Canadian Digestive Diseases Week™ 2017

CDDW™ 2017
FAIRMONT BANFF SPRINGS HOTEL
BANFF ALBERTA
MAR 3-6

EXHIBIT & ABSTRACT GUIDE

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

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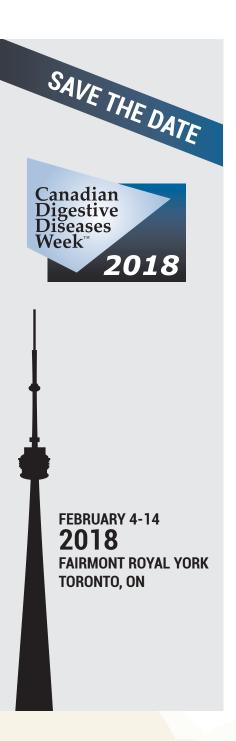
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2018

FEBRUARY 4-14
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Heritage Hall

Sir William Wallace

Rundle Bar

Upper Bow Valley Terrace

Bow Valley Grill

1888 Chop House

Frontenac

Champlain

Palliser

Princess

Victoria

McKenzie

Lacombe

Empress

Access small meeting rooms via Level 2

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Alhambra

Angus

Strathcona

Fairholme

Grapes Wine Bar

Ivor Petrak

Rundle Lounge

Curio Foyer

Trainee Program Registration

Alberta

Riverview Foyer

Medieval in the Mountains Gala

New Brunswick

Acccess to small meeting rooms on Level 1

Oval Room

Conservatory

Cascade Ballroom

Theatre
Lobby

Theatre

CDDW™
Registration

D.C.
Coleman

President's
Foyer

Sir
Edward
Beatty

Speaker
Ready Room

e-Learning
Centre

N.R.
Crump

Terrace

Baron
Shaughnessy

Van Horne Foyer

Van Horne
A

Van Horne
B/C

Exhibit Hall

Access to 2500 series,
David O'Brien and Rob Ritchie
meeting rooms
(third floor)

Company Name	Booth #
AbbVie	1001, 1002
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Allergan Canada	1008
ALPCO Diagnostics	1039
AMT Surgical	1036
ATGen Canada Inc.	1025
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Gilead Sciences Canada Inc.	

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Floor plan: N.R. Crump Speaker Ready Room/e-Learning Lounge; Van Horne A; Van Horne B/C; Registration; Booths 1001–1046; Communal; Coleman; Beatty; Shaughnessy.

* Freight door last in first out

PARTNER LEARNING THEATRE PRESENTATIONS

The Partner Learning Theatre allows sponsors and exhibitors to showcase their latest products and innovations in live, 30-minute presentations. The Learning Theatre is located in Baron Shaughnessy and lunch and nutrition break refreshments will also be available. Learning Theatre sessions are the responsibility of the company and are neither endorsed by CAG/CASL nor accredited by CAG.

SATURDAY, MARCH 4

10h30-11h00
Olympus Canada Inc.

The Tools for Successful ESD
- Dr. Peter Draganov, University of Florida

12h45-13h15
Janssen Inc.

New Therapies for the Management of Crohn's Disease
- Dr. Waqqas Afif, McGill University

15h00-15h30
Ferring Pharmaceuticals

Medical Therapy for Ulcerative Colitis: Beyond the Clinical Trials
- Dr. Laura Targownik, University of Manitoba

SUNDAY, MARCH 5

10h30-11h00
Pfizer Canada Inc.

Hot Topics on Biosimilar Infliximab - Takeaways From Most Recent Studies
- Dr. Tore K. Kvien, Dep't of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

12h45-13h15
Intercept Pharma Canada Ltd.

Intercept and the Canadian PBC Landscape
- Dr. Andrew Mason, University of Alberta and Dr. Vlad Popovic, Intercept Pharma Canada Inc.

15h00-15h30
Takeda Canada Inc.

Reflections: Living Every Day with IBD
- Dr. Mark Silverberg, University of Toronto

Industry representatives are kindly requested not to attend other companies' Learning Theatre presentations.

Company: **AbbVie**
Address: 8401 Trans-Canada
                St-Laurent, QC H4S 1Z1
Contact: Rachelle Babin
Telephone: 888-703-3006
Email: rachelle.babin@abbvie.com
Booth #:   1001, 1002

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 #:   1029

AFFINITY Diagnostics Corp. is a provider of high quality in-vitro diagnostic assays for clinical and research laboratory use. Our Featured Product for CDDW 2017 is the IDK® CALPROTECTIN ELISA. Fecal Calprotectin is a marker for inflammatory and neoplastic gastrointestinal diseases. The IDK® Calprotectin ELISA enables the differential diagnosis between Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD). Calprotectin is also an ideal marker for therapy monitoring in IBD patients. 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: **Alexion Pharma Canada**
Address: 3100 Rutherford Rd., Suite 300
                Vaughan, ON L4K 0G6
Contact:
Telephone:
Email:
Booth #:   1024

Alexion is a global biopharmaceutical company focused on developing and delivering life-transforming therapies for patients with devastating and rare disorders. Alexion is the global leader in complement inhibition and has developed and commercializes the first and only approved complement inhibitor to treat patients with paroxysmal nocturnal hemoglobin-uria (PNH) and atypical hemolytic uremic syndrome (aHUS), two life-threatening ultra-rare disorders. In addition, Alexion's metabolic franchise includes two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare disorders; hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D). Alexion is advancing the most robust rare disease pipeline in the biotech industry with highly innovative product candidates in multiple therapeutic areas.

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 #:   1008

Allergan is a global specialty pharmaceutical company that is Committed to the Gut. Allergan has a full GI portfolio which includes products like CONSTELLA®, ASACOL® 800 and SALOFALK®. Additionally, Allergan has an exciting GI pipeline in clinical development, with products for IBS-D, H pylori, gastroparesis, NASH and IBD.

Company: **ALPCO Diagnostics**
Address: 26-G Keewaydin Dr.
                Salem, NH 03079 USA
Contact: Noelle Sliney
Telephone: 800-592-5726
Email: nsliney@alpco.com
Booth #:   1039

ALPCO was founded in 1991 as a distributor of immunoassay based products for the North American life science markets and has grown into a premier channel representing over 60 collaborating partners globally. In 2007, we launched our organically developed line of diabetes and obesity research assays and continued to expand our offering into applications for HPLC, LC-MS/MS, purified antibodies, recombinant proteins, flow cytometry reagents and our STELLUX® line of chemiluminescent assays. This expansion serves a broader segment of life science research and healthcare professionals dedicated to improving patient outcomes and upholds our mission for delivering "Scientific Solutions for Life".

Company: **AMT Surgical**
Address: 20 Steckle Place, Unit 16
                Kitchener, ON N2E 2C3
Contact:
Telephone: 888-803-6799
Email: info@amtsurgical.com
Booth #:   1036

Leading the way in safety and performance, AMT is the

15

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: **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 #:   1025

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 #:   1030

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 of one pharmacy 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:
Telephone: 888-857-1990
Email:
Booth #:   1020

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

Company: **Bristol-Myers Squibb Canada**
Address: 2344 Alfred-Nobel, Suite 300
             Montreal, QC H4S 0A4
Contact:
Telephone:
Email:
Booth #:   1015

Bristol-Myers Squibb Canada Co. is an indirect wholly-owned subsidiary of Bristol-Myers Squibb Company, a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb global operations, visit www.bms.com. Bristol-Myers Squibb Canada Co. has been delivering innovative medicines for serious diseases to Canadian patients in the areas of cardiovascular health, oncology, neuroscience, immunoscience and virology for over 80 years. Bristol-Myers Squibb Canada Co. employs over 300 people across the country. For more information, please visit www.bmscanada.ca.

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 #:   1032

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 ® smartphone for at home testing. 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:
Booth #:   1046

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:
Telephone: 905-847-2002
Email:
Booth #:   1044

Canadian Digestive Health Foundation (www.CDHF.
ca). We are CAG's Foundation. We exist to support
patients, clinicians, researchers. Established in 1993,
the CDHF exists to help reduce suffering and improve
quality of life for those impacted by digestive disease.
Patients, and the health care professionals who care
for them, trust the CDHF to provide accurate, unbiased,
patient-friendly resources, increase awareness about
digestive health and disease, and fund important
research, training and knowledge translation activities.
Visit us at CDDW and be sure to ask about OneBiota
and the CDHF Human Gut Microbiota Project (www.
OneBiota.ca).

Company: **Canadian Liver Foundation**
Address: 3100 Steeles Avenue East, Suite 801
                Markham, ON L3R 8T3
Contact: Karen Seto
Telephone: 800-563-5483
Email: kseto@liver.ca
Booth #:   1045

The Canadian Liver Foundation (CLF) is a national char-
ity committed to promoting liver health and reducing
unnecessary death and suffering from liver disease.
The CLF has contributed over $26 million to liver
research in Canada and through its chapters across
the country, the CLF strives to promote liver health,
improve public awareness and understanding of liver
disease, raise funds for research and provide support
to individuals affected by liver disease. To learn more
about how the CLF is "Bringing Liver Research to Life",
visit LIVER.ca.

Company: **Cantel Medical**
Address: 90 Gough Road, Unit 1
                Markham, ON L3R 5V5
Contact: David Murphy
Telephone: 844-348-5636
Email: dmurphy@cantelmedical.ca
Booth #:   1041

Cantel Medical is a global company dedicated to
delivering innovative infection prevention products and
services for patients, caregivers, and other healthcare
providers, which improve outcomes and help save lives.
Through an expansive portfolio of endoscopy, water
purification and filtration, and healthcare dispos-
ables, Cantel Medical provides high-quality infection
prevention solutions and unsurpassed service, touching
millions of patients each year around the world.

Company: **Commonwealth Diagnostics**
                International, Inc.
Address: 39 Norman St.
                Salem, MA 01970 USA
Contact: Craig Yarwood
Telephone: 888-258-5966
Email: Inquiries@commdx.com
Booth #:   1037

Commonwealth Diagnostics International (CDI), Inc.
is an international diagnostic service provider that
specializes in bringing cutting-edge and innovative di-
agnostic products to patients and healthcare providers
worldwide. Our services assist physicians and patients
with the diagnosis of some of the common sources
of digestive distress and functional gastrointestinal
disorders.

Company: **Cook Medical**
Address: 165 Mostar Street
                Stouffville, ON L4A 0Y2
Contact: Tony Ranucci
Telephone: 800-668-0300
Email: www.cookmedical.com
Booth #:   1027

Since 1963, Cook Group companies develop healthcare
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Depuis 1963, les sociétés du Groupe Cook effectuent
le développement des dispositifs médicaux. Nous
sommes au premier rang de la recherche médicale et
du développement des produits et de la technologie des
dispositifs médicaux à effraction minimale aux fins des
interventions diagnostiques et thérapeutiques.

Company: **Crohn's and Colitis Canada**
Address: 600-60 St. Clair Ave. E.
                Toronto ON M4T 1N5
Contact: Natasha Kachan
Telephone: 416-920-5035 x234
Email: nkachan@crohnsandcolitis.ca
Booth #:   1043

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 char-
ity 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:	**ExeGi Pharma LLC**
Address:	155 Gibbs Street, Suite 506
	Rockville, MD 20850 USA
Contact:	Vanita Patel
Telephone:	240-428-6891
Email:	vanita.patel@exegipharma.com
Booth #:	1034

ExeGi Pharma is a biotechnology company focused on the development and commercialization of live bio-therapeutic and probiotic medicines. ExeGi distributes Visbiome, a high potency probiotic containing 8 strains of live bacteria in concentrations of 450 billion bacteria per sachet. Visbiome is recommended to help maintain the appropriate balance of beneficial bacteria in the bowel of pouchitis patients. Visbiome is available in 30 count sachets.

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 #:	1014

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 #:	1042

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 #:	1010

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:	**Gold Standard Diagnostics**
Address:	2851 Spafford Street
	Davis, CA 95618 USA
Contact:	Tyler Cann
Telephone:	530-759-8000
Email:	tcann@gsdx.us
Booth #:	1038

Gold Standard Diagnostics provides comprehensive diagnostic solutions and outstanding customer service that improves lab efficiency and minimizes overall costs. Offering a focused test menu for gastrointestinal diseases and therapeutic drug monitoring, we are a committed partner to provide gastroenterologists and laboratories with the best diagnostic tools available.

Company:	**Innomar Strategies**
Address:	3470 Superior Court
	Oakville, ON L6L 0C4
Contact:	Jeff Drew
Telephone:	905-847-4310 x7359
Email:	jdrew@innomar-strategies.com
Booth #:	1023

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: 416-697-6700
Email: jamie.twiselton@interceptpharma.com
Booth #: 1007

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: Ximena Camacho
Telephone: 416-382- 5910
Email: mcamac12@ITS.jnj.com
Booth #: 1003

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: **KNS Canada Inc.**
Address: 210 Silver Star Boulevard, Suite 805
Toronto, ON M1V 5J9
Contact: Shahid Khandker
Telephone: 800-233-1008
Email: shahid.khandker@knscanada.com
Booth #: 1022

KNS Canada: Bringing Innovation and point of care technologies to Liver Caregivers in Canada. After the successful introduction of FibroScan 502, 402 and Touch, KNS is launching the all new state of the art FibroScan 530 Compact which has everything that FibroScan Touch offers but more, such as 2 hours battery backup and portability. Also launching the all new and simple Rapid Hep C test kit Oraquick which has more than 99% accuracy and produces results in just 20 minutes. To learn more and see these products first hand, visit booth 1022. Take part in the raffle draw and win 20 free Oraquick Kits.

Company: **LABORIE**
Address: 2101 Boulevard Lapiniere
Brossard, QC J4W 1L7
Contact: Christine Frewen
Telephone: 450-671-5901
Email: marketing@laborie.com
Booth #: 1033

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 #: 1016

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: **MedReleaf Corp.**
Address: Markham, ON
Contact: Rebecca Siegal
Telephone: 289-317-1000 x1024
Email: rsiegal@medreleaf.com
Booth #: 1035

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Address: 85 Advance Road
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Contact: Roxanne DeAbreu-Breen
Telephone: 289-269-0204
Email: Roxanne.DeAbreu@olympus.com
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Booth #:   1006

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Company: **Physician Learning Program**
Address: 2-590 ECHA,11405-87 Avenue NW
                 Edmonton, AB T6G 1C9
Contact: Tess Friedenberger
Telephone: 780-248-1068
Email: friedenb@ualberta.ca
Booth #:   1040

The Physician Learning Program supports and advises physician members of the Alberta Medical Association at all stages of a clinical quality improvement project. From helping identify and develop a focused clinical question, through planning, design, evaluation, the PLP team recommends resource management approaches, project objectives and strategies, project scheduling and evaluation metrics. Project management resources range from turnkey project services and program management to advice and direction on obtaining ethics approvals, database selection, data analysis, interpretation and data report generation, to providing facilitated CME sessions and delivery of feedback session to review your practice data report.

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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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Company: **SuperSonic Imagine**
Address: 200 Joseph-Carrier
                 Vaudreuil-Dorion QC
Contact: Hani Sardi
Telephone: 866-904-6246
Email: hani@apexiummed.com
Booth #:   1031

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Contact:	Yvette Pitl
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Email:	Yvette.Pitl@takeda.com
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Booth #:	1005

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6th Canadian Symposium on HCV/ 6ème Symposium canadien sur le VHC

Delivering a Cure for Hepatitis C Infection: What are the Remaining Gaps?

Friday, March 3rd, 2017 / Vendredi 3 Mars 2017

The Fairmont Banff Springs Hotel, Banff, AB

Program – Programme

07h15 - 08h00	Registration, breakfast Inscription, petit déjeuner
08h00 - 08h15	Welcome and Introductions – Mot de bienvenue Dr. Naglaa Shoukry, Université de Montréal, Montréal, Canada

Biomedical Research
Co-Chairs: Dr. Selena Sagan and Dr. Angela Crawley

08:15 - 08h45	Opening Keynote: Addressing the next challenges in virus-host interactions and liver disease Pr. Thomas Baumert, Université de Strasbourg, Strasbourg, France
08h45 - 09h05	Imaging Immunity In Vivo Dr. Paul Kubes, University of Calgary, Calgary, Canada
	Oral Presentations – Présentations orales
09h05 - 09h15	Solute Carrier NTCP Regulates Innate Antiviral Immune Responses Targeting HCV Infection of Hepatocytes Dr. Che Colpitts, University of Strasbourg, Strasbourg, France
09h15 - 09h25	Intrahepatic IL-22 Correlates with Advanced Liver Fibrosis and Sensitizes HSCs to TGF-β Signaling in a p38-dependent Manner Thomas Fabre, Centre de recherche du CHUM, Montréal, Canada

Clinical Research
Co-Chairs: Dr. Carla Coffin and Dr. Curtis Cooper

09h25 - 09h55	Hepatitis C: Difficult to Cure Patients Pr. Jean-Michel Pawlotsky, Université Paris Est, Paris, France
09h55 - 10h25	Coffee Break – Pause café
10h25 - 10h45	Towards Eradication of Hepatitis C Dr. Morris Sherman, University Health Network, Toronto, Canada
	Oral Presentations - Présentations orales
10h45 - 10h55	Novel E2 Glycoprotein Tetramer Detects Hcv-Specific Memory B Cells Dr. Maude Boisvert, Centre de recherche du CHUM, Montréal, Canada
10h55 - 11h05	Evaluation of Xpert® HCV Viral Load Point-of-care Test for Detection of HCV Infection by Venipuncture-collected and Finger-stick Capillary Whole-blood Samples Dr. Jason Grebely, University of New South Wales, Sydney, Australia

Health Services Research
Co-Chairs: Dr. Naveed Janjua and Dr. Wendy Wobeser

11h05 - 11h35	Changing Minds: Popular Culture & Vaccination Myths Pr. Tim Caulfield, University of Alberta, Edmonton, Canada
11h35 - 11h55	Surveillance Systems to Support a Public Health HCV Response Dr. Mark Tyndall, University of British Columbia, Vancouver, Canada

	Oral Presentations - Présentations orales
11h55 - 12h05	HCV in the Real World: Adherence During Directly Acting Antiviral HCV Treatment Amongst Active Drug Users at a Community Based Program in Toronto Mary Guyton, RN, Toronto Community Hep C Program, Canada
12h05 - 12h15	Development of a Provincial HCV Elimination Strategy Dr. Lisa Barrett, Dalhousie University, Halifax, Canada
12h15 - 13h30	Lunch – Diner: Cascade Ballroom

Social, Cultural, Environmental, and Population Health Research
Co-Chairs: Dr. Dan Allman and Dr. Julie Bruneau

13h30 - 14h00	Strategies to enhance prevention of hepatitis C infection and reinfection in people who inject drugs Dr. Holly Hagan, New York University, New York, USA
14h00 - 14h20	Addressing barriers to integrating evidence-based public health and addiction treatment interventions Dr. Evan Wood, University of British Columbia, Vancouver, Canada
	Oral Presentations - Présentations orales
14h20 - 14h30	Short Injection Cessation Episodes as Opportunities for Hepatitis C Prevention Emmanuel Fortier, Université de Montréal, Montréal, Canada
14h30 - 14h40	Hepatitis C Treatment and Care in Big River First Nation Community: Barriers to Accessing Healthcare Services Dr. Mamata Pandey, Regina Qu'Appelle Health Region, Regina, Canada
14H40 - 15h10	Coffee Break – Pause café
15h10 - 16h10	Hepatitis C in Indigenous People Panel and Audience Discussion – Table ronde et discussion avec l'audience Panel discussion members: Alika Lafontaine, RCPSC, Carrielynn Lund, CAAN, Renee Masching, CAAN, Norma Rabitskin, CAAN Chair: Dr. Alexandra King, Simon Fraser University, Vancouver, Canada
16h10 - 16h30	Universal Access to Direct-Acting Antiviral Therapies in Australia: Early Lessons Dr. Greg Dore, University of New South Wales, Sydney, Australia
16h30 - 17h10	Panel and Audience Discussion – Table ronde et discussion avec l'audience Panel discussion members: Greg Dore, UNSW, Jean-Michel Pawlotsky, U. Paris Est, Micheal Houghton, U. of Alberta, Mel Krajden, U of British Columbia, Patricia Bacon, Action Hepatitis Canada. Chair: Dr. Jason Grebely, University of New South Wales, Sydney, Australia
17h10 - 17h15	Closing Remarks – Mot de la fin Dr. Lorne Tyrrell, University of Alberta , Edmonton, Canada
17h15 - 19h15	Cocktail and Poster Session – Cocktail et présentation des affiches: New Brunswick extension

Posters can be hung up during lunch time and coffee breaks

Organizing Committee- Comité organisateur

Lorne Tyrrell, University of Alberta, Chair	Alexandra King, Simon Fraser University
Carla Coffin, University of Calgary, Co-Chair	Mel Krajden, University of British Columbia
Thomas Fabre, Université de Montréal	Selena Sagan, McGill University
Jason Grebely, University of New South Wales	Naglaa Shoukry, Université de Montréal

For more information please contact Norma Choucha at norma.choucha@canhepc.ca
For Registration, pour s'inscrire: https://event-wizard.com/CanHepCSymposium2017/0/register/
Pour plus d'information, veuillez communiquer avec Norma Choucha @ norma.choucha@canhepc.ca

Friday March 3, 2017

18h30 – 19h30   CAHN / CASL Welcome Social Mixer

CAHN / CASL Education

Saturday March 4, 2017

CAHN Presentations:

08h00 – 08h15   Welcome

08h00 – 09h00   Street drugs - learn about where, how, what, and how
                          much
                          Dr. Ken Lee, MD

09h00 – 09h45   New DAAs: Are they as safe as what they appear?
                          Dr. D. Wong, MD, FRCP

10h00 – 10h30   CLF-CASL GOLD MEDAL LECTURE
                          Dr. Anna Lok, University of Michigan

10h30 – 11h00   Exhibits and Coffee Break

11h00 – 11h30   Management of the Compensated Cirrhotic Patient
                          Geri Hirsch RN (EC), MN, NP

11h30 – 12h00   Management of the Decompensated Cirrhotic Patient
                          Colina Yim, RN (EC), MN, NP

12h00 – 12h30   Portal hypertension: When the kidneys, heart, and lungs
                          fight back.
                          Cheryl Dale RN (EC), MScN, NP

12h30 – 13h30   Exhibits and Lunch

13h30 – 17h00   **CASL Presentations**
                     (Canadian Association for the Study of the Liver)

Sunday March 5, 2017

09h15 – 11h00   CAHN AGM

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CCC-CIHR-CAG IBD Fellowships (3)
(awards are for two years)

CAG-CIHR Fellowships (2)
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(award is for two years)

Shire-CAG Research Resident Awards (2)

Allergan-CAG Research Resident Award (1)

Ontario Association of Gastroenterology-CAG Research Resident Award (1)

CAG PhD Scholarships (2)

CAG Summer Studentships (12)

CCC Summer Studentships (6)

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- Relevant warnings and precautions regarding use with ribavirin, use in patients with decompensated cirrhosis who are infected with HCV genotype 2 or genotype 4, concurrent use with other medicinal products containing sofosbuvir, use with potent P-glycoprotein (P-gp) inducers and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4, coadministration with amiodarone (not recommended due to risk of serious symptomatic bradycardia), use in patients with severe hepatic impairment (Child-Pugh Class C), use in patients with severe renal impairment (eGFR < 30 mL/min/1.73m^2) or end stage renal disease requiring hemodialysis, use in patients who have previously failed treatment with other regimens that include an NS5A inhibitor, use in pregnancy and breastfeeding, coadministration with ribavirin during pregnancy, use in patients with recurrent HCV infection after liver transplant, use in HCV patients co-infected with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), concomitant use with tenofovir DF, particularly in those at increased risk for renal dysfunction, co-administration with an efavirenz-containing regimen, and monitoring of liver function including direct bilirubin is recommended in patients with decompensated cirrhosis

- Conditions of clinical use, adverse reactions, drug interaction and dosing information

In addition, the page contains the study parameters and reference list relating to this advertisement.

HCV=Hepatitis C virus.

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PAAB

CAG PAPER SESSION
GI PHARMACOLOGY AND DRUG DEVELOPMENT
FRIDAY MARCH 3, 08H00-09H30

A1
SEMAPHORIN3E (SEMA3E) REGULATES INTESTINAL INFLAMMATION THROUGH THE MODULATION OF DENDRITIC CELLS FUNCTIONS

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

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

Background: Inflammatory bowel diseases (IBD) involve an increase of dendritic cells (DC) infiltration and cytokines production. Recently, semaphorins have been implicated in inflammation and cell migration and has emerged as an essential axis in DC immune responses.
Aims: This study aims to determine the role of Sema3E on DC regulation during colitis using, clinical rectal biopsies from active ulcerative colitis (UC), a murine model of colitis and, DC cell culture.
Methods: mRNA expression level of Sema3E was determined in human rectal biopsies collected from healthy (n=7) and active UC patients (n=7) using RT-qPCR, and an absolute correlation analysis was conducted against pro- and anti-inflammatory markers. Bone marrow-derived DCs (BMDC) were isolated from naïve C57BL/6-deficient (Sema3E$^{-/-}$) and wild-type (WT) mice, and differentiation, IL-12p40 and interferon (IFN)-γ production were quantified by flow cytometry and/or ELISA. Colitis was induced by dextran sulfate sodium (DSS 5%) for 5 days in Sema3E$^{-/-}$ and WT mice treated or not with recombinant Sema3E-Fc. Disease activity index (DAI), macro- and microscopic scores were determined. Colonic myeloperoxidase (MPO) activity, Sema3E, TNF-α, IL-1β, IL-6, and IL-12p40 were quantified using ELISA. Splenocytes and splenic CD11C$^+$ cells were isolated from colitic groups then treated with Sema3E (10^{-6}M) or vehicle, and IL-12p40 and IFN-γ levels were assessed.
Results: In active UC biopsies, Sema3E mRNA was significantly decreased and levels of Sema3E were negatively and positively correlated with pro- and anti-inflammatory cytokines. In naïve mice, Sema3E deficiency resulted in an increase of DC differentiation, migration and antigen uptake, and CD11C$^+$ BMDC showed an increase of the intracellular IL-12p40. In colitic WT mice, Sema3E level was significantly decreased. In colitic Sema3E$^{-/-}$ mice, DAI, macro- & microscopic scores, colonic MPO activity, TNF-α, IL-1β, IL-6, IL-12p40, IFN-γ were significantly increased compared to wild-type and treatment with rSema3E-Fc abolished that deleterious effect. When compared to WT, in colitic conditions, SemaE$^{-/-}$ splenocytes and splenic CD11C$^+$ cells showed an increased production of IL-12p40 and IFN-γ, and rSema3E-Fc treatment of splenic CD11C$^+$ decreased them.
Conclusions: Sema3E signaling is critical in the pathogenesis of inflammation in both the clinical and experimental setting through the modulation of DC migration and activation. These novel findings may pave the road toward novel therapeutic strategies in IBD targeting Sema3E.

