not known. Intriguingly, Dclk1+ tuft cells express high levels of cyclooxygenase (COX)-1 and -2, the direct enzyme target of non-steroidal anti-inflammatory drugs (NSAIDs) which are known chemopreventative drugs in CRC.
**Aims:** In the present study, we aim to determine the effects of COX inhibition by NSAIDs on colitis-associated colorectal cancer.
**Methods:** Dclk1CreERT2/APC$^{flox/flox}$ mice were administered tamoxifen to induce an *APC* mutation in Dclk1-expressing cells. Mice were then exposed to the colitis-inducing agent dextran sodium sulfate (DSS), followed by daily treatment with oral NSAIDs or vehicle for the remainder of the experiment duration. The NSAIDs tested included Aspirin (non-selective COX inhibitor), celecoxib or rofecoxib (COX-2-selective inhibitors), or SC-560 (COX-1-selective inhibitor). Approximately 16 weeks post-tamoxifen, colonic tumour number and size were analyzed to determine the effect of these NSAIDs on tumour initiation and growth, respectively. Extent of inflammation was assessed by myeloperoxidase (MPO) activity and histology, and colonic tissue was taken for measurement of inflammatory mediators by qRT-PCR.
**Results:** Treatment with Aspirin and SC-560, but surprisingly, not celecoxib and rofecoxib, significantly reduced the number of colonic tumours. There was no significant difference in tumour size between vehicle and any of the NSAID-treated groups. Of note, the degree of colitis as assessed by MPO activity and histology was not significantly different between vehicle and NSAID-treated groups.
**Conclusions:** These findings suggest a role for COX-mediated inflammation in colonic tumorigenesis arising from Dclk1+ tuft cells. Our results suggest that COX-1-selective, rather than COX-2-selective, NSAIDs may be useful for chemoprevention of CRC in patients with IBD.

**Funding Agencies:** CIHR

## Poster of Distinction

A246

### ROLE OF DOUBLECORTIN-LIKE KINASE 1 (DCLK1) POSITIVE TUFT CELLS IN COLITIS-ASSOCIATED COLORECTAL CANCER

A. Shin, E. Fazio, L. Zhang, H. Good, S. Asfaha

Department of Medicine, Department of Pathology and Laboratory Medicine, Schulich School of Medicine & Dentistry, Western University; London Regional Cancer Program, Lawson Health Research Institute, London, ON, Canada

**Background:** Colorectal cancer (CRC) is the second leading cause of cancer death in Canada, with the major risk factor being chronic inflammation. How inflammation leads to cancer is not well understood. Our recent work has focused on a colonic epithelial cell known as the tuft cell that uniquely expresses the protein doublecortin-like kinase 1 (Dclk1). Using Cre-dependent lineage tracing of Dclk1-expressing cells, we showed that Dclk1 labels long-lived quiescent cells in the colon that serve as a cellular origin of CRC upon inflammatory injury.
**Aims:** The aim of the study was to determine the generalizability of inflammation-induced tumor promotion from genetically susceptible Dclk1+ cells and explore the mechanism by which inflammation contributes to tuft cell cancer initiation. We hypothesized that various colonic inflammatory insults lead to dedifferentiation of Dclk1+ tuft cells to a stem cell state susceptible to tumor initiation.
**Methods:** To investigate the various forms of injury or infection that can activate quiescent tuft cells, we crossed our transgenic Dclk1-CreER$^{T2}$ mice to both ROSA26-tdTomato and APC$^{f/f}$ mice (Dclk1/APC$^{f/f}$). Following tamoxifen induction, mice were treated with the colitis-inducing agents dextran sodium sulfate (DSS), trinitrobenzene sulfonic acid (TNBS), oxazolone or *Citrobacter rodentium*.
To examine the role of dedifferentiation in colonic tumor initiation, we crossed Lgr5-DTR-eGFP mice to our Dclk1/APC$^{f/f}$ mice. The mice were then given tamoxifen and DSS to induce tumorigenesis and diphtheria toxin (DT) post DSS injury to ablate Lgr5+ intestinal stem cells.
**Results:** Treatment with DSS, TNBS, oxazolone, or *C. rodentium* induced colonic inflammation as detected by significantly increased myeloperoxidase (MPO) activity and histologic analysis. DSS administration led to Dclk1+ cell-derived colonic tumors as previously reported. Surprisingly, administration of TNBS, oxazolone, or *C. rodentium* in Dclk1/APC$^{f/f}$ mice did not lead to colonic tumorigenesis up to 52 weeks following induction of colitis. Interestingly, ablation of Lgr5+ intestinal stem cells post colitis significantly reduced colonic tumors in DSS-treated Lgr5-DTR-eGFP/Dclk1/APC$^{f/f}$ mice.
**Conclusions:** Our data suggests that a specific inflammatory response unique to DSS-induced colitis, and not TNBS, oxazolone or *C. rodentium* infection, results in colonic tumor formation. Interestingly, the colonic transformation of Dclk1+ tuft cells in DSS

colitis appears to be mediated through Lgr5-expressing cells. These findings provide insight into the molecular pathways by which Dclk1-derived colonic tumors arise.

**Funding Agencies:** CAG, CIHRCFI

A247

**L-MENTHOL DURING COLONOSCOPY FOR ADENOMA DETECTION IN AN INTERMEDIATE RISK PATIENT POPULATION: A DOUBLE-BLIND, RANDOMIZED CONTROLLED TRIAL**

A.S. Dhillon[1], S. Alshankiti[1], A. Khorasani-zadeh[1], R. Sultanian[1], G.S. Sandha[1], A.R. Kohansal[1], A.J. Montano-Loza[2], S. Zepeda-Gomez[1]

1. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 2. Division of Gastroenterology & Liver Unit , University of Alberta , Edmonton, AB, Canada

**Background:** Adenoma detection rate (ADR) is defined as the proportion of screening colonoscopies performed by a physician that detect at least one histologically-confirmed colorectal adenoma or adenocarcinoma. Colonoscopy is considered the gold standard for detection and removal of polyps. However, despite advances in technology, there is still a significant number of missed polyps during colonoscopy.
L-Menthol (peppermint oil) has been shown to induce spasmolytic effects in human colon circular smooth muscle, it could potentially improve the visual field for the endoscopist.
**Aims:** The aim of our study was to determine the effectiveness and safety of topical L-menthol preparation in adenoma detection and effect on colonic peristalsis.
**Methods:** This was a randomized, double-blind, controlled trial conducted at the University of Alberta. Patients undergoing screening colonoscopy were consecutively recruited from the Stop Colorectal Cancer through Prevention and Education program. Patients were randomized to L-Menthol solution or the control solution (liquid simethicone) administered as spray at the cecum. Peristalsis was recorded at baseline, then at 1 and 5 minutes and graded as none, mild, moderate or severe, based on a validated classification.

The endoscopists and patients were blinded. During the procedure, insertion and withdrawal times were recorded, as were the quality of bowel preparation, total sedation, changes to patient position, abdominal pressure and the use of carbon dioxide. The location, size, removal technique and type of polyp detected were documented. All specimens retrieved were sent for histopathology. After the procedure, patients were contacted and questioned about adverse effects.
**Results:** A total of 122 patients enrolled in our study, 61 patients were randomized to receive L-Menthol. There were no significant differences in patient characteristics between the two groups. The overall ADR was 63.1%. There were no significant differences in the amount of sedation, position change, or withdrawal time. The primary end-point of ADR was 57.4% in the L-menthol group and 68.9% in placebo (p=0.260). The proportion of patients with no peristalsis at 5 minutes was 44.3% in the L-menthol group and 21.3% in the control group (p=0.002). There were no significant differences in peristalsis at baseline and after 1 minute.

No significant differences were found regarding bloating or abdominal pain between the two groups. No major side effects were reported in the two groups.
**Conclusions:** Topical L-menthol was associated with decreased peristalsis during colonoscopy after 5 minutes. L-Menthol did not increase the ADR in intermediate-risk patients, however, further studies on other patient populations should be considered.

**Funding Agencies:** None

A248

**EARLY INITIATION OF STOMACH NEOPLASIA THROUGH DUAL DELETION OF MESENCHYMAL BMP SIGNALING AND *TRP53***

C. Ouellet[3], P. Garde-Granger[4], F. Boudreau[2], N. Perreault[1]

1. Anatomie et Biologie Cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Anatomie et biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 3. Anatomie et Biologie Cellulaire - Faculté de Médecine et des Sciences de la Santé, Université de Sherbrooke, Sherbrooke, QC, Canada; 4. Université de Sherbrooke, Sherbrooke, QC, Canada

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A249

**ROLE OF LRP6 IN *KRAS* AND *BRAF* MUTATED COLORECTAL CANCER**

A. Côté-Biron[2], j. raisch[2], N. Rivard[1]

1. University of Sherbrooke, Sherbrooke, QC, Canada; 2. Anatomie et biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** Colorectal cancer (CRC) represents the second leading cause of death worldwide. Self-renewal of the intestinal epithelium is tightly regulated by intracellular signaling pathways which control stem cell proliferation and differentiation. It has been previously reported that effectors of the Wnt/β-catenin and KRAS/BRAF/MEK/ERK pathways are often mutated in early stages of CRC, leading to sustained activation of these pathways. Whereas KRAS/ MAPK and canonical Wnt/β-catenin pathways are critical for intestinal tumorigenesis, mechanisms integrating these two important signaling pathways during CRC development are however unknown. We recently demonstrated that transformation of normal intestinal epithelial cells (IEC)

by oncogenic forms of KRAS or BRAF was associated with a marked increase in phosphorylation of the Wnt co-receptor LRP6 and in β-catenin/TCF4 transcriptional activity. Notably, LRP6 phosphorylation was significantly increased in human colorectal tumors, including adenomas, in comparison with healthy adjacent normal tissues (Lemieux et al., 2015). These results suggest that LRP6 activation might represent a unique point of convergence between KRAS/MAPK and Wnt/β-catenin signaling during colorectal oncogenesis.
**Aims:** The aim of this study was to determine the role of LRP6 in the anchorage-independent growth of *KRAS* and *BRAF* mutated human CRC cells.
**Methods:** To analyze the role of LRP6 in human CRC cells, we used siRNA to specifically knockdown LRP6 expression. The cell lines analyzed displayed characteristic mutations: HCT116 (mutated for β-*catenin* and *KRAS*), HT29 (mutated for *APC* and *BRAF*) and SW480 (mutated for *APC* and *KRAS*). LRP6 phosphorylation and expression was analyzed by qPCR and Western blot. The effect of MEK inhibition on LRP6 phosphorylation was also evaluated by treating cells with CI1040 (2μM). Anchorage-independent growth was evaluated by culturing cells in soft agar for 10-15 days.
**Results:** Strong expression of LRP6 protein was observed in all CRC cell lines analyzed. Treatment of cells with the MEK inhibitor CI1040 (4h and 24h) significantly reduced LRP6 phosphorylation on serine 1490 and threonine 1572 suggesting a link between MEK/ERK signaling pathway and LRP6 activation. Most interestingly, LRP6 silencing dramatically inhibited the capacity of HCT116, HT29 and SW480 cells to grow under anchorage-independent conditions.
**Conclusions:** Altogether these results suggest that LRP6 activation controls growth of CRC cells exhibiting KRAS or BRAF mutation, suggesting that this coreceptor might represent a novel therapeutic target for CRC associated with these mutations.

**Funding Agencies:** CHUS

A250
**HNF4A'S NEW ROLE IN DNA REPAIR COULD BE A POTENTIAL THERAPEUTIC TARGET FOR COLORECTAL CANCER TREATMENT**
S. Wilson, J. Babeu, R. Drissi, D. Levesque, F. Boudreau, F. Boisvert

Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** Colorectal carcinomas typically feature an upregulation of the P2 isoform class of HNF4α. The expression of P2-HNF4α correlates with cell proliferation. Despite this link, the functional role that P2-HNF4α plays in the phenotype of colorectal cancer is poorly understood. Recently, we demonstrated that P2-HNF4α is involved in DNA repair by forming complexes with DNA repair proteins. Drugs specifically targeting DNA repair proteins have become promising avenues for treatment of colorectal cancer as of late.
**Aims:** The goal of our study was to determine whether the newly demonstrated link between P2-HNF4α and DNA repair proteins could potentially be exploited for colorectal cancer treatment.
**Methods:** The complexes of interaction of P2-HNF4α were identified by quantitative proteomics (GFP-Trap and BioID). Immunofluorescence showed HNF4α's colocalization to foci of DNA damage (γH2AX). The efficiency of non-homologous end-joining (NHEJ) was quantified by flow cytometry using a GFP reporter system. Finally, the effect of a PARP inhibitor (olaparib) coupled to knocked down P2-HNF4α expression (shRNA) will be observed.
**Results:** In total, 1066 proteins were identified, by BioID or GFP-Trap, as cofactors of P2-HNF4α. Through BioID, 1007 cofactors of P2-HNF4α were identified in the 293T and HCT116 cell lines, and 59 cofactors were identified in the 293T cell line through GFP-Trap. Many common targets are known to be involved in DNA repair and also cancerous mechanisms. Some common DNA repair targets, p53, PARP1, Rad50, and DNA-PK, were then shown to interact with endogenous P2-HNF4α in HT-29 and LoVo cells. Following genotoxic stress, induced by micro-irradiation or etoposide, immunofluorescence revealed that P2-HNF4α colocalizes to DNA damage loci (γH2AX) in the nucleus of HT-29 and LoVo colorectal cancerous cell lines. Furthermore, we observed a 35% decrease in efficiency of non-homologous end joining in 293 cells where P2-HNF4α was overexpressed. The effect of olaparib on NHEJ and concomitant P2-HNF4α loss will be quantified as well.
**Conclusions:** For the first time, we demonstrated the functional involvement of P2-HNF4α in NHEJ. Furthermore, HNF4α's involvement in DNA repair is a previously undescribed non-transcriptional role for the transcription factor. Studies are currently underway to determine whether this link between P2-HNF4α and DNA repair could be exploitable in the context of colorectal cancer.

**Funding Agencies:** CIHRNSERC

A251
**AZOXYMETHANE INDUCES INTESTINAL CRYPT ABSCESSES IN KAISO TRANSGENIC (*KAISO*$^{TG}$) MICE**
L.B. Bayer[2], S. Robinson[3], J. Daniel[1]

1. McMaster University, Hamilton, ON, Canada; 2. Biology, McMaster University, Baltimore, ON, Canada; 3. Cell Biology Program, The Hospital for Sick Children Research Institute, Toronto, ON, Canada

**Background:** Colitis associated cancer (CAC) is a poorly characterized subgroup of colorectal cancer (CRC) that afflicts ~20% patients suffering from inflammatory bowel disease (IBD). The limited understanding of CAC stems from the lack of suitable mammalian model systems, as well as a general gap in research involving the molecular mechanisms of this disease. Studies have shown that increased expression of the transcription factor Kaiso causes intestinal inflammation and tumorigenesis in mice.
**Aims:** The objective of this research is to determine the effects of environmental carcinogens on disease

progression (IBD to CAC) in Kaiso overexpressing transgenic (*Kaiso*$^{Tg}$) mice. We hypothesize that treatment with the carcinogen, azoxymethane (AOM), will exacerbate the Kaiso-mediated intestinal inflammation and lead to colitis-associated cancer (i.e. polyp formation).
**Methods:** We injected *Kaiso*$^{Tg}$ or wildtype (WT) mice with either AOM, or a PBS vehicle control once a week for 6 weeks and sacrificed them one week after the last injection. Their intestinal tissues have been collected and assessed macroscopically for inflammation and polyp formation. Immunohistochemistry (IHC) analysis was then performed for established inflammation- tumourigenesis-associated proteins (e.g. p53, NF-kB, p120$^{ctn}$, b-catenin).
**Results:** Our preliminary findings show that the intestinal tissues of AOM-treated mice exhibited atypical hyperplasia and aberrant crypt foci (ACF), which represent precursors to polyp formation. The mice also exhibited a higher quantity of NF-kB positive nuclei compared to the control, indicating increased inflammation in the experimental group. Interestingly, *Kaiso*$^{Tg}$ mice were found to have decreased levels of acetylated-p53 (K381), indicating higher p53 survival rates in overexpressing mice.
**Conclusions:** The findings from our pilot study suggests that the *Kaiso*$^{Tg}$ mouse model may hold potential as a novel genetic model for IBD-CAC progression, compared to the popular AOM/DSS mouse model that currently represents the gold standard for CAC. *Kaiso*$^{Tg}$ mice closely follow the natural inflammatory progression in mammals[SR1] , and, when treated with AOM, can be used to molecularly characterize the transition from IBD to CAC. [SR2] Mice in our expanded study of AOM-treated *Kaiso*$^{Tg}$ will be examined in December 2017[SR3] , and we anticipate that they will exhibit increased inflammation and phenotypes akin to CAC.

**Funding Agencies:** NSERC, McMaster University

A252
**METASTASIS TO THE PANCREAS: THE EXPERIENCE OF A HIGH VOLUME HEPATO- PANCREATIC BILLIARY CENTRE**
S.A. Taylor[5], K. Chiu[4], M. Byrne[2], D.F. Schaeffer[3], F. Donnellan[1]

1. Gastroenterology, Vancouver General Hospital, Vancouver, BC, Canada; 2. Vancouver General Hospital, Vancouver, BC, Canada, Vancouver, BC, Canada; 3. Vancouver General Hospital, Vancouver, BC, Canada, Vancouver, BC, Canada; 4. Vancouver General Hospital, Vancouver, BC, Canada, Vancouver, BC, Canada; 5. Gastroenterology, University of Toronto, Vancouver, ON, Canada

**Background:** Pancreatic metastases (PM) from non-pancreatic primaries are rare, but should be considered in patients with a prior history of malignancy. PM's represent less than 2% of all pancreatic neoplasms. Studies have not adequately evaluated the ideal oncologic and combined surgical approach for pancreatic metastasis.
**Aims:** The aim of this study was to investigate the clinico-pathological presentation of patients with secondary tumors of the pancreas and surgical management.
**Methods:** We retrospectively identified patients from a high volume hepato-pancreato-billiary database in Canada dating from January 1989- September 2015. Medical records were retrospectively analyzed for clinical presentation, pathologic details, time period between the diagnosis of the primary tumor to metastasis or disease free interval (DFI), tumor size, focality and surgical resectability.
**Results:** We identified 103 patients (median age 53.5) with disease metastatic to the pancreas for which cytologic material was available via endoscopic ultrasound (EUS) fine needle aspiration (n=49, 47.6%), EUS core biopsy (n=14, 13.6%) or upfront definitive surgical resection (n=38 36.7%). Renal carcinoma was the most common tumor to metastasize to the pancreas (52%), followed by lung carcinoma (10%), colonic adenocarcinoma (10%), melanoma (6%) and breast (6%) followed by 10 other primary tumors. The median DFI was 6.8 years (inter-quartile range 1.23-12.78) between diagnoses of primary malignancy to metastasis. There was a significant difference in DFI for RCC (median 9.7 years, $p < 0.05$) and 4.5 years compared to all other pathologies. 38 (36.7%) patients with a median age of 58.5 (range 33-79) were identified to have pancreatic metastasis amenable to surgical resection. The average size of the metastatic lesions in greatest dimension was 2.6 cm (range: 1.2-7cm) and the majority were a single focus. Open surgical distal pancreatectomy with or without splenectomy was the most common operation (n=10, 26%) followed by pancreaticoduodenectomy (n=9, 23%) and there were no postoperative deaths. The median survival of resected patients captured to follow-up via electronic medical record (n=18) was 31 months (range: 16-87 months).
**Conclusions:** The most common metastatic tumor to the pancreas was identified as RCC, which is in accordance with the literature. Tissue acquisition via EUS is an increasingly useful modality for guiding precision to surgical resection of pancreatic tumors with the ultimate goal of rendering a patient disease free and reducing perioperative morbidity.

**Funding Agencies:** CAG

A253
**DETERMINATION OF OPTIMAL NUMBER OF ACTUATIONS FOR AN EUS GUIDED FNA PASS**
M.S. Bawa[1], D.F. Schaeffer[2], M. Byrne[1], A. Weiss[1], F. Donnellan[1]

1. Division of Gastroenterology, Vancouver General Hospital, Vancouver, BC, Canada; 2. Department of Anatomical Pathology, Vancouver General Hospital, Vancouver, BC, Canada

**Background:** Endoscopic ultrasound (EUS) guided Fine Needle Aspiration (FNA) is an effective modality for tissue acquisition in the diagnosis of GI and non-GI pathology. The optimal method of FNA is not known. The main focus is on maximisation of each FNA pass. There is little emphasis on the number of times or actuations the needle is moved within the target lesion during each FNA pass.
**Aims:** The aim of this study was to determine the optimal number of actuations for obtaining high diagnostic yield in each FNA pass.
**Methods:** This is a retrospective study carried out at Vancouver General Hospital. EUS guided FNA of solid lesions in the GI tract were included. FNA was performed with a 22G FNA needle. Three different passes were performed on each mass lesion. A standardised technique was adopted for all passes which involved no stylet, fanning, and wet suction at 20cc. There were 10 actuations performed for the 1st pass, 20 actuations for the 2nd pass, and 30 actuations for the 3rd pass. The cellularity and diagnosis for each pass were determined by GI pathologists blinded to patient inclusion in the study.
**Results:** 32 patients were included in this study with 10 males and 22 females. The average age was 68 years with a median age of 67.5 years. Pancreatic masses were the most common tissue type with pancreatic ductal adenocarcinoma being the most common diagnosis.

The number of actuations did not affect the ability to obtain a diagnosis. Tissue obtained from all three pass types were considered adequate for evaluation by pathologists. Passes with 10, 20 or 30 actuations provided equal yield in pathologic diagnosis. The 1st pass was diagnostic in all 32 cases.
**Conclusions:** Our data suggest that lower number of actuations can reliably be used during tissue acquisition for EUS guided FNA without affecting the diagnostic yield. Fewer actuations may lower the risk of procedural complications including bleeding and seeding.

**Funding Agencies:** None

A254
**PREDICTIVE MODEL FOR NON-NEOPLASTIC PATHOLOGY RESULTS AFTER ENDOSCOPIC RESECTION OF EARLY GASTRIC NEOPLASIA**
T. Gweon

Internal medicine, The Catholic University of Korea, Incheon, Korea (the Republic of)

**Background:** The incidence of non-neoplastic pathology results is 5-10% after endoscopic resection (ER) of early gastric neoplasia. Complete removal of original tumor, incorrect localization, and pathology overestimation were main reasons for non-neoplastic pathology. However, pre-treatment characteristics for non-neoplastic pathology were not determined to date.
**Aims:** The aims of the study was to investigate predicting factors for non-neoplastic pathology.
**Methods:** Medical records of 865 patients who underwent ER for early gastric neoplasia between 2013 and 2016 were reviewed. A total of 949 cases of ER were performed during the study period. The incidence of non-neoplastic pathology was 8.7% per patients and 7.9% per lesions, respectively. Clinicopathologic data were compared between the patients who showed pathologic results or not at initial ER.
**Results:** Univariate analysis showed that whitish color, poor demarcation, flat gross appearance, adenoma with low grade dysplasia at forcep biopsy, and endoscopic mucosal resection were higher in the non-neoplastic pathology group. Open type atrophic gastritis, intestinal metaplasia and ulcer was lower in the non-neoplastic pathology group. After multivariate analysis, poor demarcation, non-prescence of ulcer, flat appearance, and adenoma with low grade dysplasia were significant contributable factors for non-neoplastic pathology. Considering beta coefficient,1 point was allocated in non-prescence of ulcer, flat appearance, and adenoma with low grade dysplasia. Two points were allocated in poor demarcation. Total points ranged from 0 to 5. Non-neoplastic pathology result in each point was as follows: point 0, 0.7% (1/139); point 1, 3.1% (6/193); point 2, 4.1% (14/344); point 3, 18.5% (22/199); point 4, 30.0% (6/20); point 5, 52.0% (26/50). Patients were categorized as low risk group (< 3) or high risk group (3 ≥) according to the total points.
**Conclusions:** We developed a predictive model for non-neoplastic pathology results of ER. Rebiopsy or pathology re-evaluation is indicated in high risk group.

**Funding Agencies:** None

A255
**IPILIMUMAB INDUCED ENTEROCOLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**
K. Witges[1], R. Zarychanski[3], A. Abou-Setta[4], R. Rabbani[5], O. Dingwall[6], C.N. Bernstein[2]

1. University of Manitoba , Winnipeg, MB, Canada; 2. University of Manitoba, Winnipeg, MB, Canada; 3. University of Manitoba, Winnipeg, MB, Canada; 4. University of Manitoba, Winnipeg, MB, Canada; 5. University of Manitoba, Winnipeg, MB, Canada; 6. University of Manitoba, Winnipeg, MB, Canada

**Background:**
Ipilimumab is a human monoclonal cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) antibody used to treat patients with stage III/IV melanoma and other solid tumors. Although treatment from an oncologic perspective may be successful, ipilimumab (a type of (CTLA-4 antibody) is associated with considerable drug-related adverse events, many serious events occurring in the gastrointestinal (GI) tract; including, enteritis, colitis, and enterocolitis. Until the introduction of ipilimumab and nivolumab (PD-1 antibody), no drugs have been reported to cause an enterocolitis that resembles inflammatory bowel disease (IBD), especially the chronic aspect of IBD.

**Aims:**
The objective of this study is to evaluate the risk of chronic (> 6 weeks) enterocolitis following ipilimumab administration.
**Methods:** We searched MEDLINE, EMBASE, CENTRAL, and reference lists of relevant articles for citations. We included only randomized controlled trials comparing ipilimumab administration with placebo/standard of care/other active chemotherapy regimens. Two reviewers independently identified trials, extracted trial-level data and performed risk of bias assessments using the Cochrane Risk of Bias tool. The primary outcome was number of individuals with enterocolits both a) acute and b) chronic reported at longest follow-up. Meta-analysis was performed using a random-effects model.
**Results:**
Of 1282 records identified, we included 7 unique trials enrolling a total of 4160 subjects. The mean age of subjects was 60 years. Five trials were evaluated as low risk of bias and two trials were evaluated as high risk of bias. Trials did not distinguish between acute enterocolitis and chronic enterocolitis. Trials did not distinguish between enteritis (small bowel involvement) and colitis. Ipilimumab was associated with an increased risk of enterocolitis (RR 11.93, 95% CI 1.51 to 94.17, $I^2$ 0%, 2 trials) and colitis (RR 10.29, 95% CI 5.92 to 17.88, $I^2$ 0%, 7 trials).
**Conclusions:** Insufficient data exist to distinguish the risk of acute enterocolitis from the risk of chronic enterocolitis after ipilimumab use. Due to the serious impact of chronic enterocolitis on quality of life, future randomized controlled trials evaluating the safety of ipilimumab and other checkpoint inhibitors should be required to report gastrointestinal events in greater detail.

**Funding Agencies:** None

A256
**COMPARING GLOBAL OUTCOMES FOR ENDOSCOPIC SUBMUCOSAL DISSECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS**
D. Daoud[1], N. Suter[1], M. Durand[1], M. Bouin[1], B. Faulques[1], A.N. Barkun[2], D. von Renteln[1]

1. Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, QC, Canada; 2. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada

**Background:** Endoscopic submucosal dissection (ESD) has become the preferred approach to remove advanced gastrointestinal lesions in Asian countries while widespread adoption in the Western world remains limited. Studies evaluating differences for ESD outcomes between Eastern and Western countries are lacking.
**Aims:** To provide a comprehensive review on outcomes of ESD between different regions.
**Methods:** A systematic review and meta-analysis was performed using PubMed, MEDLINE, Web of Science, CINAHL and EBM reviews to identify studies published between 1990 and February 2016. The primary outcome was the efficacy of ESD based on information about either curative resection, *en bloc,* or R0 resection rates. Secondary outcomes were complication rates, local recurrence rates and procedure times.
**Results:** Overall, 241 publications including 86 388 patients and 91 582 gastrointestinal lesions resected using ESD were identified. 90% of the identified studies reporting ESD on 89 283 lesions were conducted in Eastern countries and 10% of the identified studies reporting ESD outcomes in 2 289 lesions were from Western countries. Meta-analyses showed higher pooled percentage of curative, *en bloc*, and R0 resection in the Eastern studies; 82% (CI: 81-84), 95% (CI: 94-96) and 89% (CI: 88-91) compared to Western Studies; 71% (CI: 61-79), 85% (CI: 81-89) and 74% (CI: 67-81) respectively. The percentage of perforation requiring surgery was significantly greater in the Western countries (0.49%; CI: 0.09-1.08) compared to Eastern countries (0.02%; CI 0-0,05). ESD procedure times were longer in Western countries (110 vs 77min).
**Conclusions:** Eastern countries show better ESD outcomes compared to western countries. Availability of local ESD expertise and regional outcomes should be considered for decision making to treat gastrointestinal lesions with ESD.

**Funding Agencies:** None

A257
**FOLLOWING INSERTION OF SELF-EXPANDING METAL STENTS FOR MALIGNANT GASTRIC OUTLET OBSTRUCTION: WHAT LESSONS CAN BE LEARNED ABOUT PATIENT CARE?**
J. McGoran, O. Doherty, I. Maine

Belfast City Hospital, Belfast, United Kingdom

**Background:** Self-expanding metal stent (SEMS) insertion is an important management tool in restoring luminal patency for patients with palliative cancer causing gastric outlet obstruction (GOO). In recent years, it has replaced surgical gastrojejunostomy as the preferred procedure in many cases, owing to its comparable survival rate and shorter hospital stays. The objective of treatment is to permit oral nutrition which in turn can be protective against morbidity and enhance the palliative experience. The establishment of an appropriate aftercare plan and ensuring adherence to quality standards are essential components of this treatment.
**Aims:** To assess a local centre's insertion of SEMS for malignant GOO with a focus on aftercare and to develop an understanding of the improvements that could be made to this area of our practice.
**Methods:** We searched electronic records for patients who underwent SEMS insertion for malignant GOO between January 2012 and September 2017. Procedures involving immediate failure to deploy a stent and stent replacement procedures were excluded from the analysis. The available literature was searched

using PubMed to permit comparison with other centres.
**Results:** Sixty eligible patients were identified in this retrospective study. Thirty (50%) had gastric cancer, with pancreatic cancer, cholangiocarcinoma and gallbladder carcinoma representing most of the remaining cases. 30-day mortality was 21.7% (13/60). Following SEMS insertion the optimal aftercare advice was to fast for at least two hours before drinking clear fluids, with soft foods the following day under the guidance of a dietitian. This advice was given in 73.3% of cases (44/60); the remainder of records carried insufficient evidence of this direction. Post-procedure complications were identified in six patient cases, with two of these patients (bleeding and incomplete stenting) having a 30-day mortality. Seven cases on follow up had evidence of partial or complete stent obstruction, with none undergoing SEMS reinsertion.
**Conclusions:** SEMS insertion is a valuable tool in the management of patients with malignant GOO however correct patient selection, procedural skill and aftercare are all vital. Our centre's experience is comparable with the published literature. In order to drive improvement we must involve a multidisciplinary approach. Optimisation of aftercare involving patient information, routine dietetic input and physician follow-up are essential in quality improvement efforts.

**Funding Agencies:** None

A258
**SHAPLEY VALUE ANALYSIS OF FACTORS AFFECTING WILLINGNESS TO RETURN TO COLON CANCER SCREENING.**
D. Sanders[2], D. Bykov[3], L. Gentile[4], J.J. Telford[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. Internal Medicine, University of British Columbia, VANCOUVER, BC, Canada; 3. BC Cancer Agency, Vancouver, BC, Canada; 4. BC Cancer Agency, Vancouver, BC, Canada

**Background:** In 2016 colorectal cancer (CRC) was the second and third most common cause of death for Canadian men and women, respectively. Colon cancer screening can reduce the incidence and mortality of CRC. The British Columbia Cancer Agency's Colon Screening Program (BCCSP) uses the Fecal Immunochemical Test (FIT) for screening average risk participants aged 50-74. Participants with positive FITs are referred on for colonoscopy. The benefits of colon cancer screening programs are gained by initiation and repeat periodic screening if testing is negative. Participant satisfaction is an important quality indicator in colonoscopy, but there is limited data on how components of colon cancer screening drive dissatisfaction, willingness to refer the program to others, and willingness to return for repeat screening. Marketing companies have used a calculation called the Shapley Value as a tool to answer these questions.
**Aims:** We present a novel method to analyze components of participant dissatisfaction in colon cancer screening by using a statistical tool called the Shapley Value.
**Methods:** Two surveys were issued randomly to individuals in the BCCSP in 2016. One set were participants who underwent FIT screening and had a negative result. The other group had positive FITs and underwent colonoscopy. Data was collected from surveys where by participants answered responses in Likert-type scale with five possible responses ranging from with "Strongly Agree" to "Strongly Disagree". The Shapley value was calculated for collections of factors to determine which components of colon cancer screening determined dissatisfaction, willingness to refer the program to others, and willingness to return for repeat screening.
**Results:** In the FIT negative survey, an important factor in determining dissatisfaction was the information provided by the doctor about colon cancer screening. The result letter was important in terms of determining willingness to return and willingness to recommend colon cancer screening. In those participants who were surveyed after a colonoscopy, an important factor in determining satisfaction was the doctor who did their colonoscopy. An important factor in determining willingness to recommend colon cancer screening was whether participants felt their doctor had adequate knowledge of their medical history.
**Conclusions:** The Shapely value identified factors influencing colon screening participant's likelihood of returning for screening and of referring others for screening. It is important to distinguish drivers for returning to screening versus dissatisfaction, as some survey items reporting dissatisfaction were not associated with an unwillingness to return to screening or recommend screening to others. Future studies can assess whether the Shapley value results were associated with screening retention.

**Funding Agencies:** None

A259
**PHYSCIAN FACTORS ASSOCIATED WITH INAPPROPRIATE FECAL IMMUNOCHEMICAL TESTING.**
D. Sanders[2], B. Bakos[3], G. Lovedeep[4], L. Gentile[5], J.J. Telford[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. Internal Medicine, University of British Columbia, VANCOUVER, BC, Canada; 3. BC Cancer Agency, Vancouver, BC, Canada; 4. BC Cancer Agency, Vancouver, BC, Canada; 5. BC Cancer Agency, Vancouver, BC, Canada

**Background:** The Fecal Immunochemical Test (FIT) is offered in British Columbia (BC) for all patients between the ages of 50 and 74 years with the BC Colon Screening Program. The program recalls participants with a negative FIT for repeat screening in two years. Despite these recommendations, some physicians in the screening program have ordered FITs for screening program participants who have had a negative FIT prior to the program recall.
**Aims:** To identify factors associated with inappropriate

FIT utilization.
**Methods:** This is a retrospective review of all FITs ordered from November 2015 until June 2017. For each FIT, the participant's chart was reviewed to identify if a previous FIT had occurred in the prior 21 months. The British Columbia's College of Physicians and Surgeon's database was used to identify location of referring physician by postal code, date of graduation from medical school, and gender. Physician variables were examined with logistic regression to determine any association with inappropriate FIT.
**Results:** Over 25 % of all FIT participants are returning early for screening. Rural physicians were more likely to order FIT early when compared with urban physicians (OR 1.18 CI 1.11-1.26 p-value < 0.001). There were significantly lower rates of ordered inappropriate FITs for physicians who graduated from medical school after 1980 compared to those who graduated earlier (OR 0.58 p-value < 0.007). There were no differences in the rates of inappropriate FITs between male and female referring physicians.
**Conclusions:** Following a negative FIT, repeat FIT utilization prior to recommended recall was associated with rural location of the ordering physician and longer duration of practice.

