Canadian Association of Gastroenterology | L'Association Canadienne de Gastroentérologie

Canadian Association for the Study of the Liver | CASL ACEF | Association Canadienne pour l'étude du foie

CDDW DIGEST

2015 CAG Canadian Digestive Diseases Week and the Annual CASL Winter Meeting

Banff, Alberta

February 28, 2015 to March 1, 2015

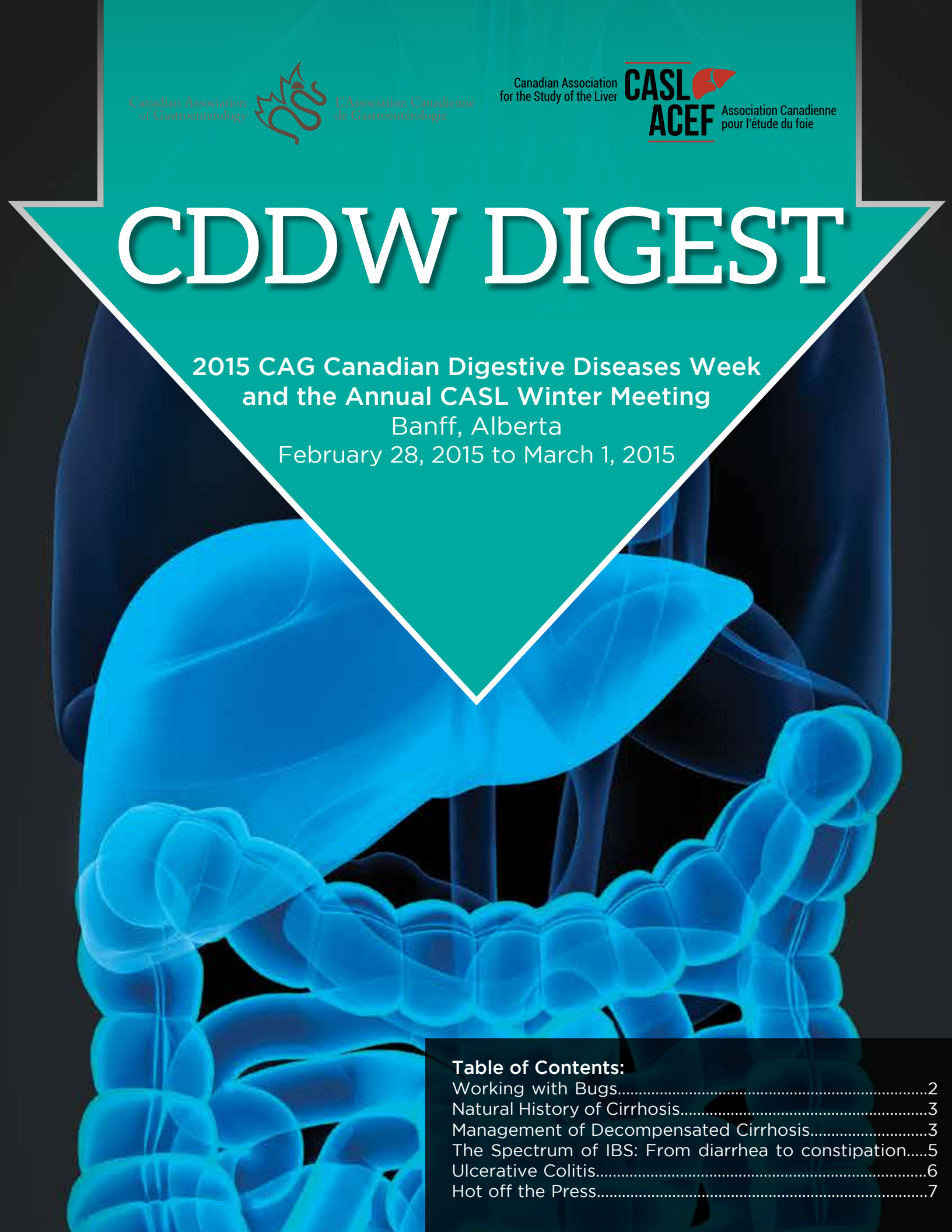


Table of Contents:

Working with Bugs

CAG Symposium

This session was co-chaired by **Dr. John Marshall** (McMaster University) and **Dr. Elaine Petrof** (Queen's University)

Not so Unculturable: Recent advances in cultivating the human gut microbiome

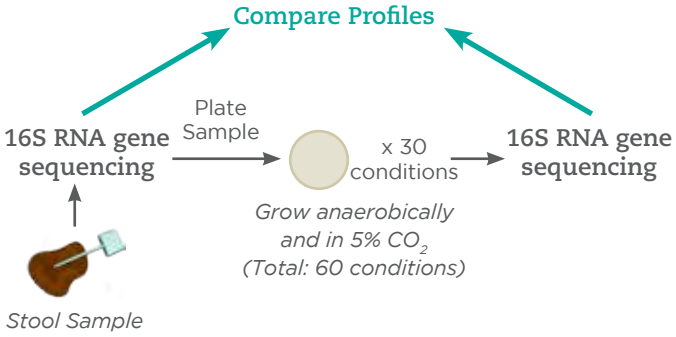
Dr. Michael Surette (McMaster University)

There have been recent advances in culturing the human gut microbiome, which are altering traditional beliefs that most of the microbiome is not culturable and requires culture-independent methods for identification.