CAG PAPER SESSION
CAG/CCC STUDENT PRIZE PAPER PRESENTATIONS
FRIDAY MARCH 3, 10H00-11H30

CAG Student Prize

A2
LOSS OF MESENCHYMAL BMPS SIGNALING SYNERGIZES WITH TRP53 MUTATION TO INDUCE GASTRIC ONCOGENIC PROGRESSION

C. Ouellet[1], P. Garde-Granger[2], F. Boudreau[1], N. Perreault[1]

1. Département Anatomie et Biologie Cellulaire - Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Faculté de Médecine - Université de Sherbrooke, Sherbrooke, QC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

CAG Student Prize

A3
A SERPIN-PRODUCING BIFIDOBACTERIA IMPROVES GLUTEN PATHOLOGY IN MICE

J. Dong[2], J. McCarville[1], A. CAMINERO FERNANDEZ[3], J. Jury[4], M. Bermudez[1], P. Langella[5], A. Mercenier[6], G. Bergonzelli[7], S. Duboux[6], E. Verdu[1]

1. McMaster University, Hamilton, ON, Canada; 2. Medical Science, McMaster University, Burlington, ON, Canada; 3. Farncombe institute, Mcmaster University, Dundas, ON, Canada; 4. McMaster, Hamilton, ON, Canada; 5. INRA, Jouy-en-Josas, France; 6. Nestle Research Center, Lausanne, Switzerland; 7. Nestle Research Center, Lausanne, Switzerland

Background: Celiac disease (CeD) is an autoimmune disorder triggered by gluten. The only treatment for CeD is a gluten-free diet, hence, there is need for adjunctive therapies. The restoration of protease/anti-protease balance in chronic intestinal disorders has become a therapeutic target. We have previously demonstrat-

ed the efficacy of the human anti-protease, elafin, expressed transgenically by *Lactococcus lactis*, in attenuating gluten-induced pathology in mice.

Aims: Here, we test the therapeutic potential of *Bifidobacterium longum* NCC 2705, a member of the commensal microbiota known to produce *in vivo* the serine protease inhibitor, serpin.

Methods: NOD/DQ8 mice were sensitized with gliadin once per week for 3 weeks, then challenged with gliadin once per week for 2 weeks. During gliadin challenge, mice were gavaged with *B. longum* NCC 2705 (*Bl* WT), the same strain containing an engineered plasmid (pMDY25) over-expressing serpin (*Bl* serpin+), or another genetically modified version of NCC 2705 knocked out from its serpin gene NCC 9035 (*Bl* serpin KO). Intestinal pathology was evaluated by CD3^{+} intraepithelial lymphocyte (IEL) quantification and villus-crypt (V/C) ratios. Microbiota composition was determined via 16S rRNA sequencing on a MiSeq Illumina platform.

Results: Serpin-producing *Bl* WT protected against gluten-induced pathology to a similar degree as the previously tested recombinant *L. lactis*-elafin. Furthermore, gliadin-challenged mice treated with *Bl* WT had lower IEL counts compared with mice receiving *Bl* serpin KO. Treatment with *Bl* serpin+ resulted in even lower IEL counts, increased V/C ratios, and reduced paracellular intestinal permeability in the small intestine compared with mice treated with *Bl* serpin KO. No significant shifts in microbiota composition were revealed in small intestinal contents, however, we did observe shifts in fecal microbiota driven by gluten exposure and in the mice receiving the *B. longum* strains.

Conclusions: *B. longum* strains expressing serpin ameliorated gluten-induced pathology in NOD/DQ8 mice, while *Bl* serpin KO did not achieve this protective effect. Thus, commensal strains expressing serpin, such as *B. longum* NCC 2705, represent a novel probiotic approach for gluten-related disorders.

CCC Student Prize

A4
DIAGNOSIS OF ASTHMA IS ASSOCIATED WITH SUBSEQUENT DEVELOPMENT OF INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED CASE-CONTROL STUDY

E. Kuenzig[5], C. Barnabe[6], C. Seow[3], B. Eksteen[6], M.E. Negron[6], A. Rezaie[2], R. Panaccione[6], E.I. Benchimol[1], M. Sadatsafavi[7], A. Avina-Zubieta[8], G.G. Kaplan[4]

1. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. Univ Calgary, Calgary, AB, Canada; 3. Medicine, University of Calgary, Calgary, AB, Canada; 4. Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada; 5. Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 6. University of Calgary, Calgary, AB, Canada; 7. University of British Columbia, Vancouver, BC, Canada; 8. University of British Columbia, Vancouver, BC, Canada

Background: Asthma and the inflammatory bowel diseases (IBD) both result from complex gene-environment interactions and share genetic and environmental risk factors.

Aims: To examine the association between asthma and the subsequent development of Crohn's disease (CD) or ulcerative colitis (UC).

Methods: We performed a population-based case-control study using health administrative data from the province of Alberta. Incident cases of CD and UC were identified using a validated algorithm based on ICD9 (CD 555; UC 556) and ICD10 codes (CD K50; UC K51). An 8-year washout period was used to distinguish incident from prevalent cases for individuals ≥10 years of age at IBD diagnosis; a 3-year washout period was used for those <10 years of age. Controls were derived from an age-stratified random sample of 10% of Albertans. The diagnosis of asthma was confirmed using a validated algorithm (ICD9 493; ICD10 J45). The odds of a asthma preceding the diagnosis of either CD (n=3,087) or UC (n=2,377) was compared to the odds of diagnosis of asthma among those without IBD (n=402,800) using logistic regression. Effect measure modification by age at diagnosis of IBD as defined by the Montreal Classification (≤16 years, 17-40 years, or >40 years) was evaluated using a likelihood ratio test. Age-stratified models are presented in the presence of effect measure modification. Logistic regression models were adjusted for age at IBD diagnosis (in the absence of effect measure modification), sex, rural/urban environment, and quintile of median income for individuals living in a dissemination area. A sensitivity analysis was conducted in which the diagnosis of asthma could either precede or follow the diagnosis of IBD.

Results: A diagnosis of asthma was associated with increased odds of incident CD (adjusted OR 1.45, 95% CI 1.31 to 1.60) with no effect modification by age at diagnosis (p=0.42). Effect modification by age at diagnosis was observed for UC (p=0.01). Asthma was associated with ulcerative colitis diagnosed at ≤16 years of age (adjusted OR 1.49, 95% CI 1.08 to 2.07) and >40 years of age (adjusted OR 1.57, 95% CI 1.31 to 1.89). There was no association between asthma and UC among individuals diagnosed between ages 17 and 40 (OR 1.05, 95% CI 0.86 to 1.26). Results were consistent in a sensitivity analysis that allowed the diagnosis of asthma to precede or follow the diagnosis of IBD.

Conclusions: Asthma is associated with an increased risk of CD, as well as early- and late-onset UC. This association requires confirmation and investigation into potential preventative strategies to reduce IBD risk, as well as identify individuals with chronic gastrointestinal symptoms who should be investigated for IBD.

CCC Student Prize

A5
**FRUCTOOLIGOSACCHARIDE EXACERBATES INFLAM-
MATION AND THE LOSS OF MICROBIAL DIVERSITY
FOLLOWING ILEOCECAL RESECTION IN A MURINE
MODEL OF POST-OPERATIVE CROHN'S DISEASE
RECURRENCE**
M. Laffin, T. Perry, N. Hotte, H. Park, R. Fedorak, B.
Dicken, K. Madsen

University of Alberta, Edmonton, AB, Canada

Background: Fructooligosaccharide (FOS) is a
fermentable prebiotic that stimulates the growth of
bifidobacteria which has been shown to have anti-in-
flammatory activity. Individuals with Crohn's disease
frequently require ileocolic resection (ICR), and disease
often recurs in the neo-terminal ileum following
surgery. Previously we have shown that ICR in a mouse
model induces gut dysbiosis, a depletion of anaerobic
microbes, including bifidobacteria, and an increase in
ileal inflammation.
Aims: We hypothesized supplementation of a post-ICR
diet with FOS in a mouse model would be effective
in stimulating the growth of bifidobacteria and thus
reducing systemic and local inflammation.
Methods: ICR was performed in IL10-/- mice (129S1/
SvImJ) with established colitis. Following surgery, mice
were subsequently fed a chow diet ± 10% FOS for 28
days (n=11), alongside diet-matched non-ICR control
groups (n=11). Serum, colon, and terminal ileum (TI)
were analyzed for cytokine expression by a MesoScale
discovery platform. DNA extracted from stool was
analyzed using 16s rRNA sequencing and qPCR. Ex-
pression of tight junction genes *occludin and ZO1* was
assessed using qPCR. Short-chain fatty acids (SCFA)
concentrations were assessed using high-pressure
liquid chromatography.
Results: A precipitous decrease in fecal bifidobacteria
and bacterial diversity was seen following ICR (p<0.05).
ICR also led to increased serum inflammatory cytokines
(IL-2, IL-12, IL-4) (p<0.05) and a complete depletion of
fecal butyrate (p<0.01). FOS-supplementation resulted
in an increase in the relative amount of bifidobacteria
and fecal acetate (p<0.01). However, contrary to our
hypothesis, the FOS diet exacerbated post-operative
systemic inflammation (elevated serum IL-6 p<0.05),
ileitis (elevated IL-1β p<0.1) and colitis (elevated IFNγ
and TNFα p<0.05). FOS-supplementation was not able
to reverse the obliteration of fecal butyrate following
ICR. Expression of *occludin* and *ZO1* was reduced
in FOS-supplemented mice (p<0.05). FOS supple-
mentation exacerbated the loss of bacterial diversity
following ICR and there was a correlation between loss
of diversity and bifidogenic effectiveness of FOS in
promoting bifidobacteria growth (r= -0.61, p<0.05).
Conclusions: FOS-supplementation of a post-ICR diet
resulted in a decrease in fecal bacterial diversity, re-
duction in barrier function, and increased inflammation.

We speculate that providing high amounts of a targeted
substrate allowed for the expansion of bifidobacte-
ria's niche, enabling a bloom of acetate-producing
organisms which consequently hindered the growth of
butyrate–producing anaerobic organisms necessary for
gut homeostasis.

Honorable Mention

A6
**PREFERENCES FOR CARE FOR ACTIVE SYMPTOMS OF
IBD IN A POPULATION BASED SAMPLE**
M.T. Bernstein, T. Chhibba, J.R. Walker, M. Ivekovic, G.
Restall, h. singh, L.E. Targownik, C.N. Bernstein
University of Manitoba, Winnipeg, MB, Canada

Background: Persons with IBD frequently attend
Emergency Departments (ED) when they are acutely ill
though many could be better served in an alternative
setting.
Aims: To determine care preferences of people with IBD
when seeking care for active symptoms.
Methods: 1143 people 18–64 yrs in the popula-
tion-based University of Manitoba IBD Research Regis-
try participated in the survey (46% response rate).
Results: 95% reported having a family doctor (FD), 10%
a nurse practitioner, 61% a gastroenterologist (GE), and
18% a GI surgeon (GIS). However, only 42% reported
being able to call a GE for advice in managing active
symptoms. Only 29% felt that they could call a GE for
an appointment within 1 week. Respondents indicated
that if they were having severe symptoms, their most
likely courses of action would be to make an appoint-
ment to see their regular GE/GIS (68%), phone regular
GE/GIS (65%), go to an ED (49%), or search the Internet
for information (48%). When asked to state most likely
course of action, 38% reported they would call a GE/
GIS, 36% would go to ED, and 17% would call their FD.
If they were having mild/moderate symptoms the
courses of action most commonly reported were to:
wait it out as long as possible before going to a doctor
(59%), make an appointment to see FD (46%), make
an appointment to see regular GE/GIS (45%), or phone
regular GE/GIS (42%); only 12% would go to ED. If
only one choice was available 30% would call or make
appointment with FD, 29% would call or make appoint-
ment with GE/GIS, and 17% would wait it out.
When experiencing severe symptoms, those with
Crohn's disease indicated they would be more likely to
go to ED (OR=2.77, 95%CI=2.10-3.66) and less likely to
adjust medications on their own (OR=.41, 95%CI=.31-
.55) than those with UC. Those who had seen a GE
within the year would be more likely to phone a GE/
GIS (OR=4.00, 95%CI=2.94-5.44) or phone a nurse
specialist (OR=1.74, 95%CI=1.28-2.35), and were less
likely to call a FD (OR=.51, 95%CI=.39-.69) or go to a
walk-in clinic (OR=.56, 95%CI=.37-.85) than those who
had not seen a GE. However, having seen a GE within
1 year did not impact on the likelihood of stating they

would attend an ED.

When participants were asked, in the event they were having urgent problems with IBD, about their likelihood of seeking services not currently available but which could be made available in the future, they reported they were very likely or likely to use the following services: telephone contact with an IBD nurse (77%), phone contact with a GE (75%), and going to a walk-in GE clinic (71%).

Conclusions: Persons with IBD are interested in choices other than accessing the ED when they are experiencing IBD symptoms; however, attending the ED remains a prominent choice. Improved access to specialized care may improve timeliness of care and reduce ED attendance.

Honorable Mention

A7
PI3KP110δ DRIVES INTESTINAL FIBROSIS IN SHIP DEFICIENT MICE
Y. Lo, J. Sauvé, S. Menzies, L.M. Sly
University of British Columbia, Vancouver, BC, Canada

Background: Crohn's disease (CD) is an immune-mediated disease characterized by inflammation along the gastrointestinal tract. One in 3 people with CD will develop intestinal fibrosis requiring surgery within 10 years of diagnosis. Despite dramatic improvements in reducing intestinal inflammation in people with CD, some still develop fibrosis and there are no treatments that target intestinal fibrosis directly.

Our laboratory has reported that mice deficient in the Src homology 2 domain-containing inositolphosphate 5'-phosphatase (SHIP$^{-/-}$) develop spontaneous CD-like ileal inflammation with arginase-dependent fibrosis. We have also reported that high arginase activity in SHIP$^{-/-}$ cells is dependent on the p110δ catalytic subunit of class IA phosphatidylinositol 3-kinase (PI3K). Based on this, we hypothesize that SHIP$^{-/-}$ mice develop CD-like intestinal fibrosis due to increased PI3Kp110δ activity.

Aims: Aim 1: To determine whether genetic inactivation of PI3Kp110δ activity prevents the development of ileal fibrosis in SHIP$^{-/-}$ mice
Aim 2: To determine whether pharmacological inhibition of PI3Kp110δ activity can block or reverse ileal fibrosis in SHIP$^{-/-}$ mice
Methods: SHIP$^{-/-}$ mice were crossed with mice deficient in PI3Kp110δ activity (PI3Kp110δ$^{DA/DA}$) to generate wild type, SHIP$^{-/-}$, PI3Kp110δ$^{DA/DA}$, and SHIP$^{-/-}$PI3Kp110δ$^{DA/DA}$ mice. Mice were assessed for fibrosis and compared at 4, 8, and 12 weeks of age.
SHIP$^{-/-}$ mice (8-week-old) were treated with the PI3K-p110δ isoform-specific inhibitor, IC87114 (or vehicle), for two weeks. Ileal fibrosis was assessed in 8-week-old SHIP$^{-/-}$ mice and compared to mice treated with inhibitor or vehicle.

Measurements of ileal fibrosis include muscle thickening, accumulation of vimentin$^+$ mesenchymal cells, collagen accumulation by Masson's trichrome staining and Sircol assay, arginase activity, and TGFβ, IL-4, and IL-13.
Results: SHIP$^{-/-}$PI3Kp110δ$^{DA/DA}$ mice have less ileal fibrosis than their SHIP$^{-/-}$ littermates including reduced muscle thickening, vimentin$^+$ mesenchymal cells, collagen accumulation, arginase activity, TGFβ, IL-4, and IL-13. Pharmacological inhibition of PI3Kp110δ activity in SHIP$^{-/-}$ mice also reduced the above parameters. Intriguingly, PI3Kp110δ deficiency or inhibition reduced ileal inflammation in SHIP$^{-/-}$ mice including immune cell infiltration and IL-1β production, suggesting that PI3Kp110δ and/or fibrosis, itself, may contribute to inflammation.
Conclusions: PI3Kp110δ activity drives ileal fibrosis in SHIP$^{-/-}$ mice. Moreover, targeting PI3Kp110δ activity effectively reverses SHIP$^{-/-}$ ileal fibrosis. Importantly, people with CD have reduced SHIP activity and so fibrosis, in people with CD, may be amenable to treatment by inhibiting PI3Kp110δ activity. Idelalisib, a PI3Kp110δ inhibitor, is already licensed for use in people with certain leukemias and lymphomas, so may be rapidly translatable into effective therapy for intestinal fibrosis in people with CD.

Honorable Mention

A8
PROLONGED FASTING ALTERS THE GUT MICROBIOME AND PROTECTS AGAINST *SALMONELLA*-INDUCED GUT INFLAMMATION
F.A. Graef[2], J. Lau[1], E.S. Bosman[2], M. Kuan[2], H. Yang[2], L.S. Celiberto[2], J.C. Berkmann[2], M. Stahl[2], S.M. Crowley[2], H. Yu[2], M. Surette[1], E. Verdu[1], K. Jacobson[2], B. Vallance[2]

1. McMaster University, Hamilton, ON, Canada; 2. Pediatrics, BC Children's Hospital Research Institute, Vancouver, BC, Canada

Background: During periods of acute sickness, all animals including humans voluntarily decrease their food intake, a behavior known as "infection-induced anorexia". Since infection-induced anorexia or fasting is highly conserved amongst mammals, we and others have proposed that it actually promotes host-defense. Several studies have demonstrated that fasting indeed attenuates disease during acute systemic infection or chronic inflammation.
Aims: Since the Gastrointestinal tract is the first organ to be affected by food deprivation, we investigated if fasting alters the course of infection and/or ameliorates intestinal inflammation using a mouse model of *S. typhimurium*-induced colitis. We furthermore examined if fasting modifies the resident gut microbiota, and whether these modifications are instrumental to alter

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the course of *S. typhimurium* infection and colitis.
Methods: *S. typhimurium* causes severe colitis in streptomycin pre-treated, orally infected mice as early as 12h post infection. C57BL/6 conventional as well as germfree mice were fed or fasted for 24h and orally infected with *S. typhimurium*, continuing the fast for another 6h to 24h. Additionally, C57BL/6 conventional mice were fed single macronutrients to gauge the effect of different nutrients on the infection. Pathology as well as *Salmonella* colonization, was assessed by histological and immunofluorescent staining and organ pathogen burden counts; inflammatory gene transcription was measured by qPCR. Microbiome profiling of intestinal contents was performed utilizing 16S rRNA sequencing.
Results: Fasting completely abrogated *S. typhimurium* infection and colitis in conventional C57BL/6 mice, whereas infection still proceeded, albeit in a reduced fashion in germfree mice in concert with minimal signs of inflammation. Microbiome profiles between fed and fasted groups differed greatly in terms of beta diversity with the fasting group showing a consistent increase in the genus *Akkermansia*. Feeding mice glucose alone was not sufficient to re-establish the infection, but preliminary results indicate that other macronutrients can partially restore *Salmonella* colonization.
Conclusions: Taken together, our findings show that prolonged fasting dramatically protects the host against *S. typhimurium* infection, in part by altering the intestinal microbiome and increasing colonization resistance, likely by limiting nutrient availability for the pathogenic bacteria. Additionally our results indicate that food deprivation impairs *Salmonella* virulence and reduces its ability to promote an inflammatory environment independent of changes in the microbiome.

CAG PAPER SESSION
ROLES OF NUTRITION AND MICROBIOTA ON GI DISEASES
FRIDAY MARCH 3, 12H30-14H30

A9
SHORT-TERM EXPOSURE TO A HIGH SUGAR DIET REDUCES SHORT CHAIN FATTY ACID PRODUCTION AND INCREASES SUSCEPTIBILITY TO COLITIS

A. Gill[1], R. Fedorak[1], H. Park[4], N. Hotte[5], R. Ginter[1], A. Hassanzadeh Keshteli[2], K. Madsen[3]

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

Background: Western diets high in refined sugar have been associated with increased susceptibility to inflammatory bowel disease (IBD), possibly through dietary-induced alterations in gut microbial composition and/or function. Short chain fatty acids (SCFA) including acetate and butyrate are produced from indigestible fibers by microbial fermentation and are critical to gut homeostasis.
Aims: The aim of this study was to examine the effects of short-term exposure to high sugar diets on host susceptibility to colitis and to determine the role of SCFA in disease susceptibility.
Methods: At 6-8 weeks of age, wild-type 129/SvEv mice were placed on chow (CH) or high sugar diet (HS) (50% sucrose: AIN76A). Fiber content was 5% (cellulose) and 5.3% (crude fiber) in the HS and chow diets respectively. After two days on the diet, mice were administered dextran sodium sulfate (DSS) for 5 days and water for 2 days (n=4-6 mice for all groups). Disease activity index (DAI) was determined by assessing weight loss, blood in stool, and stool consistency. At day 2 (prior to DSS and after 2 days on diet) and at d7, colons were homogenized for cytokine expression by MesoScale discovery platform. Short chain fatty acid (SCFA) concentrations were measured in stool after 2 days on diet. In separate cohorts, sodium acetate (300 mM) was added to drinking water concurrently with beginning the HS-diet followed by DSS.
Results: After 2 days on a HS diet, mice had reduced levels of fecal acetate (p<0.05) and butyrate (p<0.0001) but did not show any differences in basal levels of colonic cytokines Mice on the HS diet demonstrated increased susceptibility to DSS colitis compared with chow fed mice with increased weight loss, earlier blood in stool and worsened stool consistency. This was associated with significantly enhanced levels of colonic IFNγ, IL-1β, IL-6, TNFα, and IL-12p70 (p<0.05 compared with chow-fed). Mice which received acetate in their drinking water concurrently with HS diet demonstrated a similar susceptibility to colitis as did the chow-fed mice, with reduced blood in stool, less weight loss, and improved stool consistency compared with HS fed mice. An acetate-induced reduction in disease susceptibility was associated with reduced levels of pro-inflammatory cytokines to mirror those in the chow-fed group.
Conclusions: A short-term exposure to a high sugar diet significantly reduces levels of acetate and butyrate, even in the presence of similar amounts of fiber. This loss of short chain fatty acids increases susceptibility to chemically-induced colitis and can be alleviated by acetate indicating a key role for microbial fermentation processes in gut protection from insults.

CAG PAPER SESSION
MECHANISMS RESPONSIBLE FOR POST-INFECTIOUS GUT INFLAMMATORY DISORDERS
SATURDAY MARCH 4, 08H00-10H00

A10
AN ULCERATIVE COLITIS ESCHERICHIA COLI PATHO-BIONT COLONIZES THE INTESTINAL MUCOSA OF SUSCEPTIBLE HOSTS AND PROMOTES COLITIS VIA HEMOLYSIN PRODUCTION.

H. Yang[2], H.C. Mirsepasi-Lauridsen[5], E.S. Bosman[4], C. Struve[5], H. Yu[2], X. Wu[3], C. Ma[2], G. Reid[2], X. Li[6], A.M. Petersen[7], K. Jacobson[1], K.A. Krogfelt[5], B. Vallance[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Pediatrics, BC Children's Hospital Research Institute, Vancouver, BC, Canada; 3. Pediatrics, CFRI and University of British Columbia, Vancouver, BC, Canada; 4. Experimental medicine, University of British Columbia, Vancouver, BC, Canada; 5. Statens Serum Institut, Copenhagen, Denmark; 6. Cleveland Clinic Lerner Research Institute, Cleveland, OH; 7. Hvidovre University Hospital, Copenhagen, Denmark

Background: Ulcerative colitis (UC) and Crohn's disease (CD) are chronic inflammatory conditions of the gastrointestinal (GI) tract that have been linked to intestinal microbial dysbiosis. While adherent-invasive *Escherichia coli* are associated with CD, recent studies have identified E. coli of phylogroup B2 as being frequently isolated from UC patients. B2 E. coli isolated from UC patients (such as p19A) harbour extra-intestinal pathogenic E. coli virulence factors including alpha hemolysin genes (hlyI, II). Correspondingly, the p19A strain causes cell death and barrier dysfunction in human epithelial colorectal cell lines, however its role in intestinal immunopathology is unclear because of the lack of a suitable animal model.
Aims: The current study explores the potential to establish a mouse model of GI infection by the UC-associated E. coli strain p19A, as well as defines the mechanisms by which it promotes colitis.
Methods: C57BL/6 and Sigirr (Single Ig IL-1R-related Receptor) deficient mice were orally administered with 5 mg vancomycin 6 hours prior to the oral infection with 10^8 colony forming units (CFU) of P19A. Sigirr$^{-/-}$ mice were examined because they show increased susceptibility to infection by enteric bacterial pathogens. Intestinal tissues as well as feces were homogenized and plated to enumerate CFU. An *in vivo* imaging system visualized the colonization of p19A in the intact intestines. To test the impact of pre-existing p19A colonization on experimental colitis, mice were colonized with DH10B (non-pathogenic E. coli control), p19A wild-type strain or p19A-ΔhlyI, II (a mutant strain lacking hemolysin genes). The next day, mice were given 3% (wt/vol) dextran sulfate sodium (DSS) in their drinking water for 4 days. Mice were monitored daily

and euthanized to collect samples for further analysis.
Results: Vancomycin pretreatment led to persistent p19A colonization of the intestinal lumen of C57BL/6 mice, based on luciferase based imaging and fecal shedding data. Furthermore, p19A colonized the intestinal mucosal surface of Sigirr$^{-/-}$ mice. While p19A infection caused only minimal pathology on its own, it dramatically worsened the course of DSS colitis, in concert with deep penetration of the damaged colonic mucosa. Notably, a p19A strain deficient in hemolysin genes was severely attenuated in its ability to promote DSS colitis in Sigirr$^{-/-}$ mice.
Conclusions: Our findings provide evidence that a UC E. coli pathobiont can readily and persistently colonize the intestines of susceptible hosts, and significantly worsen the course of colitis. This model thus facilitates research into the role played by UC associated E. coli pathobionts in the pathogenesis of IBD.

A11
EFFECT OF FECAL MICROBIAL TRANSPLANT ON MICROBIAL AND PHAGE COMPOSITION IN PATIENTS WITH CLOSTRIDIUM DIFFICILE INFECTION

H. Park[1], B.T. Millan[2], N. Hotte[1], D.H. Kao[1], K. Madsen[1]

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

Background: The gut microbiome contains a diverse bacteriophage community that plays a largely unknown role in shaping microbial colonization and disease pathogenesis. Fecal microbial transplantation (FMT) is the most effective therapy for recurrent *Clostridium difficile* infection (RCDI) and has been shown to transfer phages along with gut microbes.
Aims: The aim of this study was to examine the effects of FMT on microbial and phage composition in RCDI patients.
Methods: Patients with RCDI (n=19) received FMT from 1 of 3 donors via colonoscopy. Stool samples were collected prior to and following FMT. DNA was extracted and indexed paired-end DNA libraries constructed using an Illumina Nextera® XT DNA kit, then sequenced on a MiSeq. Reads from individual samples were mapped to >5 kb assembled contigs using Metaphlan 2 for taxonomy, HUMAnN for gene function, and Bowtie2 with NCBI RefSeq database for prophage. To assess the metabolic state of the microbial community in RDCI patients, growth dynamics of *E. coli* were inferred from the metagenomic data by measuring the proportion of DNA copies near the origin to those near the terminus (peak-to-trough ratio (PTR)).
Results: In RCDI patients prior to FMT, *Escherichia* and *Klebsiella* dominated. RCDI patients also harbored numerous phages within the *Siphoviridae* family, including *Enterobacteria*, *Escherichia*, *Salmonella*, *Klebsiella* and *Lactobacillus* phages. In contrast,

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the gut microbiome of donors consisted primarily of Bacteroides and Firmicutes; donors also had a much reduced phage population which consisted primarily of crAssphage, a phage predicted to infect Bacteroides. Eleven patients were successfully treated with a single FMT (FMT-S) while 8 patients required multiple FMTs (FMT-M). A successful FMT resulted in the appearance of crAssphage in the RCDI recipients with a complete loss or reduction of *Siphoviridae* phages and increased Bacteroidetes and Firmicutes. There were no significant differences in microbial composition or predicted gene function between the FMT-S and FMT-M groups; however, the patients requiring multiple FMT had increased abundances of Enterobacteria phages HK542, mEp237, and phiP27. This was associated with an increased inferred growth rate of *Escherichia coli* suggesting that *E. coli* and associated phages may be driving disease pathogenesis in some RCDI patients that fail to respond to FMT.