**Funding Agencies:** None

A260
**AGREEMENT BETWEEN COLONOSCOPY-DETECTED AND PATHOLOGY-CONFIRMED COLORECTAL CANCER IN THE 2012 TIANJIN COLORECTAL CANCER SCREENING PROGRAM**
M.J. Sewitch[1], L. Zhao[2], J. Li[2], X. Wang[2]

1. Medicine, McGill University, Montreal, QC, Canada; 2. Tianjin Nankai Hospital, Tianjin, China

**Background:** The Tianjin Colorectal Cancer (CRC) Screening Program uses a questionnaire (HRFQ) to determine risk status and the initial screening test: stool testing (FIT) for average-risk and colonoscopy for high-risk individuals.
**Aims:** To determine agreement between colonoscopy-detected CRC and pathology-confirmed CRC.
**Methods:** A retrospective cohort study was conducted using the data from the 2012 Tianjin CRC Screening Program in Tianjin, China. Participants were aged 60 to 74 and residents of Tianjin who completed both the HRFQ and colonoscopy. Demographics and clinical data were obtained as well as FIT, colonoscopy and pathology results. Cohen's Kappa was used to determine agreement between colonoscopy-detected and pathology-confirmed CRC.
**Results:** In 2012, 19,096 individuals completed the HRFQ and colonoscopy, of which 10,907 (57.1%) were HRFQ positive and 7,986 (41.8%) were colonoscopy positive. Colonoscopy positive findings included 7160 polyps, 728 adenomas and 102 CRC. Of all colonoscopy positive findings, 1,256 (15.7%) were sent to pathology where 326 were confirmed CRC. Only 59 (18.1%) of the pathology-confirmed CRC were detected at colonoscopy. Agreement between CRC detected at colonoscopy and CRC confirmed by pathology was Kappa=0.22 (95%CI=0.16-0.27).
**Conclusions:** Poor agreement was found between colonoscopy-detected and pathology-confirmed CRC, suggesting that many CRCs are undetected and untreated. Effectiveness of the screening program would be improved by sending all removed tissues to pathology.

Comparison of colonoscopy-detected and pathology-confirmed colorectal cancer (CRC) in the 2012 Tianjin CRC Screening Program

| | Pathology-CRC | Pathology-no CRC |
|---|---|---|
| Colonoscopy-CRC | 59 | 16 |
| Colonoscopy-no CRC | 267 | 914 |

**Funding Agencies:** Fonds de recherche du Québec-Santé

A261
**AGE AT MENARCHE AND RISK OF COLORECTAL ADENOMA**
S. Lee[1], N. Kim[2], J. Park[1], D. Park[1], C. Sohn[1], Y. Jung[1]

1. Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Seoul, Korea (the Republic of); 2. Preventive Healthcare Center, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Seoul, Korea (the Republic of)

**Aims:** Limited data are available regarding the association between age at menarche and the risk of colorectal adenomas. Therefore, we aimed to evaluate the relationship between reproductive factors including age at menarche and the risk of colorectal adenomas.
**Methods:** A cross-sectional study was performed on asymptomatic female subjects who underwent colonoscopy between 2010 and 2014 as part of a comprehensive health screening program in Korea. The association between reproductive factors including age at menarche and the presence of adenomas was assessed using multivariate logistic regression analysis.
**Results:** Among 32,620 asymptomatic female subjects, the proportion of patients with menarche at 10-11, 12-13, 14-15, 16-17, and 18-19 years of age was 4.1%, 31.7%, 45.4%, 14.9%, and 4.0%, respectively. There was no significant association between age at menarche and risk of adenomas after adjusting for confounding factors (adjusted odds ratio, 0.99; 95% confidence interval, 0.97-1.02). In addition, parity, use of female hormones, and menopause were not associated with adenoma risk after adjusting for confounding factors.
**Conclusions:** Age at menarche, parity, use of female hormones, and menopause were not significantly associated with the risk of colorectal adenomas. Our findings indicate that reproductive factors including


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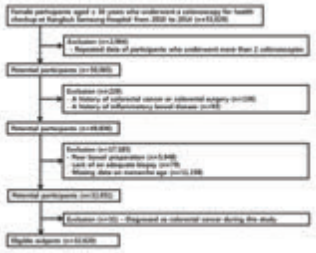
age at menarche do not affect the development of colorectal adenoma.



**Funding Agencies:** None

A262
**COLONIC MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) LYMPHOMA, A RARE OCCURENCE: A LITERATURE REVIEW AND CASE SERIES**
M. Chan, A. Rostom, C. Faught, C. Dube

University of Ottawa, Ottawa, ON, Canada

**Background:** Extranodal mucosa-associated lymphoid tissue (MALT) lymphoma is a clonal B-cell neoplasm that develops in the marginal zone of lymphoid follicles. They make up about 5% of all non-Hodgkin's lymphomas. The most common extranodal site for MALT lymphomas is the stomach, followed by the small bowel. Colonic MALT lymphomas are rare and, as a result, there are no guidelines for the workup and management of these lymphomas.
**Aims:** This case series aims to review the literature of existing cases of colonic MALT lymphoma and to share our experience with diagnosis, workup and management of colonic MALT lymphoma.
**Methods:** A literature search was conducted using an advanced PUBMED search. Charts of 4 identified cases diagnosed in 2016 - 2017 were reviewed.
**Results:** A literature review of colonic MALT lymphomas revealed a few dozen cases, either isolated or in conjunction with MALT in the upper GI tract. Presenting symptoms included abdominal pain, gastrointestinal bleeding, positive fecal occult blood test and weight loss. Workup included colonoscopy and biopsy, endoscopic assessment of the upper GI tract to assess for other foci of MALT lymphoma as well as testing for Helicobacter pylori and celiac testing, which have both been associated with gastric MALT lymphomas. Endoscopically they can appear as a polyp or mass with a smooth surface with changes in vascular pattern, but can be ulcerated if more advanced.

The management of colonic MALT lymphoma varies. Patients with limited disease were often treated with radiotherapy, surgical resection or endoscopic resection via endoscopic mucosal resection or endoscopic submucosal dissection. Patients with multiple foci of disease or lymph node involvement were usually treated with chemotherapy and/or rituximab. There have been reports of resolution of the colonic MALT lymphoma after H. pylori treatment, even in patients who were H. pylori negative.

We present our experience with the diagnosis and management of 4 cases of colonic MALT lymphoma. This includes cases of asymptomatic colonic MALT lymphoma diagnosed on routine colonoscopy which were treated conservatively with close monitoring, and a case with a concurrent gastrointestinal stromal tumor (GIST) in the stomach. In the latter case, the MALT lymphoma was treated with chemotherapy and rituximab with good response, and the GIST was surgically resected.
**Conclusions:** Colonic MALT lymphomas are considered to be rare; however, the diagnosis of 4 cases at our institution in the last 2 years would suggest otherwise. Therefore, endoscopists should be familiar with this condition and its endoscopic features. Patients with asymptomatic, limited stage colonic MALT lymphoma can be managed conservatively. Although we report one case of colonic MALT lymphoma occurring concurrently with a gastric GIST, there is no clear association between the two conditions.

**Funding Agencies:** None

A263
**MALIGNANT MELANOMA OF UNKNOWN PRIMARY WITH GASTRIC AND DUODENAL METASTASES: A CASE REPORT**
O. Gerami, N.C. Shahidi, M. Byrne

University of British Columbia, Vancouver, BC, Canada

**Aims:** This abstract presents a case of malignant melanoma of unknown with primary biopsy-proven gastric & duodenal metastases.
**Methods:** Retrospective chart review report.
**Results:** This case report presents a 65-year-old male with a distant history of melanoma of the upper abdominal cutaneous surface. He underwent a successful wide-margin excision & a right sentinel axillary lymph node, which showed a 4mm focus. A follow-up right axillary lymph node dissection removed 5 melanoma-negative lymph nodes. Given these results, he was discharged by his oncologist and continued to have ongoing cutaneous surveillance by a dermatologist.

The patient then presented with progressive fatigue, pre-syncope, dyspnea and was found to have a normocytic anemia with a Hgb of 75 g/L. His last Hgb was measured at 151 g/L three months prior on routine bloodwork. All of this occurred in the absence of any overt G.I. bleeding, abdominal pain or any other G.I. symptom, nor was there evidence of any cutaneous recurrence of his melanoma. Furthermore, the patient had a normal EGD and colonoscopy 9 months and 3 years prior, respectively. Gastroenterology was consulted for

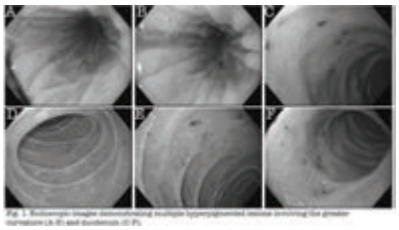
endoscopic evaluation of a possible G.I. source for his anemia.

EGD showed multiple dark, flat 1mm lesions along the greater curvature of the stomach, which were biopsied, and multiple similar lesions found in the D1 & D2 segments of his duodenum (figure 1). Biopsy results were positive for metastatic malignant melanoma.

Subsequent PET scan identified multiple metastases in the liver (the largest measuring 4.7cm) and diffuse uptake in the skeletal marrow suggesting malignant marrow infiltration. Bone marrow biopsy confirmed this with metastatic melanoma accounting for 70% of bone marrow cellularity. Oncology referral was made for chemotherapy initiation.

**Conclusions:** Malignant melanoma is a rare tumor accounting for 1–3% of all tumors. It has been observed to have GIT (GI tract) metastases in up to 50-60% of cases. However, due to being largely asymptomatic, GIT metastases are mainly diagnosed post-mortem on autopsy. Only 1-5% of all cases are diagnosed in the ante-mortem period. Furthermore, when GIT metastases are present there are often metastases to other visceral organs, and the median survival time for patients with GIT metastases is less than 1 year.

Collectively, this case highlights the potential utility for interval endoscopic surveillance in patients with a history of treated cutaneous melanoma and absence of identifiable cutaneous recurrence. Recent evidence has shown that endoscopic evaluation and diagnoses is more reliable than traditional radiographic identification of gastric metastases. Moreover, endoscopic evaluation allows for direct visualization of the gastric mucosa, direct biopsy of any identified lesions to obtain a pathologic diagnosis, and assessment of response to chemotherapy.



**Funding Agencies:** None

## HEPATOBILIARY NEOPLASIA

A264

### ADHERENCE TO ENHANCED POST-TREATMENT SURVEILLANCE IS ASSOCIATED WITH INCREASED DETECTION OF EARLY STAGE RECURRENCE AFTER RADIOFREQUENCY ABLATION BUT NOT SURGICAL MANAGEMENT OF HEPATOCELLULAR CARCINOMA

Y. Chan, S. Maclennan, L. Douglas, S.E. Congly, C.S. Coffin, E. Dixon, J. Wong, K.W. Burak

University of Calgary, Calgary, AB, Canada

**Background:** Little is known about the optimal surveillance schedule after curative intent treatment of hepatocellular carcinoma (HCC). Current guidelines advocate cross-sectional imaging at 3-6 months intervals for the first 2 years, but are not backed by strong evidence of benefit. In Calgary, we perform MRI one month after radiofrequency ablation (RFA) and 3-6 months after surgery. Thereafter we alternate contrast enhanced ultrasound and MRI every 3 months for two years and then every six months for another 3 years.
**Aims:** We conducted a retrospective study to investigate the impact of surveillance intensity on clinical outcomes following curative HCC treatment.
**Methods:** From a combined surgery and interventional radiology database in Calgary (2012-2015), 124 unique HCC patients receiving post-treatment surveillance after successful resection (n=46) or RFA (n=78) were identified after excluding patients who received transarterial chemoembolization (TACE) (n=43), failed to achieve radiological remission (n=38) or died within three months (n=10). Baseline characteristics, imaging frequency, and clinical outcomes were collected. A surveillance rate defined as sum of actual number of images performed divided by the sum of the expected number of images in the defined surveillance period for each subject was calculated.
**Results:** Baseline characteristics including age, gender and liver disease were similar in both groups. The surgery group had a higher percent of Barcelona Clinic Liver Cancer (BCLC) staging 0 (p=0.00052), non-cirrhotic (p=0.0045), and first HCC (p=0.00027) then the RFA group. The two-year disease-free survival and five-year mortality rate on Kaplan-Meier analysis, as well as mean surveillance rate (89±15% vs 84±21%) were comparable. Interestingly, BCLC B/C recurrence (n=8) was significantly associated with a lower surveillance rate as compared to BCLC 0/A (n=32) recurrence in RFA patients (76±22% vs 92±14%, p=0.015), but this was not observed in the surgical cohort. Comparison of mean imaging interval (120±47 days vs 82±29 days, p =0.038) and time to recurrence (591±245 days vs 399±222 days, p=0.048) between BCLC B/C and 0/A recurrence also differed in the RFA cohort . Univariant analysis did not identify other predictors of more significant recurrence.
**Conclusions:** In conclusion, high intensity post-treatment surveillance of HCC patients after locoregional therapy, but not surgical resection, appears to associated with detection of recurrence at an earlier stage. Ongoing follow-up will determine if this is associated with a survival benefit.

**Funding Agencies:** None

A265

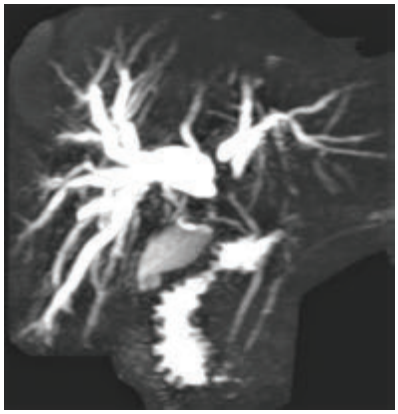
### HILAR CHOLANGIOCARCINOMA IN A YOUNG, PREGNANT WOMAN WITH NEUROFIBROMATOSIS

J. Saperia[1], V. Gupta[2], N. Coburn[1], J. Mosko[1]

1. University of Toronto, Toronto, ON, Canada; 2. St. Michael's Hospital, Toronto, ON, Canada

**Background:** Neurofibromatosis (NF) is an autosomal dominant tumor predisposition syndrome. It is associated with the development of benign and malignant tumors, including gastrointestinal neoplasms.

The commonest cause of malignancy of the biliary tract is cholangiocarcinoma. Benign tumors of the biliary tract are rare, although cases of bile duct neurofibromas have been reported. The absence of specific clinical and radiographic features makes differentiating between benign and malignant bile duct tumors challenging.
**Aims:** Describe a case of hilar cholangiocarcinoma in a pregnant woman with neurofibromatosis.
**Methods:** Case report and literature review.
**Results:** A 26 year old pregnant woman (12 weeks gestational age) with type 1 NF was found to have biliary dilation on routine obstetrical ultrasound (US).
On history, she described pruritus without abdominal pain, fever, or jaundice. She was not on medications. Her past medical history was significant for depression and tonsillectomy. She had no family history of malignancy.
On physical examination, her vital signs were normal. She had stigmata of NF including café-au-lait spots and scalp neurofibromas. Serum ALT, ALP, and bilirubin levels were 204U/L, 281U/L and 11umol/L, respectively. CA19-9 was 20kU/L.
Repeat abdominal US showed a 1.2cm mass at the bifurcation of the hepatic ducts with intrahepatic duct dilatation. On MRCP, the lesion resembled a neurofibroma. The common bile was normal at 3mm.
ERCP was undertaken for tissue acquisition. There was resistance to passage of the cholangioscope despite dilation of the common bile duct with a 4mm Hurricane balloon. Cholangioscopy revealed a hilar stricture characterized by erythema and neovascularization concerning for dysplasia. Biopsies were taken using Spybite forceps and brushings were taken for cytology. A single straight plastic stent was inserted into the right posterior hepatic duct.
Brushings were negative for SOX10, a stain specific for NF. Pathology demonstrated rare dysplastic cells that stained positive for p53, CK7 and showed patchy mitotic activity on Ki-67 immunohistochemistry, consistent with cholangicarcinoma.
Based on these results, the patient terminated her pregnancy. Her treatment plan included portal vein embolization prior to a hepatic segmentectomy of 85% of her liver.
**Conclusions:** This case highlights the diagnostic uncertainty posed by NF in the setting of an obstructive biliary lesion. While very rare, benign biliary tumors must be considered, particularly in patients with NF. The malignant nature of this patient's lesion, surprising given her age, dramatically altered her management. An added layer of complexity was her first trimester pregnancy. The association between NF and cholangiocarcinoma has not been fully elucidated and requires further study.



MRCP showing intraductal hilar obstructing lesion with secondary intrahepatic biliary dilatation.

**Funding Agencies:** None

A266
**HEPATOCELLULAR CARCINOMA PREVALENCE IN NON-CIRRHOTIC HEPATITIS C PATIENTS**
A.S. Alotaibi[3], W. Alghamdi[1], P. Marotta[2], K. Qumosani[4]

1. Gastroenterology Devision/Department of Medicine, London Health Sciences Centre, Western University, London, ON, Canada; 2. London heatlh sciences Center, University of Western Ontario, London, ON, Canada; 3. Department of Medicine, Western University, London, ON, Canada; 4. Department of Medicine, Western Univesity, LONDON, ON, Canada

**Background:** According to WHO, HCC is the fifth most common tumor in men worldwide and the second most common cause of cancer related death. In adult women, it is the seventh most commonly diagnosed cancer and the sixth leading cause of cancer death. [1] Almost 80 percent of cases are due to underlying chronic hepatitis B and C virus infection. Previous studies showed incidence of HCC in non-cirrhotic HCV patients was ranging between 4.4-10.6 %.
According to WHO, HCC is the fifth most common tumor in men worldwide and the second most common cause of cancer related death. In adult women, it is the seventh most commonly diagnosed cancer and the sixth leading cause of cancer death. [1] Almost 80 percent of cases are due to underlying chronic hepatitis B and C virus infection. Previous studies showed incidence of HCC in non-cirrhotic HCV patients was ranging between 4.4-10.6 %.

**Aims:** The aim of our analysis is to determine the prevalence of HCC among liver transplant patients with hepatitis C virus in the absence of histologic cirrhosis. Secondary outcomes are to determine the character-

istics of those patients and other possible contributing etiologies to developing HCC in the absence of cirrhosis

**Methods:** We did a retrospective charts review of transplant patients in our center. We included all HCV patients who had HCC pre-liver transplant and excluded all patients younger than 18 or with other causes of cirrhosis. We reviewed the pathology reports of all explants to determine the fibrosis stage.

**Results:** We included 98 hepatitis C patients in our analysis. 91.1% were males with the mean age of the patients of 57.1 +/- 10 years. 99% of the patients were having a viral load of > 3 x 10/6 U/L. The most common HCV genotype was 1 (68%). Alcohol was the most common cofactor contributing to cirrhosis. Two patients (2%) were found to have fibrosis stage 2 and 3. First patient was a 50-years-old male with HCV infection (unknown genotype and viral load) and alcoholic hepatitis history and no other co-morbidities. His MELD and MELD-Na scores were 7 and 13, respectively. He had multi-focal HCC on both US and histopathology of the explant with a total tumor volume (TTV) of 45 and no lympho-vascular invasion. His fibrosis stage was F3. Second patient was a 65-years-old male with HCV infection genotype 1A and a pre-transplant viral load of $7.2 \times 10^5$. His BMI was 27.2. He had OSA being treated with C-PAP. His MELD and MELD-Na were 7 and 19. His multi-focal HCC and his TTV was 26. He underwent TACE pre-transplantation. He had no lympho-vascular invasion. His fibrosis stage was F2. Regression analysis of the factors contributing to this showed no significant correlation.

**Conclusions:** Rate of HCC in non-cirrhotic HCV is still within the rate of previously reported studies. Although larger study including non-transplanted patients may revel higher incidence.

**Funding Agencies:** None

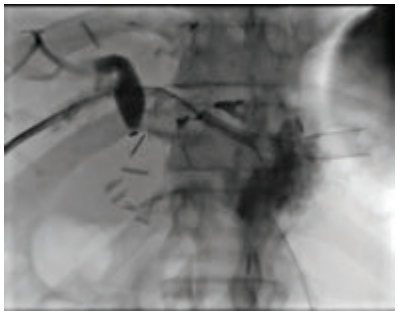
A267

**EUS-GUIDED HEPATOGASTROSTOMY POST PERCUTANEOUS BILIARY DRAINAGE IN COLLABORATION WITH INTERVENTIONAL RADIOLOGY**

A.A. Hashim[1], Y. Chen[1], D. Valenti[3], K. Waschke[1], J. Parent[1], P. Metrakos[4], s. white[5], A.N. Barkun[2], A. Bessissow[3]

1. Division of Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 2. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 3. Division of Interventional Radiology, McGill University Health Center, Montreal, QC, Canada; 4. Department of Surgery and Pathology, McGill University Health Center, Montreal, QC, Canada; 5. Royal Victoria Hospital, Montreal, QC, Canada

**Background:** Endoscopic ultrasound guided hepatogastrostomy (EUS-HGS) is a popular approach to EUS-biliary drainage especially in the setting of concomitant gastric outlet obstruction. The main disadvantage of EUS-HGS is that it requires a dilated biliary system
**Aims:** A case report (with video) describing the first conversion of a percutaneous transhepatic biliary drain (PTBD) into an HGS in a non-dilated biliary system using EUS and interventional radiology (IR) techniques.
**Methods:** A 43-year old male underwent a staged R0 hepatic resection for colon cancer metastases, during which the common bile duct was fully transected. Bilateral PTBD were placed. Definitive stable drainage was required to allow adjuvant chemotherapy. The surgical option was a Roux-en-Y hepatico-jejunostomy. HGS was chosen as less invasive option allowing faster recovery and earlier initiation of chemo
**Results:** Under EUS guidance, a non-dilated segment II bile duct was punctured with a 19-gauge needle; however, given the small ductal caliber wire passage was not possible. Via the PTBD, 2 occlusive balloons were inserted into the target duct, with one central and one peripheral to the target puncture site. Saline was infused between the balloons, dilating the isolated bile duct segment. This eased the duct puncture and passage of an 0.035-inch guidewire. The wire; however, traveled peripherally in the bile ducts but was successfully grasped with a loop-snare (via PTBD access) and pulled out the PTBD track. With control of both ends of the wire, the hepatogastrostomy tract was easily dilated to 6 mm with a balloon inserted by PTBD. During tract dilation, A 10 mmx80 mm partially covered self-expandable metal stent was simultaneously loaded through the endoscope and advanced through the HGS tract immediately following deflation of the balloon thereby minimizing the time between dilation and stent insertion, to reduce bile leak. The stent was then successfully deployed with excellent spontaneous drainage of contrast. The patient was discharged 4 days later following check cholangiogram, normalization of bilirubin and removal of the PTBD. He was pain free with no evidence of bile leak
**Conclusions:** We report the first successful conversion of PTBD to HGS using EUS and IR techniques in a non-dilated biliary system. Collaboration between endoscopists and IR can enhance the safety and feasability



**Funding Agencies:** None

A268

**A CASE OF SEVERE RIGHT UPPER QUADRANT PAIN**

**SECONDARY TO AN IGG4 RELATED INFLAMMATORY PSEUDOTUMOUR INFILTRATING THE LIVER CAPSULE**

M. Ney, M. Swain, C. Lu

University of Calgary, Calgary, AB, Canada

**Background:** IgG4 related disease has become an increasingly recognized entity over the past 15 years, with a variable presentation that can include autoimmune pancreatitis, sclerosing cholangitis, sclerosing sialadenitis, orbitopathy and retroperitoneal fibrosis amongst others. While the pathophysiology of IgG4 related disease is not fully understood, at least some degree of autoimmunity is suspected. Inflammatory pseudotumours are a rare benign lesion which primarily present in the lung, but up to 8% can be found in the liver. Rarely, these masses are associated with IgG4 related disease.
**Aims:** A 59 year old male of Korean decent with a previously presumed diagnosis of IgG1 and 2 related autoimmune cholangitis and pancreatitis with secondary compensated cirrhosis was admitted to hospital due to a 1 month history of worsening right upper quadrant pain.
**Methods:** Upon initial diagnosis 2.5 years prior, his total IgG was elevated at 34 with an IgG1 elevated at 20 and an IgG2 elevated at 10. His IgG4 was normal at 1, as was his IgG3. He was started on prednisone initially and maintained on azathioprine 100mg daily until his presentation to hospital, with a complete normalization of his total IgG and IgG subclasses. His anti-mitochondrial, anti-nuclear and anti-smooth muscles antibodies were also negative. On this presentation, a CT of the abdomen, followed by an MRI, revealed a 2.8 X 2.5cm mass in segment 5 of the liver, which extended into the capsule. Note was made of growth from a size of 2cm on an MRI from 8 months prior, on which the lesion was thought to be a perfusion abnormality. Liver enzymes and function tests were normal, as were the total IgG and IgG subclasses. A contrast enhanced ultrasound (CEUS) was completed with features concerning for malignacy (figure 1). A percutaneous biopsy of the lesion guided by CEUS demonstrated a lymphoplasmacytic predominant mass with up to 70 IgG4 plasma cells per high power field and a ratio of IgG4 to IgG of 45%.
**Results:** A diagnosis of an IgG4 related inflammatory pseudotumour was established. The patient was kept on azathioprine and prednisone was initiated at 40mg per day with a plan to taper by 5mg weekly until therapy was complete. Two weeks after the initiation of prednisone, the patient's pain had resolved and on repeat CEUS, it had become less mass-like and had shrunken slightly.
**Conclusions:** While IgG4 inflammatory pseudotumours of the liver are rare, they must be considered in the differential diagnosis of a hepatic mass, even in the setting of normal IgG4 levels and apparently stable autoimmune disease on azathioprine. In this case, the pseudotumour invaded into the liver capsule, and was cause for significant pain. Along with biopsy, CEUS was a helpful adjunct in establishing the diagnosis. Prednisone was an effective therapy for this patient.

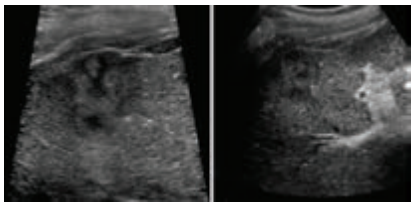


Figure 1. 59 year old male with presumed IgG1 and IgG2 autoimmune cholangitis and pancreatitis presented with acute onset of right upper quadrant pain. Gray scale ultrasound revealed a segment 5 heterogeneous mass in the liver abutting the capsule. This very unusual liver mass is superficial and appears complex with apparent small cystic black holes. The mass had rapid washout with contrast enhancement concerning for malignancy and prompted a liver biopsy. Histology was consistent with an IgG4 inflammatory pseudotumour.

**Funding Agencies:** None

A269

**THE INCREMENTAL BENEFIT OF EUS-FNA FOR DIAGNOSING MALIGNANCY AMONG INDETERMINATE EXTRAHEPATIC BILIARY STRICTURES IN ADULT PATIENTS WHO UNDERGO ERCP WITH BRUSHING CYTOLOGY**

M.D. Theriault[1], A. Chiang[3], P.D. James[2]

1. University of Medicine and Health Sciences, Embrun, ON, Canada; 2. Toronto General Hospital , Toronto, ON, Canada; 3. McMaster University, Hamilton, ON, Canada

**Background:** Currently, there is no standard approach for the evaluation of indeterminate extrahepatic biliary strictures. Endoscopic retrograde cholangiopancreatography (ERCP) with brushings is the first modality of choice, however, its diagnostic yield is only 45%. Endoscopic ultrasound with fine needle aspiration (EUS-FNA) is an alternate diagnostic tool for malignant biliary strictures with a sensitivity and specificity of 80% and 97% respectively. However, its impact after ERCP is performed has not been well established.
**Aims:** The purpose of this systematic review is to assess the current literature to determine the incremental benefit of EUS-FNA ($IB_{EUS}$) for diagnosing malignancy among indeterminate extrahepatic biliary strictures in adult patients who undergo ERCP with brushing cytology.
**Methods:** A systematic review was performed using MEDLINE, EMBASE, Cochrane, and conference proceedings from inception to July 2016. Article selection and data extraction were performed independently by two reviewers with discrepancies reviewed by a third reviewer. Pooled results were calculated using random effects model and heterogeneity was explored using stratified meta-analysis and meta-regression. The main outcome was $IB_{EUS}$ in the diagnosis of malignancy. Secondary analysis included biliary stricture location,

use of alternative imaging, study design, and study quality score.
**Results:** 8 out of 3,131 citations were selected for final inclusion (study periods from 1998 to 2010). Pooled $IB_{EUS}$ estimate with adjustment for publication bias using the 'trim and fill method' was 14% (95% confidence interval, 5-23%). Heterogeneity was not significant (Q score p-value 0. 16). Among studies that considered stricture location, $IB_{EUS}$ may be greater for distal biliary strictures (45%) when an extrinsic mass is identified on cross-sectional imaging (29%). Estimate of effect was not influenced by whether CT or MRI were involved in the evaluation, whether EUS was performed on all patients or selectively, or study design.
**Conclusions:** One in every 7 patients who underwent an EUS for an indeterminate extrahepatic biliary stricture following ERCP were diagnosed with a malignancy by EUS-FNA alone. The incremental benefit of EUS-FNA may be greater for distal strictures and when extrinsic masses are identified on cross-sectional imaging.

**Funding Agencies:** None

A270
**DEVELOPMENT OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CIRRHOSIS FROM CHRONIC HEPATITIS C VIRUS TREATED WITH DIRECT ANTIVIRAL AGENTS: THE VICTORIA EXPERIENCE**
R. Trasolini[1], J. Rauw[2], L. Bulinckx[3], R. Pai[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. BC Cancer Agency, Victoria, BC, Canada; 3. Percuro Clinical Research Ltd., Victoria, BC, Canada

**Background:** The development of direct acting antivirals (DAA) has improved sustained virologic response (SVR) rates in patients with chronic hepatitis C virus (HCV). Patients with cirrhosis from HCV have an increased risk of hepatocellular carcinoma (HCC) with a historic incidence of 1% per year. There has been recent controversy as to the rate of HCC occurrence in patients who have achieved SVR with DAA.
**Aims:** The aim of this study was to assess the risk of HCC in patients with cirrhosis from HCV treated with DAA in a Canadian population.

The primary hypothesis tested is: Does the rate of hepatocellular carcinoma in this cohort of cirrhotic patients treated with a DAA differ from published historic rates in the pre-DAA era?
**Methods:** We performed a retrospective cohort study of 147 consecutive patients at Percuro Clinical Research Limited from January 2014 to January 2017. All patients had liver cirrhosis as determined by fibroscan or liver biopsy and were treated with a DAA. Incidence rates were compared to historic rates gathered from published reviews of comparable populations treated with interferon/ribavirin based treatments.
**Results:** Interim analysis shows demographics of 61% male (90/147), 67% genotype 1 (99/147), 19% genotype 3 (28/147) and mean fibroscan 26 kPa. SVR at 12 weeks was confirmed in 80% (117/147) and 7% (11/147) were virologic failures or relapsed. 57% of patients had documented follow-up imaging and average follow-up length was 397 days.

Nine cases of de novo HCC (6%) during the follow-up period were identified with a mean time to diagnosis of 220 days from treatment end.

Further analysis will be presented based on regression or hazard analysis.
**Conclusions:** Our local experience confirms high sustained viral response rates but also suggests a higher incidence of hepatocellular carcinoma than historic data. Baseline and follow-up imaging rates were lower than expected and we would suggest considering multiphasic imaging prior to treatment commencement in patients with cirrhosis. We encourage other centres in Canada to monitor hepatocellular carcinoma rates post therapy to contribute to a future nationwide study.

**Funding Agencies:** None

## MICROBIOLOGY AND PARASITE-HOST INTERACTIONS

### Poster of Distinction

A271
**THE *HELICOBACTER PYLORI* VACA TOXIN IMPAIRS LYSOSOMAL CALCIUM CHANNEL TRPML1 ACTIVITY TO PROMOTE COLONIZATION**
M. Capurro, L. Greenfield, H. Wong, L. Robinson, N. Jones

The Hospital for Sick Children. Cell Biology Program and Departments of Paediatrics and Physiology, University of Toronto., Toronto, ON, Canada

**Background:** *Helicobacter pylori* (*H. pylori*) is a proven carcinogen for gastric cancer. The vacuolating cytotoxin A (VacA) is a bacterial virulence factor that promotes more severe disease and gastric colonization. VacA generates a unique reservoir for *H. pylori* within gastric cells conferring bacterial survival advantage. Normally the lysosome and autophagy pathways target and eliminate intracellular pathogens. VacA disrupts the endolysosomal pathway to form large intracellular vacuoles and impairs host-cell autophagy to generate the intracellular niche. However, the mechanism by which VacA alters the endolysosomal pathway is unknown. Proper vesicular trafficking, lysosomal biogenesis and autophagy pathway require a functional Mucolipin Transient Receptor Membrane Calcium channel 1 (TRPML1). Interestingly, TRPML1 deficient cells display enlarged vacuoles and disrupted autophagy, as observed in VacA-treated cells. Furthermore, TRPML1 deficient mice display hypergastrinemia and hypochlorhydria, conditions observed during *H. pylori* infections.

**Aims:** Hypothesis: We hypothesized that VacA inhibits TRPML1 to promote an intracellular niche.
**Methods:** We employed gastric cells, murine wild type and *trpml1* -/- and human organoid models as well as *in vivo* murine infection in wild type and *trpml1* -/- mice using VacA+ and isogenic VacA mutant *H. pylori*.
**Results:** We found elevated intraluminal lysosomal calcium levels in VacA-treated gastric adenocarcinoma (AGS) cells consistent with disrupted TRPML1 activity. Furthermore, using a small molecule agonist to activate TRPML1 in VacA$^{+}$ *H. pylori*-infected human gastric cell lines and organoids restores normal lysosomal and autophagic function, eliminating the intracellular protective niche and resulting in efficient bacterial killing. Consistent with these observations, we found that VacA+ *H. pylori* infected mice displayed intracellular bacteria in parietal cells. Similarly, the enlarged lysosomal-like vacuoles present in the parietal cells of *trpml1*-null mice were colonized by mutant VacA$^{-}$ *H. pylori*.
**Conclusions:** Altogether, we identify TRPML1 as a target that VacA exploits to evade host killing. We provide initial evidence that TRPML1 could serve as the first non-bacterial target to kill intracellular *H. pylori*. In this era of increasing antibiotic resistance and urgent need for research and development of new antimicrobials, we expect that TRPML1 agonists could be explored as novel therapies against intracellular pathogens.

