

THE CANADIAN CHILDREN INFLAMMATORY BOWEL DISEASE NETWORK A JOINT PARTNERSHIP OF CIHR AND THE CH.I.L.D. FOUNDATION



Paediatric IBD:
*No longer rare...
disturbingly more common!*

Message from the Network Principal Investigator *Dr. Anne Griffiths*

In late February I will have the privilege of speaking at the 3rd International Klaus Betke Symposium devoted to Paediatric Inflammatory Bowel Disease. The symposium coincides with the tenth international "Rare Diseases Day". My opening address at the meeting will address the challenge that IBD in children, whilst once rare, continues to increase in children in Canada and around the world. The Canadian Children IBD Network: a joint partnership of CIHR and the CH.I.L.D. Foundation has joined in the fight to understand the causes, to ultimately prevent and even cure, but meanwhile to also ensure the best treatment for children affected by the very variable group of intestinal chronic inflammatory disorders, which we call "Crohn's disease" and ulcerative colitis.

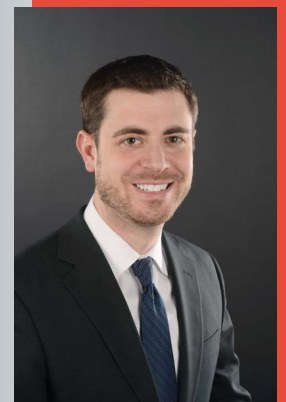


In this issue of the Newsletter you will read about research being led by several investigators in the Network. It can be difficult for families and patients to be comfortable allowing samples for research to be taken at the time of colonoscopy to confirm a suspected diagnosis of IBD, but work by Network Deputy co-chair, Dr. David Mack, and colleagues in Ottawa demonstrates the usefulness of such studies in bringing us closer to understanding why IBD develops. For patients and parents of patients, who are a part of the Canadian Children IBD Network, please read of the ongoing research in the Network, and thank-you for partnering with us to solve the many unanswered questions concerning paediatric IBD. For the CH.I.L.D. Foundation and its supporters, thank you immensely for making such a Network possible.

Canadian epidemiologic data indicate that IBD is becoming more common under age 5 years

Network Principal Investigator **Eric Benchimol**, from Children's Hospital of Eastern Ontario IBD Centre, the University of Ottawa, and the Institute for Clinical Evaluative Sciences, leads Health Services Research within the Network. His most recent work, a collaboration between the Canadian Children IBD Network and the Canadian Gastro-Intestinal Epidemiology Consortium (CanGIEC), has provided an update on the incidence and prevalence of paediatric IBD across Canada. Health administrative data from 1999 to 2010 in Alberta, Manitoba, Ontario, Quebec and Nova Scotia (the provinces where linkage to such routinely collected data has been feasible) indicate continuing increase in the youngest children, a finding that was highlighted in a recent report on CTV National News.

Dr. Benchimol is the recipient of the 2016 Canadian Association of Gastroenterology Young Investigator Award. This award is given annually to a Canadian investigator within 7 years of his/her first faculty appointment, who has demonstrated excellence in research. Eric is already well recognized internationally for the quality and importance of his epidemiologic research in IBD. The award will be given during Canadian Digestive Disease Week (March 3-6, 2017) in Banff, Alberta. Congratulations!

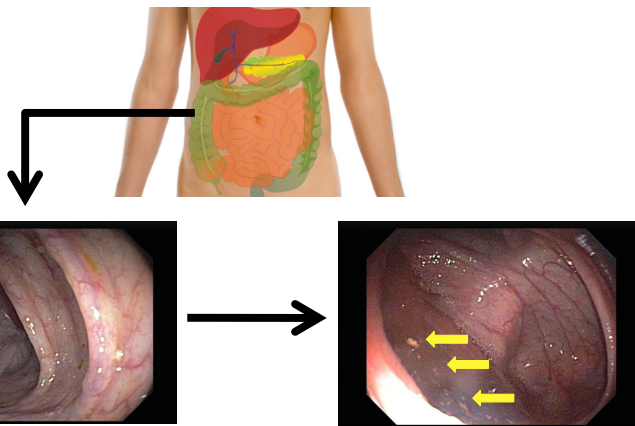


Why does IBD develop?: Recent research by Network Deputy Co-chair, Dr. David Mack



It is currently believed that organisms in the intestine (known as the intestinal microbiota) lead in susceptible children (or adults) to the development of the persistent intestinal inflammation known as IBD. Alterations in the intestinal microbiota are recognized in people with IBD, BUT it is still not known whether these differences are a cause of or the result of inflammation. The best time to study the role of the intestinal microbiota in causing IBD would be before it develops, but that is difficult! Network investigators and other pediatric IBD researchers have turned to very recent onset IBD to try to identify early changes.