Conclusions: RCDI patients had decreased microbial but increased diversity of phages compared with healthy individuals. FMT altered both bacterial and phage composition to resemble the donor. Patients who required at least 2 FMT had significant differences in their phage population suggesting that the presence of particular phages may have a role in modulating response of patients to fecal transplantation.

CAG PAPER SESSION
STROMA/EPITHELIAL STEM CELL
INTERACTION IN GI DISEASES
SATURDAY MARCH 4, 15H30-17H00

A12
LOSS OF BMPS SIGNALING IN FOXL1^{+} SUBEPITHELIAL MYOFIBROBLASTS IMPAIRS SPECIFICATION AND MATURATION OF INTESTINAL EPITHELIAL CELLS.
R. Servant, C. Ouellet, N. Perreault

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

NOT PUBLISHED AT AUTHOR'S REQUEST

CAG Paper Session
Gut Barrier Defences
Sunday March 5, 08h30-10h30

A13
PROTEOLYTIC BACTERIA PROMOTE INNATE IMMUNE ACTIVATION AND GLUTEN-INDUCED PATHOLOGY IN MICE.
H.J. Galipeau[1], A. CAMINERO FERNANDEZ[1], J. McCarville[1], S. BERNIER[1], J.a. Murray[2], J. Casqueiro Blanco[3], M. Surette[1], E. Verdu[1]

1. Farncombe Family Digestive Health Research Institute , McMaster University, Hamilton, ON, Canada; 2. Gastroenterology, The Mayo Clinic, Rochester, MN; 3. Universidad de León, León, Spain

Background: Celiac disease (CeD) is an immune-mediated enteropathy triggered by gluten in genetically susceptible individuals expressing the HLA-DQ2 or DQ8 genes. Only 2-4% of genetically susceptible individuals develop CeD, suggesting additional environmental triggers contribute to disease pathogenesis. Duodenal dysbiosis has been described in CeD, but no causative mechanisms been described. We have previously isolated *Pseudomonas aeruginosa* (Psa), an elastase-producing opportunistic pathogen, from the duodenum of active CeD patients that increases gluten peptide immunogenicity through its gluten metabolism. **Aims:** Here we determined whether microbial-derived elastolytic activity induces innate immune activation, a key step for enteropathy development in CeD. **Methods:** Altered-Schaedler flora (ASF)-colonized C57BL/6 (non-susceptible) and NOD/DQ8 (genetically susceptible) mice were supplemented with Psa prior to gliadin sensitization and challenge. Non-sensitized mice and mice supplemented with a Psa mutant lacking elastase activity (LasB) were used as controls. Small intestinal proteolytic activity, intraepithelial lymphocyte (IEL) counts and villus-to-crypt (V/C) ratios were measured following gluten challenge. **Results:** ASF-colonized C57BL/6 and NOD/DQ8 mice had low proteolytic activity in small intestinal washes and were protected from gluten-induced pathology following gluten sensitization and challenge. In ASF-colonized mice supplemented with Psa (ASF-Psa), gluten exposure increased small intestinal Psa load, which paralleled increased elastase activity in small intestinal washes. ASF-Psa colonization led to increased small intestinal IELs, independent of gluten exposure, in both the non-susceptible C57BL/6 and the genetically susceptible NOD/DQ8 mice. However, reduction in small intestinal V/C ratios was only observed in ASF-Psa-colonized NOD/DQ8 mice exposed to gluten. No increase in IELs or enteropathy were observed in ASF mice supplemented with the LasB mutant. **Conclusions:** These results suggest that bacterial-derived elastase from opportunistic pathogens, such as *P. aeruginosa*, may directly promote IEL proliferation contributing to gluten-induced pathology in genetically susceptible hosts. Microbial-derived elastolytic activity constitutes a mechanism, in addition to its gluten metabolic activity, through which tolerance to this common dietary protein may be broken. It also opens the road to adjuvant therapies to the gluten-free diet based on protease inhibitory therapy.

A14
INFLAMMASOME ACTIVATION COORDINATES INTES-TINAL MUCOSAL DEFENSE AGAINST THE ENTERIC BACTERIAL PATHOGEN *SALMONELLA ENTERICA* SEROVAR TYPHIMURIUM.

S.M. Crowley[1], F.A. Graef[1], J.M. Allaire[1], L.A. Knodler[2], B. Vallance[1]

1. BC Children's Hospital Research Institute, Vancouver, BC, Canada; 2. Paul G. Allen School for Global Animal Health, Pullman, WA

Background: Intestinal epithelial cells (IECs) play a central role in the coordination of intestinal homeo-stasis. They must strike a careful balance to temper pro-inflammatory responses against the intestinal microbiota, while remaining vigilant and rapidly responsive when exposed to a noxious stimulus such as an enteric pathogen. One early response mechanism by which IECs engage in immune defense is through the activation of an IEC-specific inflammasome. This activation triggers the extrusion of infected IEC into the gut lumen, ultimately restricting *Salmonella enteri-ca* serovar Typhimurium from escaping the gut and spreading systemically. However, it appears the role of the inflammasome in gut defense is not just restricted to IEC shedding but it also plays a key role in mucin secretion and antimicrobial lectin production.
Aims: Here, we investigate the role of the inflam-masome in mucosal defense against *S.* Typhimurium SL1344.
Methods: This study employed a streptomycin pre-treatment *S.* Typhimurium mouse infection model as well as various cell and immunofluorescent staining to characterize the role of the intestinal inflammasome.
Results: Streptomycin-pretreated C57BL/6, Casp1/11 deficient (−/−) and Casp11−/− mice were orally infected and *S.* Typhimurium loads determined for each respec-tive tissue at 18h and 72h post infection. Increased pathogen burdens were observed for both caspase-de-ficient mice compared to wild type, with increased systemic spread seen in the mesenteric lymph nodes, liver and spleen at both time points for Casp1/11−/− mice but only at 72h for Casp11 −/−. Interestingly, at 18h, despite increased bacterial loads, cecal pathology scores were decreased in both Casp1/11−/− and Casp11−/− mice, as compared to wild type. This was accompanied by increased intracellular *S.* Typhimurium immunofluorescence staining. Also, cecal mucin layer thickness, as measured by Alcian Blue as well as MUC2 immunofluorescence staining were similar amongst all mouse strains before infection, but were decreased in both Casp1/11−/− and Casp11−/− mice as compared to wild type after infection. Finally, expression of the antimicrobial lectins REG3γ and REG3β were signifi-cantly decreased in Casp11−/− mice as compared to wild type mice and minimal staining for REG3β was observed in both caspase deficient mice.
Conclusions: These results indicate that the gut epi-thelium utilizes inflammasome signaling to coordinate multiple layers of innate defense at the gut mucosal surface to ultimately restrict enteric pathogen infec-tions and systemic spread.

CAG PAPER SESSION
FROM BASIC RESEARCH TO CLINICAL TRIALS
SUNDAY MARCH 5, 15H30-17H00

A15
A PROSPECTIVE, NON-INFERIORITY, MULTI-CENTER, RANDOMIZED TRIAL COMPARING COLONOSCOPY VS ORAL CAPSULE DELIVERED FECAL MICROBIOTA TRANSPLANTATION (FMT) FOR RECURRENT CLOS-TRIDIUM DIFFICILE INFECTION (RCDI)

D.H. Kao[2], B. Roach[2], M. Silva[1], P. Beck[1], K.P. Rioux[1], K. Madsen[2], K. Goodman[2], H. Xu[3], H. Chang[2], T. Louie[1]

1. University of Calgary, Calgary, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Indiana University, Indianapolis, IN

Background: FMT is highly effective in the treatment of RCDI. Delivery of FMT by upper route and lower routes has been utilized, achieving cure rate of at least 80%. However, the ideal route of delivering FMT has not been determined.
Aims: To compare 1) the cure rate of RCDI; 2) safety; 3) patient satisfaction, preference and changes in quality of life between capsule vs colonoscopy delivered FMT.
Methods: Adult patients who had at least 3 document-ed episodes of CDI were randomized to FMT admin-istered by either capsule or colonoscopy at 1:1 ratio. Key exclusion criteria included severe and complicated CDI; inflammatory bowel disease (IBD), unless stable symptoms for ≥ 3 months; dysphagia. Seven volunteer stool donors provided stool for FMT.
Results: 116 patients (57 in capsule and 59 in colonos-copy arm) were randomized between Oct 2014 - Aug 2016 in Edmonton and Calgary. Participant baseline characteristics were shown in Table 1. The cure rate of RCDI was 96.2% in the capsule arm and 95.9% in the colonoscopy arm after a single FMT (non-inferiority p value <0.0001, Fig 1). One patient in each group died of underlying cardiopulmonary disease within 12 weeks of treatment, unrelated to FMT. Minor adverse events (AE) (abdominal discomfort, nausea, vomiting) were less frequent in capsule arm (12.5% vs 5.4%, p= 0.321). Significant improvement in quality of life measured by SF-36 occurred following FMT with no difference between groups (p>0.5). The proportion of patients rating treatment "not at all unpleasant" was higher in the capsule arm (67%; 95% CI:56-78%) than the colonoscopy arm (44%; 95% CI: 31-59%).
Conclusions: FMT administered by capsules was as ef-ficacious as colonoscopy. No serious AE attributable to FMT was identified with either delivery modality. Fewer

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minor AEs were seen with capsule. Both FMT delivery methods improved quality of life, but fewer patients found capsule to be an unpleasant treatment modality.

Table 1. Patient baseline characteristics.

Variable	Capsule (n = 57)	Colonoscopy (n = 59)
Age, mean (sd)	58.7 (18.5)	57.4 (19.1)
Females, n (%)	43 (75.4%)	36 (61%)
Charlson comorbidity index, median (Q1-Q3)	4 (2 − 5)	3 (1 − 5)
Use of immune modulator, n (%)		
• Corticosteroid	3 (5.3%)	6 (10.2%)
• Immunosuppressant	6 (10.5%)	5 (8.5%)
• Biologic	2 (3.5%)	3 (5.1%)
Body mass index (BMI), mean (sd)	25.4 (5.5)	26.6 (5.1)
Inpatient status at screening	8 (14%)	6 (10.2%)
PPI use prior to FMT	14 (24.6%)	11 (18.6%)
Number of RCDI episodes prior to FMT, median (Q1-Q3)	4 (3 − 5)	4 (3 − 4)
Number of CDI related hospital admissions prior to FMT, median (Q1-Q3)	0 (0 − 1)	0 (0 − 1)
Inflammatory bowel disease		
• Ulcerative colitis	2 (3.5%)	1 (1.7%)
• Crohn's disease	4 (7%)	6 (10.2%)
Hemoglobin, median (Q1-Q3)	136 (128 − 144)	137 (124 − 145)
WBC, median (Q1-Q3)	7.7 (6.4 − 8.6)	6.9 (5.7 − 8.4)
Albumin, median (Q1-Q3)	40 (36 − 43)	39 (37 − 42)
CRP, median (Q1-Q3)	2.1 (1 − 4.3)	3.5 (1.2 − 9.8)
Creatinine, median (Q1-Q3)	72 (62 − 86.5)	73 (61 − 84)

Figure 1. Patient Flow

CAG PAPER SESSION
CAG SELECTED CLINICAL PRESENTATIONS
FRIDAY MARCH 3, 10H00-11H30

A16
SUCCESS OF ENHANCED PRIMARY CARE PATHWAYS IN MANAGING ROUTINE GI REFERRALS.
P.J. Belletrutti[1], G. Heather[2], B. Kathol[2], M. Swain[1], R. Ward[3], L. Slocombe[3], K.P. Rioux[1]

1. Dept. of Medicine, Univ. of Calgary, Calgary, AB, Canada; 2. Alberta Health Services, Calgary, AB, Canada; 3. AHS pan-PCN Working Group, Calgary, AB, Canada

Background: GI Central Access and Triage in Calgary is a single point of entry for referrals. As in most Canadian centres, there has been a sharp increase in demand for GI consultation services resulting in prolonged wait times, especially for non-urgent referrals.

Aims: In order to address this care gap (currently >24 months), evidence-based Enhanced Primary Care Pathways (EPCPs) were developed as a unique collaboration between the GI Division and Primary Care Network leaders in the Calgary Zone in an effort to provide optimized care in the medical home without a one-on-one GI consultation.

Methods: EPCPs were developed for GERD, dyspepsia, chronic constipation, IBS and refractory H. pylori. A phased launch was conducted with the GERD and dyspepsia pathways implemented first. Specific criteria were developed to guide which patients were suitable for these pathways. If an EPCP was enacted, a formal GI consultation visit was not planned, however, a dedicated telephone hotline (GI Specialist Link) was simultaneously launched to provide access to a GI

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specialist for management advice during business hours. These patients were tracked prospectively in a database for future health system encounters. As part of the EPCP, if the suggested management failed or there was a change in symptomatology, re-referral to GI was prompted.

Results: From January 2015-June 2016, 667 cases were triaged to an EPCP thus the referral was sent back for management in the medical home. Over this time period, 54 EPCP patients (7.9%) had an emergency room visit in the Calgary zone. Of the 667 EPCP patients, the re-referral rate to GI was 9.6% (64 cases). The reasons for re-entry back into the system are shown in Table 1. All 64 patients went on to have an endoscopic procedure (EGD=47, colonoscopy=17). Forty-one of the 64 endoscopies (64%) were reported as normal. Significant findings included esophagitis (n=7), non-dysplastic Barrett's esophagus (n=3) and moderate left-sided ulcerative colitis (n=1). No malignancies were detected.

Conclusions: The majority of non-urgent GI referrals were successfully managed in a primary care setting using EPCPs thus providing an alternative to traditional queue-based GI consultations. This process has served as a template for other specialty groups in Calgary looking to address similar care gaps. Future plans include physician/patient satisfaction surveys and focus groups to determine if any additional supports are needed to aid the medical homes in caring for these patients.

Reasons for re-referral to GI after EPCP pathway enacted (n=64)

REASON	NUMBER OF PATIENTS
Worsening abdominal pain	39 (60.1%)
Symptoms despite completion of EPCP pathway	11 (17.1%)
New development of red flag features	8 (12.5%)
Abnormal diagnostic imaging	4 (6.2%)
Barrett's screening	2 (3.1%)

Funding Agencies: None

A17
LINEAR GROWTH IMPAIRMENT IN CANADIAN CHILDREN PRESENTING WITH NEW ONSET IBD: A MULTI-CENTRE INCEPTION COHORT STUDY
T.D. Walters[5], D.R. Mack[15], H.Q. Huynh[16], J. deBruyn[13], K. Jacobson[1], A. Otley[4], W. EL-MATARY[14], C. Deslandres[2], M. Sherlock[8], E.G. Seidman[10], K. Bax[17], J. Critch[9], P.C. Church[11], E.I. Benchimol[3], E. Wine[12], S. Lawrence[1], J. Van Limbergen[7], P. Jantchou[2], M.W. Carroll[12], A. Griffiths[6]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Service de gastro-entérologie, CHU Sainte-Justine, Montréal, QC, Canada; 3. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 4. Pediatrics, Dalhousie University, Halifax, NS, Canada; 5. GI, Hepatology and Nutrition, Hospital For Sick Children, Toronto, ON, Canada; 6. Hospital for Sick Children, Toronto, ON, Canada; 7. Pediatric Gastroenterology and Nutrition, IWK Health Centre, Halifax, NS, Canada; 8. Pediatric Gastroenterology, McMaster Children's Hospital, Hamilton, ON, Canada; 9. Memorial University, St. John's, , Canada; 10. Gastroenterology, Research Institute McGill University Health Center, Montreal, QC, Canada; 11. Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 12. Pediatrics, University of Alberta, Edmonton, AB, Canada; 13. Paediatrics , University of Calgary, Calgary, AB, Canada; 14. Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 15. Pediatrics, University of Ottawa/CHEO, Ottawa, ON, Canada; 16. Pediatrics, University of alberta, Edmonton, AB, Canada; 17. Western University, Schulich School of Medicine, London, ON, Canada

Background: An important target in the management of pediatric inflammatory bowel disease (IBD) is normal linear growth and pubertal development. Greater awareness of IBD and more effective therapies are anticipated to reduce the prevalence of linear growth impairment as a complication of chronic intestinal inflammation.
Aims: To evaluate the current magnitude of linear growth impairment at diagnosis in pediatric Crohn's disease (CD) and ulcerative colitis (UC).
Methods: Since April 2014, the Canadian Children IBD Network (CIDsCANN) inception cohort study prospectively enrolled patients aged $\leq$ 17 years, presenting to 12 academic centers across Canada. Recommended assessment of linear growth at presentation includes height measurement, pubertal staging, ascertainment of pre-illness heights and mid-parental height (MPH) calculation. All growth parameters are standardized utilizing the Centers for Disease Control (CDC) 2000 reference tables. 'Deficit height z-score' was calculated using the formula: 'Predicted Height z-score' minus 'Actual Height z-score'.
Results: Among the initial 800 participants (58% male; CD: 59%, UC: 30%, IBD-unclassified: 11%), median age at presentation was similar for the three disease sub-categories (12.9 yrs; IQR 10.8-15.0), but duration of symptoms prior to diagnosis was significantly longer in CD (5 months, IQR 3-12 months) vs. UC (3 months, IQR 1-6 months) (p<0.001). Macroscopic disease location based on Paris classification for UC was: 70% E4; 12% E3; 16 % E2 and for CD was: 58% L3; 23% L2; 18% L1. Linear growth impairment, based on historical growth parameters, occurred in 21% of CD patients (8% as the main presenting feature), and 3% of UC patients (but none as the main presenting feature). Predicted height z-scores (based on MPH) were normally distributed (mean 0.07, SD 0.8) with no difference noted between CD and UC patients. As shown in Table, the

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UC cohort had normal height at diagnosis, but in the CD cohort height was reduced compared to both the healthy population and predicted values. This was especially especially prominant among younger vs. older CD patients (p=0.05), despite similar symptom duration (median 5 months) prior to diagnosis (Table). Males demonstrated a greater deficit than females.

Conclusions: Linear growth impairment still occurs prior to the recognition of Crohn's disease in young patients, but its magnitude is less than in previous eras. Deficit in Height Z-score based on the Mid-Parental Height calculation appears a useful metric in quantifying linear growth impairment.

	UC	CD	CD: Age<12yrs	CD: Age>15yrs
Mean Ht z-score (SD)	0.07 (1.1)	-0.44 (1.1)		
Mean Deficit Ht z-score (SD)	-0.06 (1.1)	0.48 (1.1)	0.23 (1.2)	0.08 (1.1)

A18
IMPROVING COMPLIANCE WITH COLONOSCOPY SURVEILLANCE INTERVAL GUIDELINES
M. Borgaonkar[2], D. Pace[2], J.S. McGrath[2], J. Harding[1]

1. Gastroenterology, Eastern Health, St. John's, , Canada; 2. Memorial University, St. John's, , Canada

Background: Research suggests that colonoscopy is over utilized in patients undergoing colorectal cancer (CRC) or adenoma surveillance.
Aims: To improve endoscopist compliance with the 2013 Canadian Association of Gastroenterology (CAG) guidelines on CRC surveillance.
Methods: In 2014, a trained nurse reviewed a sample of surveillance colonoscopies conducted by each endoscopist at one of five hospitals in Eastern Health (EH) Newfoundland. The endoscopist recommendation for the next surveillance colonoscopy was compared to that of the CAG guidelines based upon the findings and polyp histology. A three-part intervention was undertaken. First, each endoscopist was informed of their own compliance rate and that of the group. Second, a survey was conducted to ascertain how endoscopists decided upon surveillance intervals and barriers to following guidelines. Finally, the group met to discuss the survey results and identify ways to optimize compliance. In 2016, the same nurse determined the endoscopist compliance rate, which was compared to 2014. Only endoscopists who contributed patients to both time periods were included in the analysis. Approximately 25 cases were chosen for each endoscopist at each time point. Data were entered into SPSS version 20.0 for analysis. The study received approval from the local Health Research Ethics Board.
Results: In 2014, 526 surveillance colonoscopies per-

formed by 18 endoscopists (10 Surgeons, 8 Gastroenterologists) were reviewed. Surveillance intervals were appropriate in 74.9% of cases. Endoscopist compliance rates ranged from 50.0% to 100%. Fourteen endoscopists completed the survey on guideline compliance. 85.7% indicated they used the CAG guidelines to determine surveillance intervals. The three most common reasons for deviating from guidelines were poor bowel preparation (71.4%), booking the next procedure prior to reviewing polyp histology (50%) and patient preference for a different interval (50%). These results prompted EH to emphasize to patients the importance of high quality bowel preparation and to utilize split dose preparations more frequently. In 2016, 533 surveillance colonoscopies performed by the same endoscopists were reviewed. Surveillance intervals were appropriate in 82.7% of cases (p=0.002 compared to 2014). Endoscopist compliance ranged from 56% to 100%. It was noted that Gastroenterologists had a higher level of compliance than surgeons (84.9% vs. 72.7%; p<0.001).
Conclusions: A multi-faceted intervention was associated with an improvement in compliance with the CAG colonoscopy surveillance guidelines. Further study is required to determine which part of the intervention was most effective and if these results are sustained over time.
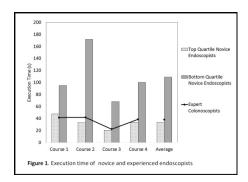
A19
DEVELOPING A COMPETENCY-BASED PERFORMANCE METRIC OF COLONOSCOPY SKILLS ACQUISITION USING MOTION ANALYSIS - STEP 1: LOW-FIDELITY BENCHTOP MODEL
C. Wang[2], M. Holden[2], T. Ungi[2], G. Fichtinger[2], C.M. Walsh[1], L. Hookey[2]

1. Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children and The Wilson Centre, Toronto, ON, Canada; 2. Queen's University, Waterloo, ON, Canada

Background: Colonoscopy is essential for the diagnosis and treatment of colonic diseases. Simulation is increasingly prevalent in colonoscopy skills acquisition as it allows controlled experiential learning without risk to patients. However, objectively assessing when trainees achieve the competence required to proceed to patients remains an outstanding challenge.
Aims: To establish a novel metric using advanced motion analysis to objectively assess colonoscopy skills acquisition across multiple simulation models.
Methods: This pilot study assessed the difference between experienced (N=9) and novice endoscopists (N=20) before and after training on a low-fidelity bench-top colonoscopy simulator developed by Walsh et al. (2009) which is designed to teach basic endoscope handling skills. Experienced colonoscopists were asked to scope four different courses with two repetitions in a random sequence to define the benchmark

workflow. Novice endoscopists were asked to scope the same course prior to and after completing a 1-hour practice session. Execution time in seconds, hand path length in meters and number of hand movements were recorded using electromagnetic position sensors attached to the left and right hands and forearms.
Results: Before practice novice endoscopists had average right hand (RH) path length, number RH movements, and total time of 6.42m, 48.7, and 153s, respectively. This was significantly higher than expert endoscopist values of 2.91m, 13.6 and 39.9s (p < 0.001 for all). Additionally, pre-practice values were significantly higher than post-practice values of 3.24m, 21.1 and 59.0s (p=0.002, p=0.003, p=0.002, respectively). Fifteen of 20 novice endoscopists reached competency after 1-hour of practice on this model; competency was defined using the second lowest performing expert's scores. **Figure 1** shows execution time of the top and bottom quartile of novice endoscopists after practice compared to the mean of experienced endoscopists.
Conclusions: We are the first group to propose a novel platform to assess colonoscopy skills acquisition using motion analysis. Novice endoscopists reliably achieve competency in basic endoscopic handling using a benchmark developed from experienced colonoscopists on a low-fidelity colonoscopy model. The range of novice endoscopist performances after 1-hour of practice reinforces the importance of competency-based assessment. We aim to apply our competency metric to objectively assess all stages of colonoscopy skills acquisition.

Figure 1. Execution time of novice and experienced endoscopists

A20
PREDICTORS OF PATIENT RELUCTANCE TO USE SPLIT DOSE BOWEL PREPARATION FOR EARLY MORNING COLONOSCOPIES
L. Shafer, C. Waldman, J.R. Walker, V. Michaud, C.N. Bernstein, L. Hathout, J. Park, J. Sisler, G. Restall, K. Wittmeier, h. singh
University of Manitoba, Winnipeg, MB, Canada

Background: European and North American guidelines strongly recommend use of split-dose bowel preparation (SDBP) for all colonoscopies based on evidence from meta-analyses. Interviews and focus groups with endoscopists indicate some reluctance to use SDBP for early morning colonoscopies because they believe patients will not agree to it.
Aims: We assessed colonoscopy patients' opinions about getting up very early in the morning to take a SDBP.
Methods: self-administered anonymous survey was distributed between August 2015 to June 2016 to patients immediately prior to their outpatient colonoscopy in 6 hospitals and 2 ambulatory care centers in Winnipeg, Canada. Multinomial multivariate logistic regression analysis was performed to determine predictors of reluctance to early morning SDBP.
Results: Of the 1336 respondents (52% females, median age 57 years), 33% had used SDBP and overall 13.5% did not complete the entire recommended laxative intake. 49% of survey respondents were willing or very willing to do early am SDBP, 24% were neutral and 27% reluctant or very reluctant. When the outcome of reluctance was compared to willing, the predictors of reluctance on multivariate analysis included more than one prior colonoscopy (OR 1.60; 95% CI: 1.04-2.47), female gender (OR 1.81; 95% CI: 1.29-2.54), lack of clear information (OR: 4.40 95% CI: 2.08-9.28), high level of anxiety for bowel preparation (score > 80 on a 0-100 scale) (OR 1.79 95% CI: 1.02-3.14), and type of laxative used (4 litres PEG alone vs. sodium picosulfalte with adjunct agent: OR 1.60 95% CI: 1.01-2.53). There was no effect of procedure time of day, indication for colonoscopy or level of education. There was an interaction effect between use of SDBP and finishing the laxative intake. Among those who finished the laxative, use of day before preparation was associated with a more than 2-fold greater reluctance to use SDBP for future colonoscopy (OR 2.24 95% CI: 1.43-3.51). The same predictors were identified when reluctance was compared to willing and neutral combined.
Conclusions: In spite of clear evidence of superior efficacy of SDBP, there continues to be limited use of SDBP in usual clinical practice. However, only a minority of patients expressed reluctance to get up early for SDBP. Efforts to clearly inform patients about the advantages of SDBP and arrangements to move the most reluctant to later morning appointments may support increased SDBP use.

A21
RANDOMIZED PROSPECTIVE STUDY: IMPACT OF THE PATIENT EDUCATION WEBSITE ON THE QUALITY OF OUTPATIENT BOWEL PREPARATION FOR COLONOSCOPY:
M.M. Suzuki[1], M. Bardi[5], O. Takach[7], C. Galorport[4], J.