**Funding Agencies:** CAG, CIHR

## Poster of Distinction

A272
**LOSS OF DISEASE TOLERANCE DURING *CITROBACTER RODENTIUM* INFECTION IS ASSOCIATED WITH IMPAIRED EPITHELIAL DIFFERENTIATION AND HYPERACTIVATION OF T CELL RESPONSES**
E. Kang[2], G. Zhou[2], M. Yousefi[2], J. Xia[2], S. Gruenheid[1]

1. Life Sciences Complex, McGill University, Montreal, QC, Canada; 2. Microbiology and Immunology, McGill University, Montreal, QC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

**Funding Agencies:** CIHRMcGill University Faculty of Medicine

## Poster of Distinction

A273
**THE CROHN'S DISEASE-ASSOCIATED PATHOBIONT ADHERENT-INVASIVE *E. COLI* (AIEC) INDUCES MITOCHONDRIAL FISSION IN EPITHELIAL CELLS IN ADVANCE OF APOPTOSIS**
N. Mancini[2], A. Wang[4], J. Shearer[3], D.M. McKay[1]

1. Physiology & Pharmacology, Uni. Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada

**Background:** Adherent-invasive *E. coli* are a putative etiological agent in a cohort of patients with Crohn's disease. Mitochondrial dysfunction has been described in inflammatory bowel disease. Mitochondria are not distinct organelles; they exist as a dynamic network that constantly remodels via the processes of fission and fusion to meet the cells energy demands and allow recycling of damaged mitochondria. This is emerging as an area of interest in host-bacterial interaction but it is unknown if (and then how) infection with AIEC affects mitochondrial dynamics in epithelia and the consequences of this for the cell. **Hypothesis**: AIEC induce mitochondrial fragmentation in intestinal epithelial cells in an invasion-dependent manner that requires ROS, resulting in apoptosis and decreased epithelial barrier function.
**Aims:** To explore the relationship between mitochondrial dynamics and epithelial function *in vitro* and determine if, then how, infection with AIEC affects mitochondrial dynamics and any consequence for epithelial barrier function.
**Methods:** Human colon-derived epithelial lines were cultured with a non-invasive *E. coli*, AIEC ($10^{4}$-$10^{8}$ cfu; 4-16h), fixed (dead) AIEC, or spent medium from bacterial cultures. Epithelia were examined: (a) ATP levels; (b) live-cell imaging of mitochondria morphology and membrane potential with confocal microscopy; (c) immunoblotting of whole cell protein extracts for the mitochondrial fusion protein Optic Atrophy Factor 1 (OPA1) and Dynamin-Related Protein 1 (Drp1); (d) ROS neutralized by the antioxidants; and, (f) measurement of barrier function and apoptosis.
**Results:** AIEC infection resulted in reduced mitochondrial membrane potential and ATP, and dramatic mitochondrial fragmentation accompanied by OPA1 cleavage and recruitment of Drp1 to the mitochondria in gut epithelia in a time- and dose-dependent manner. The mitochondrial fragmentation was not reproduced by exposure to AIEC conditioned medium or fixed bacteria cells, and was not abrogated by treatment with a general (vitamin C) or a mitochondrial-specific (mitoTEMPO) anti-oxidant co-treatment. AIEC induced epithelial barrier loses, however preliminary trials with inhibitors of fission, Mdivi1 and P110, did not prevent the AIEC-induced drop in transepithelial resistance. Mitochondrial fragmentation preceded apoptosis in AIEC-infected epithelial cells.
**Conclusions:** As a putative cause or contributor to Crohn's disease, AIEC drive massive mitochondrial fragmentation in model gut epithelia independent of ROS generation or AIEC soluble factors. Epithelial cell apoptosis is a feature of AIEC infection, which may be a consequence of excessive mitochondrial fission, that would be predicted to compromise epithelial barrier function, potentiating or reactivating inflammatory disease.

**Funding Agencies:** CCC, CIHRNSERC, University of Calgary Eyes High Funding

## Poster of Distinction

A274

### GUT MICROBIOTA REGULATES INNATE EPITHELIAL RESPONSES AGAINST AN ENTERIC BACTERIAL PATHOGEN

J.M. Allaire[2], H. Yang[2], N. Moore[2], S.M. Crowley[2], E. Verdu[3], B. Vallance[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Pediatrics, BC Children's Hospital Research Institute, Vancouver, BC, Canada; 3. McMaster University, Hamilton, ON, Canada

**Background:** Our gut microbiota plays a protective role in the GI tract, by promoting colonization resistance against enteric pathogens through nutrient competition. Antibiotic treatments in early life can lead to prolonged microbial dysbiosis and increase susceptibility to future enteric infections. Moreover, the gut microbiota have been shown to impact the development of the mucosal and systemic immune systems. Intestinal epithelial cells (IEC) are crucial cells that control interactions between the mucosal immune system and the luminal microbiota, but they also initiate innate immune responses to pathogens. Recent studies have explored the role played by the microbiota in controlling the virulence strategies of the attaching and effacing (A/E) microbe, *Citrobacter rodentium (Cr).* This pathogen directly adheres to IEC, causing diarrheal disease as well as inflammation, with commensal microbes impacting its ability to infect IEC, as well as being critical for its clearance. At present however, it is not clear whether commensal microbes influence the innate immune response by IEC to *Cr* infection. Defining the impact of commensal microbes on innate intestinal defenses may prove useful in developing new therapeutic approaches to combat enteric infections.
**Aims:** To investigate the impact of commensal microbiota on innate IEC responses to *Cr* infection.
**Methods:** This study compared the innate responses of specific-pathogen free (SPF) and germfree (GF) C57BL/6 mice to *Cr* infection. Pathogen burdens, pathology scores, qPCR and immunofluorescence staining were used to characterize the mucosal response.
**Results:** SPF and GF mice were orally infected and pathogen burdens determined on day 6 post-infection (6 DPI). Increased pathogen burdens were observed in GF mice as compared to SPF mice. Cecal tissues of GF mice showed increased pathology scores with evidence of increased *Cr* adherence to the mucosal surface. In contrast, GF mice showed reduced colon pathology scores than SPF mice, with reduced pathogen adherence. Apoptosis was characterized, with the ceca of GF mice at 6 DPI displaying massive IEC death and sloughing, while this was not seen in infected SPF mice. Interestingly, while SPF mice showed the expected upregulation in inflammatory (IL-22, IL-17A, IL-6) and antimicrobial (Reg3γ and Relmβ) responses in both the cecum and colon, GF mice showed a differential response, with dramatically higher levels of IL-22, but reduced expression of Reg3γ and Relmβ as compared to SPF mice.
**Conclusions:** These findings indicate that commensal microbes play a key role in controlling epithelial responses to A/E pathogens, promoting some responses while suppressing others. Further studies will unravel the mechanisms underlying microbiota-based regulation of IEC responses to infection, with the goal of developing novel approaches to prevent human infection.

**Funding Agencies:** CAG, CIHRFRQS, MSFHR

## Poster of Distinction

A275

### COMMENSAL BACTERIA IN THE SMALL INTESTINE INFLUENCE IMMUNE CELLS TO DICTATE HOST DRUG METABOLISM

K.L. Flannigan[1], K.M. Nieves[1], S.L. Erickson[2], L. Alston[3], S.A. Hirota[2]

1. University of Calgary, Calgary, AB, Canada; 2. Physiology & Pharmacology, University of Calgary, Calgary, AB, Canada; 3. University of Calgary, Calgary, AB, Canada

**Background:** The ability of the intestinal microbiota to influence drug responses has been recognized, however the mechanisms through which this occurs remain unexplored. Work in germ free mice has demonstrated that colonization with different microbiota influences the expression of cytochrome P450 (CYP) enzymes in the liver. Like the liver, the small intestine (SI) expresses CYP enzymes including CYP3A11 which can metabolize over 60% of commercially available drugs. The activity of CYP enzymes in the SI has been shown to influence circulating levels of orally administered drugs, but how the microbiota affects this process is unknown.
**Aims:** To investigate if distinct microbiota differentially modulate host drug-metabolism in the SI to influence drug activity and efficacy.
**Methods:** SFB-free (SFB-) mice were obtained from Jackson (Jax) and SFB+ mice were obtained from Taconic (Tac). Feces from SFB+ Tac mice were mixed in PBS and orally gavaged to mice. 14 days later sections of ileum were used for PCR array or digested in collagenase to isolate lamina propria cells for flow cytometry. A monoclonal antibody for Thy1.2 was used to deplete innate lymphoid cells (ILCs) in RAG1$^{-/-}$ mice (lacking T- and B-cells). CYP3A11 activity was determined through the colourmetric breakdown of the substrate 7-benzyloxyresorufin.
**Results:** PCR array analysis of ileal sections revealed CYP3A11 as one of the most downregulated genes in both SFB+ Tac mice and Jax mice colonized with a SFB+ microbiota when compared to SFB- Jax mice. Further analysis showed that colonization of Jax mice with a SFB+ microbiota induced IL-22 production by type 3 innate lymphoid cells (ILC3). Increase IL-22 production positively correlated with fecal levels of SFB and reduced ileal CYP3A11 expression. Colonization of



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IL-22 KO mice with a SFB+ microbiota had no effect on the ileal expression of CYP3A11. Furthermore, depletion of ILCs in RAG1$^{-/-}$ mice colonized with a SFB+ microbiota prevented a decrease in the expression of CYP3A11. In mouse SI enteroid cultures, recombinant IL-22 dose-dependently reduced the expression of CYP3A11, an effect that was blocked by the STAT3 inhibitor Stattic. IL-22 treatment also significantly decreased the ability of SI enteroids to metabolize CYP3A11 specific substrates.
**Conclusions:** Our data suggest that colonization with a specific microbiota can influence the expression and activity of the drug metabolising enzyme CYP3A11. This occurs through the production of IL-22 by SI ILC3, which down regulated CYP3A11 in a STAT3-specific manor and altered the ability of the small intestine to metabolise CYP3A11 specific substrates. These findings provide an understanding of how the intestinal microbiota modulates host drug metabolism, and how the microbiota can be manipulated to render various drug therapies, such as those for IBD, more effective.

**Funding Agencies:** CAG, CCC, CIHRAlberta Innovates

A276
**CHARACTERIZING MICROBIOTA COMPOSITION AND FUNCTION THAT PRECEDE DEVELOPMENT OF CLINICALLY RELEVANT INFLAMMATION IN UC PATIENTS**
M. Bermudez-Brito[1], H.J. Galipeau[2], A. CAMINERO FERNANDEZ[3], W. Turpin[5], L. Bedrani[5], K. Croitoru[4], E. Verdu[1]

1. McMaster University, Hamilton, ON, Canada; 2. Farncombe Family Digestive Health Research Institute, McMaster University, Hamilton, ON, Canada; 3. Farncombe institute, Mcmaster University, Dundas, ON, Canada; 4. Mount Sinai Hospital, Toronto, ON, Canada; 5. University of Toronto, Toronto, ON, Canada

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A277
**THE FIRST LINE OF DEFENSE: THE ROLE OF EPITHELIAL CELL INFLAMMASOMES IN CONTROLLING *CAMPYLOBACTER JEJUNI* INFECTION**
M. Stahl[1], T. Hoang[1], L.A. Knodler[2], B. Vallance[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. Washington State University, Pullman, WA

**Background:** *Campylobacter jejuni* is the most common cause of bacterial gastroenteritis in the developed world, often rivaling the total number of *E.coli* and *Salmonella* infections combined. Furthermore, even after the initial infection has been cleared, *C. jejuni* infection has been strongly linked to the development of Guillain Barre syndrome. Despite this, many aspects of its colonization and infection of the gut remain poorly defined. One cryptic aspect of its pathogenesis is *C. jejuni's's* ability to invade intestinal epithelial cells as it colonizes and infects the host intestine. Our previous work has illustrated that *C. jejuni* has the capacity to invade intestinal epithelial cells in the mammalian gut near the apical ends of intestinal crypts, where it resides within LAMP-1 positive vesicles.
**Aims:** The aim of this study is the characterize the role of the epithelial cell inflammasome in defending against cell invasion by *C. jejuni in vivo* and to describe the impact of inflammasome activation and cell invasion on the immune response to *C. jejuni i*nfection.
**Methods:** Using a combination of knockout mouse models and an *in vitro* primary epithelial cell model, we can now illustrate the role of epithelial cell intrinsic inflammasomes in controlling *Campylobacter* cell invasion during the course of infection. We infected mice lacking key inflammasome components, including Asc, Caspase 1, and relevant nod-like receptors, along with knockout mice in relevant inflammasome-linked cytokines, including IL18. We also used primary epithelial cells, derived from human and murine sources, and cultivated as organoid cultures, do create monolayer cultures we could infect with *C. jejuni*. This allowed us to model *C. jejuni* cell invasion of the intestinal epithelium *in vitro*.
**Results:** Mice lacking key inflammasome components lose much of their ability to limit *C. jejuni* invasion and replication inside of intestinal epithelial cells. This allows *C. jejuni* to replicate to large numbers inside of these LAMP1 positive vesicles, from where they can be released back into the intestinal lumen and infect additional epithelial cells. The consequences of impaired inflammasome function include increased pathogen burdens, a prolonged course of infection and significantly increased pathology in infected mice. Conversely, mice with functional epithelial cell inflammasomes effectively control the number of intracellular bacteria and exhibit only moderate infection induced pathology and pathophysiology.
**Conclusions:** Although much remains to be discovered regarding the role of epithelial cell invasion in *C. jejuni* pathogenesis, these findings highlight the importance of epithelial cells as an active player in combating this important enteric pathogen.

**Funding Agencies:** CAG, CCC, CIHR

A278
**ESCHERICHIA ABUNDANCE AND LOW FECAL BUTYRATE IN CHILDREN WITH INTESTINAL FAILURE**
J.K. Dowhaniuk[2], S. Chorlton[3], J. Szamosi[4], J. Owens[1], H. Mileski[1], R. Clause[1], J. Pernica[2], D.M. Bowdish[5], M. Surette[4], E. Ratcliffe[2]

1. McMaster Children's Hospital, Hamilton, ON, Canada; 2. Department of Pediatrics, McMaster University, Hamilton, ON, Canada; 3. Department of Undergraduate Medicine, McMaster Univeristy, Hamilton, ON, Canada; 4. Department of Biochemistry and Biomedical Sciences, McMaster Univeristy, Hamilton, ON, Canada;

5. Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

**Background:** Short bowel syndrome (SBS) is the leading cause of intestinal failure (IF) in children. The goal for a child with IF is to undergo sufficient intestinal adaptation to achieve enteral autonomy and thus be able to discontinue parenteral nutrition (PN). The prognosis for each child may be different depending on anatomic differences such as small intestinal length, the number of surgeries, the gestational age, and the underlying etiology. The composition of the fecal microbiome may represent an additional independent risk factor for dependence on PN.
**Aims:** We sought to compare the intestinal microbiome of children with SBS who continue to require PN (defined as SBS+IF), to those with SBS who have discontinued PN, using high-throughput sequencing to further understand host-microbe interactions in these populations. Furthermore, we sought to quantify the short chain fatty acid (SCFA) production between groups as well as total fecal bacterial load.
**Methods:** A total of 53 stool samples were collected over 6-15 months. Six children with SBS+IF submitted 34 samples and 6 children with SBS who discontinued PN submitted 15 samples; these were compared to samples from 5 control children. Fecal samples were analyzed by 16S rRNA gene sequencing using the MiSeq Illumina sequencer. SCFA levels, including butyric acid, were measured in stool samples by mass spectrometry. Bacterial load was measured by qPCR.
**Results:** Children with SBS+IF demonstrated the most significant dysbiosis with the lowest Shannon diversity and an abundance of the *Escherichia* genus seemingly attributed to the pro-inflammatory species *E. coli.* There was a significant 168-fold increase in the abundance of *Escherichia* compared to control children. Commensal anaerobes known to produce SCFA including *Ruminococcaceae* and *Lachnospiraceae* were significantly reduced in those with SBS. Similarly, measured butyric acid was significantly reduced in children with IF (median 0.37 nmol/mg; p<0.0001). Children with IF had a significantly reduced bacterial load in stool samples compared to controls (median 124.2 nmol/L vs. 1225 nmol/L; p=0.006).
**Conclusions:** Significant dysbiosis characterized by a reduction in diversity and over-population of *Escherichia* as well as a significant reduction in the critical SCFA, butyric acid, were identified in children with IF. These findings have potential implications for intestinal epithelium barrier function, intestinal permeability and host-microbe immune response in this patient population.

**Funding Agencies:** CAGRegional Medical Associates of Hamilton

A279
**COLONIZATION WITH PROTEOLYTIC BACTERIA INDUCES LOW-GRADE INFLAMMATION AND BARRIER DYSFUNCTION IN MICE**

H.J. Galipeau, J. Dong, A. CAMINERO FERNANDEZ, M. Bermudez-Brito, J. Jury, G. De Palma, A. Clarizio, C. Duque, P. Bercik, E. Verdu

McMaster University, Hamilton, ON, Canada

**Background:** In the gastrointestinal tract, proteases regulate motility, immunity, mucus cleavage, wound healing and tissue remodeling. A proteolytic imbalance has been described in inflammatory bowel disease, irritable bowel syndrome and celiac disease, but it is unclear if this imbalance is an initiator or consequence of disease. Most studies focus on host-derived proteases, while the role of bacterial proteases are poorly understood.
**Aims:** We investigated the effects induced by microbial derived proteases on host immunity and physiology, after gnotobiotic colonization of mice with bacterial strains with either high or low proteolytic activity.
**Methods:** Bacterial strains for colonization were isolated from two symptomatic patients with ulcerative colitis (UC). Strains with high proteolytic activity (HPA) or low-proteolytic activity (LPA) were selected based on *in vitro* proteolytic screening of the individual strains to generate two communities. The HPA community consisted of *Clostridium perfringens* METW, *Pseudomonas aeruginosa* C4, *Enteroccocus faecalis* FAAJ, and *Bacteroides fragilis* BHI A, and the LPA community was comprised of *Escherichia coli* K2 aer., *Ruminococcus gnavus* D5FAA1, *Enterococcus faecium* CNAG, and *Streptococcus salivarius* CAN K2. Adult germ-free C57BL/6 mice were colonized with the HPA or LPA community for three weeks, after which fecal proteolytic activity and the effects on host barrier function and immunity were determined.
**Results:** Mice colonized with the HPA had higher overall proteolytic activity, elastase activity, and gelatinase activity in fecal samples than LPA-colonized mice (p<0.001). Increased serum LPS was observed in HPA-colonized mice compared to LPA-colonized mice (p<0.05), and more HPA-colonized mice had translocation of live bacteria to the spleen (p=0.07), but no differences in colonic $^{51}$Cr-EDTA flux were detected. Using nanostring technology, we probed the colonic expression of various immune and barrier related genes. HPA-colonized mice had upregulated *Lyz1, Hif1a, Cdh1, Tjp1,* and *Ttf3* expression compared to LPA-colonized mice (p<0.05). In addition, higher *CD11b* (p<0.01), *CCR2,* and *IL-22ra2* (p<0.05) was detected in HPA-colonized mice. Quantification of polymorphonuclear cells in colonic H&E sections revealed greater inflammatory infiltrate in HPA-colonized mice (p<0.001). Finally, levels of β-defensin were increased in the feces of HPA-colonized, as measured by ELISA (p<0.05).
**Conclusions:** We successfully established an *in vivo* mouse model of microbial proteolytic imbalance. Colonization with a high proteolytic microbiota induces low-grade inflammation and an altered barrier that may contribute to the onset of gut inflammatory disorders.

**Funding Agencies:** CCC

A280

**RECOVERY OF PROBIOTIC LACTOBACILLI ADMINISTERED SINCE PREGNANCY IN TWO-MONTH-OLD CD-1 MICE OFFSPRING**

S.E. Stinson[1], A. Taibi[1], K. Henry[2], P.M. Sherman[2], E. Comelli[1]

1. Department of Nutritional Sciences, University of Toronto, Toronto, ON, Canada; 2. Cell Biology Program, Research Institute, Hospital for Sick Children, Toronto, ON, Canada

**Background:** Probiotic administration during pregnancy and lactation may be a strategy to support the establishment of a health-compatible gut microbiome. Temporary increases in *Lactobacillus* levels in infant fecal samples have been attributed to administration of probiotics during late gestation and breastfeeding. However, the effects of probiotic exposure since conception on the fecal recovery of probiotics during adulthood are unknown. Lacidofil® is a probiotic mixture of *Lactobacillus rhamnosus* R0011 and *L. helveticus* R0052, with eubiotic effects in pediatric populations.
**Aims:** The aim of this study was to assess the effect of maternal versus continuous exposure to Lacidofil® strains on probiotic recovery during young adulthood.
**Methods:** 6-8-week-old female, specific pathogen free CD-1 mice were randomized to two groups and started receiving $10^9$ CFU/mL Lacidofil® in drinking water (probiotic, P) or water alone (control, C) daily one week prior to mating; treatment continued during pregnancy and lactation. At weaning, dams were sacrificed and the offspring continued their respective mother's treatment (PP or CC) or were switched (PC or CP) (n = 6-9/sex/group). Fecal DNA was extracted at weaning and two months of age. Lacidofil® strains were quantified by q-PCR.
**Results:** Probiotic administration did not affect dams and pups body weights nor litter sizes. At weaning, strains R0011 and R0052 were detected in the feces of both dams and offspring receiving probiotics, but not in controls. In the PP study group, probiotic strains increased from weaning to two months of age, but were undetectable in two-month-old PC and CC mice. There were both maternal and pup treatment effects on fecal counts of both probiotic strains in males (R0011: dam diet, $P = 0.011$; pup diet, $P = 0.000$; R0052: dam diet, $P = 0.007$; pup diet, $P = 0.000$) and females (R0011 dam diet, $P = 0.040$; pup diet, $P = 0.000$; R0052: dam diet, $P = 0.043$; pup diet, $P = 0.000$) at two months of age.
**Conclusions:** Fecal amounts of Lacidofil® strains increase with duration of administration and depends on *in utero* exposure. Administration of Lacidofil® post-weaning, does not achieve the same bacterial colonization of the gut compared to exposure since conception. Probiotics have the potential for programming the developing gut microbiome. These novel obervations could have implications for dietary guidelines targeting pregnant and lactating mothers.

**Funding Agencies:** NSERC to EC, CIHR to PMS, OGS and NSERC CGSM to SES, Lallemand Health Solutions & Lawson Family Chair in Microbiome Nutrition Research to EC.

A281

**DOES MUC2 MUCIN REGULATE MUCUS ASSOCIATED PROTEINS AND OTHER GOBLET CELL INNATE DEFENSE MOLECULES?**

H. Gorman[1], F. Moreau[1], K. Chadee[2]

1. University of Calgary, Calgary, AB, Canada; 2. Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, AB, Canada

**Background:** In the gastrointestinal (GI) tract, goblet cells secrete MUC2 that makes up the mucus layer critical in innate host defense in separating the microbiota from the single layer of intestinal epithelial cells. Associated with MUC2 mucin are other mucus-associated proteins (mucus APs) including calcium-activated chloride channel regulator 1 (CLCA1), $F_c$ fragment of IgG binding protein (FCGBP) and kallikrein 1 (KLK1). These proteins are hypothesized to be important in stabilizing MUC2 and aiding in its protective functions but are not well characterized. Goblet cells also produce various innate host defense molecules including trefoil factor 3 (TFF3) and resistin-like molecule b (RELMb) and its unclear how these proteins interact with MUC2 to enhance innate host defences.
**Aims:** 1. To determine if MUC2 and mucus associated proteins is differentially regulated.
2. To interrogate if a common intracellular signaling pathway can regulate MUC2, TFF3 and RELMb expression and secretion *in vitro* and *in vivo*.
**Methods:** In this study, I quantified MUC2, APs, TFF3 and RELMb expression in LS174T goblet cells basally and in response to the colonic pathogen *Entamoeba histolytica* (*Eh*) and various mucus secretagogues by Q-PCR and Western Blots.
**Results:** Goblet cell proteins were developmentally regulated that coincided with maturation of the goblet cell phenotype at days 5 to 6. Cells stimulated with known mucus seretagogues that use unique signalling pathways such as PMA (PKC activator) and $PGE_2$ (cAMP signalling), simultaneously increased MUC2, mucus APs, TFF3 and RELMb expression. However, in response to *Eh*, there was a time-dependent expression of MUC2 and enhanced expression of RELMb while mucus APs and TFF3 were unaffected. I next determined if deficiency in *Muc2*$^{-/-}$ affected the expression of goblet cell innate defense proteins as compared to *Muc2*$^{+/+}$ littermates. Surprisingly, there were no significant changes in goblet cell proteins or mucus APs suggesting no negative feedback of these molecules in the absence of Muc2.
**Conclusions:** This research demonstrates that MUC2, mucus APs and goblet cells peptides are developmentally regulated and use common signalling pathways in innate host defense.

**Funding Agencies:** CIHR

A282

**EFFECTS OF *BIFIDOBACTERIUM BIFIDUM* IN MICE INFECTED WITH *CITROBACTER RODENTIUM.***

B. Wen, A. Taibi, C.R. Villa, S. Sagaidak, S. Lee, E. Comelli

University of Toronto, Toronto, ON, Canada

**Background:** Various strains of *Bifidobacterium bifidum* are probiotics with beneficial properties in intestinal inflammation, including pathogen infection. *B. bifidum* strain MIMBb75 (BB75) sustains intestinal homeostasis and mitigates intestinal discomfort in patients with irritable bowel syndrome. *Citrobacter rodentium* is a murine pathogen causing transmissible colonic hyperplasia and colitis with pathogenicity similar to foodborne enterohaemorrhagic *Escherichia coli* O157:H7 in humans and with features of inflammatory bowel disease.
**Aims:** This study aimed to examine if oral administration of *B. bifidum* MIMBb75 attenuates pathology associated with *C. rodentium* infection.
**Methods:** C57Bl6/J male mice were randomized into 4 groups; groups 1 and 2 received BB75 daily ($10^9$ CFU/ml in 200 µl PBS by gavage) starting 7 days before (group 1), or on the same day (group 2) as *C. rodentium* infection ($10^9$ CFU/ml in 100 µl LB-culture); groups 3 and 4 received sterile PBS and served as infection (group 3) and sham (group 4) controls. Mice were sacrificed at day 10 post-infection (p.i.). Fecal *C. rodentium* and *B. bifidum* load were assessed by culturing and qPCR, respectively. Crypt hyperplasia and intestinal inflammation were assessed by histology. Barrier integrity was evaluated by pathogen translocation to secondary organs and *in vivo* permeability test.
**Results:** *C. rodentium* infection resulted in colonic hyperplasia, inflammation and barrier dysfunction. Fecal *C. rodentium* viable count increased and reached a plateau ($10^{10}$CFU/g of feces) at day 10 p.i., with clearance on day 24 p.i., regardless of probiotic treatment ($p>0.05$). *B. bifidum* administration resulted in $10^7$ cells/g of feces, with no effect of timing of administration ($p>0.05$). Though, *B. bifidum* treatment did not attenuate crypt hyperplasia nor inflammation associated with the infection ($p>0.05$).
**Conclusions:** These data suggest that *C. rodentium* and *B. bifidum* can co-exist in the gut with no mutual displacement; this is in line with research showing that BB75 is well equipped for gut colonization. However, in this experimental setting, BB75 cannot counteract *C. rodentium* pathology. Findings from this study may provide insights for the understanding of probiotics behavior and their clinical relevance in intestinal inflammation.

**Funding Agencies:** NSERC and JP Bickell Foundation to Elena M Comelli; NSERC Alexander Graham Bell Canada Graduate Scholarship to Bijun Wen.

## MOTILITY AND NERVE GUT INTERACTIONS

A283

**SECRETIONS OF INTESTINAL MICROBIOTA INCREASE THE EXCITABILITY OF VAGAL AFFERENT NEURONS VIA A PROTEASE ACTIVATED RECEPTOR 2 (PAR2)-DEPENDENT PATHWAY.**

S. Pradhananga[3], A.E. Lomax[1], E. Allen-Vercoe[4], E.O. Petrof[2]

1. Queen's University, Kingston, ON, Canada; 2. Medicine, Queen's University, Kingston, ON, Canada; 3. Center of Neuroscience, Queens University, Kingston, ON, Canada; 4. University of Guelph, Guelph, ON, Canada

**Background:** The intestinal microbiota has recently been shown to have pronounced effects on the central nervous system (CNS). However, it is presently unknown how intestinal microbes signal to the CNS. There are two afferent neural pathways linking the intestine and the CNS: the spinal afferent pathway and the vagal afferent pathway. We have previously found that intestinal microbes decrease the excitability of spinal afferent neurons via the actions of serine proteases on protease activated receptors.
**Aims:** The present work was conducted to determine if intestinal microbiota can change the excitablitiy of the vagal afferent pathway as the spinal afferent pathway.

**Methods:** Perforated patch clamp electrophysiology was used to measure the excitability of the cultured vagal afferent neurons, whose cell bodies lie in the nodose ganglia. Dissociated nodose ganglion neurons were cultured overnight either in normal media or media containing supernatant from a human intestinal microbial community named microbial ecosystem therapeutics (MET-1). Nodose ganglion neuronal excitability was assayed by measuring the threshold amount of current required to elicit an action potential, the rheobase.

**Results:** MET-1 supernatant concentration-dependently increased the excitability of nodose ganglion neurons by decreasing the rheobase. The increase in excitability elicited by MET-1 supernatant was blocked by using a cocktail of protease inhibitors. Furthermore on using specific protease inhibitors, it was found that only cysteine protease inhibitor (E-64, 1:30000) was able to inhibit the effect of MET-1. Similarly PAR2 antagonist (GB-83, 10 µM) also blocked the effect of MET-1 on rheobase of nodose neurons.

**Conclusions:** In contrast to spinal afferent neurons, which are inhibited by MET-1 supernatant, vagal afferent neurons are excited. MET-1 induced increased in excitability is cysteine protease dependent and is mediated by the PAR2 receptor. The increased excitability of vagal afferent neurons in response to microbial secretions suggest that the vagal pathway may be an important neural conduit allowing microbial modulation of CNS function.



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**Funding Agencies:** CCC

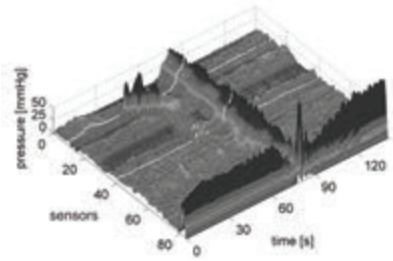
A284

**CHARACTERIZING SIMULTANEOUS PRESSURE WAVES IN THE HUMAN COLON BY HIGH-RESOLUTION MANOMETRY**

J. Chen[1], E. Ratcliffe[5], Y. Yuan[1], S.P. Parsons[2], A.D. Vincent[6], D. Armstrong[1], P. Bercik[4], P. Moayyedi[1], E. Greenwald[3], M. Xue[1], A. Wan[1], A. Eshtiaghi[1], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. Farncombe Institute, McMaster University, Hamilton, ON, Canada; 3. Internal Medicine, McMaster University, Hamilton, ON, Canada; 4. Medicine, McMaster University, Hamilton, ON, Canada; 5. Pediatrics, McMaster University, Hamilton, ON, Canada; 6. Physiology and Pharmacology, McMaster University, Hamilton, ON, Canada

**Background:** High-resolution colonic manometry promises much deeper insight into human colon motor function and their control mechanisms than hitherto possible. One motor pattern in need of full understanding is the simultaneous pressure wave (SPW), an apparent instantaneous transient pressure development in the entire colon.
**Aims:** Our aim was to provide a characterization of this motor pattern, its relationship to other motor patterns and its appearance in response to a meal, balloon distension and bisacodyl in healthy subjects.
**Methods:** High-resolution colonic manometry (HRCM) was performed using an 84 sensor (1 cm spaced) water-perfused catheter in 16 healthy volunteers. Intraluminal pressure patterns were recorded during 90 min baseline, during balloon distension, 90 min after a meal and after luminal bisacodyl administration. Quantification was performed using software, based on Image J, developed during this study.
**Results:** SPWs, with amplitudes ranging from 2.4 to 75.2 mmHg (average 12 mmHg) and duration from 2 to 75s (average 11s), occurred throughout the entire colon or they developed at the termination of proximal High-Amplitude Pressure Waves (HAPWs). SPWs progressed into the anal canal followed by anal sphincter relaxation, even at very low amplitudes. SPWs did not obliterate haustral boundary contractions, likely the mechanism by which in vivo gas can escape while stool is retained. SPWs consisted of multiple high frequency, high velocity, pressure waves that resulted in apparent instantaneous pressure development. Balloon distension, a meal or luminal bisacodyl stimulation (10 mg) resulted in high amplitude SPWs associates with gas, water or balloon expulsion. SPWs and HAPWs also occurred independently and then did not influence each other. SPWs occurred in a rhythmic fashion on 26 occasions, including responses to all different stimuli; a distinct rhythmicity was identifiable at an average frequency of 1.8 ± 0.8 cpm, ranging from 0.3 to 4.4 cpm; 13 of the clusters were observed in response to the meal where the average frequency was 2.1 ± 0.9 cpm.
**Conclusions:** The SPWs need to be incorporated into colonic function assessment by HRCM alongside HAPWs. It is the dominant motor pattern that allows gas expulsion and internal anal sphincter relaxation. Low- and high-amplitude SPWs are observed during baseline and are evoked by a meal, balloon distension or luminal bisacodyl. The rhythmicity of SPWs suggests the involvement of the ICC network at the submucosal border of the colon. The associated gas/liquid/balloon expulsion and anal sphincter relaxation provide potential diagnostic value. Their association with HAPWs suggest involvement in the defecation reflex. High resolution allows accurate quantification and 3-dimensional representation.




