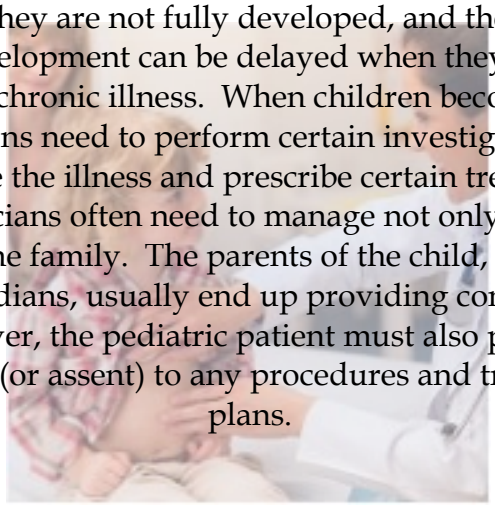
The CEGIIR Lunch'N'Learn News

1. ARE PEDIATRIC PATIENTS "MINI ADULTS"?

Children are special patients. They are not "mini adults". Children have different physiology than adults. They are not fully developed, and their growth and development can be delayed when they have to deal with chronic illness. When children become ill and physicians need to perform certain investigations to diagnose the illness and prescribe certain treatments, the physicians often need to manage not only the child, but the family. The parents of the child, as the guardians, usually end up providing consent. However, the pediatric patient must also provide consent (or assent) to any procedures and treatment plans.



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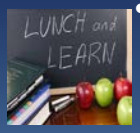


- The fourth session of the CEGIIR GI Lunch'N'Learn Series was held on July 2, 2015 in Katz 7-003

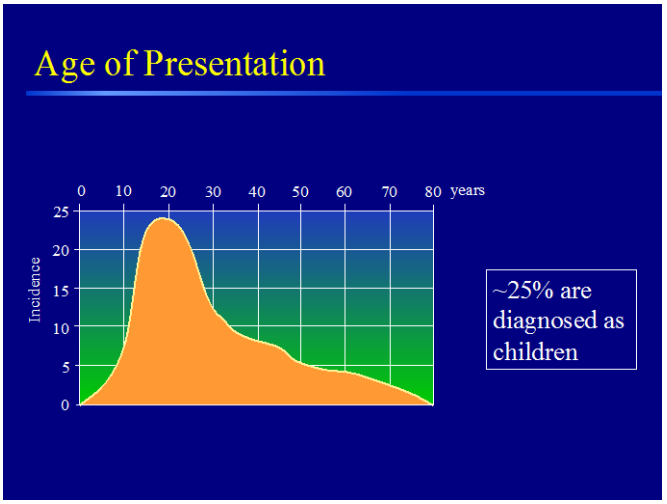
- Today's newsletter brief is a Q & A summary by Dr. Eytan Wine from this session about "Yes, Kids Get IBD Too: Unique Clinical Features and Research Opportunities".

Questions? Comments?

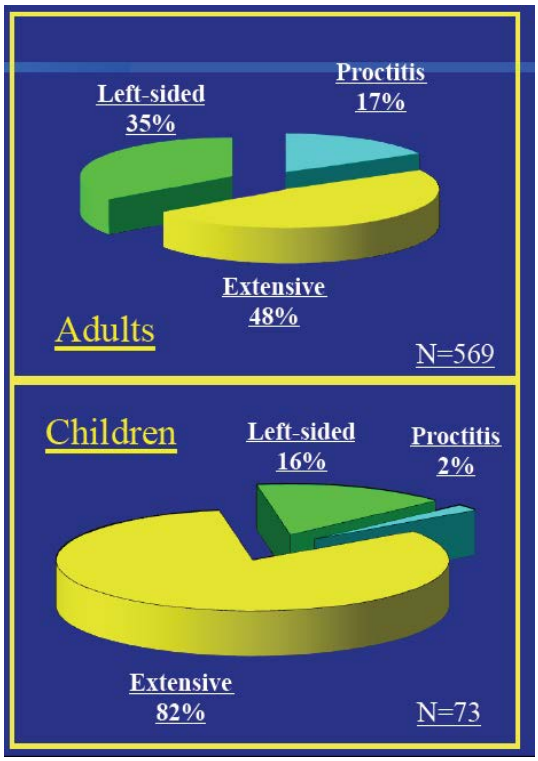
For inquiries, suggestions or feedback, please email Melissa Silva/Kayla-Marie Smith at **llcegiir@ualberta.ca**