Yonge[7], N. Harris[3], E. Lam[3], J.J. Telford[7], G. Rosenfeld[6], H. Ko[8], R.A. Enns[2]

1. Gastroenterology , Pacific Gastroenterology Associates, Vancouver, BC, Canada; 2. Medicine, St Paul, Vancouver, BC, Canada; 3. Gastroenterology, St. Paul's Hospital, Kamloops, BC, Canada; 4. Medicine, Div. of Gastroenterology, St. Paul's Hospital , Vancouver, BC, Canada; 5. Medicine , UBC, Vancouver , BC, Canada; 6. Medicine, UBC, Vancouver, BC, Canada; 7. University of British Columbia, Burnaby, BC, Canada; 8. Medicine, University of British Columbia, Vancouver, BC, Canada
Background: Low level bowel cleanliness that occurs in 25% of patients, hinders polyp detection and limits colonoscopy effectiveness. Those with inadequate preparation have incomplete examinations, fewer polyps detected, more repeat colonoscopies and higher resource utilization. Aside from pharmacological and timing of purgative factors to optimize bowel preparation, non-pharmacological factors that influence patient compliance (i.e. patient education) in the preparation phase can significantly improve bowel preparation quality.
Aims: To assess if interactive, individualized web based instruction leads to improved colonoscopy preparation through enhanced patient compliance, satisfaction and tolerability of preparation.
Methods: A randomized, prospective, single blinded trial initiated at St. Paul's hospital in Vancouver, B.C. Inclusion criteria: age >19, planned outpatient colonoscopy, and willingness/ability to participate by reading the online English material supplied by sending the subject a specific domain (which contains the educational information for their colonoscopy). Exclusion criteria: None. Consecutive patients enrolled into the study (target of 450 participants). Data Collected: demographics, cancellations, bowel preparation cleanliness scores as per Boston bowel preparation score (BBPS) and Ottawa bowel preparation score. Primary end points: percentage of patients that achieve an excellent BBPS following web-based instructions vs paper instructions. Assessment of patient satisfaction, preparation tolerability and patient activation score through post colonoscopy follow-up surveys.
Results: 450 patients have been recruited and analyzed. 197 are male; mean age 55 years (range 20-81). 223 were assigned to Group A (paper based) and 227 to Group B (web based). A Fisher's exact test showed a significant difference in the proportion of subjects achieving an excellent BBPS score ≥8 (Group A = 37% (82/223), Group B = 47% (106/227) p=0.0357) and a significant decrease in the number of subjects with inadequate preps BBPS≤3 (Group A = 8.9% (20/223), Group B = 3.5% (8/227) p=0.0191). There was no significant difference in patient satisfaction (p=0.8415), helpfulness (p=0.9847) or clarity of instructions (p=0.8936).
Conclusions: Analysis showed a significant difference in patients achieving both excellent and inadequate bowel preparation scores between interactive individualized web based instructions vs written instructions. Due this study our office has transitioned to using the web platform as standard of care. We are currently running an open label study to continue monitoring the outcomes of patient using the web platform.

CASL PAPER SESSION 1
SATURDAY MARCH 4, 08H30-10H00

A22
LIVER TYPE FATTY ACID BINDING PROTEIN (FABP1) LEVELS IMPROVE PERFORMANCE OF PROGNOSTIC MODELS IN ACETAMINOPHEN INDUCED ACUTE LIVER FAILURE
C.J. Karvellas[1], J.L. Speiser[2], M. Tremblay[3], W. Lee[4], C.F. Rose[3]

1. University of Alberta, Edmonton, AB, Canada; 2. Medical University of South Carolina, Charleston, SC; 3. CRCHUM, Montreal, QC, Canada; 4. UT Southwestern, Dallas, TX

Background: Acetaminophen (APAP) - induced acute liver failure (ALF) is associated with significant mortality. To date, traditional prognostic scores (King's College Criteria ~ KCC; Acute Liver Failure Study Group (ALFSG) prognostic index) lack discrimination in identifying patients with APAP-ALF who will die without liver transplant (LT), and those who will survive with medical management alone. Liver-type fatty acid binding protein (FABP1) is a 15 kDa cytoplasmic protein abundantly expressed in hepatocytes with potential prognostic value in APAP-ALF patients.
Aims: Our aims were to
a) Determine if elevated serum levels of FABP1 in APAP-ALF are significantly associated with 21-day mortality after adjusting for other significant covariates.
b) Determine if the addition of FABP1 improves the performance of previously described prognostic models in APAP-ALF (KCC, ALFSG prognostic index).
Methods: With serial serum samples (early; day 1 or late; day 3-5) from 198 APAP-ALF patients (99 survivors, 99 non-survivors), FABP1 was measured using solid-phase enzyme-linked immunosorbent assay. No patients in this analysis received LT. With clinical data from the prospectively collected ALFSG registry, model performance (early and late) for KCC, ALFSG index, FABP1, FABP1+KCC, and FABP1+ALFSG index were assessed using AUROC statistics. Comparisons of AUROC statistics between models (e.g. KCC vs. FABP1 + KCC) were made using the Delong method.
Results: APAP-ALF survivors had significantly lower serum FABP1 levels early (238.6 vs. 690.8 ng/ml, p <0.0001) and late (148.4 vs. 612.3 ng/ml, p <0.0001) compared with non-survivors (Figure 1). FABP1 > 350 ng/ml was associated with significantly higher risk of

death at early (p=0.0004) and late (p<0.0001) time points. Increased serum FABP1 early (log FABP1 odds ratio (OR) 1.31, p=0.027) and late (log FABP1 OR 1.50, p =0.005) were associated with significantly increased 21-day mortality after adjusting for significant covariates (MELD, vasopressor use). Areas under the receiver-operating curve (AUROC) for early and late multivariable models were 0.778 and 0.907 respectively. AUROC of the King's College Criteria (KCC) (Early: 0.552 alone, 0.711 with FABP1; Late: 0.604 alone, 0.797 with FABP1) and ALFSG prognostic index (Early: 0.686 alone, 0.766 with FABP1; Late: 0.711 alone, 0.815 with FABP1) significantly improved with the addition of FABP1 (p <0.002 for all, Delong).
Conclusions: In patients with APAP-ALF, FABP1 showed good potential to discriminate survivors from non-survivors at multiple time-points and significantly improved models currently used in clinical practice. Validation of FABP1 as a clinical prediction tool in APAP-ALF merits further investigation.
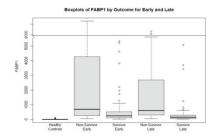
Figure 1: Serum levels of **FABP1** (ng/ml) in healthy controls, non-survivors (early ~ admission), survivors (early), non-survivors (late ~ day 3-5), survivors (late).

A23
CIRCULATING PROPIONATE AND SPLANCHNIC VASO-DILATION IN CIRRHOSIS
C. McDougall[3], A. Davila[1], A. Mason[1], S. Alghbli[1], O. Hojanepesov[1], D. Shah[1], A. Mason[1], P. Tandon[1], J. Abraldes[2]

1. University of Alberta, Edmonton, AB, Canada; 2. Liver Unit, University of Alberta, Edmonton, AB, Canada; 3. Medicine, University of Alberta, EDMONTON, AB, Canada

Background: Splanchnic arterial vasodilation is at the center of the pathogenesis of cirrhosis complications since it contributes to portal hypertension and arterial hypotension. The mechanisms of vasodilation in cirrho-sis are still not well understood which results in lack of targeted pharmacological therapies. Recently it has been shown in experimental animals that gut derived short chain fatty acids, in particular propionate, have vasoactive properties causing vasodilation.
Aims: Our aim was to assess if propionate contributes to splanchnic vasodilation in cirrhosis.
Methods: In 42 patients with cirrhosis (Child-Pugh A/B/C: 10/18/14) and portal hypertension we analysed plasma levels of propionate (LC-MS), HVPG and the transcriptome of liver biopsies. In sham-operated rats and rats with biliary cirrhosis (4 weeks of common bile duct ligation or CBDL), we assessed circulating propionate levels, and the hemodynamic effects of a continuous infusion of propionate (vs saline) on portal pressure (PP), mean arterial pressure (MAP) and superior mesenteric artery blood flow (SMABF, as a readout of splanchnic vasodilation).
Results: Cirrhosis patients showed increased circulating propionate above normal laboratory values that correlated with the degree of portal hypertension (p=0.004; Fig 1) and a downregulation of the metabolic pathway of propionate (FDR<0.000001). We then assessed in control (sham-operated) rats the effects of an infusion causing increase in propionate levels comparable to that observed in advanced cirrhosis. Propionate infusion caused an increase in SMABF (+64%, p<0.05) and hypotension (-12%, p<0.05),) without significantly modifying portal pressure (+6%, ns). Cirrhotic rats (CBDL) showed a 1.9 fold increase in propionate levels as compared to sham rats (p=0.047), that correlated with MAP (p<0.05), and a significant downregulation of liver propionate metabolic pathway (FDR<0.001). In cirrhotic rats propionate infusion induced a further worsening in cirrhosis hemodynamics, causing further decrease in MAP (-15%, p<0.05), increased SMABF (+48%, p<0.05) an increase in portal pressure (+14%, p<0.05).
Conclusions: Propionate is increased in cirrhosis and correlates with the degree of portal hypertension. In rats an increase in circulating propionate induces hypotension, increases SMABF and, in cirrhotic rats, aggravates portal hypertension. Altogether this suggests that propionate contributes to the abnormal hemodynamics of advanced cirrhosis and might be an actionable target to improve arterial hypotension and portal hypertension in these patients.

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A24
SPECIALIZED MULTIDISCIPLINARY CARE IN CIRRHO-SIS IMPROVES MORTALITY AND REDUCES ACUTE CARE UTILIZATION

M. Carbonneau[3], T. Davyduke[3], P. Tandon[1], M. Ma[1], K. Newnham[3], V. DenHeyer[3], J. Abraldes[2]

1. University of Alberta, Edmonton, AB, Canada; 2. Liver Unit, University of Alberta, Edmonton, AB, Canada; 3. Cirrhosis Care Clinic, University of Alberta Hospital, Edmonton, AB, Canada

Background: As the prevalence of cirrhosis-associated acute care utilization and mortality rise, new care models are emerging. The impact of multidisciplinary care on survival and acute care utilization is limited to one study, showing benefit. The cirrhosis care clinic (CCC) at the University of Alberta Hospital offers outpatient multidisciplinary care to patients with cirrhosis.
Aims: We aimed to evaluate the acute care utilization and survival outcomes of patients followed by the CCC compared to standard care (SOC).
Methods: We performed a retrospective chart review for 294 cirrhotic patients admitted at the University of Alberta Hospital between 2014 and 2015. Patients were included in the CCC group if they had been followed through the CCC prior to their baseline admission and patients never seen in the CCC were included in the SOC group (CCC=44, SOC=250). For the 243 survivors of the initial admission (CCC n=38, SOC n=205), re-admission time spent in hospital was collected until one-year post admission, death, or liver transplant.
Results: Patients from the CCC group had more advanced liver disease as shown by a higher prevalence of ascites, encephalopathy, and varices. However, acute care utilization was significantly lower in patients followed through the CCC with a reduction in both length of stay by a mean 6.06 days (p 0.01) and percent of transplant free survival days spent in hospital (15.7% vs 22.7%, p 0.037). CCC patients also had improved one-year transplant free survival versus SOC, with an adjusted one-year relative risk reduction of 51% (p 0.033).
Conclusions: In conclusion, for patients admitted with cirrhosis, specialized multidisciplinary outpatient care is associated with a shortened length of stay, decreased subsequent need for acute care utilization, and improved one-year transplant free survival probability.

Adjusted Predictors of Death or Transplantation

	Adjusted Hazard Ratio	95% CI		p value
		Lower	Upper	
CCC	.49	.25	.96	0.033
Ascites				0.37
First Presentation	.76	.42	1.39	0.38
Medically Controlled	.56	.28	1.11	0.12
Poorly Controlled	1.007	.54	1.88	0.99
Varices				0.80
First Presentation	1.32	.65	2.65	0.47
Yes, Never Bleed	1.02	.46	2.25	0.97
Yes, Prior Bleed	1.06	.53	2.11	0.90
Encephalopathy				0.28
First Presentation	.57	.32	1.01	0.50
Medically Controlled	.68	.31	1.51	0.30
Poorly Controlled	.82	.39	1.71	0.67
Bilirubin	1.005	1.003	1.007	0.003
Albumin	1.001	.99	1.003	0.90
Creatinine	1.05	.62	1.77	0.29
INR	.97	.94	1.002	0.84

Unadjusted Transplant Free Survival

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A25
HOME EXERCISE THERAPY IS WELL TOLERATED AND IMPROVES EXERCISE CAPACITY IN PATIENTS WITH CHILD PUGH A AND B CIRRHOSIS

C. Kruger[1], M. McNeely[1], R. Bailey[2], M. Yavari[1], J. Abraldes[5], M. Carbonneau[5], K. Newnham[5], V. Mathiesen[8], M. Ma[5], R. Thompson[6], I. Paterson[4], M. Haykowsky[7], P. Tandon[3]

1. Faculty of Rehabilitation Medicine, University of Alberta, Edmonton, AB, Canada; 2. Royal Alexandra Hospital, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. Division of Cardiology, Department of Medicine, University of Alberta, Edmonton, AB, Canada; 5. Cirrhosis Care Clinic, Department of Medicine, University of Alberta, Edmonton, AB, Canada; 6. Department of Biomedical Engineering, University of Alberta, Edmonton, AB, Canada; 7. Division of Gastroenterology, College of Nursing and Health Innovation, University of Texas at Arlington, Arlington, TX; 8. Cirrhosis Care Clinic, Department of Medicine, University of Alberta, Edmonton, AB, Canada

Background: Cirrhosis patients have reduced peak aerobic power (peak VO_2) that is associated with reduced survival. Supervised endurance training is an effective therapy to increase exercise tolerance in cirrhosis. Many patients have challenges coming in regularly for supervised training. The effect of home-based endurance exercise training (HET) on improving peak VO_2 in cirrhosis patients has not been studied.
Aims: The aim of this pilot study was to evaluate the safety and efficacy of 8 weeks of HET on peak VO_2, aerobic endurance (6-minute walk distance), thigh muscle thickness (2D ultrasound) and circumference, and quality of life.
Methods: Clinically stable patients with cirrhosis were randomly assigned to 8 weeks of HET (n=20) or usual care (controls, n=20). The HET group performed moderate to high intensity (heart rate equal to 60-80% peak VO2) cycle exercise for 3 days per week. An exercise specialist supervised an HET session once every two weeks and had regular telephone contact between these sessions. Paired t-test was used for within group comparisons and analysis of covariance was used to perform between group comparisons.
Results: The cohort (n=40) was 58% male, had a mean age of 57 ± 8 years, and 70% had Child Pugh class A cirrhosis. The between group VO_2 difference trended to significance (1.7 (-0.33 to 3.7), p=0.09) and the between group 6-minute walk test increased (33.7 (5.1 to 62.4), p=0.02). When within group differences were considered, the HET group had a significant increase in peak VO2 from baseline (17.3 ± 4.5 to 19.0 ± 6.4 mL/kg/min, p=0.03). There was also a significant increase in the thigh circumference (50.6 ± 5.8 to 52.4 ± 6.6 cm, p=0.02) and thigh muscle thickness (1.25 ± 0.40 to 1.31 ± 0.38 cm/m^2, p=0.05). There was no significant difference in quality of life and no adverse events occurred during cardiopulmonary exercise testing or HET.
Conclusions: Eight weeks of HET is a safe and effective intervention that results in a clinically meaningful improvement in aerobic endurance distance, and trends to improvement in peak VO_2 and thigh muscle mass in clinically stable patients with cirrhosis

A26
TREATMENT OUTCOMES OF HCV-INFECTED PATIENS IDENTIFIED THROUGH THE COMMUNITY POP-UP CLINIC

G. Kiani[2], R. Shahi[3], T. Raycraft[1], A. Alimohammadi[2], A. Singh[2], B. Conway[2]

1. Medicine, University of British Columbia, Vancouver, BC, Canada; 2. Vancouver Infectious Diseases Centre, Vancouver, BC, Canada; 3. Vancouver Infectious Diseases Research & Care Centre Society, Vancouver Infectious Diseases Centre, Vancouver, BC, Canada

Background: In Canada, it is estimated that over 300,000 individuals are infected with HCV, with 60,000 residing in British Columbia. The prevalence of infection on Vancouver's Downtown East Side (DTES) may exceed 70%, with relatively few individuals having been treated to date. This may relate to a lack of engagement in medical care. We developed a novel model of intervention, the Community Pop-up Clinics (CPC) as a tool to enhance access to medical care and HCV therapy in this vulnerable population.
Aims: We aim to further understand the treatment outcomes of HCV infected individuals identified through this initiative.
Methods: Participants were recruited at CPCs held at several community centres. OraQuick® HCV Rapid Antibody and HIV Rapid Antibody point-of-care testing was offered. Participants identified as HCV positive were provided the opportunity to engage in care at a multidisciplinary clinic. A questionnaire was administered to collect demographic information, HCV disease knowledge, and data regarding barriers to receiving healthcare. A $10 gift-card incentive was provided for participants who completed the demographic questionnaire and testing.
Results: A total of 2378 participants (mean age 49.9 years, 93.4% male) were tested for HCV infection, with 658 (27.7%) infected with HCV including 51 (7.7%) co-infected with HIV. Among HCV infected participants, 157 (27.6%) were linked to care (76% male, 30% First Nations, 28% homeless, 78% recent PWID), 26 (16.9%) started treatment for HCV infection, 19 (73%) completed treatment, and 16 (84.2%) achieved sustained virologic response (SVR). Groups under-represented among those engaged in care include: females (7%), lack of knowledge about how to access health care (9%), homeless (9%), perceived their health status as good (14%), First Nations (15%).
Conclusions: Our CPC approach in a neighborhood with

HCV prevalence of 70% has successfully identified over 600 HCV-infected individuals and engaged a significant proportion of them in care. Additional efforts must be undertaken to engage certain populations such as women, First Nations and those who are homeless and in ensuring that engagement leads to enhanced access to curative HCV therapies in all eligible patients.

Funding Agencies: None

A27
CHARACTERIZATION OF HCV INFECTED PWID IN THE SETTING OF CLINICAL CARE IN CANADA (CAPICA): FINAL RESULTS
J. Feld[1], B. Conway[2], J. Bruneau[3], C. Cooper[4], J. Cox[5], L. Deshaies[6], C. Fraser[7], G. Macphail[8], J. Powis[9], C. Steingart[10], K. Stewart[11], R. Thomas[12], D. Webster[13], M. Drolet[14], M. Mcgovern[14], J. Trepanier[14]

1. Centre for Liver Disease, Toronto General Hospital, Toronto, ON, Canada; 2. Vancouver Infectious Diseases Centre, Vancouver, BC, Canada; 3. CHUM:Hopital St-Luc, Montreal, QC, Canada; 4. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 5. McGill University Health Center, Montreal , QC, Canada; 6. Clinique Médicale Lauberivière, Quebec, QC, Canada; 7. Cool Aid Community Health Center, Victoria, BC, Canada; 8. Calgary Urban Project Society (CUPS), Calgary, AB, Canada; 9. Toronto Community Hep C Program, Toronto, ON, Canada; 10. Sanguen Health Center, Waterloo, ON, Canada; 11. Saskatoon Infectious Disease Care Network, Saskatoon, SK, Canada; 12. Clinique Médicale l'Actuel, Montreal, QC, Canada; 13. Dalhousie University, Saint John, NB, Canada; 14. Merck Canada, Kirkland, QC, Canada

Background: HCV-related liver disease in people who inject drugs (PWIDs) carries a heavy personal, healthcare and societal burden. Current HCV treatment uptake in PWIDs is low and related to barriers at the individual, provider and healthcare system levels.
Aims: Collect data related to demographic, medical and behavioral variables in HCV-infected PWIDs already engaged in care in Canada to help define treatment barriers.
Methods: This multicenter observational study used retrospective chart review to collect data on patients receiving care from 12 Canadian centers. Patients with chronic HCV infection (HCV RNA+) and a history of injection drug use (in the previous 12 months) were included; HIV co-infection was excluded. Data were collected from October 2015 to February 2016.
Results: Of 423 participants: 74% were male, 65% Caucasian, 12% Aboriginal, with a median age of 42 years. All clinical sites provided multidisciplinary care and 11/12 had harm reduction programs. 33% of patients injected daily and 20% recently shared needles. Most frequent HCV genotypes were 1a (47%) and 3 (29%). When the fibrosis score was known (65% cases), 55% had F0-F1 and 14% had F4. The majority of patients

were not yet being treated for HCV (83%). Of the 71 patients who received treatment, 37% (26/71) received IFN-free regimens. In the multivariate analysis, increasing age (OR = 1.10, 95% CI [1.03, 1.08]) , not using a needle exchange program (OR = 6.95, 95% CI [1.73, 27.97]), moderate alcohol consumption (males ≤ 15 or females ≤ 10 drinks per week) vs. other (OR = 3.70, 95% CI [2.05,6.69]) and a recent fibrosis assessment with F4 vs. F0-F3 (OR = 4.91, 95% CI [2.18,11.09]) were associated with a higher likelihood of receiving treatment.
Conclusions: A large number of HCV-infected PWIDs are engaged in care in Canada. Treatment rates are still low and patients are being prioritized for treatment. Barriers to treatment identified in this analysis will help to design targeted interventions for this group.

Funding Agencies: Merck Canada Inc.

CASL PAPER SESSION 2
SUNDAY MARCH 5, 09H00-10H30

CASL Student Prize

A28
INTRAHEPATIC IL-22 CORRELATES WITH ADVANCED LIVER FIBROSIS AND SENSITIZES HSC TO TGF-β SIGNALING IN A P38-DEPENDENT MANNER
T. Fabre[1], M. Flores[1], G. Soucy[1], J. Villeneuve[1], B. Willems[1], M. Bilodeau[2], N. Shoukry[3]

1. CRCHUM, Montreal, QC, Canada; 2. Liver Unit, CRCHUM, Montréal, QC, Canada; 3. CRCHUM, Montreal, QC, Canada

Background: Activation of hepatic stellate cells (HSCs) is a key event in the initiation of liver fibrosis. CD4 T cells can modulate positively or negatively this process. Briefly, Th1 cells despite their pro-inflammatory properties have anti-fibrogenic properties in contrast to Th2 cells. We and others have demonstrated that IL-17A produced by Th17 cells has pro-fibrogenic properties as it promotes activation of HSCs via different mechanisms. Th17 cells also produce IL-22, an enigmatic cytokine with proinflammatory and hepatoprotective properties. In addition, IL-10 produced by regulatory T cells (Treg) negatively modulates activation of HSCs.
Aims: We hypothesized that liver fibrosis progression results from an alteration in the Th17/Treg ratio leading to an imbalance in the pro-fibrotic cytokine profile within the liver.
Methods: We examined *ex vivo* the frequency of Th17 and Treg populations and the cytokine profile of intrahepatic lymphocytes isolated from liver biopsy samples (n=32). We validated these cytokines profiles using *in vivo* model of fibrosis in transgenic mice and primary human HSCs.
Results: We observed increased Th17/Treg ratio in advanced (F4, Metavir) as compared to moderate or

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non-fibrosis (F0-F2). Furthermore, we observed a bias towards Th17/Th9 cytokine profile in fibrotic livers with viral-hepatitis, whereas the cytokine profile was Th17/Th2 in non-viral hepatitis. All biopsies exhibited a 5-fold increase in IL-22 in fibrotic livers (p=0.0082) irrespective of aetiology. *In vivo*, lack of IL-22 signaling protects against thioacetamide-induced fibrosis. IL-22RA1 Knockout mice have reduced collagen deposition measured by picro-sirius red staining (p=0.0009) and pro-fibrotic genes expression (ACTA2, LOXL2, TIMP-I, TGFb1, COL1A1) in comparison to wild-type littermates. *In vitro* stimulation of primary human HSCs with IL-22 sensitized them to suboptimal doses of TGF-b. RNA-seq analysis demonstrated activation of p38 in HSCs in response to IL-22 and chemical inhibition of p38 suppressed the pro-fibrogenic effect of IL-22.

Conclusions: Our results suggest a dysregulated Th17/Treg ratio in advanced fibrosis coupled with distinct cytokine profile dependant on the aetiology of liver disease. Finally, we have identified IL-22 as a common factor in advanced liver fibrosis acting through sensitization of HSCs to TGF-b in a p38-dependent manner.

CASL Student Prize

A29
THE MOLECULAR INTERPLAY BETWEEN CIRCULAT-ING MIR-24, MIR-223, AND PCSK9 IN HEPATITIS C-INFECTED PATIENTS WHO ACHIEVE A TREAT-MENT-BASED VIRAL CURE
A. Hyrina[1], A. Olmstead[2], P. Steven[3], M. Krajden[4], E. Tam[5], F. Jean[1]

1. University of British Columbia, Vancouver, BC, Canada; 2. BC Centre for Excellence in HIV/AIDS, Vancouver, BC, Canada; 3. QIAGEN, Manchester, United Kingdom; 4. BC Centre for Disease Control, University of British Columbia, Vancouver, BC, Canada; 5. LAIR Centre, Vancouver, BC, Canada

Background: Hepatitis C virus (HCV) hijacks host lipid metabolic pathways as part of its replication cycle. Chronic HCV infection is associated with altered metabolism, which both contributes to disease progression and influences response to therapy.
Aims: To help understand how HCV influences important metabolic pathways of chronic liver disease, we investigated the molecular interplay between four circulating regulators of lipid homeostasis (miR-122, miR-24, miR-223 and proprotein convertase subtilisin/kexin type 9 (PCSK9)) in HCV-infected patients who achieved viral cure with interferon-based treatment.
Methods: Circulating plasma levels of microRNAs were measured at multiple time-points during antiviral therapy in individuals achieving sustained virologic response (SVR) (n=57), relapsers (n=10), and non-responders (n=27). The concentration of plasma PCSK9 was

assessed in paired samples before and after treatment in SVR (n=27) and relapsers (n=7).
Results: We report that miR-24 and miR-223 levels were significantly increased in HCV-infected patients who achieve SVR (miR-24, p-value < 0.0001; miR-223, p-value < 0.0001). In contrast, miR-122 decreased after HCV clearance (p-value < 0.0001), correlating with normalized liver-specific enzymes. Quantitative correlation between amounts of circulating miR-24 and miR-223 was also observed (r=0.91, p-value ≤ 0.0001) for all patients. Importantly, plasma PCSK9 concentrations were significantly upregulated in HCV-infected patients who achieve SVR (p-value=0.002). Also, miR-24 and PCSK9 levels were correlated (r=0.24, p-value ≤ 0.02) in HCV-infected patients, indicating for the first time an *in vivo* link between the two. A modulatory effect of PCSK9 on HCV infection was demonstrated using a cell-based system of viral infection employing recombinant human wild-type PCSK9 and PCSK9 gain- and loss-of-function mutants.

Conclusions: Together, these results provide the first insights into a novel coordinated interplay between three important molecular players in lipid homeostasis—lipoprotein-associated miR-24 and miR-223 and circulating PCSK9— whose regulation are affected by HCV infection and treatment-based viral cure.

CASL Student Prize

A30
FIRST YEAR OUTCOMES FROM A PROVINCIALLY FUNDED NON-FIBROSIS RESTRICTED HEPATITIS C TREATMENT PROGRAM IN PRINCE EDWARD ISLAND
J.W. Francheville[2], R. Rankin[1], J.n. Beck[1], C. Hoare[1], R. Khan[1], S. materniak[3], G. German[1], L. Barrett[2], N. Bunimov Wall[3], D. Smyth[2]
1. Health PEI, Charlottetown, PE, Canada; 2. Dalhousie University, Halifax, NS, Canada; 3. Horizon Health Network, Moncton, NB, Canada

Background: The availability of novel curative therapies for hepatitis C virus (HCV) infection has created a unique opportunity to mitigate complications of untreated disease, and improve both clinical programming and treatment access. Between September 2014 and October 2015 local care providers, government, industry, and HCV community groups in Prince Edward Island (PEI) created a province-wide model of care. Core components of the program include: centralized referral, triage, and intake by HCV nurse specialist; HCV treatment specialists; non-fibrosis restricted public access to direct-acting antiviral (DAA) therapy; patient education, follow-up with public and industry-affiliated nursing support; and voluntary patient enrollment into a treatment registry.
Aims: We evaluated performance of this care model, and both demographic, outcome, and treatment-effec-

tiveness measures for treated patients.

