Food Allergy/Intolerance: A practical approach to diagnosis

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Medical Director – WRHA Food and Nutrition Services
Site Coordinator GI – St. Boniface General Hospital
**CanMEDS Roles Covered**

<table>
<thead>
<tr>
<th>Role</th>
<th>Description</th>
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<tbody>
<tr>
<td>Medical Expert</td>
<td>(as Medical Experts, physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. Medical Expert is the central physician Role in the CanMEDS Framework and defines the physician’s clinical scope of practice.)</td>
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<td>Communicator</td>
<td>(as Communicators, physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)</td>
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<td>Collaborator</td>
<td>(as Collaborators, physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)</td>
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<td>Leader</td>
<td>(as Leaders, physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)</td>
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<td>Health Advocate</td>
<td>(as Health Advocates, physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)</td>
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<tr>
<td>Scholar</td>
<td>(as Scholars, physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)</td>
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<tr>
<td>Professional</td>
<td>(as Professionals, physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)</td>
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## Conflict of Interest Disclosure

(Over the past 24 months)

Name: Dr. Julia Upton

<table>
<thead>
<tr>
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<tr>
<td>CSACI (Canadian Society of Allergy and Immunology)</td>
<td>Chair of Food Allergy and Anaphylaxis</td>
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<tr>
<td>DBV, Aimmune</td>
<td>investigator</td>
</tr>
<tr>
<td>Food Allergy Canada</td>
<td>speaker honorarium</td>
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<tr>
<td>Allergy Asthma &amp; Immunology Society of Ontario</td>
<td>speaker honorarium</td>
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<tr>
<td>SickKids Foundation</td>
<td>Research Support</td>
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(Over the past 24 months)
Name: Dr. Donald Duerksen

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<tr>
<td>Canadian Celiac Association</td>
<td>Chair of Professional Advisory Council</td>
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<tr>
<td>Canadian Nutrition Society</td>
<td>Member Advisory Board</td>
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<tr>
<td>Canadian Malnutrition Task Force</td>
<td>Member Advisory Board</td>
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<td>Shire</td>
<td>Speaker’s Bureau</td>
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Objectives

• Discuss the role of the Allergist/allergy testing in two cases of GI symptoms
  – Eosinophilic Esophagitis
  – Non-specific gastrointestinal symptoms
• Recognize the limitations of Allergy testing for non-IgE mediated reactions
• Recognize when non-specific GI symptoms may be an allergic disease
• Recognize there is a risk of IgE-mediated allergic reactions in patients with EoE
Case 1

• My patient experiences abdominal pain, cramping and diarrhea
  – They think this might be a food allergy
  – Should this patient undergo food allergy testing?
Types of Food Reactions

Adverse Food Reactions

Immune mediated

Food allergy, IgE-mediated
8 foods cause 90% of food allergies. Symptoms within minutes to 2 hours after eating: Hives in 90%, “throat closing”, vomiting. Anaphylaxis can be deadly—Carry epinephrine to treat. Oral allergy syndrome is a type of food allergy

Accuracy of diagnosis:
- Skin test up to 90%
- Blood test up to 70%
- Oral challenge by allergist up to 100%. Food allergy can go away

Non-immune mediated, food intolerance
No need to carry epinephrine. No skin or blood test

Non-IgE mediated
FPIES, celiac and other gluten disorders

Mixed
IgE and non-IgE mediated: EoE (eosinophils)

Cell mediated: allergic contact dermatitis, e.g. nickel from tree nuts

Metabolic
Lactose intolerance, FODMAPs, IBS - managed by GI

Toxic
Food poisoning, Fish scombroid toxin

Other
Sulfites, MSG

Pharmacologic
Caffeine

Sensitization without food allergy = skin test or blood test is positive but patient has no allergic reaction they eat the food

Anaphylaxis

Sudden skin or mucosal symptoms and signs (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)

Sudden respiratory symptoms and signs (e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)

Sudden reduced BP or symptoms of end-organ dysfunction (e.g. hypotonia [collapse], incontinence)