Dr. Michael Surette discussed the advantages and disadvantages of common strategies to culture the microbiome (i.e. chemostats and germ free mice), as well as more recent approaches which experiment with different media or dilutions of stool samples in 384 well plates. These more recent methods have recovered a significant portion of the operational taxonomic units (OTUs) identified in sequencing. Sequencing depth is important when identifying microorganisms, as deeper sequencing allows for identification of rarer organisms.

Evidence suggests most of the gut microbiome can be cultured and diversity is currently underestimated. Using culture enriched molecular profiling (Figure 4), more than 90% of the microbiome (identified by sequencing) was cultured. Using this technique, researchers were able to identify a series of isolates that were not identified in the culture independent methods, highlighting the ability of culturing techniques to enrich for rare organisms.

Figure 4: Culture enriched molecular profiling



The ability to culture a greater proportion of the gut microbiome could improve understanding of mechanisms of disease, microbiome directed therapies, fecal microbiota transplantation and the development of novel probiotics and antibiotics.

Probiotics: Where are we and where are we going?

Dr. Karen Madsen (University of Alberta)

Dr. Karen Madsen discussed the past, present and future of probiotics, noting the concept of using bacteria to fight bacteria has been around since the work of Louis Pasteur in the 1800s. Today the definition of probiotics refers to live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Probiotics may work through a number of mechanisms which can be classified as widespread (common among studied probiotics, i.e. colonization resistance), frequent (species-level, i.e. vitamin synthesis), or rare (strain specific, i.e. neurological or immunological effects). Dr. Madsen emphasized the need to understand the mechanism required to alter human health/disease.

There are clinical applications for probiotics in chronic diarrhea, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD) and metabolic syndrome. The effects are modest in human trials and are best observed when probiotics are used as adjunctive therapy. The modest effects are likely attributed to diet of the host, existing microbiota, competitive or inhibitory effects, host adaptation or wrong strains. Controlling inflammation, prior to probiotic use, is thought to improve response, as inflammatory by-products may have a detrimental impact on probiotics.

Moving forward, microbiome research will play a key role in advancing the field of probiotics by elucidating new or optimal strains. Further research will also help determine optimal timing, concentration and duration of probiotic treatment.

FMT: past, present, future?

Dr. Christina Surawicz (University of Washington)

Fecal microbiota transplantation (FMT) is the process of transplanting stool from a healthy donor into a diseased individual's colon as a method for restoring the normal microbiome. Dr. Christina Surawicz discussed the history of FMT, which was documented as early as the 16th Century in China. However it wasn't until 2000, after the emergence of a hypervirulent strain of *Clostridium difficile*, where the frequency of FMT procedures began to rise.

For patients with recurrent *C. difficile* infection (including patients who are immuncompromised), FMT is considered to be safe and effective, with efficacy rates of approximately 90%. Thorough donor selection and screening are essential to exclude pathogens, cancer, autoimmune disease, metabolic syndrome and GI diseases/symptoms. Prior to the procedure, patients must be informed of the potential risks and counselled that long-term effects are not known. Currently, FMT is considered an investigational therapy. Dr. Surawicz recommended all patients with recurrent *C. difficile* infection receive a vancomycin pulse regimen prior to the procedure as this may be effective and obviate the need for the FMT.

> "For patients with recurrent *C. difficile* infection, fecal microbiota transplantation has efficacy rates of ~90%"
>
> - Dr. Surawicz

The future of FMT will focus on regulation, registries and research. There is a need for long-term data and standardization of indications, methodology and screening. The FDA considers stool to be a drug and biologic; Dr. Surawicz expressed concern with restricted access under this classification, stating stool could be classified as a tissue. Future areas of study should include new formulations (oral capsules, synthetic stool, etc.) and trials of FMT in refractory *C. difficile* and IBD. Advances in the next 5 years may provide more attractive solutions to recurrent *C. difficile* infection, eliminating the need for FMT.