Methods: Using a prospective observational study design, all chronic HCV referrals received from April 2015 to April 2016 were recorded in the program database. Primary analysis examined program parameters including the time from referral to assessment/treatment, as well as the number of referrals, assessments and treatment initiations. A secondary analysis involved evaluation of treatment effectiveness among all treated patients using intent-to-treat analysis.

Results: In the first year of the program, 242 patient referrals were received, 123 patients were seen for intake assessments and 93 initiated on DAAs with prioritization to patients with advanced fibrosis. This is compared to only 4 treatment initiations in the province in the 2 years prior to program implementation. The median time from assessment to treatment initiation was 3 weeks. Overall, 82 of the 84 (97.6%) patients for whom outcome data was available achieved sustained virologic response (SVR) at post-treatment week 12; 1 was lost to follow-up and 1 died following therapy completion from an unrelated event. Detailed demographics and on-treatment data was obtained from 70 patients enrolled in the voluntary treatment registry of whom 27.1% were cirrhotic, 24.3% treatment-experienced, and 82.4% reported on-treatment adverse events. No adverse events were deemed serious or resulted in treatment discontinuation.

Conclusions: Initial data from the PEI program demonstrates how comprehensive care programs can be used to facilitate timely access to assessment and initiation of HCV therapy. High SVR rates seen in our real-world cohort were reflective of that seen in registration trials including in difficult to treat patient populations. It is hoped that similar models of care throughout Canada will facilitate broader access to curative HCV therapies, especially in under resourced settings.

A31
REPROGRAMMING OF EXHAUSTED T CELLS FOLLOWING CURE OF CHRONIC VIRAL INFECTION

M.S. Abdel-Hakeem[1], P. Tonnerre[2], O. Khan[1], E. Stelekati[1], M. Ali[1], G.M. Lauer[2], E. Wherry[1]

1. Penn Institute for Immunology, University of Pennsylvania, Philadelphia, PA; 2. Massachusetts General Hospital, Harvard University, Boston, MA

Background: T-cell exhaustion is a hallmark of immunological failure to control chronic viral infection and cancer. Blocking inhibitory receptors such as programmed death-1 (PD-1) can re-invigorate exhausted T cells (T_{EX}) in animal models of chronic viral infection and in cancer patients. However, many patients still fail to achieve durable tumor control when treated clinically with checkpoint inhibitors. Thus, a deeper understanding of other molecular pathways and epigenetic mechanisms underlying reversal of T-cell exhaustion is needed. Human chronic infection by HCV represents a unique model, where treatment with novel DAAs leads to complete virological cure even following years of chronic infection. Whether T_{EX} in these cured subjects convert to functional and durable memory cells remains unknown.

Aims: To investigate whether T_{EX} become "reprogrammed" into more functional effector or memory T cells (T_{MEM}) following cure of chronic disease by non-immunological treatment.

Methods: In order to study the reprogramming of T_{EX} following cure of chronic viral infection, we will examine virus-specific T cells from chronic HCV patients cured by DAA treatment and from mice cured of chronic lymphocytic choriomeningitis virus (LCMV). We will determine the cellular, transcriptional, and epigenetic profiles of these cells. And using our well-defined tractable mouse model we will dissect the molecular pathways and mechanisms underlying the changes in T_{EX} following the elimination of continuous exposure to viral antigens. These mechanistic discoveries and predictions from the LCMV model would then be extended and tested in the HCV model in humans.

Results: Our data indicate that some markers of exhaustion (including PD-1) are downregulated, while some markers of T_{MEM} may be recovered upon cure of infection. Nevertheless, other aspects of T_{EX} biology do not appear to be corrected simply by eliminating exposure to chronic infection. Ongoing studies are investigating whether these changes are linked to selective recovery of a specific subset of T_{EX}, and whether improvements are accompanied by changes in the epigenetic landscape of these previously-exhausted T cells.

Conclusions: We expect these studies to enhance our understanding of the epigenetic signatures and the immunological mechanisms of recovery of T_{EX}. These studies should also identify candidate transcriptional circuits differentially regulated in readily-recovered T cells that could represent novel therapeutic targets for reversal of immune-exhaustion.

A32
POPULATION-BASED ESTIMATE OF HEPATITIS C VIRUS PREVALENCE IN ONTARIO, CANADA

S. Bolotin[1], J. Feld[2], G. Garber[1], W.W. Wong[3], F. Guerra[1], T. Mazzulli[1]

1. Applied Immunization Research, Public Health Ontario, Toronto, ON, Canada; 2. Medicine, University Health Network University of Toronto, Toronto, ON, Canada; 3. University of Waterloo, Kitchener, ON, Canada

Background: Hepatitis C virus (HCV) is the most

burdensome infectious illness in Canada. Current screening strategies miss a significant proportion of cases, leaving many undiagnosed. Elevated HCV prevalence in the baby-boomer cohort has prompted calls for birth-cohort screening in this group. However, Canada lacks population-level data to support this recommendation.

Aims: The aim of this study was to obtain a population-based estimate of the prevalence of HCV infection in Ontario residents born between 1945 and 1974, estimate of the number of HCV cases by age cohort in Canada, and generate evidence to underpin policy recommendations on birth-cohort screening.

Methods: We tested anonymized residual sera in five-year age-sex bands, weighted according to the population across Ontario, for anti-HCV antibody, and tested all antibody positive and 10% of negative sera for HCV RNA. We performed descriptive epidemiological analysis and used a logistic regression model to determine HCV risk-factors.

Results: Of 10,006 sera analyzed, 155 (1.55%, confidence interval (CI) 1.31, 1.79) were positive for HCV antibody. For males, who comprised 107/155 (69.03%) of positive samples, the highest prevalence was 3.00% (95% CI 1.95, 4.39), for those born between 1960 – 1964. For females, the highest prevalence was 1.56% (95% CI 0.83, 2.65), for those born between 1955 – 1959. Both male sex and year-band of birth were significantly associated with positive HCV serostatus. Eighty of 145 (55.2%) antibody positive sera were also RNA positive, and 17/993 (1.7%) antibody negative sera were RNA positive. Using a previously published cost-effectiveness model, our analysis showed that a birth-cohort screening program for Ontario would be cost-effective.

Conclusions: HCV prevalence in Ontario is highest among those in baby-boomer birth cohort, and higher than previous estimates. Given the development of highly effective, curative therapy, birth cohort screening should be strongly considered, particularly for those born between 1950 – 1969.

A33
NOVEL E2 GLYCOPROTEIN TETRAMER DETECTS HCV-SPECIFIC MEMORY B CELLS
M. Boisvert[1], W. Zhang[2], E. Elrod[2], N. Bernard[3], J. Villeneuve[1], J. bruneau[1], J. Marcotrigiano[4], N. Shoukry[1], A. Grakoui[2]

1. Centre de recherche du CHUM, Montreal, QC, Canada; 2. Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine; Yerkes National Primate Research Center, Emory Vaccine Center, Atlanta, GA; 3. Research Institute of the McGill University Health Centre (RI-MUHC) and Division of Experimental Medicine, McGill University, Montreal, QC, Canada; 4. Center for Advanced Biotechnology and Medicine, Dept of Chemistry and Chemical Biology, Rutgers University, Piscataway, NJ

Background: Hepatitis C virus infection becomes chronic in most cases while a minority (25%) can spontaneously resolve the infection. Antibodies that are specific to the envelope glycoproteins E1 and E2 are generated late during acute infection and yet their role in spontaneous clearance remains debated. Some reports described cases of viral clearance without seroconversion. Other studies demonstrated an increased rate of spontaneous resolution in individuals who developed an early HCV-specific antibody response. Investigation of the humoral responses during acute HCV infection requires identification of HCV-specific B cells.

Aims: We hypothesized that expression of a biotinylated form of the ectodomain of E2 glycoprotein and fluorescent tetramer generation would enable detection of HCV-specific B cells from patient peripheral blood samples.

Methods: We have developed an expression vector enabling production and purification of biotinylated HCV E2 ectodomain. Fluorescent tetramers were generated by incubation with fluorescent streptavidin and they were used together with phenotypic B cells surface markers in flow cytometry experiments (FACS). Longitudinal PBMC samples from individuals who became chronically infected with HCV were used to detect HCV-specific B cells. The new B cell tetramer was also used to FACS sort HCV-specific class-switched memory B cells to perform B cell receptor (BCR) deep sequencing.

Results: Our newly developed tetramer enabled us to detect HCV E2 specific memory B cells in most samples of HCV chronic infection (28/31). However, in a longitudinal study, we could detect HCV E2 specific B cells in only half of acute infection samples analysed (3/7), suggesting that in some subject the development of the humoral response might be delayed. We successfully isolated HCV E2 specific class-switched memory B cells from two samples and performed BCR deep sequencing. The BCR repertoire of both samples was focussed and had accumulated mutations, suggesting amplification of particular clonotypes and affinity maturation process.

Conclusions: Finally, our results suggest that our newly developed B cell tetramer will be very useful to study the development of the humoral response to HCV infection. We showed that most infected individuals developed HCV-specific B cell population, but in some cases, HCV-specific B cells could only be detected during the chronic phase of the infection. Future studies examining subjects that spontaneously resolved the infection will enable characterization of the protective immune response and define the role of the humoral response in spontaneous clearance of HCV infection.

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Poster Session I

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A Treatment in Chronic Hepatitis C

SIMPLE, ONCE-DAILY DOSING FOR ALL HCV GENOTYPES[1]

EPCLUSA DOSING
ONE TABLET, ONCE A DAY, 12 WEEKS[1†]

EPCLUSA (sofosbuvir/velpatasvir) is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults without cirrhosis or with compensated cirrhosis. EPCLUSA is also indicated in combination with ribavirin for the treatment of chronic HCV infection in adults with decompensated cirrhosis.

Refer to the page in the bottom-right icon for additional safety information and for a web link to the product monograph discussing:

- Contraindications in patients taking EPLUCSA in combination with ribavirin – the contraindications to ribavirin are applicable to the combination

- Relevant warnings and precautions regarding use with ribavirin, use in patients with decompensated cirrhosis who are infected with HCV genotype 2 or genotype 4, concurrent use with other medicinal products containing sofosbuvir, use with potent P-glycoprotein (P-gp) inducers and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4, coadministration with amiodarone (not recommended due to risk of serious symptomatic bradycardia), use in patients with severe hepatic impairment (Child-Pugh Class C), use in patients with severe renal impairment (eGFR < 30 mL/min/1.73m^2) or end stage renal disease requiring hemodialysis, use in patients who have previously failed treatment with other regimens that include an NS5A inhibitor, use in pregnancy and breastfeeding, coadministration with ribavirin during pregnancy, use in patients with recurrent HCV infection after liver transplant, use in HCV patients co-infected with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), concomitant use with tenofovir DF, particularly in those at increased risk for renal dysfunction, co-administration with an efavirenz-containing regimen, and monitoring of liver function including direct bilirubin is recommended in patients with decompensated cirrhosis

- Conditions of clinical use, adverse reactions, drug interaction and dosing information

In addition, the page contains the study parameters and reference list relating to this advertisement.

† No dosage adjustments are possible for EPCLUSA. Please consult the Product Monograph for complete dosage and administration instructions. HCV=Hepatitis C virus

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PAAB

POSTER SESSION 1
SATURDAY MARCH 4, 18H30-20H00

ACUTE LIVER INJURY AND HEPATOTOXICITY

A34
DARATUMUMAB DOSE DEPENDENT LIVER INJURY
M. Altuwaijri, E. Lam

University of British Columbia, Vancouver, BC, Canada

Background: Daratumumab is a recent addition in the treatment of multiple myeloma (MM). Daratumumab is a human monoclonal antibody directed against CD38. Daratumumab has no major side effects on the liver published to date. In this case report we describe a dose dependent drug induced liver injury after the use of daratumumab in the treatment of MM that has not been described previously.
Aims: To describe the first case report of Daratumumab dose dependent liver injury.
Methods: Case report
Results: A 58-year-old gentleman with IgA kappa MM which was diagnosed in January 2015 and has been refractory to three previous lines of therapy. He was admitted on an outpatient basis to the hospital in August 2016, for the treatment of his refractory IgA kappa MM, with Daratumumab. He had no recent changes in his medications and his baseline liver enzyme profile was normal. Following Daratumumab first full dose with 16mg/kg, the patient became fatigued within 48 hours and there was elevation in liver enzymes with an initial ALT of 1622 and AST of 1672. His Alkaline phosphates was 96 and total Bilirubin was 21. Viral serology (A, B, C, EBV and CMV), Acetaminophen and Ethanol level, Anti-nuclear antibody, anti-mitochondrial antibody and anti-smooth muscle antibody were negative. The dramatic increase in his liver enzymes was attributed to Daratumumab hepatotoxicity. Two days following the first dose, the liver enzymes started to trend down without intervention and gradually decreased to normal level after a period of 20 days. Subsequent doses of Daratumumab were modified at 8 mg/kg without increase in liver enzymes.
Conclusions: Daratumumab has a potential hepatotoxic effect that is likely dose dependent. Modified doses of Daratumumab may reduce the risk of liver injury.

A35
ACUTE HEPATITIS AS AN ATYPICAL PRESENTATION OF GRAFT-VERSUS-HOST DISEASE IN A PATIENT POST HEMATOPOIETIC STEM CELL TRANSPLANTATION
A. Shetty[1], R. Ramkissoon[2], K. Patel[1]
1. Gastroenterology, University of Toronto, Toronto, ON, Canada; 2. John A. Burns School of Medicine, Honolulu, HI

Background: Graft-versus host disease (GVHD) is a complication of hematopoietic stem cell transplantation (HSCT) that frequently affects the gastrointestinal tract, but can also have hepatic, ophthalmic and dermatological manifestations at time of diagnosis. GVHD that affects the liver typically presents as a cholestatic transaminitis due to biliary tree damage and dysfunction. However, this is typically mild, delayed in the clinical timeline and rarely is the presenting symptom at time of diagnosis.
Aims: To describe an atypical presentation with acute hepatitis in a patient with GVHD
Methods: N/A
Results: A 20 year old man with early T-cell precursor acute lymphoblastic leukemia (BCR-ABL+) presented with an acute hepatitis 84 days after a second, matched 9/10, unrelated allogeneic HSCT for secondary failure of the first graft. Serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT), and serum alkaline phosphatase (ALP) levels were 700 IU/L and 1282 IU/L, and 576 IU/L respectively. His total bilirubin was 59 µmol/L . He previously had received myeloablative therapy for his initial HSCT, was transfusion dependent, but was requiring IVIG and granulocyte colony-stimulating factor in an attempt to achieve consistent engraftment. Otherwise, no other hepatotoxic medications were noted and viral causes were excluded (hepatitis A, B, C, E, VZV, CMV, HSV). On day 96, he developed a lower extremity rash with skin biopsy revealing an interface dermatitis with frequent dyskeratotic cells and multifocal epidermal-dermal separation. Subsequently, a liver biopsy was done that showed marked ductopenia (>80%), cholestasis; there was little to no inflammation or ductular reaction confirming GVHD. The patient was then started on high dose methylprednisone and cyclosporine on day 106 with clinical improvement.
Conclusions: Our case highlights the importance of considering acute GVHD as part of the initial diagnosis of an acute transaminitis following HSCT. This was an atypical presentation because there were no documented cutaneous and gastrointestinal manifestations prior to diagnosis and no initial cholestatic hepatitis. Cutaneous GVHD initially presents at a median post-transplant day of 19, ranging from 5-47. Following the skin, the next most commonly affected organ is the liver in acute GVHD. The mechanism by which GVHD presents as a cholestatic versus hepatitis pattern has not been fully investigated. Some studies do suggest the overexpression of major histocompatibility complex class I antigens in hepatocytes, cytokine/T-cell subset interactions, and apoptosis induced Fas-Fas ligands may lead to this distinction. Finally, other causes of hepatocellular injury post HSCT must be excluded, including viral etiologies, drug induced, sudden withdrawl of immunosupressives, and preparative chemotherapeutic regimens.

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CLINICAL PRACTICE

A36
INFLIXIMAB INDUCED AUTOIMMUNE HEPATITIS: TWO CASES WITH DIFFERENT OUTCOME

B. Al Ibrahim[1], K. Qumosani[2]

1. Department of Internal Medicine, Division of Gastro-enterology and Hepatology Western University, LONDON, ON, Canada; 2. Department of Internal Medicine, Division of Gastroenterology and Hepatology Western University, LONDON, ON, Canada

Background: Inhibitors of tumor necrosis factor alpha (anti-TNF alpha) are an important component of treatment of number of inflammatory conditions. However, multiple adverse effects have been identified with the growing use of these agents and the prolonged follow up. Autoimmunity has been linked to Infliximab. This includes Lupus, Vasculitis and interstitial lung disease. There are a few reports in the literature regarding infliximab induced autoimmune hepatitis. We report an interesting case of infliximab-induced autoimmune hepatitis that was successfully treated by discontinuation of infliximab.

On the other hand, Infliximab induced autoimmune hepatitis can be quite dramatic. Withdrawal of infliximab and even steroid treatment might not be sufficient to reverse the process and patients might eventually need liver transplant. We are reporting a second unfortunate case where infliximab induced autoimmune hepatitis leads to fulminant liver failure requiring liver transplant.

Aims: To increase the awareness a potential side effect and improve early identification and treatment.

Methods: Case report and review of the literature.

Results: A 57 years old lady with a 1-year history of Crohn's disease, maintained on Infliximab, started 4 months prior to her presentation. She was referred to our hepatology clinic because of elevated liver enzymes. The patient was a symptomatic. Her investigations showed elevated liver enzymes as well as positive autoimmune markers. A liver biopsy was done. The biopsy Excluded element of chronicity, and the acute insult was related to Infliximab. Inflixamab was stopped and the patient was started on Vidolizumab. Her liver enzymes came down to a normal level.

The second case is a 69 years old lady with a 13 years history of fistulizing Crohn's disease with multiple small bowel resections and fistulectomy. The patient was started on Infliximab 3 months prior to her presentation and than she was noticed to be jaundiced. Subsequently, a blood work showed elevated liver enzymes with positive autoimmune markers. Imaging showed no intra or extra hepatic obstructions.During her hospitalization she showed further elevation of liver enzymes with deterioration of synthetic liver function. Additionally, The patient developed hepatorenal syndrome and encephalopathy. She was started on prednisone 20 mg daily without significant improvement. Liver biopsy was done and showed no evidence of chronicity with evidence of prominent plasma cells infiltrate suggestive of autoimmune hepatitis. Our transplant team evaluated the patient and a she underwent a liver transplant.

Conclusions: Early recognition of this entity prevents further sequela and unnecessary investigations. The presentation of infliximab induced autoimmune hepatitis can range from mild elevation of liver enzyme that can respond to discontinuation of Infliximab to a fulminant liver failure.

CLINICAL PRACTICE

A37
EFFICACY OF CTA IN DIAGNOSING NON-TRAUMATIC NON-VARICEAL GASTROINTESTINAL BLEEDING PRIOR TO TRANSARTERIAL EMBOLIZATION AFTER ENDOSCOPIC FAILURE IN MANAGING ACUTE GASTROINTESTINAL BLEEDING

A. Wadhwani[1], S. Brunet[1], J. Nguyen[2], E. Herget[1], P. Beck[1]

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

Background: Non-variceal gastrointestinal bleeding (NVGIB) is associated with a high mortality and morbidity. 10-30% of these patients tend to fail endoscopy and receive transarterial embolization (TAE) as an alternative. Studies suggest that performing pre-angiography computed tomography angiography (CTA) increases the positive yield of visceral angiography.

Aims: Our objective was to determine (1) the accuracy of CTA in diagnosing NVGIB following failed endoscopy and (2) the impact of CTA pre-TAE on the angiographic technique.

Methods: Data was collected from 83 consecutive patients who presented to the emergency department with acute NVGIB and received TAE after endoscopy failed to manage their NVGIB. Of these 83 patients, 40 underwent pre-angiography CTA. These CTA examinations were retrospectively reviewed by 2 radiology residents and 2 staff radiologists. These findings were compared to angiography, or/and surgery. Inter-reader reliability was evaluated with kappa coefficient (κ).

Results: Sensitivity, specificity, PPV, NPV, and accuracy of CTA in diagnosing NVGIB was 89%, 100%, 100%, 86%, and 93%, respectively. CTA was able to accurately diagnose the cause and source of NVGIB in 85% of the patients respectively. The inter-reader reliability coefficient for identifying the cause and source of NVGIB was κ=0.72 and κ=0.66 respectively. In 20 cases, in whom CTA localized NVGIB, no diagnostic catheter angiogram was required. In 6/20 cases, pre-TAE CTA enabled the identification of the bleeding site, which would not have been visualized on a routine diagnostic angiogram. When comparing patients that received CTA prior to their therapeutic embolization for NVGIB to the patients that did not receive a pre-embolization CTA, there was an overall reduction of 20 minutes of procedural time.

Conclusions: CTA is an accurate diagnostic modality in detecting NVGIB. Performing abdomen and pelvis CTA before TAE improves the localization of gastrointestinal bleeding and facilitates embolization by reducing the overall procedural time. Impact of pre-angiography CTA on reducing the overall number of imaging studies, amount of contrast administered, and overall mortality and morbidity needs to be further investigated.

Funding Agencies: None

A38
CLINICAL OUTCOMES OF PATIENTS UNDERGOING BALLOON-ASSISTED ENDOSCOPY FOR OBSCURE GASTROINTESTINAL BLEEDING
M. Mazurek[3], S. Zepeda-Gomez[2], B.P. Halloran[1], C.W. Teshima[4]

1. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 2. Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Gastroenterology, University of Calgary, Calgary, AB, Canada; 4. Gastroenterology, University of Toronto, Toronto, ON, Canada

Background: The etiology of gastrointestinal bleeding remains unclear in a sizable minority of patients despite extensive evaluation. In these patients, obscure gastrointestinal bleeding (OGIB) poses a significant diagnostic and therapeutic challenge, resulting in higher patient morbidity and mortality, as well as increased utilization of health care resources.
Aims: In this study, we evaluate the diagnostic yield and clinical outcomes of patients with OGIB who have undergone balloon-assisted endoscopy (BAE).
Methods: We performed a large, retrospective cohort study of 311 consecutive patients who underwent BAE at our institution. Of these, 116 cases were identified to have had OGIB and were appropriate for inclusion in our analysis. Follow-up data were available for 110 patients, with median time to follow-up of 6.1 months (range 0.3 – 37.7). The pattern of bleeding, transfusion requirements, and frequency of OGIB control were captured.
Results: BAE identified bleeding sources in 79 patient cases (68.1%), of which, 66 (83.5%) had culprit small bowel pathology. Of these, vascular lesions were the most common finding, occurring in 39 patients (59.0%), followed by neoplasia (13.6%, 9 patients), and ulcerations/erosions (12.1%, 8 patients). Diagnostic yield was highest in those patients with active overt bleeding, compared to those with inactive or occult bleeding (80.0%, 20/25 patients vs 35.2%, 32/91 patients). Overall, OGIB was controlled in 58/110 patients (52.7%). Culprit vascular lesions demonstrated poorer control rates than ulcers/erosions, tumors/polyps, or unidentified pathology (38%, 14/37 patients vs 55.8%, 29/52 patients). Among those patients with uncontrolled OGIB, median 6-month red-cell transfusion requirements were lower post-procedure compared to those pre-procedure (0.69 units/month, range 0.00 – 50.7; vs 1.00 units/month, range 0.00 – 10.3).
Conclusions: BAE is a useful diagnostic and therapeutic strategy in the management of patients with OGIB. Luminal evaluation of the small bowel with BAE should be undertaken as soon as OGIB is suspected, and preferably in proximity to active bleeding. Vascular lesions are particularly recalcitrant to endoscopic therapy and therefore warrant close monitoring.

Outcomes for patients with OGIB after undergoing BAE

	Overt re-bleeding	Hb < 100	Controlled	Total
Ulcers/erosions	1 (10%)	3 (30%)	6 (60%)	10
Vascular lesions	9 (24%)	16 (43%)	14 (38%)	37
Tumors/polyps	0	0	6 (100%)	6
Negative findings	6 (17%)	13 (36%)	17 (47%)	36
Overall	16 (15%)	35 (32%)	58 (53%)	110

Controlled OGIB is defined as the clinically stable condition meeting the following criteria: (1) the absence of any overt re-bleeding, (2) no further requirement of red cell transfusions, and (3) the resolution or absence of persistent anemia.

Funding Agencies: None

A39
A META-ANALYSIS OF COLON CLEANSING PREPARATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
S. Restellini[1], O. Kherad[2], T. Bessissow[1], C. Ménard[3], M. Martel[1], A.N. Barkun[1]

1. Division of Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 2. Department of Internal Medicine, La Tour Hospital and University of Geneva, Geneva, Switzerland; 3. Medicine, University of Sherbrooke, Canada, QC, Canada

Background: Patients with inflammatory bowel disease (IBD) are subject to several colonoscopies during their lifespan and subsequently several bowel preparations. Recent guidelines endorse the use of split-dose regimens, but only few data are available in IBD patients who are often excluded from trials for safety concerns.
Aims:
We performed a systematic review and meta-analysis to determine any existing difference in terms of effectiveness, safety and tolerability between existing colon-cleansing products in the IBD population.
Methods: Systematic searches were performed (January 1980 - September 2016) using MEDLINE, EMBASE, Scopus, CENTRAL and ISI Web of knowledge for ran-

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domized trials assessing preparations with or without adjuvants, given in split and non-split dosing, in high (>3L) or low-volume (2L or less) regimens. Bowel cleansing quality was the primary outcome. Secondary outcomes included patient willingness-to-repeat the preparation and side effects and complications.
Results: Out of 439 citations, 4 trials fulfilled our inclusion criteria (n = 449 patients). One trial (Lazzaroni et coll. 1993) assessed the impact of adding Simethicone to Polyethylene Glycol (PEG) 4L witch resulted in similar bowel cleansing effect but a better willingness to repeat. One other trial (Gould et coll 1982) compared senna to castor oil, again without any difference in term of bowel cleansing. Two trials compared the efficacy of PEG high-volume versus PEG low-volume associated to an adjuvant in split-dose regimens (Kim et al 2016, Manes et al 2016): PEG low-dose efficacy was not different to PEG high-dose; OR=0.84 (0.37 ; 1.92) A higher proportion of patients were willing to repeat low-volume preparations vs high-volume; OR 5.11 (1.31-20.0).
Conclusions: In IBD population, PEG low-volume regimen seems not inferior to PEG high-volume to clean the colon, and yields improved tolerance. Further additional research is urgently required to compare contemporary products in this specific population.