High-Resolution Colonic Manometry. A proximal pressure wave, an SPW, throughout the entire colon, IAS relaxation, and a brief EAS contraction

**Funding Agencies:** CIHRHamilton Health Sciences Organization and Canadian Foundation for Innovation John Evans Leadership Fund

A285

**MICROBIAL DYSBIOSIS ENHANCES PAIN PERCEPTION AND DRG NEURON EXCITABILITY**

C.C. Baker, J. Sessenwein, J. Segal, N. Ghasemlou, S. Vanner, A.E. Lomax

Queen's University, Kingston, ON, Canada

**Background:** Abdominal pain is a major symptom of IBD and IBS, which are associated with microbial dysbiosis. Disruption of the microbiota with antibiotics increases visceral pain and germ- free mice are prone to pain. However, the mechanisms underlying microbial modulation of pain remain elusive.
**Aims:** We hypothesized that disruption of the intestinal microbiota modulates the excitability of dorsal root ganglion (DRG) neurons. We aim to demonstrate the impact of microbial dysbiosis on pain sensitivity and identify the the mechanism by which it works.
**Methods:** Patch clamp electrophysiological recordings of DRG neuron excitability (decreased rheobase = increased excitability) were obtained from control mice and mice treated with the non-absorbable antibiotic vancomycin (50mg/ml in drinking water) for one week.
**Results:** DRG neurons from vancomycin-treated mice were hyperexcitable (~25 % decrease in rheobase, $p < 0.01$) compared to controls. Interestingly, this effect was not restricted to gut-projecting DRG neurons, suggesting an effect of gut dysbiosis on somatic pain

pathways. Consistent with this, mice treated with vancomycin were approximately 20% more sensitive to noxious thermal stimuli applied to hind paws than control mice ($p < 0.01$). Incubation of DRG neurons from naïve mice in serum from vancomycin-treated mice increased DRG neuron excitability by ~25%, suggesting that microbial dysbiosis alters circulating mediators that influence nociception. Multiplex ELISA measurements did not detect any differences in serum cytokines or chemokines between vancomycin-treated and control mice. The cysteine protease inhibitor E64 (10μM) and the protease-activated receptor 2 antagonist GB-83 (10μM) each blocked the increase in DRG neuron excitability in response to serum from vancomycin-treated mice.
**Conclusions:** Together, these data suggest that microbial dysbiosis is sufficient to alter pain sensitivity, and identify circulating cysteine proteases as potential mediators of this effect.

**Funding Agencies:** CCC

A286
**MICROBIOTA DEPLETION IN ADULTHOOD ALTERS MOUSE BEHAVIOR WITH POTENTIAL INVOLVEMENT OF MICROBIAL-METABOLITE SENSOR IN THE BRAIN**
F. Vicentini[2], Q. Pittman[4], M. Swain[1], S.A. Hirota[3], K.A. Sharkey[2]

1. Univ Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. Physiology & Pharmacology, University of Calgary, Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada

**Background:** The gut microbiota is a complex community of microorganisms that dwell in the gastrointestinal (GI) tract in a mutualistic fashion with its host. Essential for normal homeostasis, the microbiota plays a defined role in the human gut. Interestingly, the GI tract exhibits a bidirectional communication with the central nervous system (CNS), which recently has been described to be influenced by the gut microbiota – usually referred as the microbiota-gut-brain axis. Although many have shown gut microbiota influences over the CNS, mechanism(s) of how this modulation occurs have yet to be completely elucidated. Byproducts generated by the microbiota are found in the bloodstream and they are altered in accordance with microbial changes, such as in antibiotic-treated and germ-free mice.
**Aims:** Therefore, we hypothesized that gut microbiota influences brain activity and host behavior, signaling via bacterial byproducts acting at distinct receptors directly in the brain.
**Methods:** To test that, we assessed the expression of potential microbial-metabolite sensors in the brain of C57Bl/6 male mice. Moreover, broad-spectrum antibiotic cocktail was offered to mice for 2 weeks to deplete their intestinal microbiota. Following treatment, behavior was assessed by stablished behavior tests, such as the elevated plus maze, the open field test, the 3 chamber test, and the tail suspension test.
**Results:** Efficacy of antibiotic administration was verified through quantification of the bacterial load in the cecal matter after treatment. Mice treated with antibiotics had reduced bacterial load in the cecal matter, without presenting body weight alterations. No changes were observed in anxiety-like behavior and social preference. Interestingly, antibiotic-treated mice presented with a reduction in the depressive-like behavior. Measurement of microbial-metabolite sensors (e.g. aryl hydrocarbon receptor, AHR) in the brain were performed aiming to correlate their expression with the phenotypic behavior found. The brain regions selected for analyzes were the hippocampus, amygdala, and hypothalamus, chosen due to their close influence in anxiety and depressive behaviors. The mRNA of AHR was highly expressed on the three different regions of the brain. Moreover, after antibiotic treatment, AHR expression only in hippocampus was reduced, with no alterationsin the amygdala and hypothalamus.
**Conclusions:** These data suggest that changes in the intestinal microbiota, manifesting behavior alterations, may be driven, in part, by alterations in the expression and activity of microbial-metabolite sensing receptors in the brain. Further work is required to determine if AHR activity directly modulates brain regions responsible for depression-like behavior.

**Funding Agencies:** CIHR Brazilian National Council for Scientific and Technological Development

A287
**REACTIVITY OF THE EXTRINSIC AUTONOMIC NERVOUS SYSTEM ASSOCIATED WITH HUMAN COLONIC MOTOR PATTERNS**
Y. Yuan[1], J. Chen[1], E. Ratcliffe[4], S.P. Parsons[2], K. Mathewson[1], K. Zhang[1], D. Armstrong[1], P. Bercik[3], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. Farncombe Institute, McMaster University, Hamilton, ON, Canada; 3. Medicine, McMaster University, Hamilton, ON, Canada; 4. Pediatrics, McMaster University, Hamilton, ON, Canada

**Background:** The role of the autonomic nervous system (ANS) in control of colonic motility is unclear. Measurement of heart rate variability may provide diagnostic information for patients with colonic dysmotility.
**Aims:** We explored relationships between the cardiac output of the ANS through heart rate variability (HRV) and colonic motor patterns with or without sensation during high-resolution colonic manometry (HRCM)
**Methods:** Ten healthy volunteers (33 ±12 yrs; 6 male) received HRV testing in response to body position changes (supine, sitting, standing, walking). 4 weeks later HRCM was performed with synchronized HRV recording. The parasympathetic and sympathetic reactivities were evaluated by Respiratory Sinus Arrhythmia (RSA) and the Pre-Ejection Period (PEP) respectively. Colonic motor patterns were recorded at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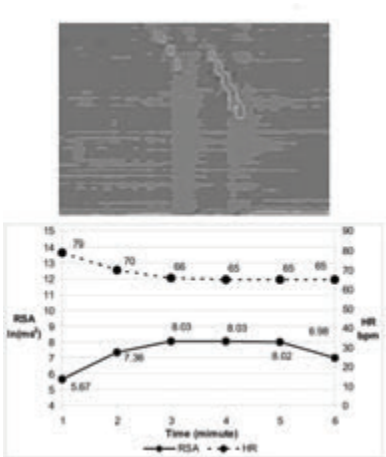
baseline and under provoking conditions: balloon distension, a meal and luminal bisacodyl
**Results:** To assess general parasympathetic and sympathetic tone, body position change from supine condition to walking showed a *decline* in RSA from 6.7±0.8 to 5.4±0.7 (P<0.05), suggesting a *decrease* in parasympathetic activity; the PEP did not show significant change from 123.2±20.0 to 113.3±16.5 (P>0.05). Colonic motor complexes, multiple high amplitude pressure waves (HAPWs) with or without simultaneous pressure waves (SPWs)(n=47), were induced by balloon distention or luminal bisacodyl. During their occurrence, RSA was *increased* from 6.7±1.2 to 7.5±1.1 (P<0.001) and PEP was *increased* from 110.5±15.3 to 116.3±14.2 (P<0.0001), suggesting i*ncreased* parasympathetic tone and *decreased* sympathetic tone. No significant autonomic change was observed during the occurrence of isolated HAPWs or SPWs. During HAPWs associated with SPWs and internal anal sphincter relaxation (n=30), RSA increased from 6.3±1.1 to 6.8±1.1 (P=0.005) and PEP did not show significant change (118.2±11.1 to 121.4±10.1; P=0.022), suggesting increased parasympathetic tone. In terms of the appreciable sensation (urge, discomfort, pain) during the occurrence of the motor pattern, both groups (109 out of 159 motor patterns with sensation and 50 out of 159 without sensation) showed increased RSA (from 6.4±1.2 to 7.1±1.2 and from 6.5±1.2 to 6.9±0.9, respectively; P<0.0001) and increased PEP (from 113.19±14.90 to 115.5±13.9, from 116.9±10.43 to 119.32±12.1, respectively; P<0.0001). There was no significant difference in RSA or PEP changes between these two groups (P>0.05), suggesting that is was motor activity that induced autonomic changes.
**Conclusions:** Colonic motor complexes and HAPWs associated with SPWs, but not isolated HAPWs or SPWs, are associated with increased parasympathetic tone and decreased sympathetic tone, measured as increased RSA and PEP respectively. The associated sensation is not reflected in ANS changes.




A colonic motor complex (2 high amplitude pressure waves (HAPWs) associated with 2 simultaneous pressure waves (SPWs) and IAS relaxation) was associated with an increase in RSA and a decrease in heart rate.

**Funding Agencies:** CIHRHamilton Academic Health Sciences Organization and the Canadian Foundation of Innovation Evans Leadership Fund

A288

## ANAL SPHINCTER RELAXATION ASSOCIATED WITH THE DEFECATION REFLEX AND GAS EXPULSION, ASSESSED BY HIGH-RESOLUTION COLONIC MANOMETRY

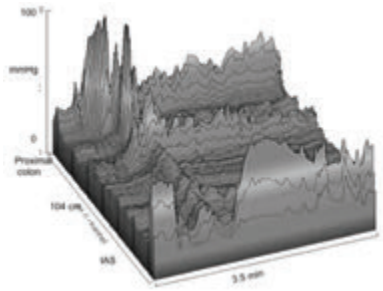
J. Chen[1], M. Shokrollahi[3], E. Ratcliffe[4], D. Armstrong[1], S.P. Parsons[2], P. Bercik[3], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. Farncombe Institute, McMaster University, Hamilton, ON, Canada; 3. Medicine, McMaster University, East Gwillimbury, ON, Canada; 4. Pediatrics, McMaster University, Hamilton, ON, Canada

**Background:** Continence and defecation require coordination between colonic motor patterns and internal anal sphincter relaxation, yet these relationships are not well understood.
**Aims:** Our aim was to investigate the coordination between human colonic motor patterns and anal sphincter activity.
**Methods:** High-Resolution Colonic Manometry (HRCM) was performed using an 84 sensor water-perfused catheter (1 cm spacing) in 14 healthy subjects. Colonic motor patterns and anorectal activity were recorded at baseline and provoking conditions (after a meal, balloon distensions, and luminal bisacodyl administration).
**Results:** A highly rhythmic alternation of contraction and relaxation of the internal AS in resting condition was observed in all subjects: a low-frequency rhythmicity at 1.2 ± 0.3 cpm with slowly developing and declining contraction, and a high-frequency rhythmicity at 15.0 ± 2.7 cpm superimposed on the slow rhythmicity. The High Amplitude Pressure Wave (HAPW) (Chen *et al.*, 2017) was not routinely associated with IAS relaxation. However, 62.5% of HAPWs were associated with a brief transient relaxation at the onset of the HAPW in the proximal colon, which did not last for the duration of the HAPW. Gas expulsion was associated with Simultaneous Pressure Waves (SPWs), pan-colonic pressurizations that penetrated into the anal canal and were most often associated with strong relaxation of the IAS. Many HAPWs terminated in the mid or descending colon but were immediately followed by an SPW and this was accompanied by IAS relaxation. A total of 61 independent SPWs with a mean amplitude of 26.3 ± 7.9 mmHg, were associated with 50.2±12.7% IAS relaxation from 65.1±15.6 mmHg to 31.5 ±11.3 mmHg. Bisacodyl induced SPWs of highest amplitude (30.3 ± 4.7 mmHg), that were followed by 63.8 ± 9.0% IAS relaxation, compared to SPWs occurring at baseline of 23.8 ± 5.6 mmHg associated with 44.3 ±12.4% IAS

relaxation. Duration of relaxation was correlated neither with the amplitude of SPW nor the percentage of IAS relaxation. Out of 44 HAPWs analyzed, 27.2% were not associated with IAS relaxation, whereas 72.8% were accompanied by a transient IAS relaxation of 51.2 ± 17.3% at the onset of the HAPW which recovered during the progression of the HAPW. 45.4% of HAPWs (103.3 ± 24.0 mmHg) were immediately followed by SPWs (18.7 ± 6.5 mmHg), which were then associated with strong IAS relaxation of 66.9 ±13.6%, going from 63.2 ±19.4 mmHg to 20 ± 8.6 mmHg.
**Conclusions:** The SPW, either in isolation and associated with gas expulsion or following an HAPW as part of the defection reflex, is consistently associated with internal anal sphincter relaxation. This relaxation reduces IAS tone which is maintained by rhythmic contractile activity.

*Chen JH, et al. (2017). Nature's Scientific Reports doi:10.1038/srep41436.*




High-Resolution Colonic Manometry (HRCM) with 84 sensors, 1 cm apart. A simultaneous pressure wave (SPW), following a High Amplitude Pressure Wave (HAPW), penetrates into the anal canal and is associated with internal anal sphincter (IAS) relaxation.

**Funding Agencies:** CIHRHamilton Academic Health Sciences Organization and the Canadian Foundation for Innovation

A289
**DELTA OPIOID RECEPTOR ACTIVATION TRIGGERS BOTH ANTINOCICEPTIVE AND PRONOCICEPTIVE SIGNALING**
J.O. Jaramillo Polanco, C.D. Lopez Lopez, D.E. Reed, A.E. Lomax, S. Vanner

Gastrointestinal Diseases Research Unit, Queen's University, Kingston, ON, Canada

**Background:** Opioid drugs are efficacious in the treatment of abdominal pain but increasing doses can activate pronociceptive signaling and paradoxically worsen pain. Although the mu opioid receptor (MOR) has been the classic analgesic target implicated in this signaling, there is growing evidence that delta opioid receptors (DOR) could also be important targets for analgesia. If so, however, they could also play a role in this paradoxical signaling.
**Aims:** The present study examined whether exposure to low and high concentrations of the DOR agonist DADLE have opposite effects on the excitability of nociceptive DRG neurons.
**Methods:** To examine the effects of high and low concentration DADLE, nociceptive mouse DRG neurons were dissociated from control mice and exposed to acute (30 min) or overnight incubation with 10 nM (low concentration) or 10 µM (high concentration) DADLE. Changes in neuronal excitability (decrease = antinociception, increase = pronociception) were recorded by measuring the rheobase (amount of current required to elicit an action potential) using patch clamp recordings.
**Results:** Patch clamp recordings of DRG neurons (small nociceptive neurons <25 pF) following acute incubation with DADLE exhibited opposing effects on excitability depending on the concentration. Acute incubation with low concentration DADLE inhibited the excitability of DRG neurons by 22.1% ($p<0.05$), whereas high concentration DADLE increased the excitability by 20.6% ($p<0.05$). Both effects were blocked by the DOR antagonist SDM25N (100 nM). Overnight incubation with low concentration DADLE had no effect on neuronal excitability, whereas the pronociceptive effect induced by high concentration persisted after overnight incubation (rheobase decreased 28.1% compared to control, $p<0.001$).
**Conclusions:** Activation of DOR can have an important analgesic effect but high doses can also trigger paradoxical increases in pain signaling. The sustained effect of overnight exposure to high dose DADLE may reflect transcription and/or post transcriptional changes in the opioid signaling pathway.

**Funding Agencies:** CCC

A290
**BILE SIGNALING TO SPINAL AFFERENT NERVES INNERVATING THE MOUSE DISTAL COLON**
Y. Zhang, D.E. Reed

Gastrointestinal Diseases Research Unit, Department of Medicine, Queen's University, Kingston, ON, Canada

**Background:** In a subpopulation of IBS patients, bile acids are increased in the colon and may trigger abdominal discomfort. However, little is known about activation of spinal afferent nerves (i.e. nociceptive nerves) innervating the colon by bile acids.
**Aims:** The aim of this study was to examine activation of these nerves by primary and secondary bile acids.
**Methods:** An *in vitro* preparation of the C57BL/6 mouse distal colon was employed to perform extracellular recordings of single serosal spinal afferent units en route to the inferior mesenteric ganglion. Human bile, mouse bile or bile acids (or their respective salt) were applied to the receptive field of a single afferent unit for 5 minutes via a small metal ring. The effect of the primary bile salt sodium cholate (300µM and 1mM) and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the secondary bile acid/salt deoxycholic acid/sodium deoxcholate (100μM-1mM) was also examined. Nerve excitability was assessed by changes in spontaneous action potential frequency as well following mechanical stimulation of the single unit's receptive field with a calibrated von Frey filament (1g) before and after application of bile acids/salts. Units were considered responders if the spontaneous firing rate increased 25% above baseline. Data are expressed as mean±SEM.
**Results:** Human bile evoked a response in all 4 units tested (control: 0.77±0.43Hz; bile: 1.68±0.23Hz). Application of diluted bile also activated single units (1:3 dilution: 3/3 units; 1:10 dilution: 3/4 units; 1:30 dilution: 2/3 units; 1:100 dilution: 2/3 units). Similarly, non-dilute mouse bile also activated 3/3 units tested (control: 0.94±0.39Hz; bile: 2.16±0.68Hz). Application of sodium cholate only activated 1/5 units when applied at concentrations of 300μM and 1mM. Deoxycholic acid or sodium deoxycholate activated 1/8 units with 100μM; 2/6 units with 300μM; and 2/9 with 1mM. Mechanical stimulation was unchanged following application of sodium cholate 300μM (10.5±2.4Hz vs 7.1±2.0; p>0.05, n=4) or 1mM (14.9±2.7Hz vs 8.3±1.8Hz; p>0.5, n=4). Mechanical sensitivity was also unchanged following deoxycholic acid or sodium deoxycholate (100μM-1mM) (p>0.05, n=6-9).
**Conclusions:** Bile is a potent stimulus to activate nociceptive nerves in the distal colon. However, a major primary bile salt and a major secondary bile acid/salt activated few of these nerves and did not change mechanosensitivity. This suggests that either a combination of bile acids/salts or another constituent within bile activates colonic afferent nerves.

**Funding Agencies:** None

A291
**INHIBITORY EFFECTS OF GHRELIN ON MEMBRANE EXCITABILITY AND RESPONSES TO SATIETY MEDIATORS IN VAGAL AFFERENT NEURONS: INVOLVEMENT OF SUPPRESSOR OF CYTOKINE SIGNALING 3**
S. Park, M.J. Beyak

Queen's University, Kingston, ON, Canada

**Background:** The orexigenic hormone ghrelin regulates feeding behavior via vagal afferent pathways. The mechanisms by which ghrelin exerts its inhibitory effects on nodose ganglion neurons are largely unknown. There is a evidence that ghrelin caused a significant increase in suppressor of cytokine signaling 3 (SOCS3) expression in nodose ganglion neurons, the cell bodies of vagal afferents.
**Aims:** The aim of this study was to examine the effects of ghrelin on excitability and satiety mediator responses and whether SOCS3 is associated with the effects of ghrelin on nodose neurons.
**Methods:** Nodose neurons from C57Bl6J mice were dissociated and incubated overnight with ghrelin (100 nM) and with/without zoledronic acid (ZA, a SOCS3 inhibitor, 10 mM). Current clamp recordings (to examine excitability) and Fura-2AM $Ca^{2+}$-imaging (to examine responses to satiety mediators) were performed 18-24 h post-dissociation.
**Results:** Ghrelin (100 nM) significantly decreased the membrane potential (-52.0±0.9 mV (n=18, control) vs. -61.5±1.9 mV (n=15, ghrelin), unpaired student t-test, p<0.001) and increased the rheobase in nodose neurons (56.7 ± 5.4 pA (n=18, control) vs. 92.7 ± 8.6 pA (n=15, ghrelin), p<0.001). The number of action potential at twice rheobase correspondingly decreased by ghrelin (2.6 ± 0.4 (n=18, control) vs. 1.1 ± 0.1 (n=15, ghrelin), p<0.01). This reduction in membrane excitability was prevented in nodose neurons incubated with ZA (10 mM). The rheobase was reduced in ghrelin plus ZA-incubated neurons (ghrelin vs. ghrelin+ZA, 74.4±4.4 pA, n=16, unpaired student t-test, p=0.064). The number of action potentials at twice rheobase was increased in ghrelin and ZA-incubated neurons (ghrelin vs. ghrelin+ZA, 1.8±0.2, n=16, unpaired student t-test, p<0.05). The proportion of $Ca^{2+}$ responses to CCK (100 nM) and 5-HT (1 mM) were examined in control and ghrelin-incubated nodose neurons. Proportion of neurons responding to CCK and 5-HT were significantly reduced by ghrelin. (CCK; control, 33/86, 38.4% vs. ghrelin-incubated, 9/49, 18.4%, Fisher's exact test, p<0.05, 5-HT; control, 22/63, 34.9% vs. ghrelin-incubated, 10/59, 14.5%, p<0.05).
**Conclusions:** Ghrelin reduced the membrane excitability and satiety responses in nodose ganglion neurons and this inhibitory effect was reversed by the inhibition of SOCS3. Thus, ghrein-SOCS3 pathway might be responsible for the inhibitory mechanism in vagal afferents and a potential therapeutic target in obesity.

**Funding Agencies:** CIHR

A292
**EFFECT OF HIGH FAT DIET ON MECHANOSENSITIVE TRP CHANNEL ACTIVATION IN VAGAL AFFERENT NEURONS**
S. Park[1], Y. YU[2], C. Zides[1], M.J. Beyak[1]

1. Queen's University, Kingston, ON, Canada; 2. GIDRU, Queen's University, Kingston, ON, Canada

**Background:** A number of studies have shown that high fat feeding in the mouse (a commonly used model of diet-induced obesity) results in impaired vagally-mediated satiety responses. Mechanical stimulation of the GI tract is an important stimulus of satiety, and can be mediated by a number of TRP channels (TRPA1, TRPV1 and TRPV4).

**Aims:** We sought to examine the effect of chronic high fat diet on responses to TRP channels known to be involved in GI afferent mechanosensation (TRPA1, TRPV1 and TRPV4).
**Methods:** C57Bl6J mice were fed a high fat diet (60% kcal from fat-HFF) and controls a low fat diet (10%-LFF). Nodose ganglion neurons were dissociated and Fura 2-AM $Ca^{2+}$ imaging was performed. In vitro

extracellular afferent nerve recordings were performed from segments of jejunum. Responses of TRPA1 (AITC), TRPV1 (capsaicin) and TRPV4 (4αPDD) were examined.

**Results:** High fat diet resulted in a decreased number of neurons responding with increased intracellular $Ca^{2+}$ to AITC (LFF; 32/72, 44.4% vs. HFF; 26/121, 21.5%, Fisher's exact test, p<0.01). Reduction in number of neurons responding to 4αPDD did not reach statistical significance (LFF; 40/88, 45.5% vs. HFF; 31/96, 32.3% p=0.07) and there was minimal change in proportion of neurons responding to capsaicin. Consistent with this, magnitude of the $Ca^{2+}$ increase induced by AITC (LFF-3.77 ± 0.43 n=19 and HFF 2.36 ± 0.33 n=20 p<0.05) and 4αPDD (LFF-2.64 ± 0.43 n=18, and HFF 1.47 ± 0.26 n=16) was reduced in HFF neurons with no change in the capsaicin response. In jejunal afferent recordings We saw a significant reduction in the afferent response to 4αPDD (p<0.01) and AITC (p<0.05), but not capsaicin.

**Conclusions:** Our results have shown decreased responses to the mechanosensitive TRP channels TRPA1 and TRPV4 at the vagal afferent cellular level as well as at the level of the nerve terminal in the intestine. The response to TRPV channel activation seems to be preserved. These results may explain some of the reduced sensitivity of GI vagal afferents to mechanical stimuli and may lead to decreased meal-induced satiety signals.

**Funding Agencies:** CIHR

A293

**SQUALAMINE INCREASES VAGAL AFFERENT FIRING FREQUENCY IN AGING MICE**

C. West[1], A. Stanisz[2], J. Bienenstock[2], D. Barbut[3], M. Zasloff[4], W.A. Kunze[2]

1. McMaster University, Hamilton, ON, Canada; 2. Brain-Body Institute, Hamilton, ON, Canada; 3. Enterin Inc., Philadelphia, PA; 4. Med-Star Georgetown Transplant Institute, Washington,

**Background:** A large portion of the aging population exhibit comorbid gastrointestinal (GI) disorders and common age-related neurodegenerative conditions often including constipation, sleep disturbance, and depression. Luminal gut contents and microbiota have the ability to influence mood and behaviour through the vagal gut-brain axis. Squalamine, an aminosterol originally isolated from the dogfish shark, is a potent stimulator of the enteric nervous system and is currently in a Phase 2a study to evaluate its effect on constipation and other non-motor symptoms of Parkinson's disease. We have recently shown that constipation in aged mice could be reversed by squalamine acting on the enteric nervous system.
**Aims:** The purpose of this study is to explore the impact of aging on vagal afferent signaling in mice and evaluates the effects of squalamine on vagal outflow in this model. We hypothesize that squalamine will increase vagal afferent firing frequency in aged mice.

**Methods:** Jejunal segments with attached mesentery from old (18-24 months) and young (3 months) male CD1 mice were excised, pinned out in a petri dish of Krebs and dissected to isolate the mesenteric nerve bundle. The jejunum was cannulated at both ends and luminally perfused with Krebs solution or Krebs with added squalamine (10μM). The mesenteric nerve bundle was sucked onto with a glass micropipette attached to a patch-clamp electrode and multi-unit electrical activity was recorded using an amplifier and signal converter. Single-unit firing was isolated using Dataview software and vagal fibres were identified by response to CCK. Basal afferent vagal firing frequency was measured in old and young mice before and after treatment with squalamine.

**Results:** Mean basal vagal afferent firing frequency was 0.58 ± 0.13 Hz (N=30[4]) in old mice compared to 1.1 ± 0.11 Hz (N=45[3]) for young mice representing a 57% reduction (p = 0.0016) in firing frequency in the elderly animals compared with the younger controls. Luminal application of squalamine increased vagal afferent firing frequency by 43% to 1 ±0.097 Hz (p < 0.0001) in old mice compared to an increase of 28% to 1.4 ± 0.11 Hz (p = 0.001) in young mice. The onset latency to the peak of the squalamine response was 15 to 20 min.
**Conclusions:** The results demonstrate that luminal exposure to squalamine: (1) stimulates vagal afferent signaling in both young and old mice, (2) the magnitude of the effect is larger in the older animals. The data suggest that diminished vagal afferent firing with aging is at least partially reversible with luminally-administered squalamine.

**Funding Agencies:** NRC

A294

**NORADRENALINE INHIBITS PROPULSIVE MOTOR PATTERNS BUT NOT SEGMENTING HAUSTRAL PROGRESSION IN THE RABBIT 3-TAENIATED COLON**

A.A. Hanman[1], J. Chen[1], S.P. Parsons[2], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. Farncombe Institute, McMaster University, Hamilton, ON, Canada

**Background:** Sympathetic inhibition may be an underestimated cause of reduced human colonic motor activity. The sympathetic nervous system has been implicated in colonic dysmotilities involving stress or anxiety.
**Aims:** Our aim was to better understand the role of sympathetic inhibition on colonic motor patterns and to formulate a hypothesis on the underlying mechanisms
**Methods:** Sympathetic activity was studied *ex vivo* using noradrenaline on four major motor patterns occurring in the rabbit 3-taeniated colon (n=11): long distance contractions (LDCs), fast propagating contractions (FPCs), haustral boundary contractions



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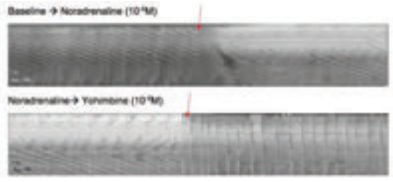
(HBCs) and ripples. Spatiotemporal maps were created to show diameter changes of the whole proximal colon over time.
**Results:** The rabbit colon displayed four motor patterns that appeared under baseline conditions in various combinations, LDCs at 0.9±0.4 cycles/min (cpm) and velocity of 3.0±0.6 cm/s, FPCs at 13.7 ± 5.1 cpm and 3.4±0.9 cm/s, HBCs at a frequency of 0.5±0.2 cpm and velocity of 8.2±2.0 mm/min and ripples at 8.6±1.6 cpm. Noradrenaline ($10^{-6}$ M) abolished LDCs, which recovered by the alpha-2 adrenergic blocker yohimbine ($10^{-6}$ M) to 0.6±0.1 cpm and velocity of 2.9±0.4 cm/s, not by the beta-adrenergic blocker propranolol ($10^{-6}$ M). The FPCs were transiently abolished but recovered in the presence of noradrenaline at 30 min with FPCs at 1.6±0.1 cpm and 4.6±1.9 cm/s, and recovered further with yohimbine at a frequency of 10.7±4.5 cpm and 3.7±1.3 cm/s. The features of HBCs in the presence of noradrenaline, a frequency of 0.5±0.1 cpm at 7.9±1.0 mm/min, were not different from control values. In the presence of noradrenaline, the myogenic ripples did not change at a frequency of 10.2±1.8 cpm.
**Conclusions:** Noradrenaline affected preferentially the propulsive motor patterns, the LDCs and FPCs, mediated by the alpha-2 adrenergic receptor. No role for the beta-adrenergic receptor was found. We propose that the human manometry equivalent of the LDC is the High Amplitude Pressure Wave (1) and that the FPCs create simultaneous pressure waves in the rabbit (2) and human colon (1). Noradrenaline did not have a marked effect on ripples or the propagating HBCs. The lack of effect on the rhythmic myogenic component of these motor patterns suggests an absence of noradrenergic communication with interstitial cells of Cajal (ICC). The HBCs also have a neurogenic component hence alpha-2 receptors appear present in some neuronal circuitries (to generate LDCs) but not in others (to generate HBCs). This knowledge may help to discover a role for sympathetic inhibition, based on motor patterns affected, as measured by high-resolution manometry in the human colon (1).

1. *Chen, J-H. et al. Nature's Scientific Reports 2017;7:41436; doi:10.1038/srep41436.*
2. *Quan, X et al., Nature's Scientific Reports 2017;7:42293:doi:10.1038/srep42293.*




Rabbit colon spatiotemporal maps of diameter changes over time in vitro. Baseline shows LDCs, FPCs and propagating haustral boundary contractions. LDCs and FPCs are inhibited by noradrenaline but LDCs recover in the presence of the alpha-2 blocker yohimbine.

**Funding Agencies:** CIHR

A295
**AN INTEGRATED MULTIDISCIPLINARY GROUP PROGRAM IMPROVES IRRITABLE BOWEL SYNDROME SYMPTOM SEVERITY: A PILOT STUDY**
M. Woo[1], Y. Tse[2], J.D. O'Brien[2], D. Klar[2], A. Sambhi[2], S. Sockalingham[2], L.W. Liu[2]

1. Queen's, Kingston, ON, Canada; 2. Medicine, University Health Network, Toronto, ON, Canada

**Background:**
Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder that is characterized by abdominal pain associated with bowel movements. IBS affects 11% of the adult population. The pathogenesis of IBS symptoms is thought to be contributed by disturbances of the brain-gut axis. Cognitive behavioral therapy (CBT) has been shown to reduce self-rated abdominal and psychiatric symptoms. Low FODMAP diet has been demonstrated to reduce abdominal pain and bloating.
**Aims:** The aim of this study is to investigate the efficacy of a formal group program that integrates psychosocial interventions and dietary education, conducted by a gastroenterologist, psychiatrist and registered dietician.
**Methods:** 9 patients with a diagnosis of IBS in a tertiary referral center were enrolled to participate in a structured group program, involving a gastroenterologist, a psychiatrist and registered dieticians. Education on IBS, mindfulness/CBT, and low FODMAP diet were provided at the initial visit (week 0). Patients returned for follow up sessions at week 4 and week 12 where additional education and practice were provided. At each session, patients completed a 7-question anxiety questionnaire (GAD-7), a 9-question depression questionnaire (PHQ-9), a 15-question questionnaire on somatic symptoms (PHQ-15), an IBS symptom severity scale (IBS-SSS), and a patient satisfaction survey assessing usefulness and satisfaction of the group session. Mann-Whitney was used to analyze differences at enrollment and exit.
**Results:** 8 patients were female (88%), with the average age of 57.3 +/- 5.5 years. Based on the IBS-SSS, 7 patients (78%) had moderate IBS and 2 patients (22%) had severe IBS symptoms. At the end of 12 weeks, 6 patients (66.7%) completed the structured group program. The mean IBS-SSS on initial visit was 269.6 +/- 60.3 and at completion (week 12) was 190.4 +/- 53.0. There was a significant reduction in IBS symptoms ($p = 0.034$). There was no significant difference seen between the anxiety, depression, or somatic symptom scores ($p > 0.10$). Overall, patients found the program useful and were satisfied, with scores > 85% in all sessions.
**Conclusions:** In this pilot study, a structured group program with a gastroenterologist, a psychiatrist and a registered dietician demonstrated a significant reduction in IBS symptoms over 12 weeks. Patients found these sessions useful and were satisfied throughout the program. Further qualitative research involving

structured interviews with participants will allow for a needs analysis to be conducted, in view of optimizing the program for future participants. In addition, future randomized control study with a longer follow-up in the optimized program will further elucidate the role of this multidisciplinary group program in the care of IBS patients.

**Funding Agencies:** None

A296

**A RHYTHMIC MOTOR PATTERN ASSOCIATED WITH HIGH AMPLITUDE PRESSURE WAVES IN HUMAN HIGH-RESOLUTION COLONIC MANOMETRY**

J. Chen[1], M. Pervez[1], E. Ratcliffe[3], D. Armstrong[1], P. Bercik[2], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. Medicine, McMaster University, Hamilton, ON, Canada; 3. Pediatrics, McMaster University, Hamilton, ON, Canada

**Background:** High Amplitude Pressure Waves (HAPWs) are the only motor pattern routinely assessed in human colonic manometry. High-Resolution Colonic Manometry is able to provide more information and shows HAPW associated motor patterns that may have clinical relevance.
**Aims:** Our aim was to characterize the HAPW associated rhythmic motor pattern, its myogenic basis based on its frequency pattern, its physiological significance and its potential diagnostic value.
**Methods:** High-resolution manometry was performed using an 84 sensor water-perfused catheter in 7 healthy subjects. Pressures were recorded at baseline, after a meal, in response to balloon distension and bisacodyl administration.
**Results:** The most consistent motor pattern that followed HAPWs in healthy adults was a characteristic rhythmic motor pattern with distinct frequency components of 6, 9,12 and 15 cpm, clearly distinguishable from the breathing frequency. This pattern had an average duration of 78.1 ± 49.6 s (24 to 165), occurring over a section of the colon of 11.5 ± 5.9 cm (6 to18) length, which is about 2 or 3 haustra. The motor pattern ended 24.0 ± 7.0 cm above the anal verge; hence it is a characteristic of the sigmoid colon. Individual pressure transients within the pattern occurred almost exclusively instantaneous. To quantify, HAPWs were evoked by balloon distention, a 1000 kcal meal, and 10 mg luminal bisacodyl. Using balloon distention, 31 HAPWs were evoked, 16.1% were followed by quiescence and 48.4% by the rhythmic motor pattern; other HAPWs were associated with spontaneous pressure waves without the occurrence of this rhythmic motor pattern. In response to a meal, 30 HAPWs were evoked, 10.0 % were followed by quiescence and 33.3 % by the rhythmic motor pattern. In response to bisacodyl, 39 HAPWs were evoked, 5.1 % were followed by quiescence and 46.2 % by the rhythmic motor pattern. This motor pattern also occurred independently of the HAPWs with dominant frequencies of 3 and 6 cpm at baseline condition, indicating the motor pattern was in a less excited state with more retrograde propagation.
**Conclusions:** A rhythmic motor pattern characteristically follows the HAPW in the sigmoid colon. Its occurrence after an HAPW suggests that this rhythmic motor pattern shares neural excitation with the HAPWs. Its frequency spectrum (3,6,9,12,15 cpm) and very fast propagation (or instantaneous appearance) suggest orchestration by a network of interstitial cells of Cajal (ICC). The frequency spectrum is identical to that in previous electrical recordings of the human colon (2). The occurrence of this motor pattern in healthy adults suggests that it may not be a biomarker of constipation in adults (1) and suggests that it may be a signature of intrinsic ICC activity.