2. WHAT IS THE YOUNGEST AGE THAT A PERSON CAN BE DIAGNOSED WITH IBD?

About 25% of patients with IBD are diagnosed as children. There is an increasing prevalence of IBD in Canadian children over the past 2 decades. There is an increase in IBD around the world. It is higher in areas that are highly developed. The highest increase is in pediatric population, specifically young children. IBD-like disease (because they are diagnosed so early, we hesitate to call them Crohn's or ulcerative colitis) has been diagnosed as young as 8 months of age!



3. WHAT IS THE DIFFERENCE BETWEEN IBD IN KIDS AND IBD IN ADULTS?



The disease behavior is different in children. Children have more severe & extensive disease. Best example: UC. In children, 80% have involvement of all of large bowel (pan-colitis). We see this in Crohn's disease as well – it is common to have pan enteric disease.

Children are supposed to be growing, and symptoms and complications of IBD reflect that. Children can present with abdominal pain, weight loss, and bloody stools just like adults. However, with children, they may present with delay in grown or puberty. They may present with different symptoms around the time of puberty or with their monthly periods. We think this is due to changes in hormones and cytokines.

Treatment of IBD in kids is different as it involves the parents. Parents are a different ballgame. We need to deal with the patient, but also the parents as well. There are different ways of dealing with this challenge - some practitioners have tried to fight this. However, we now realize we need to involve the family. We need to speak differently to the child & the parents to get the same message across.

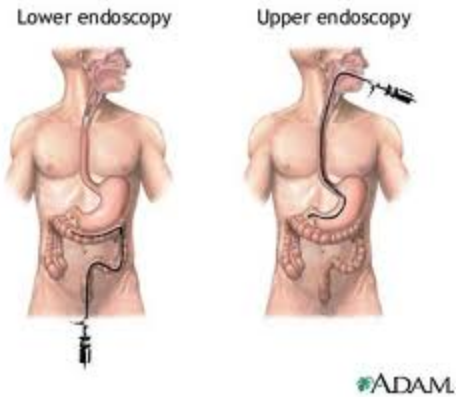
With kids it is less about intellectual ability, and more about level of comfort of dealing with medical issues and the emotional burden of dealing with a chronic illness.

4. HOW DO YOU DIAGNOSE IBD IN KIDS?

For children, evaluation for IBD includes an upper endoscopy and a colonoscopy. In adults, many only receive a colonoscopy with selective upper endoscopy, but in kids, because children are at increased risk for more extensive disease, we tend to do the full evaluation from the beginning. With an upper endoscopy, we can evaluate the upper esophagus, duodenum and small and large bowels.

We try to avoid CT scans due to the radiation. We will use MRI and other imaging tests.

We tend to do more extensive nutritional evaluation, and bone mineral density scans. Bones are very important in childhood as that is the time they are being built.



5. WHAT ARE THE MOST FREQUENT EXTRAINTESTINAL MANIFESTATIONS OF IBD IN CHILDREN?

About 15 % of children with IBD have EIM

1. Inflamed joints (2nd most common)
2. Skin rash (3rd most common) – variety seen
3. Mouth sores (canker sores)
4. Eye involvement
5. Any organ, lungs, brain, etc
6. Perianal disease (subgroup) – not always in direct contact, fissures, skin tags, fistulae most common in Crohn's

These can appear before any GI condition is diagnosed. Crohn's have more of these EIMs.