Funding Agencies: None

A40
FACTORS AFFECTING MEGAPOLYPECTOMY SUCCESS
B.H. Dubé[3], M. Brooks[2], A. Chatterjee[1], S. Murthy[1]

1. The Ottawa Hospital, Ottawa, ON, Canada; 2. University of Ottawa/OHRI, Ottawa, ON, Canada; 3. University of Ottawa/OHRI, Ottawa, ON, Canada

Background: Background:
Endoscopic management of large colon polyps is increasingly favoured over surgical resection. However, complete resection of polyps 3 cm or larger, called megapolyps, is challenging with associated risks of bleeding, perforation, and unsuccessful resection. There are numerous factors that may impact success in megapolypectomy.
Aims: Aims:
Evaluate the success rate of attempted megapolypectomy performed at The Ottawa Hospital, and identify factors which may impact success. Additionally, we reviewed complications associated with megapolypectomy.
Methods: Methods:
All endoscopic procedures at TOH are flagged based upon indication and all those from 2008 onward were captured. In addition, patients were identified retrospectively using a specific billing code for endoscopic removal of polyps 3cm or larger. Chart review was performed for data collection.
Results: Results:
356 patients with a mean age of 67 y/o and a ratio of 1:1.4 female to male patients were identified for the

study. 244 megapolypectomies were successful as defined by the absence of adenoma in 4 to 6 months follow-up. In 17 cases, where the endoscopist opined a complete resection, recurrence was found on 6 to 24 months follow up. 28 patients were referred to surgery, and 67 had no follow-up information available. The 28 polyps referred to surgery were on average 4.0cm of size, and the pathologist identified in samples no disease(28.7%), high-grade dysplasia(14.2%), and malignancy(57.1%). The endoscopist was not able to complete the resection during the first intervention of 12 cases due to non-lift sign (50%) or difficult resections (50%). The remaining 16 cases had a series of endoscopic interventions to remove residual adenoma leading to the decision of referring the patient for surgical resection due to the inability of completing the resection. Of the successful megapolypectomies, the average number of interventions required for completion was 1.3 for 3-4cm polyps, and 1.6 for 4.1-5 cm polyps (P=0.0047). On average the therapeutic endoscopists removed 3.7cm polyps successfully compared to gastroenterologists removed 3.3cm polyps successfully (P=0.043). We observed a rate of 22.6 % (N=235) incorrect impression for the first intervention. The complication rate of megapolypectomies was found to be 7.6%. 25 were bleeds (93%) and 2 were perforations (7%).
Conclusions: Conclusions:
The overall success rate of megapolypectomy at The Ottawa Hospital is 93%. Failed resections are associated with increased polyp size, polyp location, high-grade and greater dysplasia, and increased interventions. Although endoscopists appeared confident in having performed a complete resection, in 22.6% of the failed resections, the endoscopist's impression was incorrect.

Funding Agencies: None

A41
THE PRESENCE OF MELENA PREDICTS A PROXIMAL BLEEDING SITE AMONG PATIENTS WITH OBSCURE GASTROINTESTINAL BLEEDING: RESULTS OF A RETROSPECTIVE COHORT STUDY
C. Zhu[2], B. Yan[1], S. Asfaha[1], N. Chande[1], T. Ponich[1], J.C. Gregor[1], M. Sey[1]

1. Western University, London, ON, Canada; 2. London Health Sciences Centre, London, ON, Canada

Background: Melena is a hallmark symptom of upper gastrointestinal bleeding and results from the digestion of blood lost proximal to the ligament of Treitz in the majority of cases. However, whether melena also predicts bleeding in the proximal small intestine (SI) in the setting of obscure gastrointestinal bleeding (OGIB) is unknown.
Aims: The objective of this study was to determine the predictive value of melena for determining the location of SI bleeding in OGIB.
Methods: A retrospective cohort study was conducted

of all patients who underwent capsule endoscopy (CE) for OGIB at London Health Sciences Centre between 2009 and March 2016. The presenting symptoms were recorded and categorized as melena or non-melena (ie. hematochezia and occult OGIB with iron deficiency anemia (IDA)). The primary outcome was diagnosis of a bleeding site between 0 - 50% SI transit time. Baseline demographics, comorbidities, medication usage, hemoglobin, and blood transfusion requirements were noted. The association between melena and proximal SI bleeding was determined using chi-square.
Results: 312 patients underwent CE for OGIB during the study period. Mean (SD) age was 63.9 years (15.4), and 55% were female. 36% of patients had melena, 14% had hematochezia, and 48% had only IDA. Blood transfusion was required within the past 12 months in 70% of patients and 14% of cases were performed as inpatients. The mean (SD) follow-up time was 16 months (24.1). The overall diagnostic rate was 45%, with angioectasias being the most common etiology (27%). 46% of patients with melena had a bleeding site within the proximal half of the SI compared to 31.3% who did not have melena (RR 1.47, p=0.01). The mean (SD) SI transit time for bleeding site was 21.2% (25.8) for those with melena and 34.7% (33.4) for those without (p=0.008).
Conclusions: The probability of locating a bleeding site within the proximal half of the SI is 47% greater among OGIB patients with melena than those without. As such, antegrade double balloon enteroscopy without preceding CE may be warranted in this population.

Melena vs Hematochezia+IDA+Melena&Hematochezia

	Melena	Non-Melena	p-value
Bleeding site by % of SI transit time-mean (SD)*	21.2%	34.7%	0.008
Bleeding site in proximal 1/2 of SI	46%	31.3%	0.014
Bleeding site in proximal 1/3 of SI	40%	29.6%	0.08

*Among those where a SI bleeding site is found. RR for prox 1/2 SI=1.47 (1.09-2.0, p=0.014). RR for prox 1/3 SI=1.35 (0.97-1.88, p=0.08)

A42
UNDERUSE OF IRON THERAPY UPON DISCHARGE FOR ANEMIC PATIENTS WITH ACUTE GASTROINTESTINAL BLEEDING
K.J. Fortinsky[3], J. Bernick[3], a. agarwal[5], M. Bernstein[4], Y. Lin[3], Z. Gallinger[3], P. Ye[3], A.N. Barkun[1], A.V. Weizman[2]

1. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 2. Mount Sinai Hospital, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada; 4. University of Toronto, Toronto, ON, Canada; 5. University of Toronto, Toronto, ON, Canada

Background: Many patients with gastrointestinal bleeding (GIB) are discharged from hospital with anemia. One recent study found that iron therapy leads to more rapid correction of anemia in patients after GIB. Current guidelines do not address the utility of iron in these patients and recent survey data suggests that clinicians do not routinely prescribe iron therapy in this setting.
Aims: The aim of the current study is to determine iron-prescribing behavior among anemic patients discharged from hospital after GIB.
Methods: We performed a retrospective review of 191 patients who were anemic upon discharge after GIB at two quaternary care hospitals in Toronto, Ontario, Canada. Patient comorbidities, medications, endoscopic findings, hemoglobin level, need for transfusion, and iron therapy prescribed in hospital or on discharge were recorded. Descriptive statistics were carried out.
Results: The mean hemoglobin (Hgb) level at discharge was 90 g/L (range, 69 to 118 g/L). Only 70 patients (37%) were prescribed iron supplementation therapy upon discharge, most of whom were prescribed oral iron (96%) and few received intravenous iron (4%). Importantly, 31 of the 70 patients prescribed iron on discharge were already taking iron on admission. Iron studies were performed in 25 (13%) patients during admission. Patients who had iron studies performed in hospital were more likely to be prescribed iron at discharge (OR = 2.38). The majority of patients received a red blood cell transfusion in hospital (71%) but this did not affect the likelihood of receiving iron upon discharge. On average, patients with a lower Hgb level at discharge were more likely to be prescribed iron (87 vs. 92, p = 0.004).
Conclusions: Patients being discharged with anemia after gastrointestinal bleeding are not routinely being prescribed iron on discharge. Recent evidence suggests benefit from iron replacement therapy in these patients and it is unclear why clinicians aren't prescribing more iron therapy to their patients. Newer clinical guidelines should add recommendations about iron therapy in patients after gastrointestinal bleeding. Educational and quality improvement initiatives may be helpful in encouraging more clinicians to prescribe iron to these patients.

A43
EVALUATING THERAPEUTIC EFFICACY OF TRANS-ARTERIAL EMBOLIZATION IN PATIENTS PRESENTING POST-ENDOSCOPIC FAILURE TO MANAGE ACUTE NON-VARICEAL GASTROINTESTINAL BLEEDING
A. Wadhwani[1], J. Nguyen[1], S. Brunet[3], E. Herget[2], P. Beck[2]

1. Radiology, University of Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3.

University of Calgary, Calgary, AB, Canada

Background: Acute non-variceal gastrointestinal bleeding (NVGIB) is associated with a high mortality and morbidity. Endoscopy remains the initial procedure of choice for diagnosis and management. However, it is unable to achieve therapeutic hemostasis in 10-30% of these patients. Therefore, transarterial embolization (TAE) is offered as a safe and effective treatment alternative to attempt therapeutic hemostasis.
Aims: Our objective was to determine: (1) efficacy of TAE in achieving therapeutic hemostasis and preventing re-bleeding post-endoscopic failure and (2) identifying what comorbidities pre-dispose patients to fail endoscopy for achieving therapeutic hemostasis.
Methods: Data was collected from 32 consecutive patients who presented to the emergency department with NVGIB and received TAE after failing endoscopy and 24 consecutive patients in whom hemostasis was achieved with endoscopy. Their embolization results, clinical comorbidities, and clinical followup were retrospectively reviewed.
Results: Out of the 32 patients, 18 presented with upper, 9 with lower, and 5 with upper and lower NVGIB. Average of 6.1U of pRBCs was transfused. Immediate therapeutic hemostasis was achieved in all patients who failed endoscopy. 2 patients experienced re-bleeding and 1 patient died from intractable GIB in <1 month. Most patients had 4 or more clinical comorbidities such as Type II diabetes, coronary artery disease, cirrhosis, and hypertension. 14 patients were on chronic anticoagulation. 18/32 patients had a prior history of NVGIB. In the control population of 24 patients where therapeutic hemostasis was achieved with endoscopy, we found that only 1/24 patients had prior episodes of NVGIB. An average of 1.6 pRBCs was transfused in the control population at the time of presentation. Also, the overall incidence of CAD, cirrhosis, and HTN was lower in the control population.
Conclusions: Trans-arterial angiographic embolization is an effective treatment to achieve therapeutic hemostasis and prevent re-bleeding in patients presenting with post-endoscopic failure to manage acute NVGIB. Presence of multiple comorbidities and prior history of acute NVGIB tends to pre-dispose patients to endoscopic failure in managing NVGIB.

Funding Agencies: None

A44
MEASURING COLONOSCOPY QUALITY AT THE POPULATION LEVEL IN ONTARIO, CANADA
J. Tinmouth[4], N. Baxter[2], Q. Li[3], L. Paszat[3], J. Patel[4], L. Rabeneck[1]

1. Cancer Care Ontario, Toronto, ON, Canada; 2. St.Michael's Hospital, Toronto, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 4. Sunnybrook Research Institute, Toronto, ON, Canada

Aims: The importance of high quality colonoscopy is widely recognized, however, it is challenging to measure its quality for an entire population. The aim of this study is to measure on 9 key colonoscopy quality indicators for all practicing endoscopists in Ontario, Canada in 2015.
Methods: Using linked health administrative databases, colonoscopies performed between Jan. 1 and Dec. 31 2015 were identified. Endoscopists were defined as those who had performed ≥6 colonoscopies in this period. We measured 9 quality indicators at the endoscopist level: annual colonoscopy volume, polypectomy rate, cecal intubation rate, polypectomy-associated bleeding, perforations, colorectal cancers (CRC) detected, post-colonoscopy CRCs (PCCRC), poor bowel preparation rate and colonoscopies with recent normal findings (% colonoscopies in 2015 where a 2nd normal and complete colonoscopy was done in the prior 3 years). Provincial rates and median endoscopist values were reported. For less frequent events, the proportion of endoscopists is reported by number of events.
Results: In 2015, 921 endoscopists performed 464,506 colonoscopies in Ontario. Among the endoscopists, 20% were women; 57% were surgeons, 33% were gastroenterologists and 10% were internists or other practitioners. 64% practiced in hospitals, 11% practiced in private clinics and 25% practiced in both settings. See Tables 1 & 2 for quality indicators.
Conclusions: We have found that Ontario endoscopists performed well in 2015, although there is still room for improvement. These indicators will be used in centralized, province-wide provider performance reporting with the goal of improving colonoscopy quality across the province.

Table 1: Provincial rates and median endoscopist values for colonoscopy quality indicators

Colonoscopy quality indicator	Median endoscopist value (IQR)	Provincial rate
Annual colonoscopy volume	414 (202-698)	N/A[a]
Cecal intubation rate	98% (97%-99%)	98.1%
Polypectomy rate	40% (30%-51%)	42.6%
Polypectomy-associated bleeding	N/A[b]	0.3%
Perforations	N/A[b]	0.04%
CRCs detected	1.3% (0.7%-2.0%)	1.3%
PCCRCs	N/A[b]	0.1%
Poor bowel preparation rate	3% (1.5%-5.0%)	3.3%
Colonoscopies with recent normal findings	3.1% (1.9%-4.9%)	3.3%

a=Unable to calculate provincial rate as volume is calculated per endoscopist; b=Events infrequent, therefore

median is zero. See table 2.

Table 2: Proportion of endoscopists by number of events for colonoscopy indicators with infrequent events

Colonoscopy quality indicator	Proportion of endoscopists
Polypectomy-associated bleeding, #	
0	65.5%
1	23.7%
2	6.2%
3	2.9%
4-6	1.6%
Perforations, #	
0	84.7%
1	12.6%
2-5	2.7%
PCCRCs, #	
0	67.9%
1	23.7%
2-5	8.4%

A45
IMPACT OF AN ERGONOMIC INTERVENTION ON SIMU-LATED COLONOSCOPY PERFORMANCE
M.A. Scaffidi[1], W. Lee[1], A. Almazroui[1], P. Lin[1], R. Kalaic-handran[1], R. Lyn[1], C.M. Walsh[2], S.C. Grover[1]

1. St. Michael's Hospital, Toronto, ON, Canada; 2. Hospital for Sick Children and the Wilson Centre, Toronto, ON, Canada

Background: Endoscopists are at risk of musculoskel-etal injury due to the repetitive strain of motions used during procedures. Additionally, appropriate ergo-nomic practice contributes to better performance in endoscopy. Despite this, gastroenterology trainees do not receive education about ergonomics. Furthermore, there is a lack of literature on effective methods to teach ergonomic principles and behaviours to trainees.
Aims: To determine the effectiveness of an education-al intervention for novice endoscopists designed to teach proper ergonomic principles to use in performing colonoscopy.
Methods: Novice endoscopists (performed <50 previous colonoscopies) were enrolled in a simulation course in colonoscopy. The ergonomics teaching intervention consisted of the following: one hour di-dactic lecture; a video demonstrating ideal ergonomics during colonoscopy; and a self-reflection checklist on ergonomics in colonoscopy used after each simulated procedure. Participants were assessed at baseline (i.e. pre-test) and after the intervention (i.e. post-test) using the Rapid Upper Limb Assessment (RULA), an assess-ment tool of ergonomic behaviours. Higher scores on the RULA correspond to poorer ergonomic techniques.
Results: Sixteen residents completed the training inter-vention. The mean final scores based on the RULA for the pre-test was 6.31 (SD=0.70) and 5.31 (SD=1.58) for the post-test. All participants showed a significant decrease in their RULA scores (p<0.015).
Conclusions: A teaching intervention for instruction of ergonomic principles in colonoscopy, involving a video, lecture, and self-reflection tool was associated with

improved performance among novices. Further work should be performed to determine the most effective means of teaching proper ergonomic technique to novice endoscopists, and to determine if this training translates into improved clinical performance.

A46
SELF-ASSESSMENT ACCURACY OF TECHNICAL AND NON-TECHNICAL SKILLS IN LIVE COLONOSCOPIES BY NOVICE ENDOSCOPISTS
M.A. Scaffidi[1], R. Khan[1], A. Almazroui[1], P. Lin[1], C. Tsui[1], S. Iqbal[1], C.M. Walsh[2], S.C. Grover[1]

1. Medicine, St. Michael's Hospital, Toronto, ON, Cana-da; 2. Hospital for Sick Children and the Wilson Centre, Toronto, ON, Canada

Background: Accurate self-assessment, usually repre-sented by a high agreement between a self-rating and an external-rating, is an important process for skill de-velopment. In colonoscopy, skills can be categorized as technical (e.g. scope navigation) or non-technical (e.g. communication). There is a paucity of research exam-ining the accuracy of self-assessment of technical and non-technical skills in colonoscopy among novices.
Aims: To investigate the accuracy of self-assessment for technical skills and non-technical skills in live colonoscopies among novice endoscopists.
Methods: Novice endoscopists (performed <50 previ-ous colonoscopies) were recruited. Each participant completed two clinical colonoscopies. Video recordings of each colonoscopy procedure were assessed by an independent expert endoscopist, who was blinded to participant identity. Technical skills were assessed us-ing the Direct Observation of Procedural Skills (DOPS), a procedure-specific assessment tool with good valid-ity evidence. Non-technical skills were assessed using a modification of the Objective Structured Assessment of Non-technical skills (m-OSANTS), which also has good validity evidence. Participants self-assessed their performance immediately following each colonoscopy using the same instruments. Self-assessment accuracy between participant and expert ratings was determined using the intra-class correlation coefficient (ICC1,1) and paired-sample t-tests.
Results: Thirty-nine novice endoscopists participated. Agreement between participant and expert ratings as measured by the ICC was 0.36 (95% CI: 0.03-0.62) and 0.32 (95% CI: -0.01-0.59) for technical and non-tech-nical skills, respectively. There was a significant difference between technical skills scores assigned by participants and expert assessors, with a mean difference of -8.56 (p=0.03). There was no significant difference between the non-technical skills scores assigned by participants and expert assessors, with a mean difference of -0.29 (p=0.603).
Conclusions: Overall, there was generally poor-to-mod-erate self-assessment accuracy of novices for techni-

cal and non-technical skills. Moreover, novices tended to over-rate their performance, as highlighted by the negative difference scores. However, participants' scores were not significantly over-rated for non-technical skills. Taken together, these results suggest that self-assessment accuracy among novices for technical and non-technical skills in endoscopy is an area for further development.

Funding Agencies: None

A47
LONG-TERM CLINICAL OUTCOMES AFTER ENDOSCOPIC TREATMENT FOR SMALL BOWEL VACULAR LESIONS BY DOUBLE BALLOON ENDOSCOPY
T. Hansen[2], C.W. Teshima[1]

1. Gastroenterology, University of Toronto, Toronto, ON, Canada; 2. University of Manitoba, Winnipeg, MB, Canada

Background: Balloon-assisted endoscopy (BAE) has revolutionized the approach to obscure GI bleeding (OGIB) by enabling the diagnosis and treatment of bleeding sources from within the small bowel. The most common source of OGIB is small bowel vascular lesions (SBVL), and referring physicians and patients often anticipate a definitive cure once these have been endoscopically treated. The literature has predominantly focused on immediate diagnostic and therapeutic yields with relatively little attention paid to clinically meaningful outcomes. Therefore, the durability of endoscopic therapy to SBVL by BAE remains unclear.
Aims: This meta-analysis aimed to address this question by determining the risk of rebleeding in long-term follow-up after endoscopic intervention to SBVL.

Methods: A comprehensive literature search of PubMed, OVID, Medline and EMBASE was performed to identify studies reporting long-term clinical outcomes after endoscopic therapy for small bowel sources of OGIB via double balloon endoscopy, single balloon endoscopy or spiral enteroscopy. Original studies that identified patients receiving endoscopic treatment to SBVL and that reported objective measures of rebleeding such as overt bleeding signs, repeat hospitalization or intervention for OGIB and/or changes in hemoglobin levels or transfusion requirements were included. A minimum of 6 months follow up was required for study inclusion. Studies were selected using 2 independent and blinded reviewers followed by assessment of study quality. Data were extracted and then analyzed to determine the weighted pooled risk of rebleeding after successful endoscopic therapy.

Results: A literature search to April 1, 2016 yielded 1951 unique citations. After initial abstract screening, 30 articles were identified for full text review. Ultimately, 9 studies were selected for inclusion, comprising 565 patients who had received endoscopic therapy to

SBVL. There was significant heterogeneity between studies and a random effects model was required. Rebleeding occurred in 242 patients, representing a pooled rebleeding risk of 42.8% after a median follow-up of 20 months.

Conclusions: Patients with OGIB who have SBVL identified and successfully treated during BAE have significant rates of rebleeding. Therefore, ongoing clinical monitoring and consideration of repeat endoscopic investigations is recommended for these patients.

Funding Agencies: None

A48
DUODENAL ADENOCARCINOMA: A CASE REPORT
T. Hansen, W. Manishen

University of Manitoba, Winnipeg, MB, Canada

Background: Primary adenocarcinoma of the duodenum is implicated in less than 0.5% of all gastrointestinal cancers. Although rare, benign looking duodenal ulcers at time of endoscopy may represent more sinister pathology, particularly in the absence of H. pylori or NSAID use.
Aims: We report a case of an elderly man with a benign appearing duodenal ulcer at endoscopy who ultimately developed metastatic carcinoma from a primary adenocarcinoma of the duodenum.
Methods: Case report
Results: A 72 year old male presented for a routine screening colonoscopy. At time of endoscopy, the patient gave a history of vague epigastric discomfort and melena stools over the past two days. He denied ASA or non-steroidal drug use and was a non-smoker. A gastroscopy and colonoscopy were pursued. Upon examination of the duodenal bulb, a small, benign appearing ulcer was noted on the anterior wall with no active bleeding. Antral biopsies for H.pylori were negative. No intestinal metaplasia was seen. He was prescribed proton pump inhibitor and instructed to seek follow up care with his family doctor.

Approximately 8 months later, the patient began experiencing epigastric pain, nausea, early satiety and weight loss. He presented to the emergency room 11 months after the original endoscopy. A CT scan of the abdomen showed multiple hepatic metastases and lymphadenopathy at the porta-hepatis. A repeat gastroscopy revealed an ulcerated, stenotic mass at the pylorus, extending from the duodenal bulb. Biopsies of the pylorus revealed invasive adenocarcinoma, intestinal type. The patient was subsequently referred for palliative care.

Conclusions: This case highlights that not all duodenal ulcers are benign. It may be worthwhile to ensure patients follow up with their endoscopist should they develop a recurrence of symptoms, at which time biopsy of the actual ulcer, if not healed, could be performed.

A49
INNOVATIVE GROUP EDUCATION FOR A COMMON LIVER DISEASE - INCREASING ACCESS TO CARE

M. Laryea[2], M. McLeod[2], K.M. Peltekian[2], A. Sabharwal[1], G. Hirsch[1], C. Burgess[1]

1. Hepatology, Nova Scotia Health Authority, Halifax, NS, Canada; 2. Dalhousie University Faculty of Medicine, Halifax, NS, Canada

Background: Non Alcoholic Fatty Liver Disease (NAFLD) is the most common type of liver disease among Canadians that affects 20-40% of Nova Scotians with liver disease. Unfortunately, the current wait time in Nova Scotia to be seen by a hepatology specialist for NAFLD is greater than 18 months. To address this issue a group education program – The Fatty Liver Public Forum (FLPF) was developed to provide information to patients through a panel of experts. The current evidence suggests that diet and exercise are the most effective means of controlling NAFLD treatment should center on weight loss. The FLPF seeks to educate patients about fatty liver disease and provide the opportunity to institute the necessary life style changes while awaiting their clinic appointment.
Aims: To determine the effectiveness of the forum in increasing patient awareness of NAFLD and options for self treatment, as well as its effectiveness in decreasing patient wait times.
Methods: Patients appropriate for the forum were those with prior diagnosis of fatty liver disease by gastroenterologist or by ultrasound. All patients with fatty liver disease were invited to attend the FLPF as incentive to reduce their wait time to see a hepatologist. Patients with cirrhosis, hepatic decompensation, hepatocellular carcinoma were not included as these patients were not felt to benefit from the forum. The FLPF started in February 2014 and has been provided on a quarterly basis. The average wait time from referral to invitation for the FLPF is under 6 months. Furthermore, the average wait time to see the specialist is 10 months for those who have attended the forum.
Results: To date 355 individuals have been invited and 135 (38%) have attended, all of whom were asked to complete an evaluation at the end of the clinic visit. Of the 126 attendees who completed the evaluation, 120 (95.2%) reported an increased understanding of what constitutes a fatty liver, 120 (95.2%) reported improved knowledge about healthy diet choices, and 117 (92.8%) reported a greater understanding about weight loss and how to begin an exercise regimen. Preliminary follow up of these patients has shown that 65.9% of patients selected for the forum were deemed appropriate following confirmation through fibroscan or a biopsy.
Conclusions: Of the patients that attended, many patients found the forum educationally beneficial and an appropriate way to begin to manage disease prior to meeting with a specialist. The FLPF is providing improved access to healthcare, a decrease in waitlist times, and increased feelings of self-efficacy in patients with respect to self management of NAFLD.

A50
ALBERTA FAMILY PHYSICIAN ELECTRONIC ENDO-SOCPY (AFPEE) STUDY RESULTS

M.R. Kolber[2], N. Olivier[1], O. Babenko[4], R. Torrie[1], L. Green[3]

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

Background: In Canada, gastroenterologists and general surgeons perform 97% of all colonoscopies. A number of Canadian Family Physicians currently performing colonoscopies and training Family Physicians in endoscopy may help alleviate endoscopic wait times. For Family Physicians to be considered a legitimate option in the provision of colonoscopies, current FP colonoscopists must meet colonoscopy quality benchmarks.
Aims: To compare the quality of colonoscopies performed by Family Physicians in Alberta, Canada to standard benchmarks using an electronic data capturing tool.
Methods: Physicians (and their teams) collected real time data on colonoscopies performed during a six-month study period and performed pathology reconcilliation. Data was captured electronically on IPADs ™ using a colonosocpy specific tool developed by the study team and housed in REDCap.™
Primary outcomes include cecal intubation rates, proportion of patients 50 years and older (separated by gender) having first time colonoscopy with an adenoma, and immediate complication rates. All potential adverse events were independently and blindly adjudicated by two physicians not involved in the study.
Results: Nine Alberta Family Physician colonoscopists, who perform endoscopy in 11 rural sites, participated in the study.
The study physicians performed a total of 1769 colonoscopies (on 1755 unique patients) in the study for a mean of 197 colonoscopies performed per physician. Overall, 1731/1769 [97.9%, 95% CI: 97.2, 98.6] of colonoscopies attempted had a successful cecal intubation and all physicians achieve a cecal intubation rate of >95%. The proportion of males and females ≥ 50 years old who had their first colonosopy performed with an adenoma or sessile serrated adenoma (SSA) was 67.4% (95% CI; 62.1, 72.7) and 51.1% (95% CI; 45.5, 56.7) respectively. Overall, there were 120 adenomas or SSAs per 100 colonoscopies performed. There were two post polypectomy bleeds and no perforations or serious adverse events related to consicous sedation.

Conclusions: Alberta Family Physicians who participated in the Alberta Family Physician Electronic Endoscopy (AFPEE) study are meeting quality standards in colonoscopy performance. Training some Family Physicians in GI medicine and endoscopy may help alleviate endoscopic wait times and improve access for patients of rural origin. Ongoing data collection using a simple, electronic data collection system which spans endoscopy reporting platforms should be encouraged.