1. Giorgio et al. Neurogastr. Mot. 2013. 2. Sarna et al. Gastroenterology 1981.

High-Resolution Colonic Manometry: a High Amplitude Pressure Wave is followed by a Rhythmic Motor Pattern in the distal colon.

**Funding Agencies:** CIHRHamilton Academic Health Sciences Organization

A297

**FREQUENT ADVERSE CHILDHOOD EVENTS IN PATIENTS WITH IBS AND ORGANIC GASTROINTESTINAL DISORDERS**

C.V. Noejovich, M.I. Pinto-Sanchez, E. Verdu, D. Armstrong, S.M. Collins, P. Bercik

Farncombe Family Digestive Health Research Institute, Hamilton, ON, Canada

**Background:** Stressful events in childhood have been associated with the development of functional bowel disorders in adulthood, especially irritable bowel syndrome. However, it not known whether early life adverse events affect patients with common organic disorders, including celiac disease and IBD.
**Aims:** To evaluate the association between early life adverse events and gastrointestinal and extra-intestinal symptoms in patients with functional and organic gastrointestinal (GI) disorders compared with healthy controls.
**Methods:** We included adult patients with a diagnosis of IBS (Rome III criteria), organic GI disorders (celiac disease and IBD) and healthy volunteers (HV). Patients and controls were interviewed by a psychologist and early life adverse events assessed during the semi-structured interview using a modified version of the Adverse Childhood Experience (ACE) questionnaire. We quantified number of early life events and the



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presence of gastrointestinal and extraintestinal symptoms in each group. Data are presented as median (IQR) and n (%).
**Results:** We enrolled thirty subjects (16 IBS patients, 8 with organic GI disorders and 6 healthy controls). Patients with IBS had significantly increased number of early life events compared with healthy controls (12 (9-15) vs 3 (1-6); p=0.003). The number of overall early life events in IBS patients was comparable to those with a diagnosis of organic GI disorders. Compared to HV, both patients with IBS and organic GI disorders had significantly increased number of family members with alcohol or drugs abuse during childhood (IBS vs HV p=0.0028; chronic GI disorders vs HV p=0.03) and neglected parents (IBS vs HV p=0.01; chronic GI disorders vs HV p=0.004). Parental conflicts or divorce (p=0.004) and motor vehicle accidents (p=0.049) were more common in IBS patients compared to HV. The number of overall early life adverse events were strongly correlated with number of gastrointestinal (r= 0.91; p=0.01) and extra-intestinal (r=0.87; p=0.02) symptoms, but not with symptoms severity.
**Conclusions:** Our preliminary results show that adverse early life events are frequent in patients with functional and organic gastrointestinal conditions, which may contribute to symptoms in adulthood. The association between number of childhood adverse events and the presence of gastrointestinal and extraintestinal symptoms highlight the need for better psychosocial assessment in gastroenterology clinical practice to improve the management of these patients.

**Funding Agencies:** None

A298
**JACKHAMMER ESOPHAGUS: FROM MANOMETRIC DIAGNOSIS TO CLINICAL PRESENTATION**
M. Clement, W. Zhu, E. Neshkova, M. Bouin

Centre hospitalier de l'Université de Montréal (CHUM), Montreal, QC, Canada

**Background:** Jackhammer esophagus is an hypercontractile esophageal disorder recently brought to light with the advent of high resolution manometry (HRM). As Jackhammer esophagus is purely a manometric diagnosis, little is known about its clinical expression.
**Aims:** We hypothesized that the extreme esophageal contractions encountered in this disease cause upper digestive symptoms such as dysphagia and chest pain. Thus, the aim of our study was to identify the clinical characteristics associated with this new motility disorder.
**Methods:** A retrospective observational study was conducted from January 2015 to September 2017 at the CHUM gastro-intestinal motility center. Among all the HRM performed, patients with a diagnosis of jackhammer esophagus were included. This diagnosis is made when at least 20% of the swallows being studied are hypercontractile, with a distal contractile integral (DCI) of >8000 mmHg.s.cm (Chicago classification). Each patient's chart was reviewed to collect clinical data: age, sex, comorbidities, proton pump inhibitor use, along with manometry, upper digestive endoscopy, biopsies, pH-monitoring and barium swallow results.
**Results:** Among the 1046 HRM done during the study period, 34 patients with jackhammer esophagus were included (mean age 62 ± 13 years, 88% females). Their main symptoms were dysphagia (71%), pyrosis (44%), retrosternal chest pain (38%) and epigastralgia (32%). In half of the patients, at least 50% of swallows were hypercontractile. The mean DCI of the hypercontractile esophageal contractions was 11 600 ± 3600 mmHg.s.cm. Other HRM findings were hypertonia (26%) and/or inadequate relaxation (29%) of the lower esophageal sphincter. Upper digestive endoscopy results were available for 26 patients: 18 normal, 3 hiatal hernias, 2 esophageal dilatations, 2 lower esophageal sphincter hypertonia impressions and one with longitudinal striae. Among the 12 available biopsy results, 2 were abnormal: one lymphocytic exostosis and one esophagitis without eosinophilia. Pathological gastro-esophageal reflux was found in 3 of the 9 patients investigated with pH-monitoring. Among the 8 patients who had a barium swallow, 4 had a normal study, 3 had spastic contractions of the esophagus and one had an incomplete relaxation of the cricopharyngeal muscle.
**Conclusions:** Jackhammer esophagus was diagnosed in 3% of the patients referred for a HRM to our gastro-intestinal motility center. A strong female predominance is found in this study. In more than two thirds of cases, the clinical presentation of jackhammer esophagus is dysphagia. Malfunctioning of the lower esophageal sphincter can be demonstrated during manometry. Upper digestive endoscopy and biopsies seem unhelpful in suspecting the diagnosis before HRM is performed.

**Funding Agencies:** None

A299
**RARE CASE OF CONGENITAL DEFECT IN THE COLONIC MUSCULARIS PROPRIA EXTERNA CAUSING COLONIC PSEUDO OBSTRUCTION AND SEVERE CONSTIPATION IN A 10-YEAR-OLD BOY**
E.D. Greenaway[1], J. Langer[3], V. Scaini[5], B. Ngan[4], P. Marcon[2]

1. Paediatrics - Division of Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children, Toronto, ON, Canada; 2. GI , The Hospital for Sick Children, Toronto, ON, Canada; 3. The Hospital for Sick Children, Toronto, ON, Canada; 4. The Hospital for Sick Children, Toronto, ON, Canada; 5. The Hospital for Sick Children, Toronto, ON, Canada

**Background:** In children chronic constipation is common, usually functional and appropriate treatment regimens can be developed. When unresponsive to traditional therapy other etiologies are explored. Colonic intestinal pseudo obstruction (IPO) is a rare cause of severe chronic constipation.

**Aims:** A 2-year-old toilet trained male developed a Streptococcal perianal infection, painful defecation with stool withholding behaviours and chronic constipation unresponsive to medical management. He thrived with no anorexia or vomiting. He had a history of complex febrile seizures which resolved by age 6 years. He developed significant anxiety around stooling and received counselling. Family history revealed functional constipation in 4 maternal cousins. Physical examinations revealed a well grown, developmentally appropriate boy, with a normal physical exam other than copious stool on abdominal palpation. Rectal examination was unremarkable.
**Methods:** Contrast barium enema was normal. Anorectal manometry showed low squeeze pressure and ineffective bear-down but present RAIR. Full thickness rectal biopsy revealed normal ganglion cells. Immunostain for calretinin showed normal expression within mucosal nerve fibres. Nuclear medicine gut transit study demonstrated a normal pattern of gastric emptying and small bowel transit time with no evidence of colonic inertia or regional bowel abnormality. MRI of the spine, upper and lower endoscopies, celiac disease screen and abdominal ultrasound were normal. Radiography showed faecal loading primarily in the rectosigmoid region. He had treatment trials of PEG3350, Pico Salax®, Senna, prucalopride and anal sphincter botulinum toxin injection without improvement.
**Results:** He had placement of a cecostomy tube for antegrade colonic enemas and rectosigmoid resection with colorectal anastomosis. The resected segment was 5cm in circumference at the narrow margin and 15cm at the dilated margin. For 12cm extending to the narrow margin, the tenia coli separated into 2 separate longitudinal bands exposing the underlying inner circular muscular layer which appeared as cross-connecting ridges. Sections taken from the narrower segment with split tinea coli showed extensive thinning of the muscularis propria externa. Immunostains for interstitial cells of Cajal showed either absence or sparse numbers. He had one admission shortly after surgery for faecal impaction but has since managed to keep the colon clear with a cecostomy irrigation regimen.
**Conclusions:** There are few cases described of segmental congenital defects of the intestinal musculature resulting in IPO. The few cases described note hypertrophy, supernumerary muscular layers or hypoplasia, primarily involving the small bowel. This case adds to the small body of literature describing such abnormalities in the colon.

**Funding Agencies:** None

A300

**ESOPHAGOGASTRIC JUNCTION OUTFLOW OBSTRUCTION ON MANOMETRY: OUTCOMES AND LACK OF BENEFIT FROM IMAGING**

A. Liu[1], L. Wilsack[1], M.c. Buresi[3], M. Curley[3], M. Gupta[2], D.Y. Li[1], C.N. Andrews[3]

1. Gastroenterology, University of Calgary, Calgary, AB, Canada; 2. Foothills Hospital, Calgary, AB, Canada; 3. Gastroenterology, University of Calgary, Calgary, AB, Canada

**Background:** Esophagogastric junction outflow obstruction (EGJOO) is a manometric diagnosis based on the Chicago Classification defined by inadequate relaxation of the gastroesophageal junction (GEJ) with swallowing, but with sufficient peristalsis such that the criteria for achalasia are not met. Causes include structural (stricture, hiatus hernia, eosinophilic esophagitis, malignancy, and post-fundoplication) and functional/motility etiologies (early achalasia and medication side-effects), although typically most of the structural causes are ruled out by endoscopy prior to manometry. The Chicago group suggests further investigation including computed tomography (CT) or endoscopic ultrasound (EUS) to help elucidate the etiology of EGJOO, but the utility of this approach has not been proven.
**Aims:** To assess the therapeutic outcome of EGJOO by assessing which interventions are performed after an EGJOO diagnosis. To assess the proportion of patients with EGJOO who underwent further testing (e.g. CT or EUS of the GEJ) and whether that testing elucidated a cause for the EGJOO.
**Methods:** All new diagnoses of EGJOO made in calendar year 2016 at a regional motility lab were included. A comprehensive, province-wide electronic medical database (Alberta Netcare, which includes virtually all publicly-funded imaging, pathology, lab, and endoscopy results) was searched for each patient to assess diagnostic and therapeutic interventions after the EGJOO diagnosis. Ethics board-approved study.
**Results:** 80 EGJOO patients were included (mean age 63 (range 37-95), 76% female). Primary complaint was dysphagia (67.5%), chest pain (12.5%), reflux (8.8%), pre-operative assessment (7.5%), regurgitation (2.5%), or cough (1.2%). The mean IRP was 22 mmHg (range 15-43, normal <15.0). After a mean follow-up period of 439 days (range 92-631), the etiology of our patients' EGJOO remained unidentified in most cases (70.0%). In the remainder, subsequent evaluation led to a diagnosis of hiatal hernia (10.0%), medication side-effects (5.0%), spontaneous resolution (5.0%), achalasia (3.8%), stricture (3.8%), jackhammer esophagus (1.2%), and eosinophilic esophagitis (1.2%). Regarding interventions, eight patients had esophageal dilation (10.0%), nine had botulinum toxin injection to the GEJ (11.2%), and three had surgery (3.8%). A proportion of patients were investigated with CT (25.0%) or EUS (7.5%) to rule out external compression or malignancy as a cause of EGJOO; none of these tests provided any further information on the cause.
**Conclusions:** EGJOO is a relatively new manometric diagnosis with unclear clinical significance and outcome in most cases. CT and EUS of the GEJ were unhelpful at determining the cause of this entity. Few cases progressed to achalasia. Lack of familiarity with EGJOO may contribute to the low rate of subsequent intervention.


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**Funding Agencies:** None

A301

**ANTIBIOTICS INCREASE VAGAL AFFERENT FIRING IN THE MOUSE JEJUNUM**

T.N. Delungahawatta[1], C. West[1], A. Stanisz[2], J. Bienenstock[2], P. Forsythe[2], W.A. Kunze[2]

1. McMaster University, Hamilton, ON, Canada; 2. Brain-Body Institute, Hamilton, ON, Canada

**Background:** Accumulating evidence from animal studies suggests antibiotics administered to the gut lumen may act directly on the host nervous system. For instance, we have previously shown that introduction of bacitracin, neomycin and penicillin V antibiotics in mouse jejunum and colon, results in short-latency changes to neurally-dependent enteric reflexes (Frontiers in Neuroscience, in press). However, it remains to be determined whether antibiotics influence neural communication pathways to the brain. Therefore, our goal was to identify antibiotic-induced shifts to vagal spike trains recorded from the jejunal mesenteric nerve bundle. Since clinical administration of antibiotics has been associated with central nervous system excitation and convulsions, we hypothesize that antibiotics may increase the discharge activity of vagal sensory afferents.
**Aims:** To determine whether acute exposure of the gastrointestinal lumen to antibiotics modulate action potential discharge rates in vagal afferent fibres.
**Methods:** Distal jejunal segments with attached mesenteric tissue were excised from adult male Swiss Webster mice and carefully pinned out in a recording dish. The mesenteric nerve bundle was isolated by dissection under a stereomicroscope and sucked into a glass pipette attached to a patch-clamp electrode holder (CV-7B; Molecular Devices, Sunnyvale, CA). Extracellular multi-unit neuronal activity was recorded using a Multi-Clamp 700B amplifier and Digidata 1440A signal converter (Molecular Devices) while gut lumen was perfused with control Krebs solution (containing 3μM nicardipine to prevent muscle contractions) followed by the same Krebs solution with 3 mM penicillin V. Mesenteric nerve response to CCK identified single-unit vagal activity. Paired comparisons were made for before and after treatment recordings. Differences were considered significant if $p < 0.05$.
**Results:** Preliminary data show that 3 mM penicillin V significantly increased constitutive vagal firing rate by 76% (1.4 ±0.26 to 2.1±0.24 Hz, n=15(2)) within minutes of application.
**Conclusions:** We have demonstrated antibiotic-mediated increases in intrinsic vagal afferent activity. Further in vivo studies are needed to determine whether such increases in vagal firing frequency produce changes in brain neurochemistry and behavior.

**Funding Agencies:** Natural Sciences and Engineering Council of Canada Discovery Grant (2014-05517), and the Canadian-Israel Health Initiative jointly funded by the Canadian Institutes of Health Research, the Israel Science Foundation, the International Development Research Centre, Canada and the Azrieli Foundation (267429)

A302

**INAPPROPRIATE REFERRALS FOR VIDEO FLUOROSCOPIC SWALLOWING STUDIES; DEFINING THE SCOPE OF THE PROBLEM**

S. Canning[1], s. sedore[1], W.G. Paterson[2]

1. Queen's University, Kingston, ON, Canada; 2. Medicine (Gastroenterology), Queens Univ, Kingston, ON, Canada

**Background:** The first step in assessment of dysphagia is determining if it is oropharyngeal or esophageal in origin. Over half of patients with esophageal dysphagia will relate the sensation of food sticking to the cervical area. The timing of the dysphagia and associated symptoms are useful in differentiating between oropharyngeal and esophageal dysphagia with proximal referral. Unfortunately, many physicians are unaware that esophageal dysphagia is commonly sensed in the cervical area and this can lead to inappropriate referrals for videofluoroscopic swallowing studies (VFSS) by Speech Language Pathology (SLP). In our institution, a number of patients referred are found to have predominantly esophageal type dysphagia. This has contributed to long wait times for an SLP assessment and a delay in diagnosis of patients with esophageal dysphagia. The full scope of the problem remains unclear.
**Aims:** To identify the number of patients inappropriately referred for VFSS.
**Methods:** We have created a database of the VFSS studies performed by the SLP department in 2016. This was used to extract the reports of all VFSS studies and identify the patients who had normal or minimally abnormal oropharyngeal swallowing but significant abnormalities in esophageal transit. The charts of all patients referred between January 1st, 2016 and June 30th, 2016 were reviewed.
**Results:** A total of 165 referrals for VFSS were made between January 1st-June 30th, 2016. Of those, only 110 patients underwent VFSS assessment. The remainder were cancelled or not performed for reasons unavailable in the chart review. Of the 110 patients who underwent VFSS, 12 did not have results available on the electronic medical record. The remaining 98 charts for which the VFSS results were available, were analyzed. Oropharyngeal dysphagia was identified as the etiology in 70% of the patients. In 12% there was comment of mild oropharyngeal impairments with evidence of impaired esophageal transit and in 10% of cases there was normal oropharyngeal but evidence of esophageal dysfunction. 5% of patients had normal oropharyngeal dysphagia with no remarks regarding the presence of esophageal function. These studies resulted in referral to a gastroenterologist in our institution in 9% of cases. It was also noted that 16% of cases with oropharyngeal dysphagia had been previously

seen by gastroenterology.
**Conclusions:** In our institution, up to 22% of patients undergong VFSS assessments appear to have esophageal dysphagia and nearly 10% of these cases resulted in referrals to gastroenterology. This has likely contributed to the long wait times for orophyarneal dysphagia assessment and delayed appropriate assessment of patients with esophageal dysphagia. Based on this data, we plan to develop a tool to help referring physicians determine whether oropharyngeal or esophageal assessment would be most appropriate.

**Funding Agencies:** None

A303
**GASTROINTESTINAL MANIFESTATIONS IN PATIENTS WITH CONGENITAL MYOTONIC DYSTROPHY**
K. Bortolin, D. Ceballos Saenz, A. Zizzo, C. Campbell

Children's Hospital London Health Sciences Centre, London, ON, Canada

**Background:** Myotonic Dystrophy type 1 is an autosomal dominant, multisystem disease characterized by muscle weakness and myotonia. Phenotypes include congenital, childhood and classic adult onset. Congenital Myotonic Dystrophy (CDM) is the most severe occurring in neonates, characterized by severe hypotonia, mechanical respiratory failure, oropharyngeal and gastrointestinal (GI) dysmotility. Cognitive impairment and cardiac arrhythmias may develop in childhood. GI dysfunction is a common feature of the disease at all ages however manifestations have not been well characterized in pediatric patients.
**Aims:** To characterize GI manifestations in patients with CDM during infancy and childhood including growth, feeding intervention and dysmotility.
**Methods:** A multi-centre cohort of patients ages 0-13 years old with CDM was used. It was made of 2 separate prospective cohorts: A) A national active surveillance program sample, (Canadian Pediatric Surveillance Program) from 03/2005-02/2010, focusing on the burden of illness in patients with CDM from birth to 5 years old and B) an ongoing two-centre study (University of Utah and University of Western Ontario) focusing on clinical factors contributing to morbidity and mortality of patients 0-13 years old.
**Results:** A total of 88 patients were enrolled from 2 cohorts.

Cohort A: 20/38 were female. Polyhydramnios was the main complication in pregnancy 17 (45%). Term birth occurred in 23 (61%) and 22 (58%) had a normal birth weight. Feeding support was required for more than 14 days in 28 (74%); 27 (71%) via nasogastric tube (NGT), 10 (26%) via parenteral nutrition. GI complications were swallowing disorders in 28 (74%) and gastroesophageal reflux (GER) 6 (16%).

Cohort B: 23/50 were female. Baseline median age was 6 years old (6-9). Thirteen (26%) required feeding intervention; 15 (30%) used a NGT, 9 (18%) a gastric tube;. GI medications were used for: GER 9 (18%), constipation 11 (22%) and dysmotility 3 (6%);. Growth parameters included weight and height measurements. The median BMI percentile was 16.4 kg/m$^2$ (14.8-18.3). BMI was < 17 in 30 (60%) patients.
**Conclusions:** CDM is a multi-system disease presenting in neonates and manifesting in childhood with significant GI concerns including feeding intolerance and intestinal dysmotility. Few studies have focused specifically on the GI manifestations in the neonatal and early childhood period.

Future studies characterizing GI disease in these patients should specify the location of the gut dysmotility, results of diagnostic testing confirming these abnormalities, and interventions used to treat patients.

**Funding Agencies:** None

A304
**A CASE REPORT ILLUSTRATING THE NATURAL PROGRESSION OF TYPE 3 TO TYPE 2 ACHALASIA**
A. Ma[2], L.W. Liu[1]

1. Medicine, University Health Network, Toronto, ON, Canada; 2. Gastroenterology, University of Toronto, Toronto, ON, Canada

**Background:** Achalasia is characterized by the loss of esophageal peristalsis and impaired relaxation of the lower esophageal sphincter. The pathophysiology of this disease is thought to be related to the progressive loss of nitrergic inhibitory innervation in the esophagus. This hypothesis is supported by histological studies in patients diagnosed with achalasia, in whom there is a decrease of neurons containing nitric oxide synthase and interstitial cells of Cajal, a unit that likely modulates nitrergic nerve response. With the advent of high resolution esophageal manometry study (EMS) and subsequent increase in diagnostic precision, achalasia is now readily subdivided into types 1, 2 and 3. Given that the normal physiology of esophageal peristalsis and LES relaxation is dependent on nitrergic innervation, it has been hypothesized that achalasia naturally progresses from spastic type 3, to pan-pressurization seen in type 2 and finally to loss of esophageal pressurization in advanced type 1 achalasia. To date, there is no demonstrable longitudinal data supporting this hypothesis of disease progression.
**Aims:** The aim of this case report is to describe novel observations that support the hypothesis of achalasia progression.
**Methods:** We identified and reviewed the high resolution esophageal manometry studies of a patient who demonstrated a change in achalasia subtypes.
**Results:** We report a case of a previously healthy 60-year-old male who presented with dysphagia and was later diagnosed with type 3 achalasia by high resolution EMS (Figure 1a). He underwent two pneumatic dilatations without any significant clinical


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improvement of his dysphagia. Two years later, a repeat EMS demonstrated type 2 achalasia (Figure 1b).
**Conclusions:** This is the first longitudinal clinical case that demonstrates the progression from type 3 to type 2 achalasia. This novel case observation strengthens our current understanding of achalasia, which involves loss of nitrergic inhibitory nerves, with progression from spastic type 3 esophageal aperistalsis to pan-esophageal type 2 pressurization.

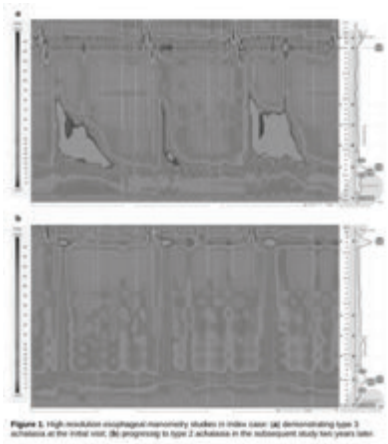

Figure 1

**Funding Agencies:** None

A305
**ERYTHROMYCIN AND RELATED MACROLIDES FOR GASTROPARESIS**
T. Wijeratne[1], P. Tan[1], F. Jowhari[2], A. Patel[2], N. Wijeratne[1], W.G. Paterson[3]

1. Queen's University, Kingston, ON, Canada; 2. Gastroenterology, Queen's University, Ottawa, ON, Canada; 3. Medicine (Gastroenterology), Queens Univ, Kingston, ON, Canada

**Background:** Gastroparesis is a chronic functional gastrointestinal disorder with considerable morbidity, caused by the failure of the stomach to pump its contents in the absence of a mechanical obstruction, and characterized by symptoms related to impaired gastric emptying. Erythromycin is a macrolide antibiotic that is known to have motilin receptor agonist activity. Having an effect similar to that of motilin, erythromycin has been shown to raise the amplitude of antral peristalsis and initiate premature migrating motor complex phase III activity, thereby stimulating gastric emptying.
**Aims:** To evaluate the safety and effectiveness of erythromycin or its derivatives in reducing symptoms and improving mechanical gastric emptying in adults diagnosed with gastroparesis.
**Methods:** Our search included Medline and EMBASE databases. Literature in all languages were searched and translated to English. Clinical trials registers including the Cochrane Library, abstracts from major gastroenterology conferences and dissertations were also screened. Randomized controlled trials, quasi-randomized studies and experimental studies without randomization/allocation concealment were included in which Erythromycin or any other macrolide or its derivative is compared with a placebo in the treatment of gastroparesis. Quality of studies was evaluated using criteria of masking of randomization, masking of intervention, masking of outcome assessment and completeness of follow-up by review authors. Statistical methods included calculation of mean difference, standardized mean difference and odds ratio when appropriate. Ninety-five percent confidence interval was used for estimates of treatment effects.

We are in the process of conducting a detailed analysis of the studies.
**Results:** From our preliminary analysis (21 studies, 717 patients), erythromycin and other derivatives do not significantly improve symptoms related to delayed gastric emptying when compared to a placebo within a 7-28 day period. Also, no significant differences were noted between erythromycin derivatives compared to placebo in reported serious adverse events. The general trend of studies showed significant improvement in mechanical emptying over 1-56 days, when erythromycin or its derivatives were compared to either placebo or metoclopramide.
**Conclusions:** From the available literature it is evident that erythromycin and other derivatives improve gastric emptying. This has potential for exploration in specific subgroups of patients where mechanical improvement would offer improved outcomes (i.e. in patients who are mechanically ventilated to avoid aspiration). The trend in evidence for symptom improvement of gastroparesis does not favour erythromycin or other derivatives although a more formal and unified assessment is warranted.

**Funding Agencies:** None

A306
**SIBO AND ASSOCIATION WITH IBD ACTIVITY.**
R.S. Rai[1], V. Jairath[2], A. Rahman[1]

1. Gastroenterology, Western University, London, ON, Canada; 2. Western University, London, ON, Canada

**Background:** SIBO is when there is an excess number of bacteria in the small intestine or when bacteria normally found in the colon are found in the small intestine. Excessive infiltration by bacteria into the small intestine is usually prevented by a number of mechanisms including an intact ileocaecal valve, gastric and bile acid secretion, antegrade peristalsis, digestion by proteolytic enzymes, IgA production and an intact mucus layer. Patients with Inflammatory Bowel Disease are believed to be at increased risk of developing SIBO. An excess number of bacteria in the small intestine can provoke diarrhoea, cause gas, and lead to malabsorp-

tion of micronutrients. Medical and surgical therapy for IBD is expensive and we may be over-treating patients with symptoms who actually have SIBO. There has only been a handful of published studies looking at the prevalence of SIBO in IBD, with no studies looking at disease activity or other clinical features.
**Aims:** The purpose of this pilot study is to estimate the prevalence of SIBO in IBD and to see if there are any clinical features associated with an increased likelihood of SIBO in CD or UC.
**Methods:** Participants are asked to do a SIBO breath test at St Joseph's Hospital. Two days prior to the test, participants are asked to eat a low fermentable carbohydrate diet, and to fast 10 hours prior. Participants provide a baseline breath sample. Then, after consuming the glucose drink (75g in 200ml water), breath samples are taken every 15 minutes for 2 hours. Concentration of hydrogen and methane in the breath are measured on the Quintron machine. Participants are deemed to have SIBO if they have an increase in either hydrogen or methane of 12 parts per million from the baseline level. We use previous information from the patients chart as well as a history from the patient to obtain data for disease history and severity using MAYO for UC and CDAI for CD. Fresh fecal and urine samples are collected in DNA/RNA free bags and sterile containers and stored at -80C.
**Results:** A total of 13 patients were recruited to participate in this pilot study. 7 patients conducted the SIBO testing, 4 with CD and 3 with UC. Of those tested, 1 was positive for SIBO and 1 had a sustantially elevated baseline hydrogen level. Both of these patients were CD patients with a previous history of small bowel resection. They were 2 of 4 with previous surgeries, the other two having an end iliostomy. These two patients also had lower CDAI scores of the 4 with CD.
**Conclusions:** This study aligns with previous studies and shows that patients with IBD have an increased risk of SIBO. It also shows that previous small bowel resection appears to be a risk factor for SIBO. Disease activity does not seem to play a role, but further studies need to be done. With a look into the stool and urine samples collected on these patients, we hope to be able to identify particular microbiota that may be associated with SIBO in IBD.

**Funding Agencies:** None

## NUTRITION, OBESITY AND AGING

### Poster of Distinction

A307
**NUTRIENTS ACUTELY MODULATE INTESTINAL PERMEABILITY INDEPENDENTLY OF THE ENTERIC NERVOUS SYSTEM**
J. Cavin, W. MacNaughton, K.A. Sharkey

Department of Physiology and Pharmacology, University of Calgary, Calgary, AB, Canada

**Background:** It is well known that diet profoundly affects intestinal physiology, with some diets contributing to a "leaky gut", possibly promoting IBD and metabolic syndrome. Recently, several studies have suggested that the enteric nervous system, composed of neurons and glial cells, could be a potent regulator of intestinal permeability. We hypothesize that nutrients, sensed at the level of the epithelium, could trigger a neuroglial response to regulate intestinal permeability.
**Aims:** We investigated whether nutrients acutely modulate intestinal permeability at the level of the small intestine and if the enteric nervous system plays a role in this effect.
**Methods:** Intact jejunum and Ileum segments from CD1 mice were mounted in Ussing chambers. Transepithelial electrical resistance (TER) and short circuit current (Isc) were recorded for 50 min after stimulation with different nutrients. Two different size probes, 400 Da Fluorescein isothiocyanate (FITC) or 4000 Da FITC-Dextran (FD4), were used as markers of intestinal permeability. Apical glucose, fructose, glutamine (10 mM) or 5% Intralipid® were used as nutrient stimuli. Enteric neurons were either inhibited with tetrodotoxin (TTX, 0.5 µM) or activated with veratridine (10 µM). Enteric gliotransmission was inhibited with the connexin 43 blocker Gap26 (20 µM).
**Results:** The nutrients used in this study were "sensed" by the intestinal epithelium as illustrated by a rapid change in Isc following stimulation (+14, +7, -28 µA/cm$^2$ for glucose, glutamine and Intralipid, respectively, in the jejunum; +132, +42, -14, -56 µA/cm$^2$ for glucose, glutamine, fructose and Intralipid in the ileum). Addition of 5% Intralipid to the luminal side increased TER in both jejunum (+10 Ω/cm$^2$) and Ileum (+10 Ω/cm$^2$). Glutamine triggered a significant ($p<0.05$) increase of the transport of FITC across the intestine (+600% in jejunum and +60% in ileum after 50 minutes). On the other hand the transport of both FITC and FD4 was significantly reduced in the presence of Intralipid (-73% and -27%, respectively, in the jejunum and -74% and -31%, in the ileum). Results were similar when germ free mice were compared to conventionally raised mice. Neither the activation or inhibition of enteric neurons or the inhibition of gliotransmission affected TER or the transport of the fluorescent probes across the mouse intestine. Additionally, the use of the neuronal blocker, TTX, did not reverse the glutamine- or Intralipid-induced alteration of FITC and FD4 transport across the intestine. Blocking the calcium-sensing receptor did not alter the response to glutamine.
**Conclusions:** We have shown glutamine and Intralipid® to be potent regulators of intestinal permeability acting independently of the enteric nervous system, the microbiota, and the calcium-sensing receptor. We are currently investigating the potential endocrine contribution to these effects.

**Funding Agencies:** Human Frontier Science Program, Alberta Innovates


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## Poster of Distinction

A308

**HNF4A ORCHESTRATES PHYSIOLOGICAL REGULATIONS FROM THE INTESTINE THROUGH INCRETINS**

R. Girard, M. Darsigny, C. Jones, F. Maloum, S. St-Jean, J. Coulomb, N. Perreault, M. Plourde, F. Boudreau

Université de Sherbrooke, Sherbrooke, QC, Canada

**Background:** HNF4α is a transcription factor known to regulate the intestinal epithelium homeostasis. Since HNF4α is also involved in nutrient metabolism, we questioned its ability to regulate systemic physiology from its specific alteration in the intestine. Upon a conditional deletion of *HNF4A* from the intestinal epithelium, we evidenced a deficiency for incretins (GIP and GLP-1) that favors glycemic and fat metabolism improvements in a murine model.
**Aims:** To demonstrate how sensitive is the physiology to intestinal changes in expression of the transcription factor HNF4α and enteroendocrine-derived incretins.
**Methods:** Control and HNF4αΔ$^{IEC}$ mice were fed with a chow diet or a high fat diet (HFD: 45% calories from fat) for 14 weeks. Effect of HNF4α on *GIP* transcription was assessed by luciferase-reporter assays. The endocrine system components were measured by ELISA. Physiological parameters were measured using metabolic cage and indirect calorimetry. Gross intestinal absorption of calories was estimated by measuring residual fecal calories using a calorimeter bomb. Glucose (GTT) and Insulin tolerance test (ITT) were performed intraperitoneally with 2 mg/g and 0.75 mUI/g doses, respectively.
**Results:** HNF4αΔ$^{IEC}$ mice fed with either high fat or chow diet displayed lowered circulating GIP and GLP-1 levels as compared to controls. These observations were reminiscent to a reduction of *GIP* and *GCG* gene transcript levels in the intestine. Coincidently, HNF4α was able to regulate transcriptional activity of the *GIP* promoter. Despite incretins deficiency, HNF4αΔ$^{IEC}$ mice harbored similar weight gain, feeding behavior, intestinal calories absorption and most intriguingly, similar GTT as compared to controls. However, ITT resulted in faster blood glucose clearance in HNF4αΔ$^{IEC}$ mice suggesting better insulin sensitivity in this context. Since obesity links insulin resistance and type 2 diabetes, HNF4αΔ$^{IEC}$ and control mice were fed with HFD to study their sensitivity to obesity. Once again, HNF4αΔ$^{IEC}$ mice displayed similar feeding behavior and intestinal calories absorption, but significant reduced weight gains as compared to controls under HFD, indicative of a higher energy expenditure. In parallel, fat metabolism was investigated using indirect calorimetry and showed a higher lipid consumption profile occurring in HNF4αΔ$^{IEC}$ mice during the dark cycle.
**Conclusions:** These data are the first to link HNF4α as a common transcriptional regulator for incretins. Incretins downregulation following the intestinal epithelial loss of HNF4α improved native insulin sensitivity under chow diet and improved fat metabolism under HFD. Therefore, our study emphasizes on the key role of the intestinal epithelium and enteroendocrine function in nutrients metabolism following absorption and their impact on whole physiology.