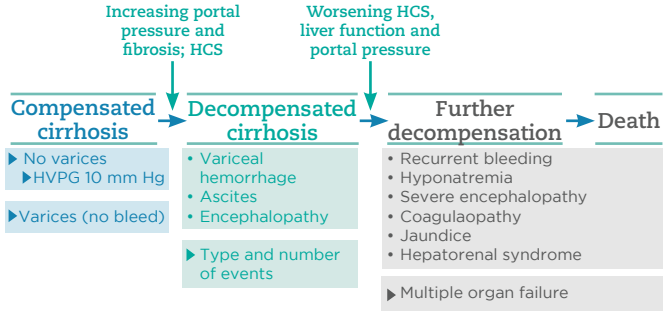
Natural History of Cirrhosis

CLF-CASL Gold Medal Lecture

Dr. Guadalupe Garcia-Tsao (Yale School of Medicine, Conneticut)

This year the Canadian Liver Foundation (CSL) and Canadian Association for the Study of the Liver (CASL) honoured Dr. Guadalupe Garcia-Tsao with a Gold Medal for her contributions to the current understanding of the natural history of cirrhosis. In her lecture, Dr. Garcia-Tsao discussed cirrhosis as a dynamic and potentially reversible disease, involving progression across different prognostic stages: compensated, decompensated and further decompensated (Figure 1). Progression through the stages of cirrhosis is characterized by increasing portal pressure which correlates with fibrosis level. She noted that hepatic venous pressure gradient (HVPG) is a useful diagnostic marker, where patients with an HVPG >6 mm Hg are considered cirrhotic.

Figure 1: Stages of cirrhosis and stratifying factors



HCS: hyperdynamic circulatory state

Dr. Garcia-Tsao emphasized that compensated and decompensated cirrhosis are distinct disease entities, with different clinical characteristics, mortality rates and predictors of death. She reviewed histological, clinical, hemodynamic and biological parameters for each stage, highlighted in Figure 2. Patients with compensated cirrhosis can be further stratified based on the presence or absence of varices without bleeding. Of note, the main predictor of the development of varices is an HVPG >10 mm Hg.

Figure 2: Classification of chronic liver disease

	F1-F3	F4 (Cirrhosis)		
Histological				
Clinical	*Non-cirrhotic*	*Compensated*	*Compensated*	*Decompensated*
Symptoms	None	None (no varices)	None (varices present)	Ascites, VH, Encephalopathy
Sub-stage	–	Stage 1	Stage 2	Stages 3 and 4
Hemodynamic (HVPG, mmHg)		>6	>10	>12
Biological	Fibrogenesis and Angiogenesis	Scar and X-linking	Thick (acellular) scar and nodules	Insoluble scar

VH: variceal hemorrhage.
Adapted from Garcia-Tsao et al. Hepatology. 2010;51:144-9.

Increasing portal pressure and fibrosis, as well as a hyperdynamic circulatory state, can result in the transition from a compensated to decompensated state. Decompensated cirrhosis is characterized by the presence of clinically evident complications such as variceal hemorrhage, ascites and encephalopathy. Heterogeneity between patients with decompensated cirrhosis is attributed to the type and number of complications. Once decompensated, patients have a median survival of 2 years.

Further decompensation occurs following an acute insult such as bacterial infection or liver injury. This stage is characterized by recurrent variceal hemorrhage or hepatic encephalopathy, non-responsive ascites, hyponatremia, hepatorenal syndrome, coagulopathy and jaundice, which can result in multiple organ failure. Higher mortality rates were associated with extrahepatic vs. intrahepatic insults, suggesting patients with decompensation may be further stratified.

Understanding a patient's stage of cirrhosis allows for individualized management approaches based on pathophysiology, including removing or reducing the cause of damage; reducing fibrosis and angiogenesis; reducing portal pressure or preventing acute insult. Liver transplantation should be considered for patients with decompensated cirrhosis.

The Management of Decompensated Cirrhosis: Controversies and new developments

CASL Symposium

This session was co-chaired by **Dr. Eberhard Renner** (University of Toronto) and **Dr. Mang Ma** (University of Alberta).

Minimal Hepatic Encephalopathy - Can we continue to ignore this in clinical practice?

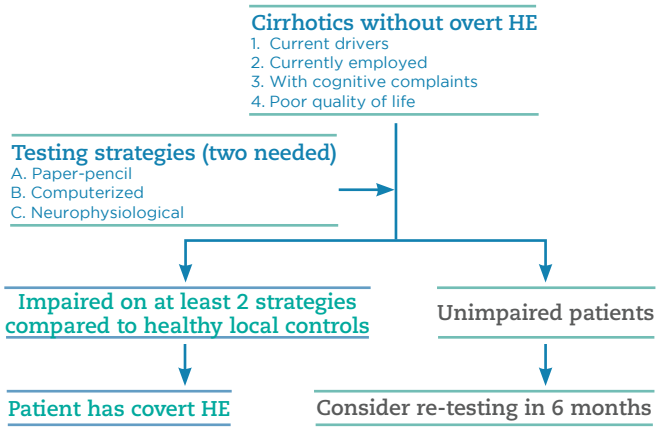
Dr. Jasmohan Bajaj (Hunter Holmes McGuire VA Medical Center, Virgina)