Dr. David Mack in collaboration with Drs. Alain Stinzi and Daniel Figeys at the University of Ottawa has recently reported (published on-line in Nature Communications November 2016) elegant studies to address causality of alterations of intestinal bacteria (microbiota) in the development of new-onset as-yet untreated Crohn's disease of children. To understand the interactions between the intestinal microbiome and the patients, both the proteins produced by the patients and the intestinal microbiota were studied from samples taken during colonoscopies at the site of their disease.



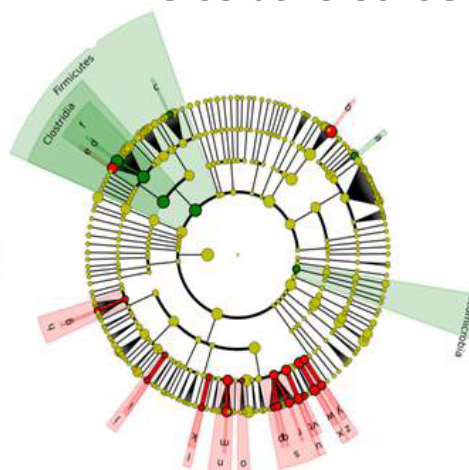
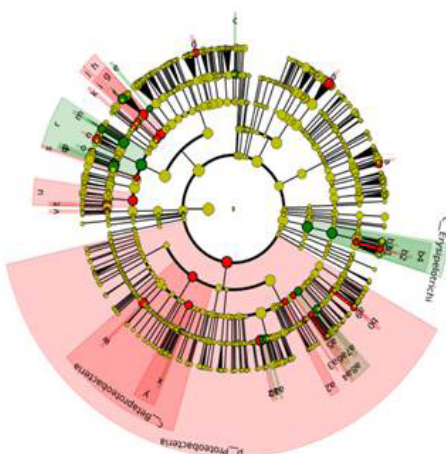
What was discovered was a deleterious cycle of events leading to development of inflammation that included changes in the balance of 'anti-inflammatory' bacteria which lead to impaired ability of the patient to detoxify pro-inflammatory bacterial products which, in turn, allowed for these latter bacteria to flourish. Altogether, the results emphasized the importance of the interactions of intestinal bacteria and their interplay with the children's protective mechanisms in leading to inflammation in Crohn's disease.

The study points to potential for new avenues for treatment such as targeting the key drivers of the altered microbial networks or targeting the metabolic imbalances created by the altered balance of microbes.

Dr. Mack's technique for obtaining samples at the mucosal luminal interface directly at the site of disease at the time of colonoscopy is being utilized in the Canadian Children IBD Network to explore, particularly, IBD developing in South Asian children.