**Funding Agencies:** CIHR

A309

**EFFECT OF MIXED LIPID, ω-3 FISH OIL AND ω-6 SOYBEAN OIL PARENTERAL LIPID EMULSIONS ON LIVER DISEASE, HEPATIC LIPID AND PHYTOSTEROL COMPOSITION IN NEONATAL PIGLETS.**

D. Migliarese Isaac[1], A. Alzaben[4], V.C. Mazurak[4], J. Yap[1], P. Wizzard[1], P.N. Nation[5], Y. Zhao[4], J.M. Curtis[4], C. Sergi[5], P. Wales[3], D.R. Mager[4], J. Turner[2]

1. Division of Pediatric Gastroenterology and Nutrition, Department of Pediatrics, University of Alberta, Edmonton, AB, Canada; 2. Stollery Children's Hospital, Edmonton, AB, Canada; 3. The Hospital for Sick Children, Toronto, ON, Canada; 4. Department of Agricultural Food and Nutritional Science, University of Alberta, Edmonton, AB, Canada; 5. Department of Laboratory Medicine & Pathology, University of Alberta, Edmonton, AB, Canada

**Background:** Determining the optimal lipid emulsion in parenteral nutrition (PN) for pediatric intestinal failure (PIF) patients remains an important clinical question given the risk of PN associated liver disease (PNALD).
**Aims:** Using a neonatal piglet model, this study compared mixed lipid (ML; ω-6:ω-3 fatty acid [FA] 2.5:1), ω-3 fish oil (FO; ω-6:ω-3 FA 1:8), and ω-6 soybean oil (SO; ω-6:ω-3 FA 7:1) emulsions for the following markers of PNALD: i) hepatic histology, neutral lipid (NL), FA and phytosterol (PS) composition, and ii) biochemical cholestasis.
**Methods:** Neonatal piglets received iso-nitrogenous PN with variation in the dose (5=5g/kg/d or 10=10g/kg/d) and type of lipid provided: SO5 (n=5), SO10 (n=5), FO5 (n=5), and ML10 (n=5). Biochemical evidence of cholestasis was assessed by measuring bile flow, γ-glutamyl transpeptidase (GGT), bile acids (BA) and total bilirubin (TB). Liver tissue was assessed on day 14 of PN for: histology, NL accumulation using Oil Red O (ORO) staining, hepatic FA composition in triglyceride (TG) fraction, and PS composition. Data were expressed as mean ± standard deviation. Chi-square was used for categorical variables, and one-way Anova for continuous variables.
**Results:** TB was significantly higher ($p<0.02$) and bile flow significantly lower ($p<0.001$) in SO groups versus (vs) FO5 and ML10. Serum BA were 3-fold higher in SO vs FO5 and ML10 piglets ($p=0.04$). There were no differences in GGT ($p=0.19$), NL accumulation ($p=0.3$), or overall liver histology scores ($p=0.16$) between groups; however, only SO piglets showed cholestasis on histology (SO10 n=2, SO5 n=1). Total FA in the TG fraction was higher in SO vs FO5 and ML10 groups ($p<0.03$), with SO10 levels 4-fold greater than FO5 ($p=0.02$). Eicosapentaenoic acid and docosahexaenoic acid were higher in FO5 and ML10 vs SO piglets

(p<0.001), with no significant differences between ML10 and FO5. The ω-6/ω-3 FA ratio was significantly higher in SO groups (SO5 9.0 ± 0.7, SO10 8.7 ± 1.8, p<0.0001), but not different between ML10 and FO5 (1.5 ± 0.3 vs 0.4 ± 0.3, p=0.32). FO5 and ML10 were markedly lower in campesterol than SO (p<0.0001). Stigmasterol and β-sitosterol were not detected in FO5, but were significantly higher in SO than ML10 (p<0.0001). β-sitostanol was only detected in the SO10 group.
**Conclusions:** ML and FO lipid emulsions were associated with reduced cholestasis and lower hepatic lipid and PS accumulation. Alterations in hepatic lipid and PS composition in piglets given SO emulsions may contribute to PNALD. Considering typical infant diets, ML provided a more balanced ω-6/ω-3 hepatic FA composition than SO and FO. These results provide guidance on lipid selection for PIF patients receiving PN.

**Funding Agencies:** CIHRLiver Foundation Research Grant; Industry Partner Fresenius Kabi (provision of parenteral nutrition); and Saudi Cultural Bureau, Ministry of Education, Saudi Arabia (personal training funding for Abeer Alzaben).

A310
**DAILY ADMINISTRATION OF *LACTOBACILLUS PLANTARUM* IMPROVES MOUSE JUVENILE GROWTH KINETICS BY SUSTAINING SOMATOTROPIC AXIS ACTIVITY UPON UNDERNUTRITION.**
M. Schwarzer[2], P. Poinsot[1], A. Lambert[2], S. Goeffroy[2], N. Peretti[3], F. Leulier[2]

1. Gastro-entorology paediatrics, CHU Montréal, Hopital Sainte Justine, Montreal, QC, Canada; 2. Institut Génomique Fonctionnelle de Lyon, Lyon, France; 3. CarMen Laboratory, Lyon, France

**Background:** Chronic undernutrition, a condition currently affecting more than 17 millions of children under five years of age, has severe long-term consequences including stunting. Epidemiologic studies have emphasized that undernutrition cannot be ascribed to food insecurity alone and gut microbiota has been shown to play an active role in disease aetiology. In mammals, post-natal growth is controlled by the activity of the somatotropic axis. Undernutrition leads to a decrease of the Insulin like Growth Factor 1 (IGF-1) and a state of Growth Hormon (GH) resistance.
**Aims:** Previously we have shown the capacity of selected *Lactobacillus plantarum* strain to maintain growth in infant mono-colonized mice during chronic undernutrition. Here we show that L. plantarum retains its growth promoting capabilities also in a conventional mouse model.
**Methods:** C57BL6 male mice were weaned at 21 days and bred on a standard or an experimental (isocaloric, hypoprotidic and hypolipidic) diet until young adulthood. One group of mice on experimental diet received an *Lp*$^{WJL}$ oral supplementation (2*10^8 CFU/day; 5 days per week) and the other group received placebo. Length and weight were measured weekly. Mice were sacrificed at day 56 to study the impact of the *Lp*$^{WJL}$ oral supplementation on IGF-1 levels and organ growth. Somatotropic axis activity was tested at Day 28 by injecting the mice with GH and measured by the STAT5 phosphorylation level.
**Results:** At D56, mice fed with the experimental diet were smaller than the standard diet group (7.7 vs 8.9 cm; p< 0.01). Undernourished mice had a lower hepatic level of IGF-1 (113±39 vs 174±35 pg/mg tissues; p<0.01) and a lower plasmatic level of IGF-1 (150±50 vs 388±103 ng/mL; p< 0.01) compared with the standard diet group. Body length of mice fed experimental diet was longer in *Lp*$^{WJL}$ –supplemented group compared to the placebo supplementation (8.02±0.19 vs 7.73±0.16 cm; p<0.0001). *Lp*$^{WJL}$-treated mice showed 23% increase in daily growth gain compared to placebo without the change in the mean daily food intake. In the *Lp*$^{WJL}$ group, mice had a higher hepatic IGF-1 level (108±12.5 vs 59.8±18.5 pg/mg tissues; p< 0.0001) and a higher plasmatic IGF-1 level (209±51 vs 148±32 ng/mL; p< 0.001) compared to the placebo group. At day 28, mice exposed to *Lp*$^{WJL}$ during starvation process showed an increase of the sensibility of the hepatic GH receptor to GH according to the STAT5 phosphorylation level.
**Conclusions:** Oral supplementation by *Lp*$^{WJL}$ alleviates the GH resistance and improves juvenile growth of conventional infant mice upon undernutrition.

**Funding Agencies:** None

A311
**LEPTIN'S ANOREXIGENIC EFFECTS ARE SWITCHED IN DIET INDUCED OBESITY**
Y. YU[2], S. Park[1], M.J. Beyak[1]

1. Queen's University, Kingston, ON, Canada; 2. GIDRU, Queen's University, Kingston, ON, Canada

**Background:** Leptin is well known as a satiety hormone to regulate energy balance by inhibiting hunger. However, an inability for leptin to act normally occurs in obesity, a phenomenon named leptin resistance. Considerable attention has focused on leptin resistance in the hypothalamus. However there has been relatively little attention on vagal afferents, which transmit satiety signals to the CNS. Interestingly, selective knockout of leptin receptor in vagal afferent neurons prevents high fat diet-induced weight gain (de Lartigue, 2014), whereas underlying mechanisms remain unknown.
**Aims:** Thus, this study aimed to examine the effects of leptin on satiety signaling via vagal afferents.

**Methods:** All experiments were performed on male C57/BL6 mice in accordance with the guideline of Canadian Council for Animal Care. Obese and control mice were fed on a high (HFF, 60% calories from fat) and low (LFF, 10%) fat diet respectively. Membrane excitability of nodose neurons was assessed by whole cell patch clamp. Afferent discharge was recorded from

jejunal mesenteric nerves.

**Results:** Incubation of serum from HFF mice overnight resulted in lower excitability of nodose neurons from normal mice compared to LFF mice serum, evidenced by increased rheobase (78.6±16.1 vs. 32.7±5.1 pA, P<0.01, N≥14, unpaired t-test) and reduced number of action potentials at twice rheobase (1.5±0.2 vs. 4.0±0.6 P<0.001, N=14, unpaired t-test). These differences were absent in nodose neurons from leptin receptor deficient mice. Leptin's inhibitory effect on nodose neuron excitability was blocked by zoledronic acid, an inhibitor of suppressor of cytokine signalling-3 (SOCS3). Effect of leptin on afferent signaling induced by CCK was examined in LFF and HFF mouse jejunum. Co-application of leptin and CCK moderately potentiated afferent response to CCK in LFF mice (P<0.05, one-way ANOVA, N=7), whereas leptin inhibited CCK signaling dose-dependently in HFF mice (P<0.01, one-way ANOVA, N=7). The inhibitory effects of leptin on CCK signaling was blocked by zoledronic acid (P<0.05, Bonferroni test, N=7).

**Conclusions:** These data suggest that leptin's anorexigenic actions were switched to orexigenic in obesity, and this will provide new strategies for obesity treatment.

**Funding Agencies:** CIHR

A312

**POST MARKET USE OF TEDUGLUTIDE IN CANADA IN PATIENTS WITH SHORT BOWEL SYNDROME ON HOME PARENTERAL NUTRITION: THE REAL WORLD SETTING**

J. Noelting[5], B. Jurewitsch[3], L. Gramlich[1], D. Duerksen[7], M. Raman[6], D. Armstrong[2], M.L. Ponta[5], O. Saqui[5], C.K. Arca-Juico[5], P. Kim[5], B. Stewart[5], J. Allard[4]

1. Alberta Health Sciences, Edmonton, AB, Canada; 2. McMaster University, Hamilton, ON, Canada; 3. St. Michael's Hospital, Toronto, ON, Canada; 4. Toronto General Hospital, Toronto, ON, Canada; 5. Gastroenterology, University Health Network, Toronto, ON, Canada; 6. University of Calgary, Calgary, AB, Canada; 7. University of Manitoba, Winnipeg, MB, Canada

**Background:** Patients with intestinal failure due to short bowel syndrome (SBS) are dependent on parenteral support (PS). Teduglutide, a glucagon-like peptide-2 (GLP-2) agonist, can reduce PS requirement by enhancing absorptive capacity of the remaining intestine. As it was only approved for use in Canada in October 2015 and it is indicated for a very select group of patients, not much is known on real-world experience using this drug in Canada.
**Aims:** The aim of this study was to describe the current experience in Canada in using teduglutide.
**Methods:** Data was obtained: 1) from a brief survey on the use of teduglutide, distributed to the HPN programs participating in the Canadian HPN Registry and; 2) from the home parenteral nutrition (HPN) registry itself, where patient data are entered prospectively by HPN teams across Canada. If teduglutide was initiated prior to the patient's baseline entry in the Registry, data was also collected retrospectively.
**Results:** Fifty two patients from 5 provinces were referred by their respective HPN programs for funding of teduglutide. Of these, 21 patients are currently on the drug while 4 had the drug discontinued and 11 were not eligible due to lack of funding. The remaining patients are being assessed or awaiting initiation of the drug. Of those on teduglutide, 18 patients (7 male, 11 female) were entered in the HPN Registry, and, of those who discontinued, 2 (1 male, 1 female) were also entered in the Registry (total: 20). Patients in the Registry are between 26 and 70 years old (mean age 51), with 20cm to 225cm of small bowel and have been on PS from 1 to 29 years (median 5) prior to initiation of the drug. Since initiation of tedulgutide, six patients have discontinued HPN, although 4 of them still receive IV hydration. Of those on teduglutide for 6 and 12 months, PS was reduced by an average of 29% and 43% based on volume and 32% and 34% based on calories, respectively. Fifty-three percent and 82% of patients were able to reduce PS volume by at least 20% after 6 and 12 months of therapy with teduglutide, respectively. The drug was discontinued in two participants due to increased fistula output in one person with uncontrolled Crohn's disease and increased carcinoembryonic antigen in the other.
**Conclusions:** In patients with intestinal failure due to SBS, teduglutide therapy results in reduced dependence on PS. Given the long term complications associated with PS and the limitations of alternative therapies such as intestinal transplantation, teduglutide is a promising new treatment that has the potential to improve the prognosis of this condition. Further, long term studies are needed to determine the sustainability of this therapy and its side effects.

**Funding Agencies:** Ontario Medical Supply, Baxter

A313

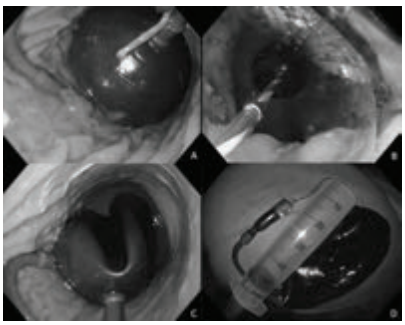
**INTRAGASTRIC BALLOON REMOVAL: PUNCTURE, DILATE, DEFLATE**

V. Falk[3], J.K. Eccles[1], S. Karmali[4], R. Sultanian[2]

1. Division of Gastroenterology, University of Alberta , Edmonton, AB, Canada; 2. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Gastroenterology, University of Alberta, Stony Plain, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada

**Background:** The growing obesity epidemic has led to the development of a number of endoscopic bariatric weight-loss procedures, including intragastric balloons (IGB). The US FDA-approved IGB devices are the Orbera (Apollo Endosurgery), ReShape (ReShape Medical Inc), and Obalon (Obalon Therapeutics Inc), whilst two other internationally recognized IGB systems are the Spatz (Spatz Medical) and the Elipse (Allurion Technologies). Each device is made of silicone and filled with 0.9% saline solution to a total volume between 400-950cc. As per FDA approval, the IGB should be removed after 6

months. The most common side effects are nausea/vomiting, abdominal pain, and reflux, requiring early IGB removal in up to 9% of patients. Other complications include balloon deflation± migration, gastric ulcers, perforation, and pancreatitis. The mortality rate is 0.05%. Adverse events specific to removal of IGBs include aspiration pneumonia, esophageal tears and perforation. Although IGBs were CDFA-approved in Canada in the early 2000's, few endoscopists currently practice this procedure. Increasing international use of the IGB combined with the rising incidence of Canadians traveling abroad for bariatric procedures means that Canadian endoscopists will be faced with managing these devices and their complications.
**Aims:** We describe the case of a patient who presented with complications due to IGB and detail our endoscopic approach to its safe removal.
**Methods:** A 51-year-old male presented 14 months after IGB placement in Saudi Arabia with intractable reflux, nausea and vomitting. The balloon manufacturer was unknown. At ultrasonography, the IGB volume was 550cc. All laboratory investigations were normal.
**Results:** The gastroscopy was performed under general anesthesia with endotracheal intubation. The IGB was identified and no significant complications noted within the stomach or esophagus. After an esophageal overtube was inserted, the wall of the IGB was punctured with an injector needle, but with poor drainage of fluid with aspiration alone. The puncture site allowed introduction of a JAG 0.035 wire into the balloon with subsequent dilatation of the opening by CRE balloon to 15mm and successful evacuation of fluid. Once decompressed, the balloon was grasped via snare and removed through the overtube. Repeat gastroscopy showed unharmed gastric and esophageal mucosa. The IGB was subsequently identified as a non-FDA/CDFA approved Spatz adjustable balloon (Image 1).
**Conclusions:** The increased incidence of endoscopic bariatric interventions means that endoscopists will need to become familiar with management of IGBs and their complications. We recommend that IGBs be removed under general anesthesia using an esophageal overtube for safe extraction by following a “puncture, dilate and deflate" technique as described with an endoscopic assessment of gastric and esophageal mucosa post removal.



A) Inital endoscopic appearance
B) IGB puncture/dilation
C) Deflated IGB
D) Extracted IGB

**Funding Agencies:** CAG, None

A314
**A CHARACTERIZATION OF NUTRITION STATUS AND GUT MICROBIOTA IN OBSESSIVE-COMPULSIVE DISORDER (OCD) IN YOUTH**
E.C. Macphail, R. Reimer, P.D. Arnold

University of Calgary, Calgary, AB, Canada

**Background:** Obsessive compulsive disorder (OCD) affects ~5.2-10.4 million North Americans. Most commonly diagnosed in childhood and adolescence, it can result in years of struggle and has been listed among the top ten causes of disability by the World Health Organization.

Zinc is physiologically essential and integral for optimal health; however, zinc deficiency is quite prevalent. Not only are youth (particularly females) more likely to have zinc deficiency risk factors, but they are also in a life stage where zinc deficiency is more problematic, based on its importance developmentally. Neural zinc levels have implications for neuroplasticity (a factor in cognitive flexibility, a feature of executive function that is impaired in OCD). Additionally, zinc supplementation has been demonstrated to improve mental health, and in animal models, zinc deficiency has been shown to alter the gut microbiota.

Gut microbiota profiles have been linked to anxiety and depression (potentially due to interactions with the enteric nervous system). Given the high co-occurrence rates between these and OCD, as well as the fact that patients with OCD have been reported to have higher rates of gastrointestinal distress than controls, an investigation into nutrition and gut microbiota profiles in youth with OCD is a logical step.
**Aims:** The aim of this study was to assess the role of zinc and of the gut microbiota in OCD in youth, and to determine any differences between youth with and without OCD.

It was hypothesized that higher zinc intake and status, as well as greater gut microbial diversity, would be associated with greater cognitive flexibility and with decreased OCD symptom severity. It was also thought that youth with OCD would be more likely to have non-optimal nutrient intake/levels and dysregulation of gut microbiota than youth without OCD.
**Methods:** Zinc status analysis was conducted via 3-day dietary record, serum levels, and hair levels. Berg's Card-Sorting Test and Trail-Making Tests A&B were used to assess cognitive flexibility; clinical interview and self-report scales measured anxiety, depression, and OCD symptoms; and gut microbiota was quantified


To view enlarged images and tables, please refer to Abstract Library.

via stool samples analyzed using qPCR and 16S sequencing. Data were compared for youth with OCD versus youth without OCD.
**Results:** Commonalities among dietary intake patterns and nutrient status for youth with OCD, as well as their gut microbiota profiles in comparison to youth without OCD, will be discussed.
**Conclusions:** Nutritional status' impact on mental health is underexplored, and no literature to date combines analysis of zinc, cognitive flexibility, and gut microbiota, particularly in OCD. This study's characterization of nutrient intake/status and gut microbiota has the potential to aid development of alternative therapies for youth with OCD.

**Funding Agencies:** Ferring Canada, Branch-Out Neurological Foundation, Mathison Centre for Mental Health Research & Education

A315
**EFFECT OF CONTINUOUS ADMINISTRATION OF FLAXSEED AND FLAXSEED COMPONENTS ON THE GUT MICROBIOTA IN FEMALE MICE**
Z. Lin[1], A. Taibi[1], D. Lepp[2], K.A. Power[3], L.U. Thompson[1], E. Comelli[1]

1. Nutritional Science, University of Toronto, Markham, ON, Canada; 2. Agriculture and Agri-Food Canada, Guelph, ON, Canada; 3. University of Ottawa, Ottawa, ON, Canada

**Background:** Flaxseed (FS) contains FS oil (FSO), α-linolenic acid (ALA); lignan, secoisolariciresinol diglucoside (SDG); and 30% dietary fiber. FS and SDG have previously been shown to decrease early markers of colon cancer such as reducing epithelial cell proliferation and number of aberrant crypts and aberrant crypt foci. SDG and fiber are bio-transformed by the gut microbiota into enterolignans and short-chain fatty acid, respectively. These are at least partially responsible for FS beneficial effects. However, a comprehensive analysis of the effects of FS and its components on the gut microbiota is lacking.
**Aims:** To investigate the effect of continuous administration of FS or FS components, FSO and SDG, on the gut microbiota in C57BL/6 mice.
**Methods:** Fifty-six female C57BL/6 mice 4-5 weeks of age were randomly assigned into one of the four diet groups and fed for 3 weeks: i) Basal AIN-93G, ii) 10% FS, iii) 37% FSO or iv) 1.48% SDG. The experimental diets were supplemented with their respective components, FSO and SDG, at the level present in the FS and formulated to ensure that diets were isocaloric. After 21 days of intervention, the mice were sacrificed and feces and caecum contents (CC) were collected. 16S rRNA gene sequencing was performed on DNA extracted from CC (day 21) or feces collected at the baseline (day 0) or day 21 on a MiSeq instrument. UniFrac distances were calculated and β-diversity was assessed by PERMANOVA and principal coordinate analysis (PCoA) with QIIME.
**Results:** In the longitudinal analysis, PCoA of unweighted UniFrac distance matrixes resulted in 2 predominant clusters associated with the FS and BD/FSO/SDG diets in fecal samples. In line with this, at sacrifice samples clustered based on dietary treatment but FSO could not be distinguished from BD in both caecum and feces. Taxa known to be involved in enterolignans production were identified in the FS group.
**Conclusions:** FS and SDG diet modify gut microbiota diversity in a different manner. Separation between FS and SDG clusters suggest that effect of FS is due not only to its SDG content but also to its fiber. This is significant as it suggests that FS and FS components act in both a differential and a complementary manner to potentiate positive health outcomes in the colon.

**Funding Agencies:** NSERC (LUT, EMC), NSERC Canada Graduate Scholarship for Master's to ZL. Lawson Family Chair in Microbiome Nutrition Research at the University of Toronto (EMC).

A316
**CANADIAN CANCER PATIENTS ON HOME TOTAL PARENTERAL NUTRITION (HTPN): A 10-YEAR ASSESSMENT**
V. Tran[4], B. Bielawska[5], A. teterina[7], M. Raman[3], S. Whittaker[6], D. Armstrong[2], L. Gramlich[1], J. Allard[5]

1. Community Services Centre, Edmonton, AB, Canada; 2. McMaster University, Hamilton, ON, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. Faculty of Medicine, University of Toronto, Toronto, ON, Canada; 5. University Health Network, Toronto, ON, Canada; 6. Providence Health Care, Vancouver, BC, Canada; 7. University Health Network, Toronto, ON, Canada

**Background:** For cancer patients with intestinal failure, malnutrition is a common and recognized predictor of poor prognosis. While home total parenteral nutrition (HTPN) may improve nutritional status, quality of life, and potentially survival, its use in this population varies considerably across different countries. In Canada, the number of cancer patients receiving HTPN has increased significantly over the last decade. However, there seems to be a disparity among provinces regarding access and indication for HTPN.
**Aims:** The objectives of the present study were to characterize the population of cancer patients on HTPN across Canada and assess clinical outcomes using data from the Canadian HTPN Registry.
**Methods:** This retrospective analysis included all cancer patients enrolled in the Canadian HTPN Registry from 2005 to 2016. Patient demographics, nutritional status, Karnofsky Performance Status (KPS), tumour type, and HTPN duration were described at both national and provincial levels. Kaplan-Meier survival curves were analyzed by tumour type and province with the log-rank test.
**Results:** There were 164 cancer patients on HTPN (107 females, 57 males; mean age 54.9 ± 13.0), which comprised 22.6% of the total HTPN population. The

majority of cancer patients on HTPN were from Ontario (54.3%) and Alberta (41.5%). The most common tumour categories were gastrointestinal (54.2%) and gynecological (31.8%). Patients on HTPN for ≥ 3 months had a higher baseline KPS (65 vs. 50; $p < 0.05$) and albumin (33.5 vs. 25.0 mmol/L; $p < 0.05$) compared to those on HTPN for < 3 months. There were no differences in survival based on location of tumour ($p = 0.887$), but patients in Ontario had better median survival compared to those in Alberta (11.3 vs. 7.1 months; $p = 0.037$). Ontario had a significantly higher proportion of cancer patients with short bowel syndrome (32.5% vs. 8.8%; $p < 0.001$), mucosal defects (7.9% vs 0%; $p = 0.019$), and/or surgical complications (21.8% vs. 4.4%; $p < 0.001$) relative to Alberta.
**Conclusions:** This is the first study to assess HTPN use in cancer patients across Canada. Cancer is now a relatively frequent indication for HTPN but primarily in Ontario and Alberta, suggesting potential access issues in other provinces. Patients with greater baseline functional and nutritional status received HTPN for longer periods of time, which may indicate better prognosis. The greater survival in Ontario may be due to more selective HTPN indications. This study serves as a first step in optimizing the management of the growing population of cancer patients on HTPN.

**Funding Agencies:** None

A317
**A SYSTEMATIC REVIEW OF NUTRITION SCREENING, NUTRITION ASSESSMENT AND CLINICAL OUTCOMES IN INFLAMMATORY BOWEL DISEASE**
S. Li[1], M. Ney[3], T. Eslamparast[2], M. Raman[3], P. Tandon[2]

1. Department of Internal Medicine, University of Alberta, Edmonton, AB, Canada; 2. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Division of Gastroenterology and Hepatology, University of Calgary, Calgary, AB, Canada

**Background:** Malnutrition is highly prevalent in inflammatory bowel disease (IBD) but is not routinely screened or assessed. Multiple nutrition screening (NST) and assessment tools (NAT) have been developed for general populations, but the ideal tools and their predictive validity for clinical outcomes in IBD remain unclear. We hypothesize this knowledge gap may be a reason why NST and NAT are not routinely utilized in this at risk population.
**Aims:** To provide a review of the evidence in IBD populations:
1. Correlating NST or NAT to clinical outcomes
2. Correlating NST to NAT for diagnosis of malnutrition
**Methods:** We performed a comprehensive search strategy including Medline, CINAHL Plus and PubMed with study selection and quality assessment carried out by two independent reviewers. A third reviewer resolved disagreements.

Inclusion criteria: Diagnosis of IBD; Age ≧18 years; studies correlating NST to NAT or correlating NST/NAT to clinical outcomes; RCT/case-control/cohort/cross-sectional study

Exclusion criteria: Use of BMI or lab values as sole NST/NAT
**Results:** 1052 articles were identified from the initial search. 41 full-texts were reviewed against inclusion/exclusion criteria; 5 studies with a total of 494 patients were analyzed (CD n=447, UC n=47). Reasons for exclusion were: no predictive clinical outcomes (n=22) and no formal screening/assessment method (n=14).

NST included the Nutritional Risk Screening 2002 (NRS-2002, n=1), Malnutrition Universal Screening Tool (MUST, n=1), Nutritional Risk Index (NRI, n=1), and Malnutrition Inflammation Risk Tool (MIRT, n=1). NAT included Body Impedance Analysis (BIA, n=2), Skeletal Muscle Index (SMI, n=1) and Subjective Global Assessment (SGA, n=1).

Four studies assessed correlation of NST or NAT to outcomes and three studies assessed NST to NAT. Two studies demonstrated correlation between NST of MIRT with outcomes (hospitalizations [R=0.398, p=0.003], flares [R=0.299, p=0.03], surgeries [R=0.371, p=0.006], complications [R=0.333, p=0.015]) and low NRI (< 97.5) with poor response to biologics (p=0.037). Two studies found associations between NAT (low SMI, BIA [Increased skeletal muscle percentage]) and surgical complications (OR 9.24 and 0.487 respectively). Three studies demonstrated NST (MUST, NRS-2002, MIRT) correlated with BIA (FFMI), SMI and SGA.
**Conclusions:** There is limited evidence correlating NST, NAT and clinical outcomes in IBD populations. Our review found statistically significant associations between NST/NAT with outcomes, and between NST with NAT, was present in all studies. Despite this, the small number of studies and differences in NST/NAT methods did not allow for further meta-analysis. Further prospective studies are necessary to evaluate the performance of these tools to determine the most effective nutrition screening/assessment algorithm for IBD patients.

**Funding Agencies:** None

A318
**DO IMPROVEMENTS IN METABOLIC SYNDROME POST BARIATRIC CARE ASSOCIATED WITH BETTER ORAL HEALTH?**
M. Alghamdi[1], M. Glogauer[1], T.D. Jackson[2], A. okrainec[2], J.P. Allard[2]

1. University of Toronto, Toronto , ON, Canada; 2. University of Health Network, Toronto, ON, Canada

**Background:** Obesity and diabetes may predispose to periodontal disease (PD) which is a polymicrobial inflammatory disorder destructing periodontium and promoting chronic systemic inflammation. Proposed mechanisms are increased salivary glucose level from hyperglycemia and hyposalivation, with both affecting

the oral microbiome. Bariatric surgery is an effective treatment for obesity with improvements in body weight and insulin sensitivity. Bariatric care protocol also includes a very low calorie diet (VLCD) with Optifast®, used for 2-3 weeks pre-op to facilitate laparoscopic access. VLCD can also reduce weight and blood glucose.
**Aims:** This study aims to determine the effect of the bariatric protocol (pre-bariatric VLCD and bariatric surgery) on oral inflammatory load (OIL), a surrogate marker for PD, and stimulated salivary flow rate (SFR) in obese patients.
**Methods:** Patients were recruited from the Toronto Western Hospital. Sample collection took place at 3 time-points: pre-VLCD, post-VLCD (surgery day) and 1-month post-surgery. A 30-second mouth rinse was collected to determine neutrophils count using hemocytometer. Subjects were asked to chew on a piece of parafilm to determine salivary flow rate. Blood tests were performed to measure fasting insulin, glucose, and HbA1c. Anthropometric measurements including height, weight, and body mass index (BMI) were measured. Results are expressed as mean ± SD.
**Results:** Twenty patients (18 females, 2 male) were recruited of which 4 were diabetic. Mean age of the patients was 50.5 ± 8.6 years, and BMI was 46.4 ± 5.4 kg/m2. The mean VLCD duration was 16.7 ± 3.5 days. At baseline, 3 patients, assessed by OIL, were diagnosed with PD and one patient had SFR < 0.5ml/min. Overall, weight and blood tests significantly improved after VLCD except for HbA1c (BMI $P$ <0.001, Glucose $P$= 0.016, insulin $P$= 0.013, HOMA-IR $P$= 0.016). Additionally, parameters significantly improved 1-month post-surgery compare to baseline (Glucose $P$= 0.004, insulin $P$= 0.008, HOMA-IR $P$= 0.009, HbA1c $P$= 0.001, BMI $P$ <0.001). During the bariatric care protocol, the changes of oral measurements were not statistically significant (OIL $P$= 0.316, SFR $P$= 0.588).
**Conclusions:** These results suggest that both VLCD and bariatric surgery improve glucose metabolism and weight. However, these preliminary results do not suggest that the bariatric care protocol has a significant impact on oral parameters.

**Funding Agencies:** CIHR

A319
**THE MURINE CECAL DEVELOPMENTAL MICRORNA SIGNATURE**
A. Alraefaei, A. Taibi, E. Comelli

Nutritional Sciences, University of Toronto, Toronto, ON, Canada

**Background:** MicroRNAs (miRNAs) play a key role in intestinal gene expression regulation and their dysregulation has been observed in paediatric intestinal pathologies such as necrotizing enterocolitis and inflammatory bowel disease. In this context, miRNAs are being considered as diagnostic and prognostic markers. Though, little is known about the intestinal miRNA signature during postnatal maturation.
**Aims:** To investigate the murine cecal miRNA signature during postnatal maturation
**Methods:** Specific-pathogen-free C57BL/6-Elite male and female mice 6-8 weeks old were housed in sterile conditions. Mice were bred harem-style; at weaning (postnatal day (PND) 21), offspring were caged based on sex and dam. Each litter ($n$=7) was followed longitudinally and offspring were sacrificed at PND 14, 21 and 36 ($n$=1 male per litter and time point). Total RNA was extracted from cecal tissue and used to profile the expression of 578 miRNAs with the nCounter® Mouse V1.5 miRNA Expression Assay (NanoString Technologies, Inc.). Data was analyzed with nSolver™ Analysis Software 3.0 and statistical analysis and hierarchal clustering were completed in R. Target prediction was completed in TargetScan Release 7.1 and miRDB databases.
**Results:** 207 miRNAs were detected in cecal tissue. Of these, 10 miRNAs were significantly differentially expressed over time ($p$<0.05, FDR<0.05) in which 4 miRNAs were overexpressed at both PND 21 and 36 compared to PND 14 (2.0-7.7 fold change) and 6 miRNAs were underexpressed (0.2-0.6 fold change). When comparing PND 36 to PND 21, 2 miRNAs were overexpressed (1.9-16.7 fold change) and 5 miRNAs were underexpressed (0.3-0.6 fold change). Samples clustered according to postnatal age based on the expression profile of these 10 miRNAs. Prediction analysis identified 3,525 genes as potential targets of these miRNAs, including genes involved in the intestinal barrier function and immune system.
**Conclusions:** This study shows that the cecal miRNA signature evolves during early postnatal life with potential implications for intestinal homeostasis. Selected miRNAs may serve as nutritional or pharmacological targets.

**Funding Agencies:** NSERC Discovery grant to EMC. AA is the recipient of a full scholarship from Kuwait University, State of Kuwait. EMC holds the Lawson Family Chair in Microbiome Nutrition Research at the University of Toronto.