Hepatic encephalopathy (HE) is a neuropsychiatric and neurocognitive complication of acute and chronic liver disease, which can be classified into covert HE and overt HE. Covert HE is the term ascribed to patients with minimal HE or a Grade 1 classification according to the West Haven Criteria, and is often ignored in clinical practice. Dr. Jasmohan Bajaj emphasized the importance of identifying covert HE, as it can prognosticate overt HE, indicate poor quality of life (QoL) and reduced socioeconomic potential, and is also associated with a higher risk of falls and driving impairment.

Dr. Bajaj discussed how covert HE requires specialized testing that should only be performed on patients who are likely to benefit, i.e. those who drive, are employed, have cognitive complaints or a poor QoL. Patients with other causes of neurocognitive dysfunction should not be tested as this may confound results. A diagnosis of covert HE can be made if patients are impaired on at least two testing strategies (neuropsychological tests, psychometric hepatic encephalopathy scales, rapid automated tests or sophisticated neurophysiological tests) (Figure 3). The Stroop test (available as a free app) and the sickness impact profile are simple screening methods.

Once identified, patients with covert HE and their caregivers, should be counselled about the disease and the potential driving impairment associated with the disease. Treatment is not standard of care for these patients; however, trials with lactulose, rifaximin and probiotics have shown improvements in health-related QoL and lactulose has been found cost-effective.

Figure 3: Diagnosis of covert HE



Acute-on-Chronic Liver Failure: A distinct clinical entity?

Dr. Richard Moreau (Inserm, Clermont-Ferrand, France)

Dr. Richard Moreau discussed acute-on-chronic liver failure (ACLF), which is acute decompensation (AD) associated with organ failure(s) and a high risk of short-term mortality. ACLF is distinct from decompensated cirrhosis.

Until recently there was no evidence-based definition for ACLF. CANONIC is the first evidence-based study designed to define and identify patients with ACLF. The definition of ACLF was based on the presence of AD (ascites, gastrointestinal [GI] hemorrhage, hepatic encephalopathy; present in all patients), organ failure (predefined by the CLIF-SOFA score) and a high 28-day mortality rate. Using this classification system, patients with ACLF can be stratified into four categories depending on severity (Table 1).

Table 1: Classification of ACLF

Classification	Organ Failure	28 day mortality
No ACLF	No organ failures*	4.7%
ACLF-1	Single organ failure*	22.1%
ACLF-2	2 organ failures	32.0%
ACLF-3	>3 organ failures	76.7%

*Simplified definition – see *Gastroenterology. 2013;144:1426* for comprehensive criteria.

Precipitating factors could not be identified in 50% of patients with ACLF. Patients with ACLF were younger and had a higher prevalence of alcoholic cirrhosis; however, ACLF is not exclusive to severe alcoholic hepatitis. ACLF mortality was greater in patients with no prior history of AD and was associated with loss of organ function and a high white cell count (a marker of systemic inflammation).

Portal Vein Thrombosis: Cause or result of decompensation?

Dr. Guadalupe Garcia-Tsao (Yale School of Medicine, Conneticut)

Patients with cirrhosis are prone to developing portal vein thrombosis (PVT), and until recently it was not clear if PVT was the cause or consequence of liver disease progression. Dr. Guadalupe Garcia-Tsao presented evidence suggesting PVT indicates the presence of severe liver disease and is not an independent predictor of decompensation and death. Portal vein thrombosis occurs in sicker patients; predictors of development include the presence of varices and prothrombin time.

The presence of PVT becomes a concern in the liver transplant setting, where occlusive PVT is a predictor of post-transplant mortality. Partial PVT does not increase mortality post-transplant.

> "Portal vein thrombosis is the result of severe liver disease. It is not an independent predictor of decompensation or death"
>
> - Dr. Garcia-Tsao

There are currently no treatment guidelines for PVT and patients should be managed on an individualized basis. Anticoagulant therapy is recommended for patients with symptomatic superior mesenteric vein (SMV) thrombosis; patients on a transplant list with recent occlusive PVT, extension of PVT or extension into SMV; and for patients with a prothrombotic disorder. These patients should also receive prophylaxis for variceal hemorrhage prior to anticoagulation. Anticoagulation is not recommended for patients with partial PVT, those who have contraindications to anticoagulant therapy or patients who require frequent monitoring. A transjugular intrahepatic portosystemic shunt (TIPS) can be considered as second-line therapy for PVT.

Varices: Is carvedilol a superior therapy? When are beta-blockers unsafe? Is variceal hemorrhage a novel indication for statin therapy?