Crohn's Disease

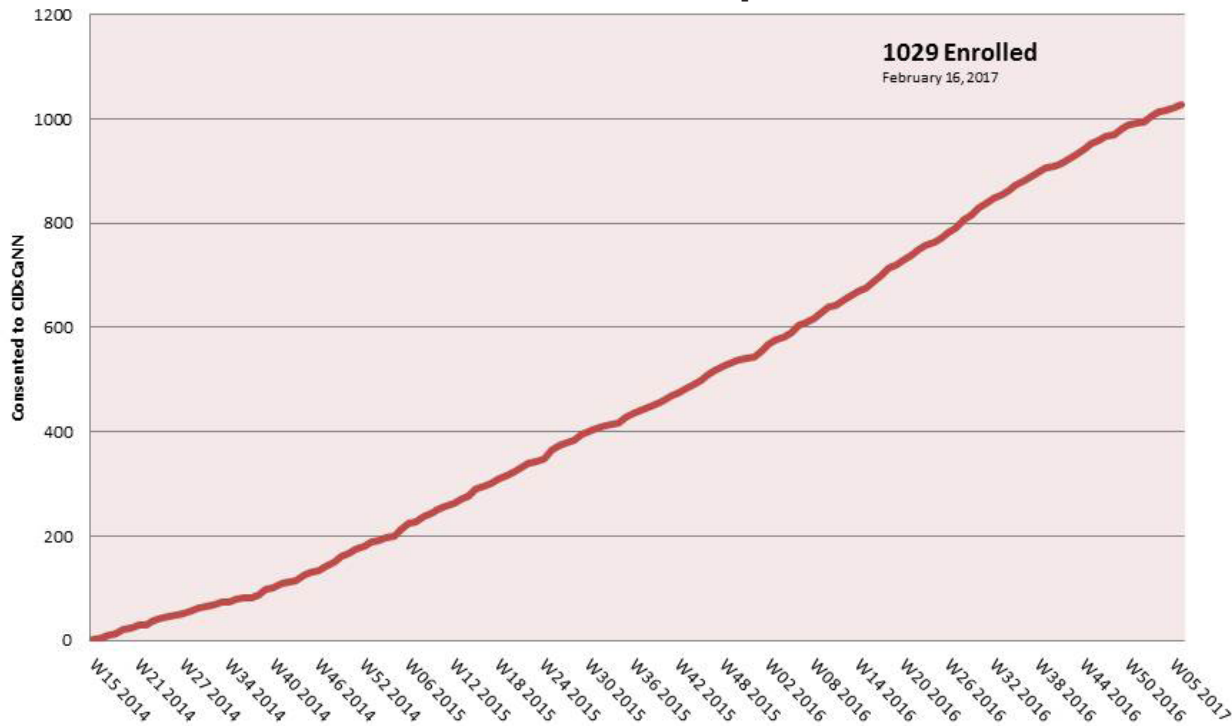
Ulcerative Colitis



Differences in intestinal microbiota at mucosal luminal interface between children with IBD and healthy children

The Network's inception cohort study

Inception Cohort Recruitment



Over 1000 children and adolescents with newly diagnosed Crohn's disease or ulcerative colitis across Canada have been registered in the Network's inception cohort study. One quarter are aged 10 years or under, which would not have been the case several years ago, and speaks to the fact that IBD is becoming increasingly common in younger children.

Patient Engagement

Research Prioritization in paediatric IBD



Dr. Tony Otley has led the Network's efforts to engage children and youth with IBD, their parents, families, and their clinicians to help determine the top ranked research questions relating to paediatric IBD. Thank you to all across Canada, who completed the on-line questionnaire giving us your key unanswered questions and uncertainties. The steering committee is synthesizing and will reduce the concerns to a list of 30 top research questions relevant to children and adolescents with Crohn's disease and ulcerative colitis.

Current and former patients and parents will come together with clinical experts at an all-day meeting on March 26, 2017 to determine the final top 10 list of research questions. This is a highly interactive process developed by the James Lind Alliance with all participants playing an active role. This top ten list will go on to inform what areas need more research, and where research funds should be allocated.

Stay tuned to learn what patients and families affected by paediatric onset IBD identify as the top 10 research uncertainties to be addressed! See <http://www.lindalliance.org> for more details

Therapeutic drug monitoring

For more than a decade, biologic therapies, particularly antibodies targeting TNFalpha, a pro-inflammatory cytokine or messenger in the body, have made a huge difference in the treatment of IBD occurring in children. Compared to historical treatments, they are more effective at healing the intestine, which is particularly important in children, who have such long lives ahead. Like any therapy, however, use of anti-TNF antibodies is most effective, when tailored to the individual child. One size does not fit all.

The Canadian Children IBD Network has attempted to move the field of paediatric therapeutic drug monitoring forward by examining drug levels during the first and very important "induction" phase of therapy in children. The Network has allowed IBD centres separated geographically to work together to much more quickly determine how anti-TNF therapy is best administered. We were able as a group to advocate with the marketing pharmaceutical company to make measurement of drug levels available three times yearly for children. These data will be presented at the upcoming meeting of the European Crohn's and Colitis Organization in Barcelona, Spain (February 18, 2017).

EARLY USE OF THERAPEUTIC DRUG MONITORING TO INDIVIDUALIZE INFLIXIMAB THERAPY IN PAEDIATRIC IBD

Crowley E, Carman N, Arpino V, Frost K, Ricciuto A, Sherlock ME, Critch JN, Mack DR, Benchimol EI, Jacobson K, Lawrence S, deBruyn J, El-Matary W, Otley AR, Huynh HQ, Muise A, Church PC, Walters TD, Griffiths AM.

**On behalf of the Canadian Children Inflammatory Bowel Disease Network:
A Joint Partnership of CIHR and the CH.I.L.D Foundation**



Alberta Children's Hospital



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