A320
**COW MILK PROTEIN ALLERGY - THE GREAT MASQUERADER**
N. Laverdure[2], J. Trebichavsky[2], D. Dal Soglio[4], L. Oligny[2], K. Grzywacz[1], V. Marchand[3]

1. CHU Sainte Justine, Montreal, QC, Canada; 2. CHU Ste Justine, Montreal, QC, Canada; 3. CHU Ste Justine, Montreal, QC, Canada; 4. CHU Ste Justine, Montreal, QC, Canada

**Background:** Cow milk protein allergy is a very common disease, with a prevalence of 2 to 7.5% in the pediatric population. The diagnosis is often made clinically and appears early, usually during the first few months of life. Common clinical presentations include: reflux, atopic dermatitis, failure to thrive, chronic diarrhea, as well as rectal bleeding or enterocolitis.
**Aims:** Severe, life-threatening, presentations are very

rare.The 2 reported cases show that cow milk protein allergy may have a very early and severe presentation and can even mimic some surgical diagnoses.
**Methods:** Case n°1
An 8-day-old formula-fed male infant with no significant personal or family history of atopic disease was transferred to our hospital with bilious vomiting and abundant hematochezia. Small intestinal volvulus was suspected, but laparotomy was normal. In the face of persistent rectal bleeding and severe anemia (Hgb 73g/l), rectal biopsy and upper endoscopy were performed and showed mild colitis and severe gastritis with mucosal desquamation. Biopsies revealed an important infiltration of eosinophilic cells (>100/HPF in the stomach and severe eosinophilic proctitis). Peripheral eosinophil count was initially normal, but hypereosinophilia appeared at day 3 of admission (maximum 2600 $10^6$/L at 16 daysof life). After 8 days of bowel rest with total parenteral nutrition, progressive refeeding was initiated, with an amino acid based formula and was well tolerated.
**Results:** Case n°2
A newborn female infant was transferred to our hospital for suspected intestinal obstruction. She was breastfed and had a brother with cow's milk protein allergy. She presented with bilious emesis and mild rectal bleeding a few hours after birth. Abdominal X-ray showed small bowel dilatation. Ultrasound and small bowel opacification did not demonstrate volvulus or malrotation. Enteral feeding was started with standard formula 48 hours after admission.Three days later, she suddenly deteriorated and developed acute diarrhea with hypernatremic dehydration (Na: 165mmol/l) and metabolic acidosis (pH: 7.145, bicarbonate level: 11mmol/l). Feedings were stopped but 24 hours later she once again developed rectal bleeding. A severe colitis was seen on endoscopy and biopsies showed eosinophilic infiltration of the mucosae with >70 eosinophils/HPF. Rectal bleeding stopped 3 days after she was made NPO. Peripheral eosinophilia (max 3000 $10^6$/L) appeared at day 6 of life. She responded well to an amino acid based formula and peripheral hypereosinophilia resolved.
**Conclusions:** The above cases show that cow milk protein allergy can have an acute and severe presentation and can even mimic surgical pathologies in early life. Atypical clinical manifestations of cow milk protein allergy need to be recognized by pediatricians and primary care physicians in order to improve the management of these patients.

**Funding Agencies:** Ste Justine Fundation

A321
**CANADIAN HOME TOTAL PARENTERAL NUTRITION REGISTRY: 10 YEARS OF DATA ENTRY**
M.L. PONTA[4], N. Somlaw[4], O. Saqui[7], D. Stevenson[11], M. Boudreault[12], E. Marliss[10], M. Raman[5], D. Duerksen[6], S. Whittaker[8], D. Armstrong[3], B. Jurewitsch[9], K.N. Jeejeebhoy[2], L. Gramlich[1], J. Allard[4]

1. Community Services Centre, Edmonton, AB, Canada; 2. Mary Bridge Children's Hospital, Toronto, ON, Canada; 3. McMaster University, Hamilton, ON, Canada; 4. Medicine, University Health Network, Toronto, ON, Canada; 5. University of Calgary, Calgary, AB, Canada; 6. University of Manitoba, Winnipeg, MB, Canada; 7. University Health Network, Toronto, ON, Canada; 8. Providence Health Care, Vancouver, BC, Canada; 9. St. Michael's Hospital, Toronto, ON, Canada; 10. McGill University Health Centre, Montreal, QC, Canada; 11. Regina Qu'Appelle Health Region, Regina, SK, Canada; 12. Hotel-Dieu l'Hopital , Quebec, QC, Canada

**Background:** Ten large HTPN centers collect and enter clinical data in the Home Total Parenteral Nutrition (HTPN) registry. This is the first Canada-wide registry looking at this population
**Aims:** To assess the 10-year clinical data in this cohort of patients
**Methods:** A web-based database prospectively collecting information on Patient demography, Nutritional assessment, Medications, Indications for HTPN, Gastrointestinal anatomy following surgeries, HTPN, Blood, Vascular access, Hospitalizations, Mortality, Liver complications, Metabolic bone disease, Quality of life on a two-year bases
**Results:** A total of 735 patient charts have been entered in the database, with a total of 1380 entries. Four centers reached the 10-years follow-up time point. The median age of patient population is 60 years (IQR: 51-70), with 62.5% being females. Short bowel syndrome (SBS) represents 42% of indications, tumours represent 24%, surgical complications 23%, motility disorders 13%, mucosal defects 6%, pancreatic disorders 1%, and other indications are 16%, with some overlap. Considering patients who reached the 10 years mark, mean values at baseline and at 10 years follow-up are the following: AST 51.5 ± 48.5 U/L vs. 35.2 ± 16.9 U/L, ALT 39.9 ± 36.7 U/L vs. 36.7 ± 27.7 U/L ALP 275.1 ± 329.0 U/L vs. 213.8 ± 244.3 U/L and total bilirubin 12.9 ± 8.0 U/L vs. 23.9 ± 44.3 U/L respectively, with statistically significant difference for ALP (p-value <0.02). Liver disease was reported in 186 patients representing 26% of population (n=721); in 108 patients, physicians judged it TPN-related (58% of liver disease). To treat liver disease, in 80% of cases lipids and/or dextrose content has been reduced in the regimen (dextrose only reduction in 9%, lipids only reduction in 39% and both in 32%). In addition, 146 patients were prescribed with ursodeoxycholic acid, 48 took antibiotics, 54 used carnitine and 4 were supplemented with choline (with some overlaps between them). Intralipid and SMOF are lipid emulsions used respectively in 53% and 43% of patients. Overall, 54% of patients have a Karnofsky Performance status of 80 or greater
**Conclusions:** The HTPN registry is a valuable tool to collect relevant information on HTPN patients. SBS is still the leading indication, however cancer and surgical complications are becoming a more frequent indication for TPN. TPN related liver disease is not uncommon, and typically managed by adjusting lipid and/or dextrose content in TPN solution. There is no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significant effect of TPN on liver enzymes modification nor on bilirubin and a favorable impact on ALP

**Funding Agencies:** Baxter and Ontario Medical Supplies

A322

**NON-ALCOHOLIC FATTY LIVER DISEASE: DOES A CLINIC SPECIALIZED COUNSELLING ON NUTRITION AND EXERCISE REGIMEN HAS A CLINICAL IMPACT?**

M.L. PONTA, S. Saber Hamishegi, J. Allard

Medicine, University Health Network, Toronto, ON, Canada

**Background:** Non-alcoholic fatty liver disease (NAFLD) is a disease spectrum which includes benign simple steatosis (SS) and the more severe non-alcoholic steatohepatitis (NASH), affecting 20% to 30% of the general population in North America. It is linked to obesity and diabetes mellitus type II. Treatments options include healthy diet, physical activity and weight loss.
**Aims:** To assess the clinical impact of a specialized nutrition clinic that provides counselling on nutrition and exercise regimen.
**Methods:** This is a prospective cohort study. Patients data included here are patient demography, anthropometry (weight, BMI, waist circumference) and blood works (liver enzymes, HbA1c, glucose, lipid profile). Bloodwork and anthropometry were repeated at 6 months. Nutritional counseling and exercise regimen tailored to the patients were provided by a nutritionist and included oral supplements (Omega-3, Vitamin E, Vitamin D and Vitamin C). Significance of differences has been evaluated with Wilcoxon signed rank test for non-parametric data.
**Results:** Among 77 patients referred to the NAFLD clinic, 42 consented to the study. The median age was 49.5 years (IQR: 39, 56), with 53% females and 58% non-Hispanic white. 17 subjects were seen at 6 month-follow-up visit, 11 did not show and 14 are pending. For the 17 patients, baseline to 6 months measurements were: weight (mean 92.8 +/- 19.1 vs mean 90.7 +/- 19.0 kg); BMI (mean 33.3 +/- 6.0 vs mean 32.5 +/- 6.0 kg/m$^2$); waist circumference (mean 107.8 +/- 13.0 vs mean 105.6 +/- 12.2 cm); AST (mean 45.8 +/- 31.5 vs mean 30.3 +/- 14.6 microU/L), ALT (mean 66.2 +/- 45.8 vs mean 45.2 +/- 30.5 microU/L). We observed a statistically significant difference for body weight (p-value <0.005), BMI (p-value <0.01) and AST (p-value <0.005). Of the 17 seen at 6 months, 3 lost $\geq$ 5% of their weight, representing 11% of those who came back at 6 months and those who were lost to follow-up.
**Conclusions:** Six-months results suggest a favorable trend toward improvements in anthropometry and liver enzymes but there is a significant number of patients lost to follow-up. Therefore, it is too early to determine if a nutritional clinic dedicated to NAFLD has a significant clinical impact.

**Funding Agencies:** None

A323

**INVESTIGATION OF THE NUTRITION CURRICULUM IN THE UNDERGRADUATE EDUCATION PROGRAM OF A CANADIAN MEDICAL SCHOOL**

S. Hanninen, M. Rashid

Dalhousie University, Halifax, NS, Canada

**Background:** The role of nutrition in health and disease is well recognized. Previous research had revealed students' dissatisfaction with the nutrition curriculum at Canadian medical schools and their lack of confidence in this clinical domain upon graduating.
**Aims:** To investigate the content of undergraduate medical education (UGME) nutrition curriculum at Dalhousie University medical school in order to identify areas of strength and deficiency.
**Methods:** The 4 year UGME curriculum was reviewed in depth utilizing the University's online curriculum map and course syllabi and compared to the Nutrition Curriculum Guide for Training Physicians (NCGTP, 2002, www.nhlbi.nih.gov). Nutrition curriculum was considered to have strengths if the learning objectives were consistent with NCGTP and to have gaps if the objectives lacked consistency with NCGTP. Strengths and gaps were organized into themes. The unit heads of undergraduate courses and clinical rotations were also consulted by telephone interviews to clarify any questions arising from the review. Responses were transcribed in writing and organized into themes.

**Results:** Nutrition education occurs longitudinally over the first 3 years of the UGME program. Most instruction is provided in first year in a brief but specific nutrition course. The UGME met 70% of the high priority learning objectives as indicated in the NCGTP. Strengths of the nutrition curriculum included: health promotion, obesity, pediatrics, women's health, chronic disease, gastrointestinal disease, anemia, metabolism of nutrients, energy requirements, and of the role of nutrition in health, disease, growth, and development. Gaps in nutrition education included: knowledge regarding food sources of nutrients, Dietary Reference Intakes, ability to obtain and assess diet histories, malnutrition and nutrition support and geriatric nutrition.

**Conclusions:** There are significant gaps in the UGME nutrition curriculum. Changes are required to improve medical students' overall knowledge of food including their ability to obtain adequate dietary histories, identify and manage malnutrition, and knowledge of nutrition support. Instruction in nutrition curriculum could be further enhanced by adding self-directed learning, case-based education, online modules, clinical training, and practical experiences through interprofessional learning with registered dietitians. Medical schools should systematically analyze their curriculum in nutrition to identify knowledge gaps and develop strategies for improvement.

**Funding Agencies:** None

A324

**ASSESSMENT OF STUDENTS' PERCEPTION OF THE NUTRITION CURRICULUM IN THE UNDERGRADUATE MEDICAL EDUCATION PROGRAM**

S. Hanninen, M. Rashid

Dalhousie University, Halifax, NS, Canada

**Background:** Nutrition is important in disease prevention and clinical management of patients. Students have previously reported overall dissatisfaction with the nutrition curriculum at Canadian medical schools and unpreparedness in their knowledge and skills in this area.
**Aims:** To investigate students' perspectives about the undergraduate curriculum in nutrition at Dalhousie University medical school.
**Methods:** All students in their second (Med-2), third (Med-3), and fourth year (Med-4) of medicine at Dalhousie University were invited to anonymously complete a 23-item online survey. Responses were graded on a 5-point Likert scale with 1 indicating Very Dissatisfied/Strongly Disagree and 5 indicating Very Satisfied/Strongly Agree. The study was conducted at beginning of the second half of the academic year.
**Results:** Of the 340 students, 89 (26.2%) completed the survey. Mean satisfaction with the nutrition curriculum was 2.9±0.81. Most students (81.5%) agreed that they received sufficient training regarding nutrition assessment (mean 3.98±0.89). Students were uncertain about adequacy of training regarding basic nutrition principles (mean 3.51±0.92), nutrition in disease prevention (3.14±1.12), nutrition and disease management (mean 3.48 ±1.00), role of registered dietitians (mean 2.97±1.05)) and credible nutrition sources (mean 3.14±1.09). Most students did not feel they received sufficient training in dietary intake assessment (mean 2.72±0.94), nutrient requirements across the lifecycle (mean 2.58±0.91), strategies to address food security(mean 2.4±0.95), and malnutrition(mean 2.74±0.93). Med-4 students were significantly more likely to believe they received adequate training about role of dietitians compared to Med-2 ($p<0.003$). All questions asking about the importance of nutrition were ranked as Agree/Strongly Agree. The majority (79%) agreed that more nutrition instruction is needed. Recommendations to improve learning included a longitudinal nutrition curriculum, clinical application of nutrition principles, evidence-based nutrition sources, and a healthy food environment. When compared to a similar national survey done in 2010, satisfaction with curriculum in nutrition remains unchanged and most students still want more instruction.
**Conclusions:**
Medical students recognize the importance of nutrition and would like more education in this area. The undergraduate nutrition curriculum should be enhanced by making it longitudinal and incorporating a variety of education tools to cover competencies such as dietary intake assessment, food security and malnutrition.

**Funding Agencies:** None

A325

**HEALTH PROFESSIONAL AND COMMUNITY PERCEPTIONS REGARDING NUTRITION GUIDELINE CONTENT FOR THE GLUTEN FREE DIET.**

A. Liu[3], P. Marcon[2], J. Turner[1], K. Radmanovich[3], D.R. Mager[4]

1. Stollery Children's Hospital, Edmonton, AB, Canada; 2. GI , The Hospital for Sick Children, Toronto, ON, Canada; 3. Agriculture Food & Nutritional Sciences, University of Alberta, Edmonton, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada

**Background:** Celiac Disease (CD) is a common autoimmune gastrointestinal disorder in children, treated through strict adherence to a gluten free diet (GFD). Gluten free (GF) foods often have high levels of simple sugars, glycemic index, glycemic load and saturated fat, and are low in important micronutrients. This can lead to an increased risk for suboptimal nutrient intake and for obesity. Current national guidelines (Canada's Food Guide to Healthy Eating) do not address the optimal GFD. Thus, a specialized GF food guide to help families make healthy gluten free food choices would be beneficial. This should target health professionals, individuals with CD and their caregivers to ensure the nutritional needs of children and youth consuming the GF diet is met.
**Aims:** To probe health professionals (HP), CD patients and their caregivers with in regards to content development for a gluten free nutrition guide.
**Methods:** Two internet surveys (one for HP, one for members of the community) were disseminated via the Canadian Celiac Association –Chapter's Facebook/ web-pages. Survey content addressed demographic variables (province, urban/non-urban, CD diagnosis, type of HP practice) and perceptions regarding the content of a food guide (nutrition topics, menu planning, etc). Descriptive statistics and thematic analysis were used to analyze closed and open-ended questions, respectively.
**Results:** 405 individuals responded to the surveys (246 HP and 159 families). Respondents in the HP survey were mainly registered dietitians (80%) who saw pediatric CD 1-5 times per month (82%). Family respondents were caregivers, 31-40 years old (34%), who has a child with CD (51%) from Alberta (74%). HP wanted to see information on plant-based meal plans (64%), label reading (93%) and selection of processed foods (81%). Family respondents wanted to see information on CD (95%) and restaurant menu choices (72%). Both groups wanted modules on school friendly recipes and cafeteria menu options and information on added sugars (80%) and iron (82%).
**Conclusions:** HP and families want a resource that includes information on micronutrient deficiencies in the diet and topics such as label reading and restaurant menu selection.



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**Funding Agencies:** Canadian Celiac Association - Edmonton Chapter

## PANCREATICO-BILIARY DISEASE

### Poster of Distinction

A326

**THE IMPACT OF DELAYED SOURCE CONTROL AND ANTIMICROBIAL THERAPY IN 196 PATIENTS WITH CHOLECYSTITIS-ASSOCIATED SEPTIC SHOCK**

V. Dong[1], C.J. Karvellas[2], J. Abraldes[1], E. Lester[1], A. Kumar[3]

1. University of Alberta, Edmonton, AB, Canada; 2. Hepatology/Critical Care Medicine, University of Alberta, Edmonton, AB, Canada; 3. University of Manitoba, Winnipeg, MB, Canada

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A327

**THE IMPACT OF ENDOSCOPIST CASE VOLUMES RELATED TO ERCP**

A.S. Dhillon, J. Kassam, S. Zepeda-Gomez, G.S. Sandha, V. Bain, A.J. Montano-Loza, R. Sultanian

University of Alberta, Edmonton, AB, Canada

**Background:** Endoscopic retrograde cholangiopancreatography (ERCP) is a common procedure used to diagnose and treat a variety of hepatobiliary and pancreatic conditions. ERCP has transitioned from a diagnostic test to a therapeutic intervention, with the complexity of cases becoming more challenging and the possibility of subsequent complications increasing. Previous studies have demonstrated that high volume endoscopists (HVE; >75 ERCP /year) have greater success compared to low volume endoscopists (LVE), despite performing more complex procedures. After our previous study demonstrated the benefit of having ERCP performed by HVE, our site transitioned to all procedures performed by HVE.
**Aims:** The aim of our study was to determine if this strategy resulted in improved ERCP outcomes at our centre.
**Methods:** A retrospective chart review of all ERCPs completed between September 2014 - September 2016, collecting data on cannulation success rate, ERCP complexity score, and any significant post-ERCP complications. These results were compared to ERCP patient outcomes performed between January 2010 - December 2012 which were completed by mixed volume endoscopists (MVE).
**Results:** From January 2010 - December 2012, six MVE performed a total of 1246 ERCP while only four HVE performed a total of 1385 ERCP from September 2014 to September 2016. Patient demographics were similar between both groups.

Successful cannulation was achieved in 92.5% for the HVE group, in comparison to 89.8% for the MVE group (OR 1.40, 95% CI 1.07-1.84, P=0.02), while the overall success rate was 89.2% in the HVE group versus 86.7% for the MVE group (OR 1.27, 95% CI 1.00-1.60, P=0.05).

Once adjusted for ERCP complexity, the OR for successful cannulation was 1.32 (95% CI 1.04-1.68, P=0.03), and for successful completion of the procedure was 1.32 (95% CI 1.00-1.74, P=0.05).

The rate of unintentional cannulation of the pancreatic duct (PD) was not different between the HVE and MVE groups (18.7% and 17.2%, respectively; OR 1.11, 0.91-1.35, P=0.3); however, the PD injection was lower in the HVE compared to the MVE group (5.4% vs. 9.8, P<0.001).

The risk of post-ERCP pancreatitis rates was not different for the HVE and MVE groups after adjustment for complexity score (3.4% vs. 2.9%, OR 1.08, 95% CI 0.80-1.49, P=0.6).

The risk of perforation was lower in the group of HVE compared to MVE, after adjusting for complexity score (0.2% vs. 0.6%, OR 0.25, 0.06-0.96, P=0.04). There was no mortality in either group.
**Conclusions:** The outcomes of patients undergoing ERCP at our centre has significantly improved with limiting ERCP to be performed by select HVE. While this data only reflects the experience at a single centre, transitioning complex care of ERCP patients to expert facilities performing HVE may result in improved patients outcomes.

**Funding Agencies:** None

A328

**A RETROSPECTIVE ANALYSIS ON SERUM CHROMOGRANIN-A LEVELS IN THE DIAGNOSIS OF PANCREATIC NEUROENDOCRINE TUMORS AT A CANADIAN INSTITUTE**

M.H. Laghari[1], K. Chiu[3], D.F. Schaeffer[4], F. Donnellan[2]

1. Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 2. Gastroenterology, Vancouver General Hospital, Vancouver, BC, Canada; 3. Anatomical Pathology, University of British Columbia, Vancouver, BC, Canada; 4. Anatomical Pathology, Vancouver General Hospital, Vancouver, BC, Canada

**Background:** Pancreatic Neuroendocrine Tumors (PNET) are rare neoplasms, diagnosed via CT, MRI, Octreotide scan or EUS, which has the highest sensitivity & tissue obtaining ability. Management is based on resection, dependent on size & spread. Serum Chromogranin-A (CgA) is still widely used in diagnosis

despite its lack of evidence. Hence, the North American Neuroendocrine Tumor Society (NANETS) and the Canadian expert group considers serum CgA diagnostic utility a controversial area and advise caution in its interpretation, requiring further studies in its validation
**Aims:** Despite the widespread use of serum CgA in PNET diagnosis, we believe serum CgA has poor diagnostic utility
Aims include:
1. Evaluate the diagnostic sensitivity of serum CgA in our cohort
2. Delineate different modalities utilized in tissue diagnosis
**Methods:** Retrospective chart review of patients with a histological diagnosis of PNET from a pathology database covering Vancouver BC, Canada, from January 1st, 2011 till July 31st, 2016
Exclusion criteria:
1. Patients with a nonpancreatic primary neuroendocrine tumor
2. Patients with no CgA levels prior to diagnosis
We correlated serum CgA levels, patient characteristics, disease manifestations and characteristics such as size and metastases, dianostic modalities used and treatments undertaken
**Results:** 143 patients with histological diagnosis of PNET. Mean age 60 & 58% females. EUS used in diagnosis of 90 (63%), surgical resection in 34 (24%) & remaining had percutaneous or intra-operative biopsy. Serum CgA prior to tissue diagnosis was performed in 60% (87) and had a sensitivity of only 48% (42/87), median of 109 U/L (normal <40 U/L) & 212 ug/L (normal <94 ug/L) from two different lab assays. Comparing CgA positive versus negative patients, no significant difference was found in location of PNET (most commonly in the tail in 33% & 37% of positive & negative patients respectively, 95% CI -17.3-24.8%, p=0.69). A significant difference was found in the size of the lesion in patients with a positive CgA as compared with the negative group (mean 3.31cm vs. 2.32cm; 95% CI 0.11-1.86, p=0.02). A significant proportion of CgA positive patients had metastatic disease as compared to CgA negative patients (38% vs. 15%; 95% CI 2.97-41.53, p=0.015)
**Conclusions:** PNET are rare neoplasms, usually diagnosed via EUS. We corroborated this with approximately two thirds of our cohort undergoing EUS sampling for diagnosis. Serum CgA, although thought to have some diagnostic utility, has a very low sensitivity with less than half of our cohort of patients having positive CgA levels. Hence, CgA levels should not be used as a diagnostic modality in PNETs, and if negative, should be interpreted cautiously. CgA levels may however, have a utility in helping identify metastatic disease and thus altering surgical management

**Funding Agencies:** None

A329
**CAN THE CALGARY BILE LEAK RULE AVOID THE NEED FOR REPEAT ERCPS IN OTTAWA? A VALIDATION STUDY**
U. Khan[1], Z. Meng[2], H. Dhaliwal[2], A. Chatterjee[2], S. Grégoire[2], S. Heitman[3], P.D. James[4]

1. Faculty of Medicine, University of Ottawa, Ottawa, ON, Canada; 2. Department of Medicine and The Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, ON, Canada; 3. Department of Medicine, University of Calgary, Calgary, AB, Canada; 4. Department of Medicine, University Health Network, University of Toronto, Toronto, ON, Canada

**Background:** ERCP with biliary stent placement is currently the standard treatment for postsurgical bile leaks. However, the best method (ERCP or gastroscopy) and timing of stent removal is controversial. The Calgary Bile Leak Rule suggests that patients who present with bile leaks after a laparoscopic cholecystectomy, have a normal postsurgical ALP, and have a small or no leak with no other pathology identified on initial ERCP can safely have their stent removed via gastroscopy 4 to 8 weeks after stent insertion.
**Aims:** We aimed to validate this prediction rule using the Ottawa Advanced Endoscopy Service experience.
**Methods:** A retrospective chart review of patients who were endoscopically managed for surgical bile leaks between 2005 and 2017 at The Ottawa Hospital (TOH) were identified. The primary outcome was presence of persisting bile leak or other pathology on follow-up ERCP. Sensitivity, specificity, and the positive and negative predictive values were calculated for the Calgary Bile Leak Rule.
**Results:** 71 cases met inclusion criteria and had sufficient data available to be considered for the validation analyses. 29 cases met most inclusion criteria but did not have sufficient data. 54 (76%) of bile leak cases had no leak identified during the follow-up ERCP and 17 (24%) had a persisting leak. The Calgary Bile Leak Rule demonstrated a sensitivity of 87% (95% CI, 75%-95%), a specificity of 6% (95% CI, 0%-29%), a positive predictive value of 75% (95% CI, 64%-85%), and a negative predictive value of 13% (95% CI, 2%-50%).
**Conclusions:** The Calgary Bile Leak Rule demonstrated high sensitivity for predicting the need for repeat ERCPs after surgically induced bile leaks are treated with biliary stenting. Further evaluation using larger prospective data sources are needed prior to recommending this rule for clinical practice.

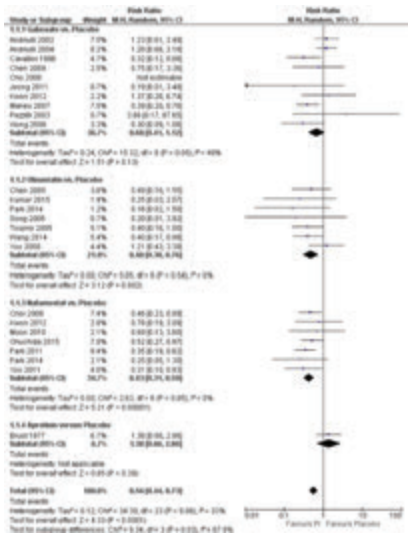
**Funding Agencies:** None

A330
**PREVENTION OF POST-ERCP PANCREATITIS: DO PROTEASE INHIBITORS HAVE A ROLE?**
A. Hu[1], Y. Yuan[2], G. Leontiadis[2], F. Tse[2]

1. McMaster University, Toronto, ON, Canada; 2. McMaster University, Hamilton , ON, Canada

**Background:** Acute pancreatitis is the most common complication of endoscopic retrograde cholangiopancreatography (ERCP). Rectal Indomethacin and

prophylactic pancreatic stent placement have been shown to be effective for the prevention of post-ERCP pancreatitis. However, there remains considerable controversy regarding the usefulness of protease inhibitors (PIs) in preventing PEP.
**Aims:** This systematic review of randomized controlled trials (RCTs) aims to compare PIs with other pharmacological agents and/or placebo.
**Methods:** CENTRAL (*the Cochrane library)*, MEDLINE, EMBASE, and CINAHL databases, and major conference proceedings from DDW, UEGW and ACG up to July 2017 were searched for RCTs examining PIs against other pharmacological agents and/or placebo. Study selection, data extraction and quality assessment were conducted independently by two authors. The primary outcome was PEP. Secondary outcomes included severity of PEP and other ERCP-related complications such as bleeding, perforation, cholangitis, cholecystitis and mortality. The outcomes were pooled into a meta-analysis using risk ratios (RR) with 95% confidence intervals (CI; Mandel-Haenszel method; random effects model). Heterogeneity was assessed by $Chi^2$ test ($P<0.15$) and $I^2$ test (> 25%). The risk of bias was assessed using the Cochrane Risk of Bias Assessment Tool.
**Results:** 23 RCTs (7091 patients) comparing four different types of PIs with placebo were included in this review. Overall, there was a significant reduction in the risk of post-ERCP pancreatitis with PIs compared with placebo (RR 0.56, 95% CI 0.44-0.73, $I^2 = 33\%$). Among the seven studies that compared Ulinastatin with placebo, the incidence of PEP was 3.9% in the PI group vs. 8.3% in the placebo group (RR 0.48; 95% CI 0.30-0.76; $I^2 = 0\%$). Among the seven studies that compared Nafamostat with placebo, the incidence of PEP was 3.8% in the PI group vs. 8.2% in the control group (RR 0.43; 95% CI 0.31-0.59, $I^2=0\%$). There was no statistically significant difference found in the comparison between Gabexate versus placebo (RR 0.68; 95% CI 0.41-1.12; $I^2 = 48\%$). In the one study that assessed Aprotinin versus placebo, there was no statistically significant difference (RR 1.38, 95% CI 0.66-2.86). Overall, the risks of bleeding (1.5%), perforation (0.2%), cholangitis (1.2%) and mortality (0.3%) appeared to be low.
**Conclusions:** Protease inhibitors, specifically Nafamostat and Ulinastatin, are effective in preventing PEP. Further studies are needed to assess the optimal dose, timing and duration of PI, as well as the cost-effectiveness in different subgroups of patients. As well, the role of PIs along with prophylactic PD stent placement and rectal NSAIDs will need to be further elucidated in RCTs.



Post-ERCP Pancreatitis in PIs versus Placebo

**Funding Agencies:** None

A331
**QUALITY GAPS IN THE MANAGEMENT OF PATIENTS WITH ACUTE PANCREATITIS**
O. Ahmed[1], C.W. Teshima[2], H. Akram[1], J. Mosko[3]

1. University of Toronto, Toronto, ON, Canada; 2. Gastroenterology, University of Toronto, Toronto, ON, Canada; 3. Medicine, University of Toronto, Toronto, ON, Canada

**Background:** Acute pancreatitis is the most common gastrointestinal (GI) cause for hospitalization and is associated with high morbidity and mortality. Multiple clinical guidelines outline best practices for the management of these patients. However, recent studies suggest that adherence to such guidelines is poor.
**Aims:** In this study, we aim to audit current practice to identify potential targets for quality improvement initiatives.
**Methods:** A retrospective chart review of all patients admitted directly to St. Michael's Hospital (a tertiary-care hospital) from the Emergency Department with a diagnosis of acute pancreatitis between July 1, 2016 and December 31, 2016 was performed. Complex patients transferred from another hospital to the ICU or GI ward were excluded. Patients were identified using ICD-10 discharge codes. Potential quality indicators were extracted from the recent AGA, ACG and recently published Canadian guidelines on the management of acute pancreatitis. Individual charts were reviewed and the following data was extracted: laboratory values, imaging results, dates of admission and, discharge, interventions/procedures performed, antibiotic use and nutrition. The data was were then used to determine baseline characteristics and adherence to guidelines.

**Results:** A total of 55 patients were included in the study. The mean age was 50 (range 16 to 92) years and 31 (56%) were male. The most common cause of acute pancreatitis was idiopathic (36%), followed by alcohol (22%) and gallstones (20%). The average Charlson co-morbidity index was 2.4 (+/- 2.6). The average length of stay was 5.8 (range 1 to 46) days. 3 patients required ICU admission. Ultrasound was performed within 48 hours of admission in 28 (51%) patients, while 23 (42%) patients had a CT scan during their admission. The most common reason for CT was for diagnostic evaluation (52%), followed by investigation for underlying etiology (30%). 25% of patients did not obtain any imaging during their admission. 2 (4%) patients did not receive nutrition within 48 hours, with the average time to nutrition being 1 day. Antibiotic prophylaxis was started in 4 (7%) patients. The average fluid resuscitation rate was 113 (+/- 64) mL/hour. No patients had appropriate lab values drawn to calculate Apache or other severity index scores. Only 3 patients had CRP measured. For patients with biliary pancreatitis, 5/13 required ERCP during their admission (all for ongoing biliary obstruction), and only 36% underwent cholecystectomy within the same admission.
**Conclusions:** The management of patients presenting with acute pancreatitis remains quite variable, with the most common deficiencies relating to imaging for potential etiologies, risk stratification, under resuscitation with intravenous fluids and delay to cholecystectomy.