Table 1 EXTRAINTESTINAL MANIFESTATIONS OF INFLAMMATORY BOWEL DISEASE

Musculoskeletal	**Ophthalmologic**	**Renal**	**Vascular**
Arthralgia	Uveitis	Nephrolithiasis	Thrombosis
Arthritis	Episleritis	Obstructive hydronephrosis	Vasculitis
Ankylosing spondylitis	**Hepatobiliary**	**Oral**	**Growth**
Osteopenia/Osteoporosis	Primary sclerosing cholangitis	Aphthous stomatitis	Growth failure
Dermatologic	Autoimmune hepatitis	Cheilitis	Pubertal delay
Erythema nodosum	Cholelithiasis	**Hematologic**	**Constitutional**
Pyoderma gangrenosum	**Pancreatic**	Iron deficiency anemia	Fever
	Pancreatitis	Vitamin B12 deficiency	
		Anemia of chronic disease	

6. WHAT ARE THE MAIN COMPLAINTS OF CHILDREN WITH IBD?

Quality of life questionnaire studies have been done a lot in children and parents, and show that the concerns from parents and from children are different. With parents, they are concerned about the future (job, marriage, having children etc). Children tend to have practical concerns such as "can't go to school because having diarrhea" or "look different on steroids because of puffy face". Children have more psychological and emotional difficulties dealing with disease. Often we need to work with psychiatry or psychology. We need to ask children questions when alone in the clinic. This is more routine with teenagers – asking about cigarette smoking, drugs, emotions. The physical part is easy to detect and treat. The emotional aspects are harder to detect in children.

7. IS THE TREATMENT OF IBD IN CHILDREN DIFFERENT THAN IN ADULTS?

For the most part, we use similar medications in children with IBD as in adults with IBD. Most of the studies for drugs were done in adults, but through experience and a few clinical trials, we have found them to be safe and effective in children. For example, when first diagnosed with Crohn's, the typical four options presented are:

1. Mild - 5-ASA
2. Steroids (effective, lots of SE, avoid in kids, affect bone health/growth/dev., external SE include swelling of face, stretch marks, acne)
3. Biologics
4. Nutritional therapy (unique) – not a med, no side effects, safe, difficult to do.

Treatment	Induction of Remission	Maintenance	CD	UC
Steroids	☑ Moderate - severe	☒	☑	☑
Enteral Nutrition	☑ CD only	☑ But difficult to do	☑	☒
5-ASA	☑ Mild UC	☑	☒ Maybe in very mild cases	☑ Mild
AZA/MTX	☒	☑ CD > UC	☑	AZA
Anti-TNF	☑	☑	☑	☑

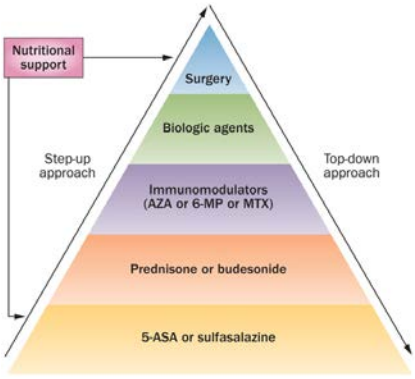
8. NUTRITIONAL THERAPY – FOR CHILDREN ONLY?

Nutritional therapy is unique for children, and not as effective in adults. Instead of eating a normal diet, children are put on a strict regimented liquid diet, using something like Nutren, which is similar to Ensure. This works in kids due to principle of exclusion (by excluding what we have in food products). Here we give a partially broken up diet that heals the bowel as effectively as steroids.

This therapy is difficult to do because it is 8 weeks long. Two ways of taking nutritional therapy are 1) drinking it, and 2) placing a nasogastric tube. However, nutritional therapy can be monotonous, lacks flavor, and requires support and resources.

We do not know exactly why it works, but we think it is because it removes food antigens that stimulate the immune system. Nutritional therapy provides excellent nutrition to the gut. It is liquid, and thus easier to tolerate for some Crohn's patients who cannot tolerate solid chunks of food. It affects gut bacteria because food is not stagnating in the bowel, and because food is already broken down. Nutritional therapy changes bacteria in an effective way.

9. WHAT ABOUT NEWER DRUGS IN CHILDREN WITH IBD?



Children are protected from newer drug trials. The typical trial is randomized – e.g. infliximab or placebo. However, we know now that drugs like infliximab work well in children. Doing these studies in the present day would be unethical. Using placebo is not ethical as we have other drugs we can use. How do we fit kids in this reality (if we know this works on adults – does it work well in children?). There are drugs out there we want to use, but do not know if this works in kids. Fortunately, as an academic center, we have more to work with.