Sudden gastrointestinal symptoms (e.g. crampy abdominal pain, vomiting)

Evaluation: History

Cramping and Diarrhea

- Timing? Usually <2 hrs for IgE-mediated
- Associated IgE-mediated symptoms?
  - Skin: itch, hives, swelling
  - Chest: wheezing, SOB
  - CVS: BP, faint
Most Allergies caused by a few foods

- In Canada, there are nine priority food allergens (substances which causes allergies):
  - peanuts
  - tree nuts (almonds, Brazil nuts, cashews, hazelnuts [filberts], macadamia nuts, pecans, pine nuts [pignolias], pistachio nuts, and walnuts)
  - sesame seeds
  - milk
  - eggs
  - fish (including shellfish and crustaceans)
  - soy
  - wheat
  - Mustard
  - (sulphites)

History: Food trigger?

- GLUTEN:
  - IgE-mediated allergy
  - Celiac Disease: If the patient identifies GLUTEN as a culprit for their symptoms
    - risk ranging from 2% to 42% of having undiagnosed celiac disease
  - Other Non-IgE mediated reaction such as FPIES
  - Non-Celiac Gluten Sensitivity
  - Non-Immunological causes: eg FODMAP

FPIES: Food Protein Enterocolitis

- A non-IgE mediated food related reaction
- Under-recognized gastrointestinal food allergy affecting primarily infants and toddlers, can rarely be seen in adults
- Acute onset of vomiting and diarrhea hours after ingesting a food
- A chronic form can be less dramatic
- Diagnosed by Oral Food Challenge (OFC) or by a clear history (allergy testing will not show)
- In children up to 30% will develop positive allergy tests over time
  - Positive tests modify the OFC protocol and may help in prognosis


### Clinical Presentation of Acute and Chronic FPIES

<table>
<thead>
<tr>
<th>Acute FPIES</th>
<th>Chronic FPIES</th>
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<td>Food ingested intermittently</td>
<td>Food ingested on a daily basis (e.g., cow’s milk or soy infant formula)</td>
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<tr>
<td>Vomiting (onset 1 to 3 hours)</td>
<td>Intermittent vomiting</td>
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<tr>
<td>Lethargy</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Pallor</td>
<td>Lethargy</td>
</tr>
<tr>
<td>Dehydration</td>
<td>Weight loss</td>
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<tr>
<td>Diarrhea (onset 5 to 8 hours)</td>
<td>Failure to thrive</td>
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<tr>
<td>Bloody diarrhea</td>
<td>Bloody diarrhea</td>
</tr>
<tr>
<td>Abdominal distention</td>
<td>Abdominal distention</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Dehydration</td>
</tr>
<tr>
<td>Hypothermia</td>
<td></td>
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*FPIES = food protein-induced enterocolitis syndrome.*

Leonard SA, Nowak-Wegrzyn A. Manifestations, Diagnosis, and Management of Food Protein-Induced Enterocolitis Syndrome. Pediatric Annals. 2013;42(7):e145-e150
Non Celiac Gluten (or Wheat) Sensitivity

- Non-specific and vague symptoms
- No diagnostic test
- Assess with Controlled elimination, ideally Blinded

Burkhardt JG, Chapa-Rodriguez A, Bahna SL. Gluten sensitivities and the allergist: Threshing the grain from the husks. Allergy 2017;00:1–10.

What about IgG4 tests? (Drugstore/Naturopath)

There is no body of research that supports the use of IgG4 testing to diagnose adverse reactions to food or to predict future adverse reactions.
There may be a future for food specific IgG4 tissue testing to evaluate EoE

Bottom Line: Non Specific GI Symptoms and Allergy

• In PEDIATRICS: GI-limited symptoms may represent non-IgE mediated allergy such as chronic FPIES
  – Non-IgE is not testable other than by history, elimination and challenge
  – These patients often have allergic comorbidities and have a risk of having/developing IgE-mediated allergy which is testable

• In ADULTS: There is a small chance that GI-limited symptoms may represent non-IgE mediated allergy (more work is needed to clarify any relationship)
  – Not testable other than by history, elimination and challenge
  – If no concerning features of IgE-mediated allergy may not need allergy referral
Case 2