**Funding Agencies:** None

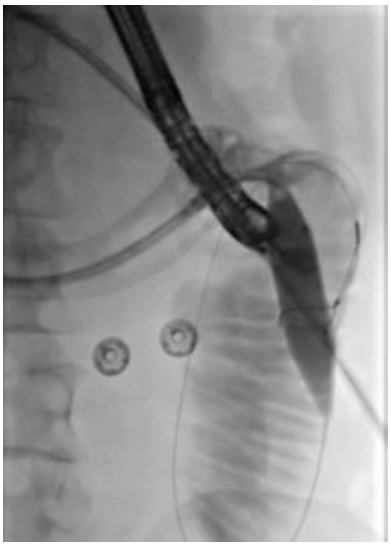
A332

**FIRST REPORTED EUS-GUIDED DOUBLE BYPASS PERFORMED IN COLLABORATION WITH INTERVENTIONAL RADIOLOGY**

A.A. Hashim[3], A. Bessissow[4], D. Valenti[4], K. Waschke[3], J. Parent[3], A.N. Barkun[1], J. Barkun[5], s. white[2], Y. Chen[3]

1. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 2. Royal Victoria Hospital, Montreal, QC, Canada; 3. Division of Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 4. Division of Interventional Radiology, McGill University Health Center, Montreal, QC, Canada; 5. Department of Surgery, McGill University Health Center, Montreal, QC, Canada

**Background:** Endoscopic ultrasound-guided double bypass (EUS-DB) is a novel technique in the management of concomitant biliary and gastric outlet obstruction. It involves the creation of both an EUS-guided gastroenterostomy and hepatogastrostomy
**Aims:** To describe the first reported case in the literature (with video) of EUS-DB performed in collaboration with interventional radiology (IR)
**Methods:** A 54-year old male known for locally advanced pancreatic cancer was referred for recurrent cholangitis and gastric outlet obstruction despite previous duodenal stenting and transhepatic percutaneous biliary drainage (PTBD). Endoscopy confirmed complete obstruction of the duodenal stent due to tumor tissue ingrowth. A decision was made to proceed to EUS-DB to optimize nutritional status, biliary drainage, and patient comfort
**Results:** IR introduced a guidewire through the PTBD traversing the enteral stent and advanced to the jejunum. A 20 mm dilating balloon with an overlapping snare attached was then introduced over the PTBD wire and advanced across the enteral stent to the ligament of Treitz where the balloon was inflated under fluoroscopy. Overall, 500 ml of both saline and contrast was then injected percutaneously to dilate the small bowel segment proximal to the balloon. EUS-guided puncture of the balloon was performed transgastrically with a 19-gauge needle. Bursting of the balloon confirmed successful puncture in the desired jejunal segment. An 0.035-inch guidewire was then advanced through the needle and grasped with the snare and pulled through the percutaneous access thereby creating wire tension on both ends of the wire. Track dilation was performed with a 4 mm dilating balloon. A Lumen-apposing metal stent (15 x 10 mm) was then deployed under EUS guidance. Contrast injection confirmed a patent gastroenterostomy. Attention was then shifted to the HGS. Under EUS a dilated hepatic segment III left intrahepatic bile duct was visualized. A transgastric puncture of the duct was performed with a 19-gauge needle, followed by the advancement of an 0.035-inch guidewire into the common bile duct. The HGS track was then dilated using a 4mm dilating balloon followed by successful deployment of a 10 x 80 mm partially covered self-expanding metal stent. A full stent diet was initiated 48 hours post procedure with excellent tolerance. PTBD was removed 3 days later with the bilirubin having decreased by more than 50 % at the 1-week follow-up
**Conclusions:** We describe the first reported EUS-guided double bypass performed in collaboration with IR. Combining endoscopic and interventional radiology techniques may enhance the safety and ease of this novel approach. Further studies; however, will be needed to validate this technique



**Funding Agencies:** None

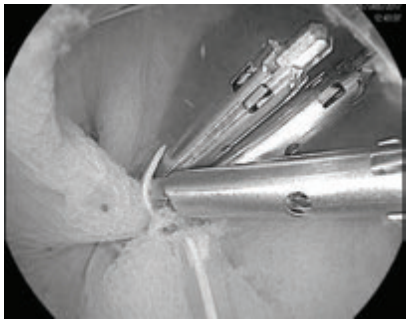
A333

**REMOVAL OF A MIGRATED BILIARY STENT IMPACTED IN THE COLONIC WALL: A CASE DESCRIPTION OF ENDOSCOPIC REPAIR.**

K. Hnaris, R. Bechara

Gastroenterology, Queens University, Kingston, ON, Canada

**Background:** Endoscopically placed biliary stents are commonly used for the treatment of pancreaticobiliary disorders. Plastic biliary stent migration is a complication that is well described in the literature and is estimated to occur in 5 to 10% of cases. The stents are usually expelled without incident within a few weeks if they migrate into the intestine. Perforation of the GI tract secondary to stent migration is a rare event occurring in less than 1 % of cases. Reported cases of perforation secondary to stent migration have required surgery for stent removal and repair. Advances in therapeutic endoscopy has led to an increase in potential complications including iatrogenic perforations. Recently, there has been an increasing interest in the use of clips and endo loops for the closure of iatrogenic colonic perforations, and for closing defects following large polypectomy Developing techniques to manage these complications is crucial to further advancement of the field.
**Aims:** To describe a case of perforation secondary to biliary stent migration that was repaired endoscopically.
**Methods:** Case report and review of the literature.
**Results:** The case is that of a 90-year-old female known for recurrent biliary obstruction secondary to gallstones and Mirizzi's syndrome which had been managed conservatively for many years with sequential biliary stent exchanges via ERCP. The patient initially presented to hospital with sudden onset severe abdominal pain following a week of intermittent post-prandial pain. A CT scan identified a migrated biliary stent in the ascending colon with one end through the colonic wall and surrounding fat stranding, which was concerning for a perforation. The patient was admitted under the general surgery service for treatment with intravenous antibiotics and observation. Her condition stabilised and her pain subsided within 24 hours, however the stent remained lodged in the colonic wall as visualized on serial abdominal x-rays. In view of multiple comorbidities that precluded surgery, a colonoscopy was performed on day 4 of her admission. We identified the stent impacted in the wall of the ascending colon. It was dislodged with the use of a snare, leaving behind a defect in the colonic wall. We then proceeded to endoscopically close the defect with the use of 3 clips. The perforation was further approximated using an endo loop around the 3 clips, to bring the mucosa closer together. The patient recovered uneventfully and was sent home on oral antibiotics.
**Conclusions:** This is the first description of a migrated plastic biliary stent removed endoscopically with repair of the colonic perforation using a previously described endoscopic technique. Our case further emphasizes the potential for endoscopic repair of gastro-intestinal perforations, especially in non-surgical candidates with multiple comorbidities.



Endoscopic repair of mucosal defect using clips and an endo-loop

**Funding Agencies:** None

A334

**CHRONIC MIRIZZI SYNDROME CAUSING SECONDARY SCLEROSING CHOLANGITIS AND CIRRHOSIS: A CASE REPORT.**

R. Homenauth[2], M.M. Wells[1], A.R. Kohansal[1], R. Sultanian[3]

1. University of Alberta, Edmonton, AB, Canada; 2. Adult Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada

**Background:** Mirizzi syndrome (MS) is an uncommon presentation in which a gallstone becomes impacted in the cystic duct or neck of the gallbladder causing compression of the common bile duct (CBD) or common hepatic duct (CHD), with resultant biliary obstruction. Most common symptoms include abdominal pain, jaundice and fever. Patients can present with concurrent cholangitis and acute cholecystitis. Diagnosis can be confirmed by imaging modalities including ultrasound, MRCP, EUS or ERCP. Initial management of MS includes supportive care, and relief of biliary obstruction via ERCP. Surgery is the definitive treatment for MS. Secondary Sclerosing Cholangitis (SSC) refers to a chronic and progressive liver disease characterized by inflammation, fibrosis and obstruction of the intra and extrahepatic biliary tree. The etiology is varied but includes chronic biliary obstruction. MS has not been described as a potential etiology for SCC as it is typically an acute presentation requiring emergent treatment. To date there have been no documented reports of chronic MS or MS causing SSC.
**Aims:** We present a case of chronic MS leading to SSC and cirrhosis.
**Methods:** A literature search was performed between July 1997 and July 2017 in the PubMed and Google Scholar databases using the terms "Mirizzi syndrome", "chronic Mirizzi syndrome", "secondary sclerosing cholangitis", either individually or in combination. Citations among the identified publications were also reviewed.
**Results:** A previously healthy 44-year-old female presented to the emergency department with a 15-month history of intermittent right upper quadrant pain and fevers. Her labs at the time of presentation revealed an elevated WBC of 13.8, ALT 234, AST 234, Total Bilirubin 535, ALP 1389, GGT 290 and albumin 30. MRCP imaging showed intrahepatic and CBD dilation concerning for biliary obstruction. She was referred to Gastroenterology for an ERCP which demonstrated markedly dilated intrahepatic biliary system with a 2-cm stone in the cystic duct causing external compression of the CBD consistent with MS (image1). She was then referred to hepatobiliary surgery where the diagnosis of MS was further confirmed surgically. Intraoperatively, note was made of severe intrahepatic and peri-portal inflammation with fibrosis, suspicious for SSC and portal hypertension. An intraoperative liver biopsy was consistent with the diagnosis of secondary sclerosing cholangitis. Screening workup for other causes of liver disease was negative and liver enzymes were normal prior to her presentation.
**Conclusions:** MS is an uncommon and invariably acute complication of gallstone disease. This is the first reported case of MS as a chronic presentation since patients typically require emergent treatment. Consequently, this is also the first case of chronic MS as a cause of SSC and portal hypertension in the available literature.

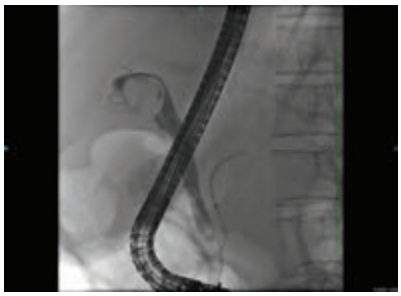


Image 1

**Funding Agencies:** None

A335
**EUS-GUIDED CYSTOGASTROSTOMY IN MANAGING PANCREATIC PSEUDOCYST-PORTAL VEIN FISTULA WITH REFRACTORY HEPATIC ABSCESS**
J.K. Eccles, P. D'Souza, G. Sandha

University of Alberta , Edmonton, AB, Canada

**Background:** Pancreatic pseudocysts can fistulise into the portal venous system and seed to the liver with subsequent abscess formation. Percutaneous drainage and antibiotics may only offer temporary improvement.
**Aims:** We look at the role of EUS-guided cystogastrostomy and metal stent insertion in facilitating definitive resolution of secondary infected hepatic pseudocysts.
**Methods:** In the case of a 64-year-old presenting with abdominal pain, CT abdomen showed a pancreatic pseudocyst, portal vein thrombosis and a multiloculated liver lesion. Despite antibiotics for presumed liver abscess, he later re-presented with enlargement of both liver cyst and pancreatic pseudocyst, communicating with the pancreatic duct and portal vein on CT imaging. Fluid from the liver cyst showed an elevated amylase level. The pseudocyst did not fully resolve with CT-guided percutaneous drainage, so we did an EUS-guided cystogastrostomy with plastic double-pigtail stent insertion. Follow-up CT, however, showed pseudocyst enlargement, requiring further EUS-guided cystogastrostomy and fully covered metal stent insertion. Follow-up CT two months later showed almost complete resolution of both liver and pancreatic collections. For a 54-year-old also presenting with abdominal pain, abdominal CT identified an ill-defined, multiloculated liver mass and extensive portal venous thrombosis. The liver abscess was treated with antibiotics and drainage. Three months later, he re-presented and abdominal CT showed complex fluid within the portal venous system, suspicious of a pancreatic origin. MRCP confirmed a pancreatic ductal stricture with decompression into a pseudocyst and evidence of secondary cavernous transformation of the portal vein extending into the liver. Percutaneous aspiration of the large liver cyst confirmed amylase-rich fluid. We proceeded with EUS-guided cystogastrostomy and fully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covered metal stent deployment. Abdominal CT two weeks later showed successful decompression of the pseudocyst and resolving liver cyst.
**Results:** These patients demonstrate that secondary liver pseudocysts, *refractory* to percutaneous drainage, may resolve completely after decompression of their feeding "primary" pancreatic pseudocyst through EUS-guided cystogastrostomy and metal stenting. Failure of percutaneous drainage alone may be explained by persistent feeding with proteolytic material via the connection between the primary pseudocyst and portal vein.
**Conclusions:** In conclusion, liver fluid collections may develop in association with pancreatic pseudocysts through an "embolic" phenomenon mediated through the portal venous system. Furthermore, failure of liver cyst resolution could be attributed to ongoing "feeding" from its parent pancreatic pseudocyst. We suggest that consideration be given to EUS-guided pancreatic cystogastrostomy and metal stent placement for long-term resolution.

**Funding Agencies:** None

A336
**AN UNUSUAL FINDING AT ERCP**
M. Strohl[2], A. Hashim[1], L. Stein[1], K. Waschke[2]

1. Radiology, McGill University Health Center, Montreal, QC, Canada; 2. McGill University Health Center, Montreal, QC, Canada

**Aims:** We present a rare complication during ERCP of portal vein cannulation emphasizing the importance of recognition of this to avoid potentially ominous complications.
**Methods:** Our case will be presented below with a review of the literature
**Results:**
A 56-year-old male known for dyslipidemia presented to a community hospital with a 3-week history of new postprandial epigastric pain and a 15 pound weight loss. An EGD demonstrated a duodenal mass partially obstructing D1. Biopsies of the mass revealed poorly differentiated adenocarcinoma. A CT abdomen showed eccentric thickening of the gastric antrum with aneurysmal dilation and abnormal appearance of D1 and D2. Abnormal tissue was described at the head of pancreas making it difficult to identify the origin of the mass. MRCP showed eccentric D1 and D2 thickening highly suggestive of a primary duodenal neoplasm (7.3x5.0x4.6cm). The mass did not appear to arise from the pancreas. Two additional masses, thought to be possible metastatic lymphadenopathy were described. The patient was transferred to a tertiary care center. While admitted there an elevated cholestatic liver enzyme pattern was noted to be worsened with no signs or symptoms of cholangitis.

ERCP was arranged for suspected biliary obstruction prior to planned chemotherapy. During the ERCP the duodenal mass was easily traversed. The papilla had a normal appearance. Cannulation with sphincterotome and guidewire was performed. Contrast was injected however the biliary tree did not appear to opacify. Despite injecting significant amounts of contrast, it appeared as if the contrast was dispersing rapidly. Multiple fluoroscopic images were taken while adjusting the views as this was very atypical. It became apparent that the portal vein had been cannulated and the contrast was flowing through the portal vein. The procedure was aborted. No immediate complication occurred as a consequence of the PV cannulation during the ERCP. A percutaneous biliary drain was inserted the same day.
**Conclusions:** Portal vein cannulation or opacification of the portal venous system during ERCP is an exceedingly rare complication with a reported incidence of less than 1/6000 [1]. The majority of cases reported in the literature have been in the context of pancreatic cancer and after sphincterotomy [2-5]. One portobiliary fistula was described pre-procedure [6]. Two cases have been reported in non-pancreatic cancer cases with standard wire guided cannulation technique [7, 8]. Although many complications including bleeding, sepsis and portal thrombosis are possible none of the reported cases have described any complications. Similarly, in our case no immediate post procedure complication arose. However, had stenting been undertaken the consequences would likely have been more detrimental. This exceptionally infrequent complication is therefore important to recognize promptly during ERCP, which should then be terminated immediately.

**Funding Agencies:** NoneNone

## PEDIATRIC LIVER DISEASE

A337
**KABUKI SYNDROME: A NEW ADDITION TO THE DIFFERENTIAL DIAGNOSIS OF LOW-GGT NEONATAL CHOLESTASIS**
F. Briglia[2], O. Guttman[1], O. Popescu[3], C. Senger[1], R. Schreiber[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Gastroenterology, BC Children's Hospital, Vancouver, BC, Canada; 3. BC Children's Hospital, Vancouver, BC, Canada

**Background:** Neonatal low-GGT cholestasis has a unique differential diagnosis centered on congenital disorders of bile acid transport or synthesis. Kabuki syndrome is a genetic condition with distinctive facies, developmental delay, and skeletal, renal and cardiac defects. While Kabuki has been associated with high-GGT cholestatic conditions including biliary atresia, patients with low-GGT cholestasis have not previously been described.
**Aims:** To describe 2 patients with Kabuki syndrome and low-GGT neonatal cholestasis
**Methods:** Chart review.
**Results:** Case 1: A female infant of non-consanguinous South Asian parents was born at 35 6/7 weeks.

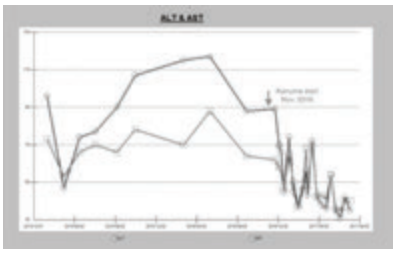
Antenatal US was normal. Facial dysmorphisms and hypotonia were noted at birth. Whole exome sequencing analysis confirmed Kabuki syndrome with *de novo* deletion in the KMT2D gene. Ventilation was needed from birth, with right-sided heart failure from pulmonary hypertension. She required TPN. Cholestasis was identified at 6 weeks: conjugated bilirubin 175umol/L, AST 404U/L, ALT 121U/L, ALP 289U/L, GGT 64U/L (70-130). Abdominal US: hepatosplenomegaly and ascites without biliary abnormalities. CMV infection occurred at 12 weeks. Liver biochemistry improved with ursodeoxycholic acid, cessation of TPN and CMV resolution. She was discharged home at 7 months.
Case 2: A male infant of non-consanguinous Filipino parents was born at 25 4/7 weeks. He had a patent ductus arteriosis and solitary renal cyst but no dysmorphisms or other congenital abnormalities. He required TPN. Intractable pulmonary hypertension necessitated prolonged ventilation. Cholestasis was identified at 4 weeks. Stools were initially pale. HIDA scan was non-excretory. Liver biopsy: giant cell transformation, mild portal fibrosis, no bile duct proliferation. Stools later became pigmented. A jaundice gene chip (EGL) found no mutations of familial intrahepatic cholestasis (PFIC). Kabuki syndrome was diagnosed at 4 months on chromosome array. Peak liver biochemistry: conjugated bilirubin 512umol/L, AST 731U/L, ALT 345 U/L, ALP 891U/L, GGT 65U/L. Repeat liver biopsy at 3 months: extensive giant cell transformation. EM: canaliculi with markedly reduced stubby microvilli, with finely granular to filamentous material suggesting BSEP deficiency (PFIC type 2). He died at 5 months from pulmonary hypertension.
**Conclusions:** These are the first reported cases of Kabuki syndrome with low-GGT neonatal cholestasis. KMT2D gene mutations should be considered on the short list of genetic disorders causing low-GGT cholestasis. We hypothesize that in Kabuki syndrome, KMT2D gene mutations modify lysine methytransferase activity and impair FXR expression of target gene products including BSEP, leading to phenotypic PFIC type 2 disorders. Kabuki syndrome gene mutations should be included in next generation jaundice gene chip panels for neonatal cholestasis.

**Funding Agencies:** None

A338
**LYSOSOMAL ACID LIPASE DEFICIENCY (LAL-D): FROM DIAGNOSIS TO THERAPY IN CANADA**
D. Ashok[1], C. Prasad[1], J. Walsh[2], S. Colaiacovo[3], T. Rupar[1]

1. Pediatrics, Western University, London, ON, Canada; 2. Western University, London, ON, Canada; 3. Children's Hospital Western Ontario, Canada, ON, Canada

**Background:** Lysosomal Acid Lipase (LAL-D) deficiency is an ultra-rare lysosomal storage disorder. Clinical features in the late-onset form include dyslipidemia (elevated LDL, low HDL), elevated liver enzymes, hepatomegaly, and splenomegaly. This can progress to liver fibrosis and cirrhosis. LAL-D is caused by deficient activity of the LAL enzyme, resulting in the accumulation of cholesteryl esters and triglycerides throughout the body, predominately in the liver, spleen, gastrointestinal tract, and blood vessel walls. Supportive management with lipid-modifying agents, hematopoietic stem cell and liver transplant has been tried without major success.
**Aims:** We describe our centre's experience of 3 patients with LAL-D. We describe our preliminary experience in treating this condition with Enzyme Replacement therapy (Sebelipase Alfa Kanuma®)
**Methods:** Over the last 20 years, we have had three patients with a confirmed diagnosis of LAL-D. Two adult patients, currently 31 and 40 years old, were diagnosed at 11y and 14 y with LAL activities at about 7% of control mean using fibroblasts and peripheral blood leukocytes after presenting with hepatosplenomegaly. Both adult patients were lost to follow up.
A nine year old girl of French and Welsh background presented in 2014 with hepatomegaly, elevations in liver enzymes and dyslipidemia - high total cholesterol 7.4 mmol/L, high LDL cholestrol (4.7) mmol/L and low HDL cholestrol (0.83) mmol/L. LAL enzyme showed low levels of 13 pmol/hour (normal 80-230) in dried blood spots. Liver biopsy showed severe microvesicular steatosis and bridging fibrosis. She has c.684delT and c.894G>A pathogenic mutations.
**Results:** The child with LAL-D has received Sebelipase Alfa Kanuma® intravenous therapy every two weeks at 1 mg/kg. She has tolerated the infusions well for the last twelve months with no adverse effects. The liver enzymes and lipid profile have normalized.
Liver stiffness measured by transient elastography at baseline was 8.6kPa; after10 months of therapy liver stiffness improved to 7.4 kPa.
**Conclusions:** Enzyme replacement therapy for LAL-D appears to be safe and preliminary results are encouraging. The therapy was started after significant advocacy from the family as the drug is not yet approved for coverage in Canada.




Improvement in ALT and AST

**Funding Agencies:** None

A339
**NOT ALL CYANOSIS IS CARDIAC- VARIED PRESENTATION OF ABERNATHY MALFORMATION: SINGLE CENTRE EXPERIENCE**


To view enlarged images and tables, please refer to Abstract Library.

s. amin[1], s. sharma[2], v. kumaran[3]

1. the hospital for sick children,Toronto and Kokilaben Ambani Hopsital, India, TORONTO, ON, Canada; 2. kokilaben ambani hospital, Mumbai, India; 3. kokilaben ambani hospital, Mumbai, India

**Aims:** To present long term manifestations of Abernathy malformation( AM) type 1 and 2 and establish the need for early diagnosis and management.
**Methods:** Nine patients were diagnosed with Abernathy malformation and managed at a single tertiary center between 2015 – 2017 .Data on presentation, clinical course, management and outcome is presented.
**Results:** Nine patients were assessed at the liver unit (4 males) at a median age of 11 (range 3 -29) years. All patients presented previously with dyspnea, cyanosis (oxygen saturations 55 – 65 % at room air; clubbing grade 2 to 3), failure to thrive and normal heart structure on echocardiogram with evidence of high pulmonary pressures. All patients were erroneously diagnosed with idiopathic pulmonary hypertension and treated with vasodilators with no significant improvement. Upon arrival to our clinic screening abdominal ultrasound showed type 1 AM in 3 patients and type 2 in 6. Among AM type 1, one patient had hepatopulmonary syndrome (HPS), liver focal nodular hyperplasia, and brain abscess due to long standing cyanosis. She was treated with a LDLT and recovered very well. The other two had failure to thrive with cyanosis and HPS. Both were offered liver transplant. All type 2 AM patients (N=6) presented with pulmonary arterial hypertension. Five patients underwent shunt closure surgically (n=3) or via catheterization (n=2). One patient is on vasodilators for pulmonary hypertension and has been offered device closure. On 6 months follow up a 2d echocardiogram has shown significant improvement in pulmonary pressures and saturations at room air in treated patients.
**Conclusions:** Not all cyanotic cases are cardiac related . Early diagnosis of Am can prevent long term complications in childhood including impaired growth and development and portal hypertension related pulmonary pathologies. All children with idiopathic pulmonary hypertension must undergo evaluation for abnormal Porto venous connection with abdominal scan before being labelled as idiopathic.

**Funding Agencies:** None

## VIRAL HEPATITIS

A340
**IDENTIFICATION OF A G4-QUADRUPLEX STRUCTURE MOTIF IN HEPATITIS B VIRUS GENOME: A POTENTIAL NOVEL DRUG TARGET**

V. Meier-Stephenson[1], S. Schultz[2], C.S. Coffin[1], T. Patel[2]

1. University of Calgary, Calgary, AB, Canada; 2. University of Lethbridge, Lethbridge, AB, Canada

**Background:** Approximately 240 million people worldwide are chronically infected with hepatitis B virus (HBV), one of the leading causes of liver cirrhosis and hepatocellular carcinoma (HCC). HBV persistence is due to the presence of its compact, stable, covalently closed circular DNA (cccDNA), which resides in the nucleus and acts as the template for all HBV mRNA transcripts. While current antiviral therapies are effective at viral suppression, they do not target HBV cccDNA and cannot eradicate infection, necessitating prolonged, if not lifelong therapy.

The transcription of cccDNA is under the guidance of numerous host factors, which bind to the various promoter regions to aid the replication of HBV. In the pre-core promoter region, specifically, interrupting host-protein interaction via a single nucleotide mutation studies can abrogate the HBV production.

Recently, we have found a unique structural motif in the pre-core promoter region—a G4-quadruplex—a distinct, stacked, four-guanosine folding arrangement of the DNA. Such quadruplexes are being discovered at key transcription and translation sites of numerous organisms and are thought to be important regulators of these processes.

We hypothesize that the host proteins bind at the pre-core promoter site through a G4-quadruplex, and disruption of this inhibits binding, hindering replication.
**Aims:** (1) Demonstrate that oligomers of the pre-core promoter region forms a quadruplex in its wildtype form; (2) Demonstrate that these motifs form in physiologically-relevant samples.
**Methods:** The wild-type and single-nucleotide mutation oligomers of the pre-core binding region were solubilized and purified through FPLC. Fractions of the purified products underwent circular dichroism, electrophoretic mobility shift assay, and small angle X-ray scattering analyses. Next, a known quadruplex-binding protein, DHX36 was produced using an E.coli expression system with an added His-tag and purified using a cobalt bead column. Pull-down assays of the DHX36 with the two oligomers were performed. Finally, cccDNA was extracted from an HBV-infected explanted liver via the Hirt extraction method and a similar pull-down assay was performed.
**Results:** Using several biophysical methods, we demonstrate that the wild-type oligomer forms quadruplex structures, while the mutant oligomer does not. As well, we show a known quadruplex-binding protein, DHX36 to bind only to the wild-type oligomer and provide evidence for an analogous in vitro process with cccDNA.
**Conclusions:** This novel finding of a quadruplex in the pre-core region provides a unique opportunity to study a critical host-protein interaction in cccDNA transcription. Through the pursuit of high-resolution structural data, we will be creating the framework for designing a novel inhibitor of the resilient HBV cccDNA, the master template for HBV replication.

**Funding Agencies:** Cumming School of Medicine Seed Grant, University of Calgary

A341

**ANALYSIS OF SERUM HEPATITIS B VIRUS RNA LEVELS IN A MULTIETHNIC COHORT OF PREGNANT CHRONIC HEPATITIS B CARRIERS**

N.H. Patel[1], S. Joshi[4], K. Lau[3], E. Castillo[5], C.S. Coffin[2]

1. University of Calgary, Calgary, AB, Canada; 2. Medicine, University of Calgary, Calgary, AB, Canada; 3. Microbiology, Immunology, and Infectious Diseases, University of Calgary, Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada; 5. University of Calgary, Calgary, AB, Canada

**Background:** Mother to child transmission (MTCT) of HBV is one of the most common routes of transmission worldwide. All infants born to HBV+ mothers should receive complete immunoprophylaxis with HBV immune globulin (HBIG) and vaccine. In some mothers with high HBV DNA levels (>2x $10^5$ IU/mL), antiviral therapy is recommended to further reduce MTCT risk. We had previously documented HBV immune (cytokine) and alanine aminotransferase (ALT) flares in pregnancy; as well as, HBV DNA correlation with quantitative (q) HBV surface antigen levels[1,2,3,4]. There are no prior studies quantitavely assessing other HBV replication markers (i.e., HBV RNA and pre-genomic RNA levels) in pregnancy.
**Aims:** To analyze HBV RNA levels in association with HBV DNA, qHBsAg, genotype and ALT levels in pregnant and/or post-partum Chronic Hepatitis B (CHB) carriers.
**Methods:** In total, sera and plasma from 38 CHB pregnant and/or post-partum women were tested for HBV DNA, including 34/38 for qHBsAg levels by standard clinical assays (Abbott Architect). Serum HBV RNA levels was assessed by in-house qPCR using HBV X gene specific primers (based on a plasmid dilution standard curve). The HBV genotype was determined in (31/38, 82%) by commercial line probe assay (LiPa) or in-house nested PCR using HBV S gene specific primers and Sanger sequencing, according to previously published protocols. Data was analyzed using indepdendent and paired t-test where $p<0.05$ was considered significant.
**Results:** In 38 pregnant CHB carriers (median age 32 y, 53% Asian, 32% African, 15% other), were 79% (30/38) HBeAg negative, and 21% (8/38) on antiviral therapy with Tenofovir Disoproxil Fumarate. In 31/38 patients with HBV genotype results, showed 13% A, 36%B, 19%C, 19%D and13%E. The median ALT, HBV DNA and qHBsAg levels were 19.5 U/L; 2.85 $\log_{10}$IU/mL and 3.3 $\log_{10}$ IU/mL, respectively. Analysis of serum RNA levels showed undetectable HBV RNA in 21% (8/38), detectable but not quantifiable in 32% (12/38), and quantifiable levels in 47% (18/38) tested. In 6 matched pregnant vs. post-partum samples, the serum HBV RNA decreased from a median of 3.47 to 3.01 log10 IU/mL. There was no significant association between HBV RNA levels and HBV DNA levels, qHBsAg, genotype or ALT levels tested.
**Conclusions:** In this multiethnic cohort of CHB carriers in pregnancy, serum HBV RNA levels are not associated with HBV DNA, qHBsAg, genotype or ALT levels. Further studies involving assessment of other HBV virological and serological markers (i.e., HBV pre-genomic RNA, quantitative HBV core antigen) may help increase understanding of HBV natural history in pregnancy.

**References:**
1. Joshi et al; AJRI; 2017.
2. Kochaksaraei et al; JVH; 2016.
3. Kochaksaraei et al; Liver Int; 2016.
4. Virine et al; PLos One; 2015.

**Funding Agencies:** None

A342

**POST-TREATMENT LIVER STIFFNESS MEASUREMENTS PREDICT THE DEVELOPMENT OF LIVER-RELATED COMPLICATIONS IN PATIENTS WITH HCV CIRRHOSIS WHO ACHIEVE SVR POST-DAA THERAPY**

F. Nguyen, C. Galanakis, C. Cooper, C. Tsien

University of Ottawa, Ottawa, ON, Canada

**Background:** Chronic hepatitis C virus (HCV) infection may lead to cirrhosis and liver-related complications (LRC) such as hepatocellular carcinoma (HCC), ascites, hepatic encephalopathy (HE) and esophageal varices. Transient elastography (TE) is a non-invasive measurement of liver fibrosis in HCV, and may predict LRC. HCV therapy with sustained virologic response (SVR) appears to decrease liver stiffness (LS) however, whether this is also associated with fewer LRC is unclear.
**Aims:** To evaluate whether a reduction in LS post-HCV treatment with SVR is associated with a lower incidence of LRC in cirrhotic patients within 24 months of therapy.
**Methods:** We included all cirrhotic patients (LS >12.5 kPa) treated with direct acting antivirals (DAAs) between May 1, 2013 and June 1, 2016 with SVR and pre- and post-treatment TE. We excluded patients with new/worsening LRC before post-treatment TE. Those with baseline LRC were included, and evaluated for worsening LRC, as defined by progression of post-treatment grading of the LRC compared to baseline. The absence of new/worsening LRC was recorded as 'non-event'. ROC curves and Kaplan-Meir analysis were used. Person-time was calculated from the post-treatment TE date to the last clinic visit up to 24 months post-treatment.
**Results:** Of 57 patients, we excluded 4 patients with new LRC prior to post-treatment TE. TE was performed a median 32 weeks after end of treatment (IQR 28.5 weeks). 40/53 (75.5%) patients had reduction in LS, with a mean decrease of 10.7 kPa (SD 10.4). There were no differences in baseline characteristics of patients with/without decreased LS. Post-treatment, 4 events occurred during follow-up: 1 new varices, 1 new HCC, and 2 progression known varices. The incidence rate for patients with increased LS was 0.47/100

person-weeks, vs. 0.19/100 person-weeks for patients with decreased LS (RR 2.5, p=0.40, 95% CI: 0.26-24.0), with no significant difference in mean time to event (74 weeks vs. 79 weeks, respectively, p=0.55). All events occurred in individuals with LS >20.75 kPa, while no events occurred in individuals with LS score <20.75 kPa (4/20 vs. 0/33, p=0.02). This LS cutoff also had the best AUC (0.786) with a sensitivity of 100% and specificity of 67%. Post-treatment, 20/53 (37.7%) patients still had a LS above 20.75 kPa.
**Conclusions:** In our cohort of patients with early cirrhosis (Child-Pugh class A), successful antiviral therapy led to a reduction in LS in most patients. Prior studies have identified a LS cutoff of 20 kPa as associated with clinically significant portal hypertension, and this was confirmed in our post-treatment cohort. Many (37.7%) patients remained above this cut-off and require LRC monitoring post-SVR. The predictive value of long-term, serial LS measurements requires evaluation.

**Funding Agencies:** None

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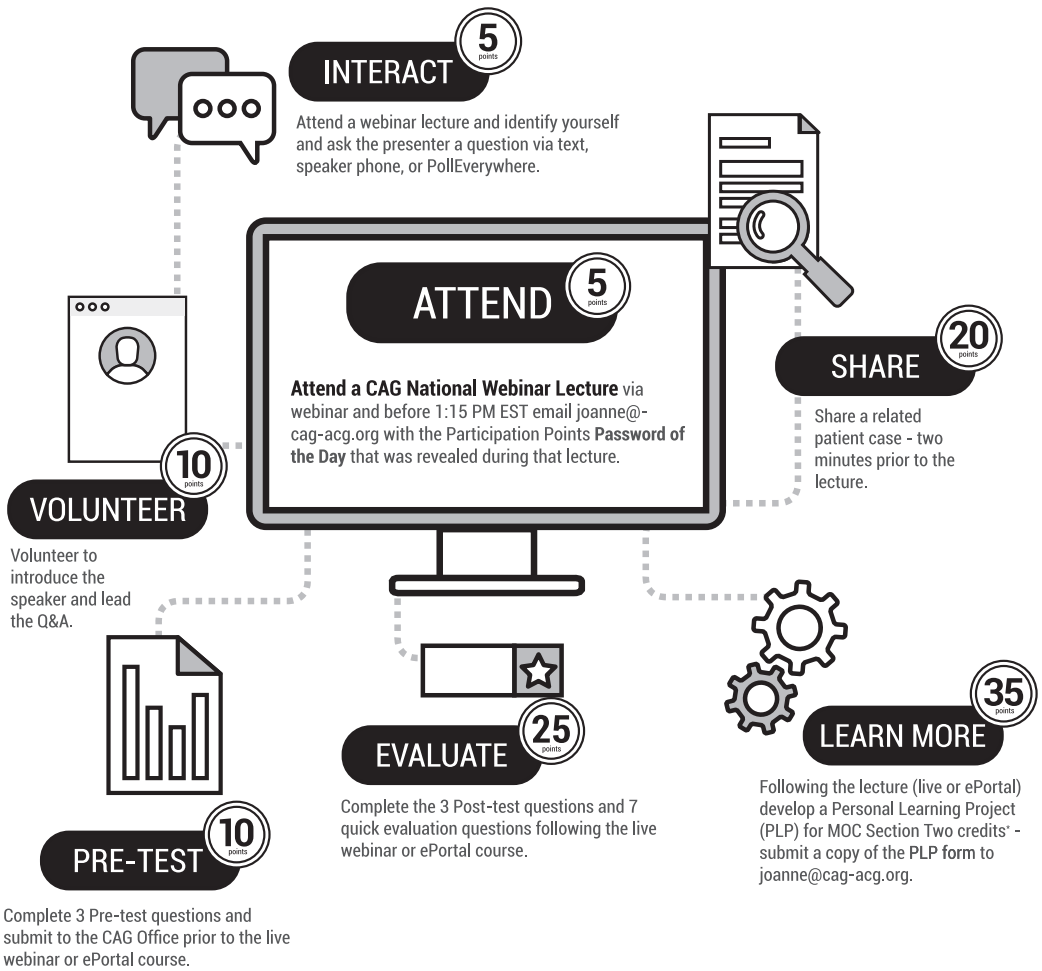


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**Reference: 1.** HUMIRA Product Monograph. AbbVie Corporation. July 28, 2017.

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