We have to realize that we cannot use the concept "test on healthy, white, male, volunteer" and now even for adult trials we test drugs on variety of background, gender etc.

10. HOW DO CHILDREN WITH IBD TRANSITION CARE WHEN THEY BECOME ADULTS?

The transition from pediatric care to adult care is an important step for teens with inflammatory bowel disease (IBD), and is often a challenging one. Health professionals face many barriers to successful transition, including the physical and emotional immaturity of patients, resistance from parents, and their own hesitations to the subsequent transfer.

A transition plan should be introduced as soon as possible in pediatric patients, allowing adequate time to facilitate a smooth process. Early preparation can help build patient confidence, assuage reservations and resistance from parents, and establish a clear set of goals for the transferring provider. Transitioning focuses on patient education and the development of the necessary skills to independently and successfully manage their IBD in a new and unfamiliar setting.

The pediatric provider should guide and prepare the patient for the new culture of adult health care. The adult patient is expected to articulate his/her medical history, tolerate minor physical discomfort, take initiative in asking questions, and participate in more decision making. The adult provider often focuses more on the disease and less on the psychosocial context, favors the patient's autonomy over nurturance, and treats the individual instead of the patient's family.

A successful transition includes:

- Customizing an approach that takes into account the maturity and personal development of individual patients
- Openly recognizing and addressing barriers inherent to the transition process
- Recognizing that transition is a process, not a single point in time
- Creating a developmentally appropriate program aimed at moving adolescent patients toward self-management
- Starting the process early to establish the necessary skills for self-management, including proper treatment adherence, a general understanding of disease activity, and recognition of flares

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)

Did you know?

You can find updated information on Pediatric IBD research at:

http://www.naspghan.org/

You can find additional information on Pediatric IBD at:

http://www.gikids.org/

In The Media

Young Immigrants at risk of developing IBD:

http://www.ctvnews.ca/health/younger-immigrants-at-greater-risk-of-developing-ibd-study-1.2272470

Fast Facts:

- Nearly 1 in 4 patients diagnosed are under 20 years old.
- The exact cause of IBD is unknown, but both genetic and environmental factors may be involved.
- IBD can affect parts of the body outside the GI tract, such as the skin, joints, eyes, or liver.

11. HOW DO YOU CONDUCT RESEARCH ON CHILDREN?

When recruiting pediatric patients for research, there are many differences compared to research in adult patients.

- Ethics is an important obstacle
  - we need consent from children who can write and read
  - we need permission from children and parents
  - we give the children a brief explanation of what we are doing, children can check off and sign the consent form, even if the parents sign for them.
  - some children do not want details out there, while others are more protected.

- Adults are easier to convince about the importance of research. We often do not argue with kids when they refuse to participate in research, as this occurs. It is important to build trusting relationship.

- Taking samples: we need to budget this, so we do not take unnecessary amounts. Additionally, needles are an issue with kids, so we try to take blood samples at the time they are getting blood work for clinical care

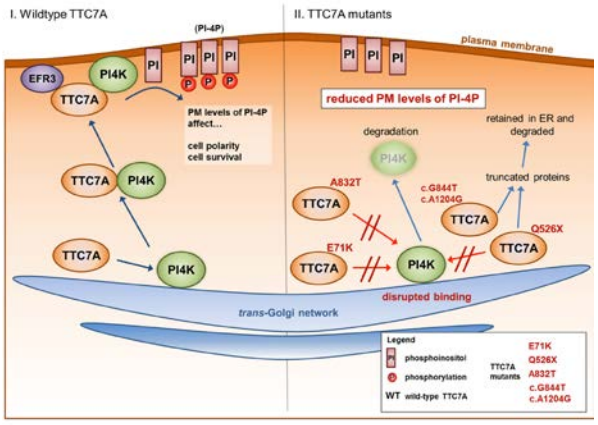
- Numbers: less kids with IBD than adults (harder to collect 100 patients for good sample sizes)

- Opportunities: there are many hints to understanding IBD that occurs in childhood. We can study origins of disease, even for factors before birth. We believe IBD is due to the fact that the immune set point has changed (hygiene hypothesis). First born child seems to have higher risk. Pets, veg, zoo, farms, etc. prove to play a protective role on a statistical level. We can look at adults retrospectively and notice that early exposure does have impact. Therefore, there is a huge opportunity to study diseases in children as they first develop.