Dr. Juan Abraldes (University of Alberta)

Non-selective beta blockers (NSBBs) are the mainstay of therapy for portal hypertension in patients with cirrhosis; however, their safety has been questioned in patients with refractory ascites. Dr. Juan Abraldes reviewed current evidence for the risks and benefits of NSBBs. In patients with ascites, use NSBBs only when blood pressure can be monitored and frequent blood tests performed. Non-selective beta blockers should be discontinued if systolic blood pressure decreases below 95 mm Hg; at the onset of orthostatic symptoms; or if creatinine levels increase. They should not be used during septic episodes.

Dr. Abraldes also discussed the role of carvedilol in the prevention of variceal bleeding, noting its effectiveness over propranolol for decreasing portal pressure. Carvedilol may be more effective than endoscopic banding ligation (although based on limited evidence). It should be reserved for well compensated patients with normal or high arterial pressure and should not be used in patients with ascites.

The rationale for statins as a treatment of variceal bleeding was addressed in the BLEeding Prevention with Simvastatin (BLEPS) study, which showed simvastatin improved survival after variceal bleeding in patients with cirrhosis versus placebo. This benefit was seen exclusively in patients with Child-Pugh A/B (not Child-Pugh C). Simvastatin had no effect on the rate of rebleeding.

The Spectrum of Irritable Bowel Syndrome: From diarrhea to constipation

CAG Symposium

This session was co-chaired by **Dr. Christopher Andrews** (University of Calgary) and **Dr. Stephen Collins** (McMaster University).

Microbiota and the Gut-brain Axis: Implications for etiology and management

Dr. Premysl Bercik (McMaster University)

Irritable bowel syndrome is a chronic GI disorder, often triggered by stress, which is associated with a high prevalence of anxiety and depression. Dr. Premysl Bercik presented data showing how gut microbiota may contribute to these intestinal and behavioral manifestations of IBS.

Symptoms of IBS can be triggered by infection. The microbiota profiles of some patients with IBS are abnormal, although no specific microbial signature has been identified. There is a relationship between IBS symptoms and antibiotic use, where antibiotic treatment has been shown to improve or trigger IBS symptoms in a subset of patients.

Researchers have identified altered metabolomic profiles in an IBS microbiome, which may explain how the microbiomes of diseased and healthy individuals could cluster together. These findings suggest it may be less about 'who' is present and more about 'what metabolites' are present. The microbiota of patients with diarrhea predominant IBS (IBS-D) induces faster intestinal transit, alters intestinal barrier function, and has been found to induce immune activation.

In patients with functional GI disorder, presence of anxiety/depression correlated with the severity of GI symptoms. Mice developed anxiety-like behavior when colonized with microbiota from patients with IBS and anxiety/depression. This suggests microbiota from patients with IBS-D have the capacity to alter behavior of the host.

Dietary Management of IBS: Ready for prime time?

Dr. Melanie Stapleton (University of Calgary)

The majority of IBS patients believe certain foods trigger their GI symptoms, consequently these patients often restrict their diet. While this is a safe and accessible management approach, there is limited dietary guidance available for patients with IBS. Dr. Melanie Stapleton reviewed the current views and dietary recommendations for fibre, gluten and fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAPs) in patients with IBS.

Although large-scale reviews suggest fibre has no effect on IBS symptom improvement, these trials are associated with several limitations. Dr. Stapleton stated that fibre should be considered a reasonable option for patients with IBS, but more data is required to determine the optimal type of fibre and patient populations.

Symptomatic improvements have been observed with gluten-free diets; however the current belief is this is a result of restricting FODMAPs, a component of foods high in gluten. The rationale and mechanisms for how FODMAPs could result in IBS symptoms were discussed. FODMAPs are poorly absorbed in the small intestine, osmotically active and can be rapidly fermented by bacteria. However, the mechanism(s) behind the symptomatic improvements seen with a FODMAP-restricted diet are not clear.

Dr. Stapleton recommends a FODMAP-restricted diet for patients with IBS. It is important to seek guidance from a registered dietician and obtain tools/resources to assist with implementation. Access to resources (counselling, food preparation, socioeconomic, etc.) can be a frequent barrier to a FODMAP-restricted diet. Caution should be used as this approach is for symptomatic management and does not address underlying psychological or social issues.