Funding Agencies: Alberta Rural Physician Action Plan, Northern Alberta Family Medicine Fund

A51
COMPARISON OF THE BOSTON BOWEL PREPARATION SCALE WITH AN AUDITABLE APPLICATION OF THE US MULTI-SOCIETY TASK FORCE GUIDELINES
V. Heron[7], M. Martel[8], T. Bessissow[9], Y. Chen[6], E. Desilets[10], C. Dube[11], Y. Lu[7], C. Ménard[2], J. McNabb-Baltar[1], R. Parmar[3], A. Rostom[5], A.N. Barkun[4]

1. Brigham and Women's Hospital, Harvard Medical School, Montreal, QC, Canada; 2. Medecine, CHUS, Sherbrooke, QC, Canada; 3. Internal Medicine, McGill, Montreal, QC, Canada; 4. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 5. University of Ottawa, Ottawa, ON, Canada; 6. Division of Gastroenterology, Johns Hopkins Hospital, Baltimore, MD; 7. McGill University, Montréal, QC, Canada; 8. McGill University Health Center, Montreal, QC, Canada; 9. Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 10. Gastroenterology, Université de Sherbrooke, St-Basile-le-Grand, QC, Canada; 11. medicine, the ottawa hospital, Ottawa, ON, Canada

Background: Existing bowel preparation scales (BPS) are limited in their ability to predict interval to next colonoscopy. The US Multi-Society Task Force (MSTF) recommends screening or surveillance colonoscopies be repeated within the year if the preparation does not allow for detection of polyps greater than 5 mm in size.
Aims: To assess reliability and validity of an auditable application of the MSTF in comparison with the Boston BPS (BBPS).
Methods: We developed an auditable application of the MSTF guidelines which we termed the Montreal Bowel Preparation Scale (MBPS). We compared this with the BBPS using a total cut-off score of 6 with each segment score ≥2 (BBPS 2-6). In sensitivity analyses, we applied the MBPS using a cut-off of 3mm rather than 5mm, and also assessed the BBPS using an adequacy threshold of total score ≥5 (BBPS 5). Video recordings of 83 colonoscopies (8 for intra-rater agreements) were independently evaluated by nine physicians trained to use the different scales. Weighted kappas quantified intra- and inter-rater agreements. Intra class correlations were used to assess agreement of the BBPS as a continuous scale. Associations between scores and clinical outcomes were assessed.

Results: The BBPS 2-6 and 5mm MBPS showed moderate to substantial intra-rater agreements (κ=0.44-0.63 and κ=0.50-0.53, respectively), while inter-rater agreements were only fair to moderate and slight to moderate (κ=0.25-0.48 and κ=0.19-0.50, respectively). Similar results were noted using alternate thresholds of BBPS 5 and 3mm MBPS. No significant associations were found between scores and clinical outcomes.
Conclusions: For all scales, intra-rater kappas were superior to inter-rater values with the latter reflecting at best moderate agreement. This modest performance may reflect the dichotomized interpretation of the scales (adequate vs inadequate) contrary to previous studies which compared scores assessed as continuous variables. Further validation studies of existing ordinal bowel preparation scales should aim to assess reliability in a categorical manner based on proposed adequacy thresholds in order to determine optimal interpretation with regards to interval to next colonoscopy.

Inter- and intra-rater agreement

		BBPS 5	BBPS 2-6	5mm MBPS	3mm MBPS
Inter-rater agreement (κ, 95% CI)	All raters	0.22 (0.18; 0.25)	0.39 (0.35; 0.43)	0.31 (0.28; 0.35)	0.44 (0.40; 0.47)
	Senior group	0.35 (0.28; 0.42)	0.48 (0.41; 0.55)	0.19 (0.12; 0.26)	0.39 (0.32; 0.46)
	Junior group	<0	0.25 (0.16; 0.34)	0.50 (0.41; 0.58)	0.52 (0.43; 0.61)
Intra-rater agreement (κ, 95% CI)	All raters	0.68 (0.55; 0.88)	0.55 (0.53; 0.90)	0.52 (0.59; 0.83)	0.76 (0.45 ; 0.74)
	Senior group	0.65 (0.34; 0.99)	0.50 (0.21; 0.72)	0.52 (0.22; 0.74)	0.78 (0.50; 1.00)
	Junior group	0.74 (0.40; 1.00)	0.63 (0.15; 1.00)	0.53 (0.15; 0.92)	0.73 (0.57; 0.89)

Funding Agencies: None

A52
PERORAL ENDOSCOPIC MYOTOMY (POEM) FOR TREATING ACHALASIA: A SINGLE CENTER'S RESULTS
M. Woo[1], R. Bechara[2]

1. Queen's University, Kingston, ON, Canada; 2. Queens University, Kingston, ON, Canada
Background: Achalasia, a primary esophageal motor disorder characterized by insufficient 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.
Methods: 11 consecutive patients with achalasia (8 men, 3 women, mean age 51.82 years [range 31–80], mean duration of symptoms 100 mo [range 10 mo–30 yrs]) from a single tertiary center in Kingston, Ontario underwent 12 peroral endoscopic myotomies (POEM) between March 2016 and Sept 2016. A submucosal tunnel extending to the gastroesophageal junction was created endoscopically and then an endoscopic myotomy (mean length 12.92±2.84cm in the distal esophagous, 3.17±0.43cm in the cardia) of the circular muscle bundles was performed. The mucosal defect was closed with hemostatic clips (5±0.43). The mean operating time was 117.17±30.8 min. Pre- and post-operative assessments included Eckhardt scores, barium swallow, endoscopy and manometry.
Results: There were no complications. The mean Eckardt score pre-procedure was 7.90±1.1 (range 6-10). 9 patients underwent follow-up [mean duration 2.33±1.5 mo, range 0-5 mo] with post-procedure Eckardt score of 0.78±0.97 (range 0-3). The improvement was statistically significant ($p<0.05$).
There was no significant difference in the improvement of symptoms in patients with type 2 achalasia ($n=2$) [pre-procedure Eckardt 8.67, post-procedure Eckardt 0.00, difference 8.67] and patients with type 3 achalasia ($n=5$) [pre-procedure Eckardt 8.17, post-procedure Eckardt 1.00, difference 7.17].
Patients with >1 previous treatments ($n=3$) for achalasia, including balloon dilation, botox injection and Heller myotomy, experienced statistically significant improvement in their symptoms [mean pre-procedure Eckardt 8.00±0, mean post-procedure Eckardt 1.33±1.55, $p<0.05$].
Of four patients who underwent follow-up endoscopy, none had any endoscopic evidence of esophagitis.
A difficulty score involving tunnel distension, abnormal contractions, submucosal oozing, submucosal fibrosis, tunnel orientation was calculated (mean score 2.67). The mean difficulty score per morphology was as follows: non-sigmoid non-dilated, 2.17; non-sigmoid dilated, 2.50; sigmoid S1, 2.50; sigmoid S2, 4.00. Difficulty score was found to strongly correlate with operative time ($r=0.88$).
Conclusions: POEM is a safe and effective method of managing achalasia, specifically in groups that have been previously shown to be less responsive to surgical therapy, e.g. type 3 achalasia and those with previous anti-achalasia procedures. A difficulty score has been shown to correlate with operative time and warrants further investigation.

Funding Agencies: None

A53
EVALUATING THE DIAGNOSTIC YIELD OF PATIENTS PRESENTING FOR COLONOSCOPY WITH ISOLATED ABDOMINAL PAIN
M. Nunn[2], G. Williams[1], S.E. Gruchy[1]
1. Division of Digestive Care & Endoscopy, Department of Medicine, Dalhousie University, Halifax, NS, Canada; 2. Dalhousie University , Halifax, NS, Canada

Background: Colonoscopy is used as a diagnostic and therapeutic procedure to assess patients with lower gastrointestinal disease. Practice guidelines from the American Society of Gastrointestinal Endoscopy (ASGE) outline accepted indications for colonoscopy; however, there is disagreement over there use in patients who present with abdominal pain in the absence of other symptoms. These guidelines state that colonoscopy is generally not indicated for chronic abdominal pain, noting that there are "unusual exceptions in which colonoscopy may be done once to rule out disease, especially if symptoms are unresponsive to therapy". The diagnostic yield of colonoscopy for the isolated indication of abdominal pain is thought to be low, though few studies have been published that confirm this. While it is generally considered a safe procedure, colonoscopy carries potentially serious risks including perforation, bleeding, discomfort, and issues related to anxiolysis. Furthermore, colonoscopy is a limited resource with multiple firmly established indications.
Aims: The aim of our study was perform a quality initiative to assess the diagnostic yield of colonoscopy and procedure related complications for the isolated indication of abdominal pain.
Methods: We performed a retrospective analysis of all patients undergoing colonoscopy in the Central Zone of Nova Scotia Health Authority for the isolated indication of abdominal pain, from April 1, 2015 to March 30, 2016. Data was retrieved from the Clinical Outcomes Research Initiative (CORI) database, including patient demographics, supplemented by information obtained from regional Horizon Patient Folder. The primary outcome was endoscopic findings, and secondary outcome was procedure related complications.
Results: In total, 98 participants received a colonoscopy for isolated abdominal pain. Participants had a mean age of 52 years (range 16-84), of which 63.3% were female. Abnormal colonic findings were identified in 48% of colonoscopy reports, with biopsies taken in 56% of cases. Colonic polyps and diverticulosis were each detected in 24.5% of participants and were the most frequent diagnostic findings. Other findings at time of colonoscopy included hemorrhoid (3.1%), malignancy (1.0%), and Crohn's disease (1.0%). No immediate complications were reported.
Conclusions: Over half of the patients underwent a biopsy during the procedure and approximately 1 in 4 patients were found to have polyps. The diagnoses of Crohn's disease, malignancy and diverticular disease may account for patients' abdominal pain; however, these finding represented only 27% of our study population. This quality analysis reveals a low diagnostic yield for significant findings that may be attributable to the patients' abdominal pain at our center. More research is needed to determine what subgroups of patients with abdominal pain may benefit from colonoscopy.

A54
IMPROVEMENTS OF GLOBAL RATING SCALE (GRS) CANADA SCORES IN SEVEN ENDOSCOPY UNITS IN THE EDMONTON REGION USING AN INTEGRATED QUALITY IMPROVEMENT PROGRAM

S. Veldhuyzen van Zanten[1], L. Bistritz[3], M. Greenaway[4], R. Ennis-Davis[5], k. kostiuk[6], R. Sultanian[2], b. walters[7], V. Selvarajah[3], n. hoque[8]

1. University of Alberta, Edmonton, AB, Canada; 2. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 3. Gastroenterology, University of Alberta, Edmonton, AB, Canada; 4. alberta health services, Edmonton, AB, Canada; 5. alberta health services, Edmonton, AB, Canada; 6. alberta health services, Edmonton, AB, Canada; 7. university of alberta, Edmonton, AB, Canada; 8. University of Alberta, Edmonton, AB, Canada

Background:
The recently developed GRS-Canada is a validated instrument whose implementation leads to improved quality and patient experience of colonoscopy. The GRS-C has two dimensions dealing with clinical quality and quality of the patient experience. Both have ratings for 6 different categories resulting in a total of 12 dimensions for the "total" GRS-C score. The GRS-C has four grading levels, going from D, the lowest level, to level A, the highest. In order to reach a certain level all questions in each domain need to be answered positively. 18 months ago the GRS was introduced in seven of the eight hospital sites where endoscopy is performed in the Edmonton Zone: University of Alberta Hospital, Royal Alexandra, Grey Nuns, Misericordia, Sturgeon, Leduc and Fort Saskatchewan. The 8th hospital WestView recently also started.
Aims: The aim is to get all sites up to an A level over the next four years. Here we report on how scores improved as a result of an integrated QA program that was launched.
Methods: The CAG website created for online submission of the GRS and associated improvement process was used to enter scores. This was done once every year.
Results:
As can be seen marked improvements were seen in 6 of the 7 hospitals all of whom have been actively working on the project for at least 1 year. In many dimension there was improvement from a D level to a C. One site was unchanged and an eighth site is just starting. Patient surveys have been started which will further help improve scores over time.
Conclusions: Important improvements were seen in GRS-Canada scores in Edmonton Zone endoscopy units using an integrated QA program. The program was supported by a project manager.

	Royal Alexandra Hospital		University of Alberta Hospital		Misericordia Hospital		Grey Nuns Hospital		Sturgeon General Hospital		Leduc Community Hospital		Fort Saskatchewan Community Hospital		Westview Community Hospital	
	2014	2016	2014	2016	2014	2016	2014	2016	2014	2016	2014	2016	2014	2016	2014	2016
CONSENT PROCESS	D	C	D	C	D	C	D	C	C	C	D	C	D	D	N/A	D
SAFETY	D	D	D	D	D	D	D	D	D	D	D	D	D	D	N/A	D
COMFORT	D	C	D	C	D	D	D	C	C	C	D	C	C	C	N/A	D
QUALITY OF PROCEDURE	D	D	D	D	D	D	D	D	D	D	D	D	D	D	N/A	D
APPROPRIATENESS	D	D	D	D	D	D	D	D	D	D	D	D	D	D	N/A	D
COMMUNICATING RESULTS	D	D	D	D	D	D	D	D	D	D	D	D	D	D	N/A	D
EQUALITY OF ACCESS	D	D	D	D	D	D	D	D	D	D	D	D	D	D	N/A	D
TIMELINESS	D	D	D	D	D	D	D	D	D	D	D	D	D	D	N/A	D
BOOKING AND CHOICE	D	C	D	C	D	D	D	C	D	C	D	C	D	D	N/A	D
PRIVACY AND DIGNITY	D	C	D	C	D	D	D	C	D	C	D	C	D	D	N/A	D
AFTERCARE	D	C	D	C	D	C	D	C	D	C	D	C	D	D	N/A	D
ABILITY TO PROVIDE FEEDBACK	D	B	D	B	D	B	D	B	D	B	D	C	D	D	N/A	D

A55
ASSESSMENT OF THE APPROPRIATE USE OF GASTROINTESTINAL ENDOSCOPY AT A TERTIARY CARE CENTRE

J. Yonge, C. Galorport, B. Bressler, H. Ko, J.J. Telford, R.A. Enns

St. Paul's Hospital, Vancouver, BC, Canada

Background: Knowledge of appropriate indications for colonoscopy is essential for quality endoscopic practice and ideal future management of patients. The American Society for Gastrointestinal Endoscopy (ASGE) published guidelines for the appropriate use of endoscopy to help hospitals, endoscopy units, and endoscopists achieve safe and responsible endoscopic practice. These guidelines outline indication statements that specify the circumstances in which colonoscopy is indicated.
Aims: The primary objective of this study is to determine whether the endoscopic procedures performed at St. Paul's Hospital are appropriate according to ASGE guidelines.
Methods: A total of 400 consecutive charts (161 male and 239 females; mean age 57.9 +/- 14.3 years) were retrospectively reviewed to assess the appropriateness of colonoscopy performed by gastroenterologists at St. Paul's Hospital. Appropriateness was determined by comparing the procedure indication to the ASGE guidelines. Fisher's exact test was used to assess detection of significant lesions. A p-value of < 0.05 was considered significant.
Results: 98% underwent colonoscopy for an appropriate indication, while it was only considered inappropriate for 2% of patients. Detection of significant lesions (colon cancer and adenomatous polyps) was higher in appropriate colonoscopies compared to inappropriate

(39.5% vs. 0.0%, p=0.025). The most frequent indications for colonoscopy were bleeding (40.8%), screening/surveillance for colonic neoplasia (35.6%), and IBD affecting the colon where more precise diagnosis or determination of the extent/activity of the disease would influence management (6.3%).

Conclusions: The vast majority of colonoscopy procedures being done at St. Paul's Hospital are for appropriate indications (98.0%). The greater yield of significant lesions from appropriate procedures suggests the effectiveness of the ASGE guidelines, however, additional steps should be taken to make the guidelines more specific and to standardize them across sites with a wide variety of patient populations to ensure uniformity in care.

Funding Agencies: None

A56
ENDOSCOPIC PROCEDURE REPORT COMPLETENESS IMPROVES FOLLOWING IMPLEMENTATION OF A DICTATION TEMPLATE AT ST. PAUL'S HOSPITAL
J. Yonge, N. Harris, C. Galorport, M. Suzuki, J. Amar, B. Bressler, C. Brown, E. Lam, T. Phang, A. Ramji, S. Whittaker, J.J. Telford, R.A. Enns

St. Paul's Hospital, Vancouver, BC, Canada

Background: Following colonoscopy or esophagogastroduodenoscopy (EGD), the physician reports their findings, which are typically transcribed and kept in patient's medical records. The completeness of endoscopic dictation reports are quality indicators for endoscopic practice. Several guidelines outlining the key elements of endoscopic reports were used to develop a dictation template at St. Paul's Hospital in 2013.

Aims: The purpose of this study is to assess and compare the quality and completeness of endoscopic procedure reports from 2008 and 2014 for physicians currently working at St. Paul's Hospital to determine if key quality elements of documentation were more consistently included following institution of a dictation template.

Methods: A retrospective chart review of endoscopic reports of 9 physicians were reviewed at two time points, before (2008) and after (2014) the introduction of the dictation template. 150 charts were reviewed for each doctor in each year. Data was collected from a comprehensive EMR review that included demographics, patient history, procedure report details (appropriate quality indicators as outlined by ASGE Guidelines), and length of procedure. Cecal visualization rate and polyp detection rate were also calculated for colonoscopy reports. This study was approved by the IRB at St Paul's Hospital.

Results: The overall completeness for colonoscopy reporting for all quality data points improved from 70.5% in 2008 to 90.6% in 2014 (p<0.001) when looking at all variables that were included on the dictation template. The overall completeness for EGD data points improved from 81.1% in 2008 to 87.1% in 2014 (p<0.001). Most variables remained consistent or increased; however, reporting of comorbidities, medications, and patient comfort remained low at both time periods for both endoscopic procedures. The biggest improvement in reporting was seen in withdrawal time for colonoscopy and consent for EGD.

Conclusions: The use of the dictation template has improved documentation of quality parameters from 2008 to 2014 in both colonoscopy and EGD. Most variables not included in the dictation template were frequently underreported and educational maneuvers as well as other adjustments to include these variables in future procedure reports can be targeted at these items.

Presence of endoscopic procedure report variables

Presence of dictation item, %	2008 (n=1336)	2014 (n=1350)	2008 (n=985)	2014 (n=977)
	Colonoscopy		EGD	
Preoperative diagnosis	98.7	99.3	99.7	98.5
Post-operative diagnosis	98.7	99.3	99.4	97.0
Procedure performed	99.5	99.4	99.8	99.6
Clinical preamble/indications(s)	99.3	94.6	91.0	88.4
Consent	44.3	88.5	46.7	72.2
Endoscope used	42.8	97.0	53.0	58.3
Quality of bowel preparation	59.0	89.4	N/A	N/A
Sedation (type and dosage)	85.9	96.4	82.5	94.9
Digital rectal examination	55.8	89.0	N/A	N/A
Extent of examination	99.8	99.9	99.9	43.4
Complications (if any)	17.7	62.6	22.8	99.6
Withdrawal time	0.4	71.8	N/A	N/A
Rectal retroflexion	28.5	77.6	N/A	N/A
Findings	99.8	100.0	100.0	100.0
Pathology specimens taken	90.2	91.6	92.0	98.0
Location of sample	91.5	88.3	91.7	96.7
Recommendations for subsequent care	93.8	95.9	76.7	86.7
Overall completeness of procedure-related items, %				
Mean (SD)	70.51 (7.41)	90.63 (10.00)	81.07 (10.02)	87.08 (7.92)
Median (IQR)	70.59 (64.71, 76.47)	94.12 (82.35, 100.00)	83.33 (76.92, 84.62)	84.62 (84.62, 92.31)
Range	(41.18, 88.24)	(52.94, 100.00)	(53.85, 100.00)	(53.85, 100.00)

Funding Agencies: None

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CLINICAL PRACTICE

A57
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

Medicine, Div. of Gastroenterology, St. Paul's Hospital , 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 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 a 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 colonos-copy, 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 instructions.
Results: Preliminary data analysis (n = 333) shows that 86% of patients have achieved a score demonstrating adequacy on the BBPS (mean 7.2; adequate score considered ≥ 6) and 90 % have scored adequately on the OBPS (mean 3.6 ; adequate considered ≤ 7). 92% of patients scored the web education tool as "Very Helpful" (8 or higher out of 10 on our usefulness scale), and 90% scored as "Very Clear" (8 or higher in terms of the clarity of information presented to them). Com-pared to our historical control (examining the BBPS of 983 patients) displaying a mean 6.2, our interim results suggest that our online education tool results in a superior BBPS score.
Conclusions: Our interim analysis has demonstrated a strong improvement in preparations overall with this instruction pathway. Additionally, it is uniquely modified for each patient and limits the instruction re-quired 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. Further data collection and analysis will provide insight into the feasibility of implementing this program in the medical clinic and determining the limiting factors to the access and use of it.

A58
PATIENT SATISFACTION WITH ENDOSCOPY UNITS: THE EDMONTON EXPERIENCE

L. Bistritz[1], R. Ennis-Davis[2], A. Mulgrove[2], M. Green-away[2], S. Veldhuyzen van Zanten[1]

1. University of Alberta, Edmonton, AB, Canada; 2. Alberta Health Services, Edmonton, AB, Canada

Background: Endoscopy services in the Edmonton Zone (EZ) are provided by 8 endoscopy units. Implementa-tion of the Global Rating Scale (GRS) as a measure of endoscopy unit quality in the EZ was previously based at individual sites, with no coordination across the EZ. This led to poor uptake of the GRS. In September 2015, Alberta Health Services leadership partnered with Gastroenterology to provide quality improvement (QI) resources across the EZ to support the GRS. Part of this project involved introducing a patient satisfaction survey to be utilized by all EZ endoscopy units to inform the ongoing QI process.
Aims: The project aim was to develop and implement a uniform process to assess patient satisfaction with endoscopy units across the EZ.
Methods: A patient satisfaction survey was developed using multiple stakeholders from the five principal endoscopy units within AHS and Covenant Health, including departments of Integrated Quality Manage-ment, Patient Engagement and Primary Data Support, as well as EZ Gastroenterologists. Survey distribution began April 1, 2016. At each site, two patients undergo-ing colonoscopy were randomly selected to receive the survey daily. The survey was discussed with patients pre-procedure and distributed at discharge by nursing staff. After six months, data was collated and reported to the EZ GRS/Quality Committee and individual endoscopy units.
Results: 595 surveys were distributed from April 1, 2016 to Sept 30, 2016. Overall response rate was 220 (37%), which varied by site (range 30-47%). 99.5% of respondents felt they had been treated with courtesy and respect. Respondents reported confidence/trust in endoscopy staff (100% for endoscopist, 99.6% for nurse), and satisfaction with explanations received (99.0% for endoscopist, 99.5% for nurse). 92.7% of patients were comfortable/very comfortable during the colonoscopy. Higher than expected numbers of respondents were not made aware by endoscopy unit staff that they were free to withdraw consent at any time (39.3% for endoscopist, 34.3% for nurse). 39% of patients reported difficulty with bowel preparation; of these 31.7% did not have a number to call with ques-

tions. 9.2% of patients reported requiring a translator, but only 33% of these were offered one.
Conclusions: This zone-based patient satisfaction survey has enabled the EZ to identify ways to improve the patient endoscopy experience, such as clarifying our pre-procedure consent information, and improving pre-procedure support and translation. Bowel preparation information will require more work. GRS items across the EZ improved due to implementation of the patient survey. The provision of centralized resources and personnel by AHS was integral to the success of this process, and will be required to entrench QI as part of usual business for EZ endoscopy units.

A59
FACTORS ASSOCIATED WITH ANXIETY ABOUT COLO-NOSCOPY: THE PREPARATION, THE PROCEDURE, AND THE ANTICIPATED FINDINGS
J.R. Walker, L. Shafer, V. Yang, A. Singh, C. Waldman, V. Michaud, C.N. Bernstein, J. Park, L. Hathout, J. Sisler, G. Restall, K. Wittmeier, h. singh

University of Manitoba, Winnipeg, MB, Canada

Background: Previous research has assessed anxiety related to colonoscopy but has not specifically considered anxiety related to different aspects of the situation – bowel preparation, the procedure itself, and the anticipated findings. A better understanding of anxiety related to the various aspects of colonoscopy may help guide the development of resources or interventions to lessen colonoscopy-related anxiety.
Aims: We aimed to assess anxiety immediately before a colonoscopy and evaluate variables associated with anxiety about different aspects of the procedure.
Methods: A self-administered anonymous survey was distributed between August 2015 to June 2016 to patients immediately prior to their outpatient colonoscopy in Winnipeg's 6 hospitals and 2 ambulatory care centers. Anxiety was assessed with a visual analogue scale in which respondents indicated their anxiety about each of bowel preparation, the procedure and the findings on a 0 to 100 scale. A score of 70 or more was considered a high level of anxiety. Multivariate logistic regression analysis determined predictors of high anxiety.
Results: Of the 1336 respondents (52% females, median age 57 years), 18% reported high anxiety about the bowel preparation, 29% about the procedure, and 28% about the findings of the procedure. Predictors of high anxiety about bowel preparation were: female gender (OR 2.90; 95% CI: 1.97-4.25), finding bowel prep information confusing (OR 3.29; 95% CI: 1.64-6.63), unfinished laxative intake (OR 1.71; 95% CI: 1.05-2.80), and high anxiety about the procedure itself (OR 3.06; 95% CI: 2.09-4.49). Predictors of high anxiety about the procedure were: female gender (OR 1.41; 95% CI: 1.02-1.94), high anxiety about bowel prep (OR 3.04; 95% CI: 2.07-4.47), and high anxiety about the findings

(OR 4.58; 95% CI: 3.30-6.35), while lower anxiety was seen in those with more than one previous colonoscopy (OR 0.38; 95% CI: 0.24-0.58) and coming direct to scope (OR 0.71; 95% CI: 0.51-0.99). Predictors of high anxiety about the findings were polyp/cancer surveillance (OR 1.98; 95% CI: 1.18-3.30) or symptom investigation (OR 2.02; 95% CI: 1.36-3.00) as reasons for the procedure and anxiety about the procedure (OR 4.51; 95% CI: 3.26-6.24). There was no association between anxiety and educational attainment or the use of the split dose preparation for any of the aspects of the procedure.
Conclusions: Fewer people had high anxiety about preparation than about the procedure and findings of the procedure. There are unique predictors of anxiety each of these factors. Higher quality information about preparation, the colonoscopy itself, and findings of the colonoscopy may help to reduce anxiety for some patients.

A60
IMPROVING PROCESS IN THE EDMONTON PEDIATRIC INFLAMMATORY BOWEL DISEASE CLINIC: AN INFLIXIMAB INFUSION QUALITY IMPROVEMENT PROJECT
M.W. Carroll[1], C. Kluthe[4], P. Medvedev[1], E. Wine[2], H.Q. Huynh[3]

1. Pediatric Gastroenterology, Univeristy of Alberta, Edmonton, AB, Canada; 2. Pediatrics, University of Alberta, Edmonton, AB, Canada; 3. Pediatrics, University of alberta, Edmonton, AB, Canada; 4. Alberta Health Services, Edmonton, AB, Canada

Background: There is a growing body of literature demonstrating that sustained clinical remission using infliximab is related to adequate trough serum drug levels and inversely to the development of antibodies against the drug. Antibody formation typically occurs when serum drug levels fall too low; this might happen when scheduled infusion treatments are delayed and not given as planned.
Although there is little literature specifically reviewing the outcomes of patients with respect to adherence to scheduled dosing intervals, it stands to reason that patients who repeatedly receive their infusion outside of the intended treatment window may be at greater risk of low drug levels & loss of response to therapy.
Aims: We sought to audit the use of infliximab amongst patients of the Edmonton Pediatric IBD Clinic (EPIC) by retrospective analysis of the duration between infusions to determine how many patients fall outside of their intended treatment window.
Methods: PDSA Cycles:
Data Inadequacy
Our initial audit revealed significant deficiencies in our established data collection and patient tracking processes. These were in part due to :a mix of medical day

unit infusions, community infusion center infusions and out of province infusions leading to inconsistent data; unreliable Infliximab Infusion Patient Report forms (clinical report forms); unscheduled visits: ER visits and hospitalizations inconsistently recordedImplementation of Revised Data Collection Processes

Revision of process to ensure report forms consistently returned
New EMR flow sheets to capture ER visits, surgeries and hospitalizations.Prospective Data Collection Utilizing Revised Processes - 95 patients tracked over 12 months
Results: 90% adherence to prescribed dosing interval
Dose changes & frequency changes mostly related to symptoms and/or low infliximab serum levels/development of anti-infliximab antibodies
Most changes were in fact a reduction in scheduled interval
This informs us that out of window infusions are not the driving cause of antibody development and therapeutic loss of response.
Conclusions: As a result of these findings and an increased awareness of the shortfalls in our data collection and patient tracking, EPIC has now developed and implemented a comprehensive patient registry which collates and tracks multiple facets of daily patient care, patient oriented outcomes (such as quality of life scores and patient satisfaction) and clinically focused outcomes (such as steroid free remission, hospitalizations and surgical interventions, growth and development). In doing this, we have been able to improve the way in which we personalize patient care, track patient outcomes and recognize new areas for continuing quality improvement.