- 30 year old man has a 10 year history of intermittent difficulty swallowing
- Solid foods may stick especially if he eats quickly
- He had to occasionally swallow water to ‘push’ food from the esophagus into the stomach
- There is no history of GE reflux or heartburn
- He present to the ER after getting a piece of chicken stuck in his esophagus
Case 2

- A gastroscopy is performed
- The food bolus is lodged in the distal esophagus and gently pushed into the stomach
- There is no evidence of a stricture
- There is ‘trachealization’ of the esophagus and longitudinal ridging
  - Biopsies confirm increased eosinophils
- He is given a Rx for Flovent (swallowed) and a follow-up is booked for 3 months
3 months
• At follow-up he states he is feeling well
• He started a gluten free diet in an effort to improve his health
  • He has never been tested for celiac disease
• He has not started flovent as his swallowing has not really been a problem

9 months
• Remains well with no difficulty swallowing
• Adherent to a gluten free diet
  • States he is very strict and doesn’t knowingly ingest gluten
• He is wondering whether he can liberalize his diet and remain well with respect to his swallowing.
Case

- Is it safe to reintroduce small amounts of gluten?
- Is there any risk of developing an allergic response?
Eosinophilic Esophagitis: Symptoms

• In older children and adults with EoE
  – solid food dysphagia
  – food impaction
  – non-swallowing associated chest pain

• In younger children and infants
  – reflux-like symptoms
  – Vomiting
  – abdominal pain
  – food refusal
  – failure to thrive

• Esophageal inflammatory infiltration remitted after exclusively feeding patients with amino acids-based elemental diets

Allergy and EoE

• Personal history of atopy is documented prior to EoE diagnosis in 50–60% of cases
  – Most EoE patients are sensitized to aeroallergens or food allergens (skin or blood tests)

• High prevalence of anaphylaxis has been documented in EoE patients

• Case series have reported approx. 2.7% patients undergoing oral immunotherapy (OIT) for progressive desensitization from IgE-mediated food allergy eventually develop EoE which remits after discontinuation of OIT.

• Child had excellent history of drinking milk with no immediate allergic symptoms
• Avoided milk for EoE
• When milk was reintroduced, anaphylaxis occurred

• Patients with EoE who are found to have positive skin test results to foods should be appropriately evaluated for immediate hypersensitivity reactions and prescribed epinephrine, if indicated.

• Medically supervised food reintroduction might be necessary for patients with previous allergic reactions to a food or IgE-mediated sensitivity documented by SPT responses, serum food-specific IgE levels, or both

• Significant reactions may occur on reintroduction due to a loss of tolerance during food avoidance

6 Food Elimination for EoE

• “Six”-food elimination diet (avoiding milk, wheat, egg, soy, peanuts/tree nuts, and fish/shellfish)
  – Histological improvement in over 70% of adults (versus less than 1/3 of adults have histological improvement based on allergy test directed avoidance)


6 Food Elimination Diet

Your patient failed PPI treatment and is on empiric avoidance for EoE....

• Does avoidance have to be complete?
Milk Ladder

- Milk has different levels of allergenicity depending on the MATRIX and the COOKING.
Some pts with EoE tolerate Baked Milk

• In eosinophilic esophagitis (EoE), strict milk avoidance is commonly recommended for its therapeutic effect

• Some children with EoE can tolerate BAKED MILK diets
  – Leung et al. reported the endoscopy results of 15 children (age 6-17 years) with milk-implicated EoE who had ingested sufficient baked milk products for at least 6 weeks.
  – Eleven patients had maintained disease remission and 4 had disease recurrence as defined by histological criteria of >10 eosinophils per high powered field
  – It is not known if continuing BM in the diet could prevent the development of IgE mediated allergy seen in some patients with EoE on milk-restricted diet

Upton J, Nowak-Wegrzyn A. The Impact of Baked Egg and Baked Milk Diets on IgE- and Non-IgE-Mediated Allergy. Clinical Reviews in Allergy & Immunology. DOI: 10.1007/s12016-018-8669-0.