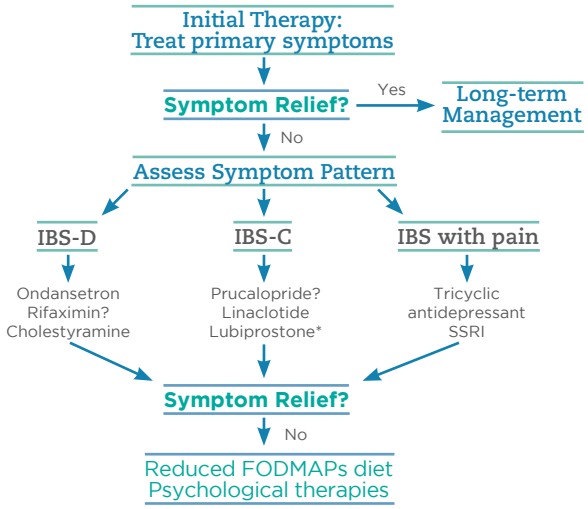
Medical Management of IBS in 2015

Dr. Jan Tack (University Hospital Leuven, Leuven, Belgium)

Dr. Jan Tack spoke about the medical management of IBS, highlighting the appropriate patient work-up and treatment algorithm. Initial management should focus on primary symptoms, including antispasmodics or peppermint oil for pain; fibre, dietary measures or laxatives for constipation; and antidiarrheals (i.e. loperamide) for diarrhea.

For refractory patients, second-line treatment should be based on the dominant symptom (IBS-D, constipation predominant IBS [IBS-C] or IBS with pain). The recommendations are shown in Figure 5. Prucalopride is not approved for use in IBS-C; however, it has shown benefits on symptoms of bloating and discomfort, reminiscent of some IBS symptoms, but the studied patient population was selected on rather severe chronic constipation. At this time, rifaximin is not approved for use in IBS-D, and a recently finalized re-treatment trial, requested by regulatory agencies to provide information on long-term efficacy, is currently being evaluated. For patients who still do not respond to treatment, psychological therapies and a FODMAP-restricted diet should be considered.

Figure 5: Management of IBS



*Not approved for IBS-C in Canada or Europe
SSRI: selective serotonin reuptake inhibitor

In reviewing new medical therapies and approaches for IBS-C, Dr. Tack highlighted the guanylate cyclase-C agonist, plecanatide along with bile acid transport inhibitors as promising novel treatments. New therapies under investigation for IBS-D include ibodutant (neurokinin 2 antagonist) and eluxadoline (combined mu opioid receptor agonist and delta opioid receptor antagonist).

Ulcerative Colitis

CAG Symposium

This session was co-chaired by **Dr. Edmond-Jean Bernard** (Université de Montréal) and **Dr. Brian Bressler** (University of British Columbia).

Therapeutic drug monitoring to optimize management of UC

Dr. Niels Vande Casteele (University of California San Diego)

Dr. Niels Vande Casteele discussed the rationale for therapeutic drug monitoring (TDM), noting the causal relationship between tumour neciosis factor (TNF) antagonist exposure and efficacy. The inter-individual variability in pharmacokinetic and pharmacodynamic profiles can impact overall exposure and magnitude of response.

Data show a concentration-effect relationship on clinical response, mucosal healing and clinical remission for infliximab, adalimumab and golimumab in ulcerative colitis (UC). Results from the TAXIT trial showed dosing infliximab by TDM was more cost effective than dosing based on clinical features, as it allowed for dose reductions and a 28% cost savings. This study also demonstrated a causal relationship between exposure and response in patients with Crohn's disease (CD), but not UC. No difference in remission rates were observed between the two dosing strategies.

A similar relationship between exposure and response was also observed with the novel anti-adhesion monoclonal antibody, vedolizumab, during induction; however, more data is required to confirm whether this is a casual relationship. A 95% saturation of the $\alpha_4\beta_7$ receptor was observed after one infusion of vedolizumab.

These findings support a role for TDM as a guide for treatment decisions upon secondary loss of response, or for optimizing dosing in responder patients to improve cost-efficiency.

Overview of the CAG clinical practice guidelines for moderate to severe UC

Dr. John Marshall (McMaster University)

Dr. John Marshall presented the new Canadian Association of Gastroenterology (CAG) guidelines for the management of UC which represent the first Canadian guidelines for non-hospitalized UC, and the first guidelines to include new therapeutic classes worldwide. The development process and grading system was reviewed along with the definitions for remission and response in UC.