- Confounding factors - children have less concomitant medical conditions outside of IBD. They also have fewer cigarettes smoking (risk for CD). Lastly, there is less time from development of first symptoms to first diagnosis.

Examples of opportunities for research in pediatric IBD:

- ❖ Very early onset IBD group: Kids diagnosed before age of two are of interest.
- ❖ Crohn's-like infantile IBD: seen in as early 10 month olds. Looks like Crohn's, unique group.
- ❖ Extensive genetic workup. Many appear to have Crohn's, need to do genetic workup.
- ❖ Gene TTC7a = results in severe colitis from first week of life, work up for intestinal transplant, last known patient died at 7 mo.
- ❖ In IBD, not only single gene responsible. Older children: genetic component richer than even adolescents and adults.



Very Early Onset IBD – Gene TTC7A

PROFILING TRAINEES SECTION

The following students are conducting research in pediatric GI diseases. Studying pediatric GI disease is extremely important for understanding pediatric GI diseases, for diagnosing pediatrics GI diseases, for managing pediatric GI diseases, and for improving the health of pediatric patients with GI diseases. Thank you for your hard work and good luck this summer!

Lucas Churchill is an undergraduate summer student in Dr. Wine's lab. Lucas is studying insight into the pathogenesis of pediatric IBD using probe-based confocal laser endomicroscopy (pCLE).

Deenaz Zaidi is a graduate student in Dr. Wine's lab. Deenaz' is studying the increase in epithelial gaps in pediatric IBD patients and its correlation with inflammation and microbial virulence.

Natalie Klostermann is a graduate student of Dr. Kroeker. Natalie is studying the improvement of healthcare transition for young adults with inflammatory bowel disease using a novel educational intervention that improves medication adherence, IBD knowledge and self-management skills.

Thank you for attending the fourth session of the CEGIIR GI Lunch'N'Learn series.
We look forward to having you participate in future sessions and incorporating your feedback!

Next CEGIIR GI Lunch'N'Learn newsletter:

What? "Demystifying the Microbiome"

Who? Dr. Karen Madsen

Proposed future topics to be discussed this summer:

- Lab techniques
- Qualitative research
- How to make abstracts and posters
- Upper GI Disease

Cartoon of the Day

Lastly…

Special thanks to Dr. Vivian Huang for founding the CEGIIR Lunch'N'Learn series, Brian Reuter, Melissa Silva, contributing scientists (you know who you are), and of course, YOU, for all your help with participating in our fourth session.

Contributing author: Dr. Eytan Wine; Editor: Dr. Vivian Huang, Melissa Silva, Kayla-Marie Smith

REFERENCES

- **Pediatric IBD**
  - https://s3.amazonaws.com/hcplive/v1_media/_image/Doctor_checking_little_girl_stomach.jpg
- **Age of presentation picture**
  - **Used with permission from Dr. Eytan Wine**
- **Pediatric UC Differs from Adult-Onset UC**
  - **Used with permission from Dr. Eytan Wine**
- **Diagnosing IBD in children**
  - http://www.refluxrebels.com/test/wp-content/uploads/2015/04/egd.jpg
- **Extraintestinal Manifestations**
  - https://www2.luriechildrens.org/ce/online/article.aspx?articleID=247
- **Treatment Table**
  - **Used with permission from Dr. Eytan Wine**
- **Enteral Nutrition Pictures (Nutren, NG Tube)**
  - **Used with permission from Dr. Eytan Wine**
- **Treatment of Pediatric IBD Algorithm**
  - http://www.nature.com/nrgastro/journal/v11/n2/full/nrgastro.2013.158.html
- **Transitioning Pediatric IBD patients**
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- **Sidebar**
  - **www.naspghan.com**
  - **Fast Facts**
    - **http://www.gikids.org/content/7/en/ibd**
- **Very Early Onset IBD – Gene TTC7A**
  - **http://www.neopics.org/**
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