Table 2. Practical tips for dietary therapy in EoE.

1. Due to convenience, cost and safety profile consider PPI therapy in EoE patients before either topical corticosteroids or elimination diets.
2. Ponder cautiously any elimination diets for patients already on multiple dietary restrictions due to IgE-mediated food allergy. Severe symptomatic patients may benefit best from topical corticosteroids. Compliance issues with diets may arise in older children, adolescents, and young adults.
3. Elemental diet is unfeasible in clinical practice and should be exclusively reserved for refractory patients.
4. Food allergy skin and blood testing-guided diet is discouraged for adult patients. Its efficacy is variable in children, with conflicting results in literature.
5. Efficacy rates for empiric elimination diets are consistent between children and adults. Cow’s milk, wheat, and eggs are the most common food triggers of EoE in children and adults from the United States, Spain, and Australia.
6. A step-up approach for empiric elimination diets might be cost-effective and improve patient uptake for dietary therapy. Therefore, a six-food elimination diet must be reserved for highly motivated patients unresponsive to a two- or four-food elimination diet.
7. All diets should be followed for a minimum of 6 weeks. Its efficacy should be evaluated through symptoms and inflammation improvement in esophageal biopsies obtained during an endoscopic procedure. Sedation for endoscopic procedures is key to engage patients with empiric elimination diets.
8. After remission eliminating several foods or food groups, foods should be individually reintroduced while continuing on the diet (one at a time) for a minimum of 6 weeks, with an endoscopic procedure after each individual food reintroduction.
9. The final goal is to identify which food trigger esophageal inflammation and which do not, in order to design an individualized diet for each patient, avoiding exclusively causative foods in the long run.
10. When available, dietary counseling should be considered for patients on elemental diet, six-food elimination diet, and patient responders to empiric diets with long-term avoidance of multiple food triggers.

Summary: What can Allergy Testing in EoE NOT do?

• Allergy testing will not diagnose EoE
• Allergy testing does not have a clear role in defining which foods to avoid for EoE management
• Allergy testing cannot tell you if the food you reintroduced is causing EoE
  – EoE management is predominantly PPI, then empiric diet or steroids and dilation procedures
  – Empiric elimination is better than allergy testing based methods
Summary: What CAN Allergy Testing do?

• Assess if there are concomitant IgE-mediated food allergies – these patients need epinephrine autoinjectors and education

• Discover if the patient has developed an IgE-mediated allergy after avoidance:
  – these patients may need observed food challenges for reintroduction

• Diagnose other comorbid conditions (environmental allergies, asthma etc)
• As an alternative to biopsies, there is a swallowed sponge under investigation

• Is it safe (from an EoE point of view) to reintroduce small amounts of gluten?
  – It is not known in this case if he has a histological cure (would need histology)
  – If it was the gluten avoidance, it is not known if complete avoidance is needed to avoid EoE recurrence
    • The way to know if wheat is relevant to his EoE is histological

• Is there any risk of developing an allergic response?
  – There is a risk, likely it is low in adults
  – Risk almost non-existent if there were no concerns about IgE-mediated allergy symptoms and if the allergy tests are negative prior to re-introduction
    • We can test for risk of IgE-mediated allergies, even on avoidance diets (unlike celiac)
Bottom Line: EoE

• Refer to Allergy for:
  – Comorbidities
  – risk of IgE-mediated allergic reactions

• Testing is not better than empiric elimination for EoE related dietary avoidance advice
Summary

• Allergy testing (prick and blood tests) cannot **diagnose** non-IgE mediated reactions and cannot **identify** the culprit food or the **response** to re-introduction
• Non-specific GI symptoms can be a **non-IgE-mediated** disease (celiac, FPIES) or **non-immunological** (eg FODMAP, others)
• Allergists can help with management of EoE co-morbidities
• Allergists can help planning for food reintroductions (with FPIES and when risk of IgE-mediated)
• Allergists can assess to rule out and rule in IgE-mediated reactions
Please download the CDDW™ app to complete the session evaluation and to receive your certificate of attendance.