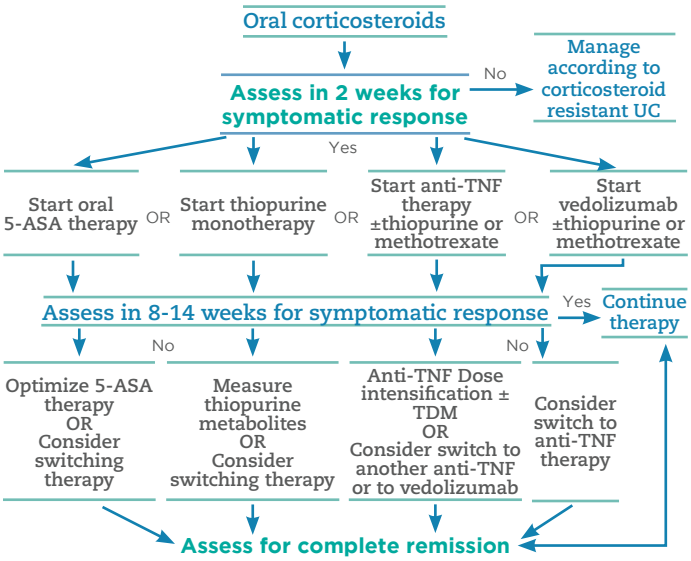
The new guidelines include recommendations according to whether a patient has mild-moderate, moderate-severe or steroid-resistant/dependent UC. 5-aminosalicylic acid (5-ASA) Therapy should be considered first-line for patients with mild-moderate UC. For 5-ASA treatment failures, corticosteroids should be considered second-line to induce complete remission.

In patients with moderate-severe UC (Figure 6), oral corticosteroids should be considered first-line to induce, but not maintain, clinical remission, while thiopurine monotherapy can be used to maintain complete remission. Oral 5-ASA therapy is suggested for select 5-ASA-naive patients who achieve symptomatic remission on oral corticosteroids while being assessed for corticosteroid-free complete remission.

For patients who fail thiopurine or corticosteroids, anti-TNF therapy (adalimumab, golimumab or infliximab), in combination with thiopurine or methotrexate, is recommended to induce complete remission. Vedolizumab (anti-integrin) can be considered in primary or secondary anti-TNF failures, or in patients with moderate-severe UC who fail corticosteroids or thiopurines, to induce complete remission. TDM is recommended for dose optimization in patients with secondary failure.

Probiotics and FMT are not recommended to induce or maintain complete remission.

Figure 6: Treatment algorithm for moderate to severe UC



Complete remission in UC

Dr. Remo Panaccione (University of Calgary)

The guidelines endorse complete remission as the treatment target for patients with UC, which involves both symptomatic remission and endoscopic healing. Patients who achieve endoscopic healing are more likely to have sustained remission and fewer adverse outcomes.

Dr. Remo Panaccione presented evidence supporting the guideline concept of complete remission and whether clinicians should instead target histological remission. Histological remission decreases flares and reduces the risk of developing dysplasia and colorectal cancer. This endpoint is currently not a recommended target, but may be a desirable future goal.

There is a role for non-invasive, serological markers to monitor endoscopic healing long term, particularly for asymptomatic patients. These markers should correlate with intestinal inflammation, lesions and treatment response. There is evidence for fecal calprotectin and serum CRP as biomarkers of intestinal inflammation. Elevated CRP predicts the future need for colectomy and may be useful for prognosis. Fecal calprotectin has been shown to correlate with endoscopic lesions, predict relapse and response to treatment.

For patients with an IBD flare, baseline measures of fecal calprotectin, CRP, hemoglobin and platelets prior to and during treatment are recommended. For patients with quiescent IBD, Dr. Panaccione recommends measuring these surrogate markers in patients who have achieved remission as confirmed by endoscopic assessment. Monitoring should be performed every 3 to 6 months, or before a treatment decision is made, although more data is required to optimize cut off values.

Hot off the Press

CAG Symposium

This session was co-chaired by **Dr. Robert Enns** (University of British Columbia) and **Dr. Paul Moayyedi** (McMaster University)

Narcotic use and misuse in Crohn's disease

Dr. Charles Bernstein (University of Manitoba)

Patients with IBD present with abdominal pain, often resulting in the usage of narcotics to manage disease symptoms. Dr. Charles Bernstein discussed a study from Crocker et al. *(Inflamm Bowel Dis. 2014;20:2234-8)* investigating narcotic use and misuse in CD. This retrospective study assessed narcotic use in patients with CD according to whether or not they had functional gastrointestinal disorder (FGID). Narcotic misuse was defined as narcotic prescriptions filled from four or more prescribers and at four or more different pharmacies in a 12 month period.

Twenty percent of patients with CD were using narcotics, with higher rates in patients with concomitant FGID (44%). Of these, 60% were misusing narcotics (12% of CD patients overall). The authors found narcotic misuse was associated with patients who had FGID, disability, anxiety, depression or substance abuse.

Dr. Bernstein highlighted a number of similar studies on the prevalence and predictors of narcotic use in IBD, emphasizing a study by Targownik et al. *(Am J Gastroenterol. 2014;109:1613-20)*. Overall, a significant percentage of narcotics use among IBD patients was reported, particularly in females, substance abusers, smokers, patients taking more than 5 medications, and those with a comorbid psychiatric diagnosis, disability or history of chronic opioid use prior to IBD diagnosis. Heavy opioid use was found to be associated with an increased risk of death in patients with IBD.

These findings can be leveraged to counsel patients against opioid use. Steps must be taken to address the significant issue of narcotic misuse in IBD and solidify the role for gastroenterologists in helping identify and wean patients from opioids.

Visceral abdominal obesity is associated with an increased risk of irritable bowel syndrome

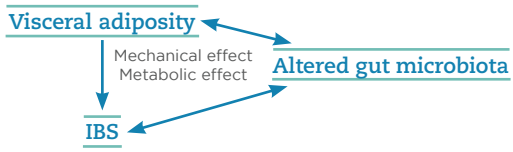
Dr. Paul Moayyedi (McMaster University)

Obesity is considered a risk factor for various GI symptoms; however, until recently, its relationship with FGID was not clear. Dr. Paul Moayyedi presented data from Lee et al. *(Am J Gastroenterol. 2015;110:310-9)*, who found visceral abdominal obesity to be associated with an increased risk of IBS.

This case-controlled study compared measures of obesity (visceral adipose tissue [VAT], subcutaneous adipose tissue [SAT], waist circumference, VAT/SAT ratio, and BMI) in patients with and without IBS. In a multivariate analysis, they found visceral abdominal obesity (VAT, VAT/SAT ratio) and waist circumference were associated with an increased risk of IBS-D (odds ratio of 10). No association was identified with SAT or BMI, corroborating studies in cardiology which found BMI to be a poor predictor of risk.

The authors proposed a mechanism for the link between visceral adiposity and IBS (Figure 7). Dr. Moayyedi noted a few caveats with the study's conclusions: increasing obesity trends do not correlate with an increase in IBS prevalence over time; a higher prevalence of obesity is observed in the US vs. Canada, however, rates of IBS are similar; and obesity increases with age, whereas IBS typically affects younger age groups. It was noted that the observed association between obesity and IBS should not be interpreted as a causative relationship.

Figure 7: Proposed link between visceral adiposity and IBS.



These findings can play a role in helping to unravel factors which contribute to IBS and should encourage more research into microbial components similar between obesity and IBS. They also can be leveraged when counselling patients to lose weight.

Living with IBD: A Crohn's and Colitis Canada survey.

Dr. Subrata Ghosh (University of Calgary)

There is a need to better understand IBD disability and the impact of therapy, which has been limited by the lack of validated assessment methods. Dr. Subrata Ghosh presented the results of a recent Canadian survey by Becker et al. *(Can J Gastroenterol Hepatol. In press)* that assessed the impact of IBD on patients and their families.

This study, performed in conjunction with Crohn's and Colitis Canada, assessed 360 responders using a non-validated, web-based survey. There was a selection bias in the study, with the majority of respondents being women and from urban centres. The survey found IBD impacted participation in leisure activities, interpersonal relationships, mental well-being and financial burden. Patients with IBD felt a greater impact than those without (i.e. family members). No impact was reported on plans to have children, plans to obtain advanced education or career.

Dr. Ghosh also presented data from a paper by van der Have et al. *(Inflamm Bowel Dis. 2015;21:369-77)* assessing factors related to self-reported disability. Using the IBD disability index, which was recently validated against disease activity, this study prospectively assessed patients with CD and UC every 3 months for 2 years. They found disability to be associated with clinical characteristics (emotional response) and illness identity. Disability was not associated with disease duration or complications.

These studies provide the first glimpse at understanding the impact of IBS disability. Similar studies are needed using objective markers of inflammation to eliminate bias associated with symptom reporting. This is an important area of research for influencing public policy on IBD, as disability is proportionate to the direct cost of illness, and for managing disability in the future.

Canadian Association of Gastroenterology | L'Association Canadienne de Gastroentérologie

Canadian Association for the Study of the Liver | CASL ACEF | Association Canadienne pour l'étude du foie

CDDW DIGEST

CDDW Platinum Sponsors:

abbvie

Takeda

CDDW Gold Sponsors:

Actavis

Janssen Pharmaceutical Companies of Johnson & Johnson

The Fairmont Banff Springs

OLYMPUS

GILEAD

Produced and Published by:

MEDUCOM HEALTH INC.
Science meets Strategy

www.meducom.ca

The information contained in this report is intended to reflect content from selected sessions at the 2015 CAG Canadian Digestive Diseases Week and the Annual CASL Winter Meeting held in Banff, Alberta, February 28, 2015 to March 1, 2015.

Any therapeutics mentioned in this report should be used in accordance with federally approved prescribing information. Please consult respective product monographs for complete dosage and official product information. No claims or endorsements are made for any products, indications or dosages not approved in country of usage or presently under investigation. No endorsement is made or implied by coverage of such unapproved use. Information provided herein is not intended to serve as the sole basis for individual care. No responsibility is taken for errors or omissions in this publication.