Average Infliximab Interval Discrepancy

A61
AN ASSESSMENT OF THE EDUCATIONAL EXPERIENCE OF MEDICAL STUDENTS AND RESIDENTS AFTER THEIR GASTROENTEROLOGY AND HEPATOLOGY ROTATIONS
N. Jawaid[2], Z. Gallinger[1], K.J. Fortinsky[1]

1. University of Toronto, Toronto, ON, Canada; 2. Internal Medicine, University of Toronto, Toronto, ON, Canada

Background: Trainee educational experience on gastroenterology (GI) and hepatology rotations can vary between hospitals. Routine practice in GI takes place predominantly in an ambulatory setting, while core rotations are known to expose trainees to mainly inpatient medicine in the form of a consult service. As a result, obtaining knowledge across a wide variety of gastrointestinal disorders during a 1 month rotation may not be feasible.
Aims: To assess the education experience of medical students and residents after their gastroenterology and hepatology rotation in order to identify key topics which may not be adequately covered.
Methods: A web-based survey was sent to 130 medical students and residents who completed a rotation in GI and hepatology within the University of Toronto hospital network. The survey included demographics and questions regarding frequency of teaching, quality of teaching, and breadth of topics covered during their rotation. There were additional questions pertaining to the utility of novel resources as a learning supplement. Data was analyzed using descriptive statistics.
Results: The survey response rate was 50% (65/130) with medical students accounting for 29% while residents (PGY 1-3) accounted for 71% of the respondents. Most (72%) do not plan on pursuing a career in GI and had completed only 1 rotation. The vast majority (98%) reported spending 75% or more of their rotation managing inpatients rather than outpatients. Most learners (79%) felt their learning experience could have been improved, as the overall educational experience was rated a 5 on a 10-point likert scale. Many (80%) felt the amount of teaching differed significantly between the staff on service, and only 23% reported receiving daily formal teaching. The most pronounced deficits in clinical exposure and formal teaching topics included viral hepatitis, irritable bowel syndrome, gastrointestinal malignancies, and pregnancy-related gastrointestinal disorders. Only 49% of respondents received resources to supplement their learning. The vast majority (91%) agreed that receiving a daily question-and-answer resource spanning a variety of topics could improve their learning during the rotation.
Conclusions: Current rotations are not addressing many core topics within gastroenterology and hepatology. There is wide variation in teaching between different hospital sites and staff. Most learners are not reporting high levels of satisfaction with their rotations, which can be partly explained by the lack of clinical exposure or teaching around common gastrointestinal disorders. Additional resources are not routinely being provided leading to significant gaps in knowledge. This study lends support towards creating a novel question-and-answer based resource to supplement learning and ensure core topics are being addressed

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during each rotation.

A62
POST COLONOSCOPY COLORECTAL CANCERS IN ALBERTA. A PROCESS FOR IDENTIFYING TRUE CASES
M.S. Mohamed[1], D. Johnson[2], D. Sadowski[1], C. Wong[1]

1. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 2. Physician Learning Program, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, AB, Canada
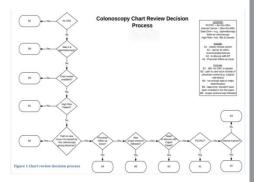
Background: Determining Post Colonoscopy Colorectal Cancer (PCCRC) rates is one of the most important measures of colonoscopy quality. Most commonly, PC-CRCs are the result of technical factors surrounding the colonoscopy such as inadequate bowel preparation, in-complete examination, missed early lesions and failure to adhere to follow-up guidelines. As these factors are amenable to quality interventions, we set out to identify PCCRC cases from a population perspective with a view to calculating incidence rates.
Aims: Our objective was to develop a framework for data gathering and analysis in order to identify PCCRC cases and rates in Alberta in order to obtain a clearer understanding of the underlying causes of PCCRC where potential quality interventions might be applied.
Methods: This was a retrospective population based review of all cases of colorectal cancer (CRC) diag-nosed in Alberta in 2013. Data from the Alberta Cancer Registry (ACR) was linked to the Discharge Abstract Database (DAD), the National Ambulatory Care Re-porting System (NACRS) and Alberta Ambulatory Care Reporting System (AACRS) databases to determine the timing of antecedent colonoscopies. We defined a PC-CRC as a case identified in the ACR with ICD-10 codes for colorectal cancer with an antecedent colonoscopy greater than 6 months but less than 3 years prior to the diagnosis of CRC. Individual chart reviews were carried out to exclude high-risk groups such as IBD or genetic syndromes and to determine lesion location.
Results: Before a PCCRC rate could be calculated, we identified that the initial data linking process provided a number of cases that required further in depth review to determine if they met inclusion and exclusion criteria. Subsequently, through an iterative process of chart review, we developed a decision analysis framework (see Figure1), that provided a rational basis for case exclusion as well as systematic categorization of PC-CRC root causes. Our analysis also identified areas for future quality improvement initiatives: such as the fail-ure to arrange follow-up after poor bowel preparation or advanced lesions. We also identified cases where access to timely care resulted in the development of a PCCRC.
Conclusions: Attempts to identify cases of PCCRC through database linkage identifies cases that require in depth analysis to determine eligibility. We have developed an algorithm that provides a rational basis for case exclusion as well as systematic categorization of PCCRC root causes.

Figure 1 Chart review decision process

A63
COLONOSCOPY QUALITY IN COLORECTAL CANCER SCREENING: HOW BEST TO CAPTURE THE DATA?
N. Nemecek[1], M. Webber[1], C. Wong[2], D. Sadowski[2]

1. Alberta Colorectal Cancer Screening Program, Alber-ta Health Services, Calgary, AB, Canada; 2. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada

Background: Colonoscopy quality indicators have been developed to ensure performance of accurate and safe colonoscopies as part of screening for colorectal can-cer. Measurement of these indicators requires timely recording of data during the colonoscopy procedure to allow for subsequent calculation of indicator rates. While various data capture methods currently exist, ranging from paper-based to electronic record systems, there is very little guidance available regarding the necessary requirements for accurate data entry into these systems.
Aims: In this outcomes project, our objectives were to assess both the uptake and barriers to implementation of quality data capture using a standardized bedside data collection form.
Methods: A pilot project was conducted in the Coaldale Screening Centre in southern Alberta over a 6-month period in 2016. This centre is a stand-alone endoscopy unit solely dedicated to performing colonoscopies for colorectal cancer screening. A standardized data collection form was developed to capture key quality indicators of interest as well as information regarding colonic polyps removed. The endoscopy theatre nurse completed the form during each procedure. Data from the completed forms were then entered into a central-ized electronic reporting system (Synoptec). Site visits, surveys and interviews were carried out to determine satisfaction with the method and to identify barriers to broader implementation of this quality initiative in other

units. A manual audit was performed to determine the accuracy of data collection and entry.

Results: During the study timeframe, 660 cases were entered into Synoptec and available for analysis. Feedback from the site visits, interviews and user surveys demonstrated the following concerns a) disparity between the endoscopists and nursing record regarding confirmation of landmarks b) concern over duplicate data entry and, c) extra time required to collect quality data resulting in delayed theatre turnover. An audit was completed on 10% (n=67) of the total cases to determine the level of agreement between the data collected on the standardized form (nurse) to the colonoscopy report (endoscopist). Findings indicated data were comparable for all quality indicators with the exception of withdrawal time; 75% case disparity. 54% of cases had a variance in withdrawal time within 1 minute and 30% were more than 2 minutes.

Conclusions: Institution of a colonoscopy quality program requires a culture of quality in the endoscopy unit that facilitates clear and purposeful communication between colonoscopist and theatre nurse, avoids duplication of data entry and builds quality data collection into the main work flow of the endoscopy unit.

Funding Agencies: None

A64
PERFORMING ERCP AT A CANADIAN ACADEMIC INSTI-TIUATION: QUALITY PROCEDURES START WITH THE RIGHT INDICATION.
A. Alghamdi, G. Williams, S.E. Gruchy

Dalhousie University, Halifax, NS, Canada

Background: Endoscopic Retrograde Cholangiopancreatography (ERCP) has diagnostic as well as therapeutic potential. However, given the availability of non-invasive diagnostic modalities, such as Magnetic Resonance Cholangiopancreatography (MRCP), the indications for performing ERCP have now shifted towards therapeutic procedures. In 2015, the American Society of Gastrointestinal Endoscopy (ASGE) published quality indicator guideline in ERCP. An appropriate procedural indication was considered a priority indicator and the task force selected a performance target of > 90%. There are no recent practice audits that review the indications for ERCP in Canada.

Aims: Our primary outcome is to measure how often ERCP is performed in accordance with the ASGE guidelines for procedural indication. Secondary outcome measures include the diagnostic yield and adverse event rates when an ERCP is performed outside of the ASGE guidelines for clinical indication.

Methods: An observational, retrospective review of all ERCPs in the central zone of the Nova Scotia Health Authority (NSHA) over a one year period between April 2015 and March 2016 was performed. New ERCP procedures were considered for inclusion in the review. 560 patients met the inclusion criteria during this time period. We accessed the patients electronic files through the Clinical Outcomes Research Initiative (CORI) data base. Basic demographic data was extracted. The procedural indications were recorded and compared with the ASGE clinical guidelines to access our compliance. The procedures that were not consistent with guidelines were analyzed further to determine a diagnostic yield and complication rate.

Results: Of the 560 procedures, 14 (2.5%) were performed for an indication inconsistent with the ASGE clinical guidelines. 6 patients (43%) met the clinical criteria for biliary Sphincter of Oddi dysfunction type III, and 4 cases (29%) were performed for biliary pancreatitis without evidence of biliary obstruction. Among the 14 ERCP procedures, common bile duct stones/sludge were actually found and removed in 5 cases (36%). There was no procedure related complications reported, however, one patient had transient oxygen desaturation during the procedure.

Conclusions: The procedural indication for ERCP in our institution during this quality analysis appear to be consistent with the ASGE guidelines in about 97% of procedures, which is within the performance target recommended by the ASGE quality indicator guideline. In cases when ERCP was performed outside the recommended guidelines, MRCP is a reasonable option to identify the hepatobiliary pathology prior to ERCP. Although no serious adverse events were determined in this audit, larger numbers of patients over a longer period of time would be needed to conclude this.

Funding Agencies: None

A65
SEVERE CYTOMEGALOVIRUS COLITIS MASQUERADING AS RECURRENT ISCHEMIC COLITIS IN PATIENT WITH END-STAGE RENAL DISEASE
R. Huang[2], A. Benmassaoud[1], S. Mayrand[1]

1. Division of Gastroenterology, McGill University Health Centre, Montreal, QC, Canada; 2. Division of Internal Medicine, McGill University Health Centre, Montreal, QC, Canada

Background: Severe Cytomegalovirus (CMV) colitis is a rare condition, most commonly seen in immunocompromised patients. We describe a case of CMV colitis masquerading as recurrent ischemic colitis in a patient with end-stage renal disease (ESRD).

Aims: Describe a case of severe CMV colitis presenting as recurrent ischemic colitis.
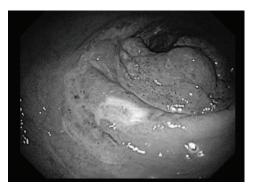
Methods: Case report

Results: Case: A 44 year-old man with atherosclerotic risk factors including hypertension, diabetes mellitus, ESRD on hemodialysis and morbid obesity presented twice to our emergency department (ED) within 14 days with hematochezia, acute abdominal pain, fever, leukocytosis, and an elevated serum lactate. Computed tomography scan of the abdomen (CT-Abdo) demonstrated changes consistent with isolated right

colon ischemia (IRCI). Colonoscopy showed circumferential ulcerated mucosa with greyish discoloration and sloughing of the mucosa starting at the hepatic flexure and extending proximally, potentially due to ischemic colitis (figure 1). There was a sharp demarcation between the normal and ulcerated mucosa, and, in view of possible ischemia, the endoscope was not introduced further. A colonic biopsy at the edge of demarcation was taken and showed non-specific small ulcerations. The patient improved with conservative management including intravenous fluids and antibiotics. He was discharged home with resolution of symptoms.

He unfortunately returned to our ED two weeks later with a third episode of hematochezia, abdominal pain and hemorrhagic shock. Repeat CT-Abdo showed persistent IRCI with new pneumatosis intestinalis. As he failed to improve with vasopressors, blood transfusions, and antibiotic therapy, an urgent right hemicolectomy was performed. On pathology, multiple CMV organisms were identified with ulcerations and perforation, consistent with severe CMV colitis. CMV PCR was only minimally elevated (80copies/mL). IV ganciclovir was initiated. On follow-up visit, the patient demonstrated sustained clinical improvement, and no recurrence of symptoms.

Conclusions: IRCI is an uncommon form of ischemic colitis, but occurs more frequently in patients with significant atherosclerosis and hemodialysis. Despite initial improvement, the patient's symptomatic recurrence was initially attributed to his severe vasculopathy, coupled with ongoing hemodialysis causing fluid shifts. In a review of the literature of 14 cases with ESRD and CMV GI disease, 72% presented with lower GI bleeding, colonoscopy showed ulceration or polypoid lesions, and was associated with a 35% mortality. CMV colitis should be suspected in atypical cases of ischemic colitis, and early diagnosis may avoid significant morbidity.

Sharp area of demarcation with circumferentially ulcerated and sloughing mucosa

A66
ABNORMAL THYROID FUNCTION IN CHILDREN WITH CELIAC DISEASE AT DIAGNOSIS AND FOLLOW-UP IN MANITOBA
V. Deora[1], W. EL-MATARY[2]

1. Section of Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 2. Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada

Background: The increased prevalence of autoimmune disorders in patients with celiac disease, including thyroid disorders, has been previously reported. However, data on abnormal thyroid function in children with celiac disease are limited.
Aims: The aims of this study were to:
1) Determine the prevalence of abnormal thyroid functions in children with known celiac disease (CD) in Manitoba; at diagnosis, as well as at 6 and 18 months post diagnosis.
2) Examine predictive factors for abnormal thyroid function in celiac patients.
Methods: Children (<17 years) with CD had anti-tissue transglutaminase (TtG) IgA antibody titers, and thyroid function (TSH and T4) measured at diagnosis, 6 and 18 months after diagnosis. Histopathological changes of the small intestine at diagnosis were documented using modified Marsh classification. Abnormal thyroid function tests were defined following laboratory normal values for TSH (0.7 − 5.7 mU/L) and T4 (8.0 − 20.8 pmol/L).
Results: 140 children with CD [mean age; 7.8 ± 4.01 years, 87 (62.1%) girls] were consecutively enrolled. Over the study period, ten (7.1%) patients with celiac disease had abnormal thyroid function. Out of those 10 patients, three (30%) had abnormal thyroid function at diagnosis and seven (70%) after 6 and 18 months post-diagnosis. Serum TtG IgA antibody titers at diagnosis and follow-ups had no correlation with thyroid abnormalities. However, there was a significant association between histopathological changes at diagnosis and prevalence of abnormal thyroid function (p <0.05; OR=4.8; 95% C.I=1.071−23.414).
Conclusions: Approximately 7% of children with CD had abnormal thyroid functions over 18 months of follow-up in Manitoba. The degree of villous atrophy at diagnosis was significantly associated with abnormal thyroid function. Several children with CD had abnormal thyroid function at follow-up with almost no clinical symptoms such as goiter. This observation highlights the importance of measuring thyroid function tests on annual bases.

CLINICAL PRACTICE

A67
PERFORMANCE OF COMPUTED TOMOGRAPHY IN MANITOBA
A.S. Dhillon[2], h. singh[1], I. Kirkpatrick[1]

1. University of Manitoba, Winnipeg, MB, Canada; 2. Gastroenterology , University of Manitoba, Winnipeg, MB, Canada

Background: Colorectal cancer (CRC) is the third most common cancer in the world and the second most common cause of cancer related deaths in North America. The incidence of CRC has been declining in the North America at least partly due to implementation of CRC screening aimed at detecting premalignant polyps from which CRC arise. Various screening tests are currently available including Fecal Occult Blood Test, Flexible Sigmoidoscopy, Computed Tomography Colonography (CTC) and Optical Colonoscopy.

CTC is a non-invasive modality which has become highly reliable in detecting CTC and large colon polyps. The US Preventive Services Task Force (USPTF) recently added CTC to the list of acceptable screening modalities.

In Manitoba, CTC is performed only in the Winnipeg Regional Health Authority (WHRA). It has been performed since 2009.
Aims: Assess performance of CTC in usual clinical practice in Canada: including indications for CTC, specialty of the ordering physicians, proportion of procedures that detect polyps, and colonic and extra-colonic findings and recommended follow up.
Methods: Retrospective review of CTCs reports within the WHRA. Follow-up imaging reports were also reviewed. Descriptive statistics are used to describe the data.
Results: In the year 2012, 195 CTC were performed. The majority (54%) were ordered by gastroenterologists, followed by surgeons (27%), family physicians (13%) and a few by general internists (0.05%). Incomplete colonoscopies were the major reason for ordering CTC (70%), while only (24%) were used as a primary screening modality. 17% of the CTCs reported colonic polyps and 52% extra-colonic lesions, of which 37% were recommended follow-up radiological imaging which occurred in less than half of those for whom it was recommended.
Conclusions: CTC is primarily being used in Manitoba by gastroenterologists for assessment of incomplete colonoscopies. A high proportion of CTCs in usual clinical practice report extra-colonic findings, a follow-up of which is recommended in a large portion. Reasons for lack of recommended radiological follow-up need to be studied and measures developed to ensure completion of the recommended follow-up. The data for other years is being reviewed and will also be presented.

A68
IMPACT OF VIDEO CAPSULE ENDOSCOPY ON THE MANAGEMENT OF CHILDREN WITH GASTROINTESTI-NAL DISORDERS
R. Ortiz[1], V. Deora[1], W. EL-MATARY[2]

1. Section of Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 2. Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada

Background: The impact of video capsule endoscopy (VCE) on the decision-making of clinical care for children with different gastrointestinal (GI) disorders is currently under-investigated.
Aims: The aim of this study was to examine how VCE impacts the management of children with different GI disorders in real world clinical practice
Methods: A retrospective chart review was performed for all consecutive children who under-went VCE at the Children's Hospital, Winnipeg, Manitoba from April 2012 to July 2016. Variables collected included any changes in diagnosis or treatment that took place based on VCE findings.
Results: A total of 41 VCE studies for 37 children (median age 13 years, IQR = 10.5 – 15.5 years) with different GI disorders were included. There were changes in the diagnoses of 6 (15%) participants based on their VCE findings. Diagnostic categories included three children with inflammatory bowel disease (IBD), two participants with small bowel polyposis, and one with protein losing enteropathy secondary to primary intestinal lymphangiectasia. IBD was ruled out in 8 studies (20%) based on normal VCE. There were 12 studies (29%) where VCE resulted in meaningful changes in management including major changes in participants' treatment. VCE findings were discordant with findings from other small bowel imaging techniques in 15 (37%) studies.
Conclusions: VCE is a useful tool with major impacts on clinical management of children with different GI disorders.

A69
PATIENT WAIT TIME RECALL ACURRACY FOR GASTROENTEROLOGY SPECIALTY CONSULTATION IN NOVA SCOTIA
H. Mathias, C. Heisler, J. Jones

QEII Health Sciences Centre, Halifax, NS, Canada

Background: Inflammatory Bowel Disease (IBD) is a chronic disease with lifelong health, social, and economic burden. The province of Nova Scotia (NS) has the highest age-adjusted incidence and prevalence rates of IBD in Canada, with Canada having the highest

prevalence rates of IBD in the world. The Canadian Association of Gastroenterology guidelines suggest wait times between 2 weeks and 2 months for those with active IBD symptoms. Despite these guidelines, the 2015 audit of the NS Health Authority (Central Zone) showed 50% of IBD referrals were seen within 81 days and 90% of referrals were seen in 732 years. Long wait times can lead to increased anxiety, decreased quality of life, and reduction in patient satisfaction and overall health. Estimating wait times is complex but essential in order to evaluate access to specialty care.
Aims: 1) To determine whether patients referred to GI specialty services in NS can accurately estimate the length of time between GP referral and first GI specialty appointment; 2) To examine demographic, disease-related, and system factors which may influence the accuracy of patient wait time estimates.
Methods: Questionnaires were distributed to patients following their appointment with a luminal GI or IBD nurse practitioner. Patients were asked to estimate their wait time for seeing a GI specialist. They were also asked to report on factors that could influence their wait time recall (geographic locale, age, employment status, completed education, disease severity, and relevant comorbidities). Completed questionnaires were returned to the on-site research associate, who then conducted retrospective chart reviews to validate the patients' responses.
Results: A total of 29 patients were enrolled as of October 2016. Twenty (69%) patients were female, with a mean age of 49 years (SD=20.95 years). When patients were asked to estimate their wait time between their referral and seeing a GI specialist, they reported an average of 36 weeks. Following retrospective chart reviews, the patient estimates were shown to be conservative. In reality, records showed the average patient waited 40 weeks from the time the referral was sent to seeing a GI specialist. A Spearman's correlation was used to determine the relationship between patient estimates and referral dates. There was a strong positive correlation between patient estimates and referral dates (r_s=0.680, N=29, p<0.001).
Conclusions: This study is the first of its kind to look at patient recall of wait times for gastroenterology in NS. The initial pilot data highlights the reality of excessive wait times in NS for patients seeking care from a GI specialist. Future research will look at access to GI care using a healthcare systems mapping approach to better inform clinical care pathways in the province.

A70
ACCURACY OF IBD PATIENT WAIT TIME ESTIMATES BY GASTROENTEROLOGISTS IN NOVA SCOTIA
H. Mathias, C. Heisler, J. Jones

QEII Health Sciences Centre, Halifax, NS, Canada

Background: Inflammatory Bowel Disease (IBD) is a chronic disease with profound health and socioeconomic burden. Approximately 1 in 150 Canadians live with IBD: the highest prevalence rate in the world. Within Canada, Nova Scotia has the highest age-adjusted incidence and prevalence rates of IBD. High levels of need have translated into prolonged wait times: one of the main indicators of healthcare access. Extended wait time can negatively impact physical and mental health outcomes, as well as patient satisfaction of care. The Canadian Association of Gastroenterology has recommended GI wait times between 2 weeks and 2 months. However, the 2015 audit of the Nova Scotia Health Authority (NSHA) Central Zone shows referred patients are waiting over 2 years to see a specialist.
Aims: 1) To determine whether physicians can accurately estimate the length of time that patients have waited between the referral and intake specialist appointment; 2) To examine physician-related factors that may influence the accuracy of wait time estimation.
Methods: Luminal gastroenterologists and IBD nurse practitioners practicing within the NHSA Central Zone were administered questionnaires designed to measure practice, practitioner, and systems factors which could influence accuracy of physician wait time estimate. Specialists were asked to estimate the wait time for each of their patients seen that day, based on the level of assigned triage urgency. A retrospective chart review was conducted to verify referral date and wait time duration.
Results: A total of six specialists were enrolled as of October 2016. Four (67%) participants were male, with a mean age of 51.60 years (SD=11.06 years). All participants reported working in an academic practice with an existing triage process. Five physicians reported using a central triage system for referrals, while one physician completed personal reviews of referrals. When physicians were asked to estimate the wait time for patients between the referral and seeing specialist, they estimated an average of 32 weeks. According to patient health records, patients waited an average of 49 weeks. When comparing physician-estimated wait times to referral dates a moderate positive association was found (r_s=0.542, N=6, p <0.001).
Conclusions: Initial results demonstrate a disconnect between perceived patient wait times by specialists and true wait times. These findings support previous research which has suggested, despite increased levels of healthcare expenditure, wait times for medically necessary treatment have not improved. Additional recruitment is ongoing and will allow further analysis of practitioner and system-related factors that effect physician estimates of patient wait times.

A71
INFORMED CONSENT AND BOOKING METHOD IN COLONOSCOPY
AUTHORS: JULIA MORRISON, ALISON HARDING, STACEY WILLIAMS
J.B. Morrison[1], A. Harding[2], S. Williams[1]

1. Nova Scotia Health Authority, Halifax, NS, Canada; 2. Digestive Disease and Endoscopy, QEII Health Science Centre, Bedford, NS, Canada

Background: Within the Nova Scotia Health Authority, patients are booked for colonoscopy via various routes. Many are seen for consultation in clinic and the informed consent discussion is held with their physician. Patients are also booked directly for colonoscopy ("direct access") based on information provided in the original referral without having been seen by their physician. Recently, a third route to booking has been introduced which involves consultation in person or via telephone with a registered nurse as part of the Nova Scotia Provincial Colon Cancer Screening Program. This evaluation includes education about the procedure and the bowel preparation. There have been concerns raised as to whether patients booked via direct access have an adequate level of pre-procedural education and are able to provide true informed consent. It is not clear whether patients who have had a pre-procedural consultation with either a physician or nurse are better equipped to provide informed consent compared to those booked direct to procedure.
Aims: This study aims to evaluate the levels of informed consent for colonoscopy patients depending on the method by which they were booked for their scope.
Methods: This study is questionnaire-based with surveys being administered to colonoscopy patients at two sites within the NSHA. Surveys are provided to all patients seen for outpatient colonoscopy outside the context of a clinical trial. Patients who have had previous colonoscopy were excluded. The questionnaire was validated based on the input of several health care practitioners and feedback from patients.
Results: To date, there have been 17 responses from the pilot study, and 29 responses to the finalized version. Of these, 18 responses were first-time colonoscopy patients and therefore relevant to this study. Data acquisition is ongoing. Thus far, 6 patients (33.3%) were booked after seeing a physician, 7 patients (38.9%) after being screened by a nurse, and 5 (27.8%) were booked direct to procedure. All patients reported being either satisfied (61.1%) or very satisfied (38.9%) with their level of understanding prior to their procedure. All patients stated that they understood the benefits and risks of colonoscopy prior to their procedure. All patients stated that they felt adequately prepared about what was happening to them.
Conclusions: his pilot project confirms that patient satisfaction levels with the pre-procedural education they receive before colonoscopy are high. Greater numbers of survey responses will help determine if there are subtle differences in patient satisfaction dependent on the method of booking. This study implies that nurse-driven pre-screening results in similar patient satisfaction levels as the traditional approaches to booking.

A72
BUILDING A SMARTPHONE APPLICATION FOR COLONOSCOPY PREPARATION USING A PATIENT-CENTERED APPROACH
M.J. Sewitch[1], C. Fallone[2], P. Ghali[2], C.A. Soulellis[2], P. Wong[2]

1. McGill University and the Research Institute of the McGill University Health Centre, Montreal, QC, Canada; 2. McGill University and the McGill University Health Centre, Montreal, QC, Canada

Background: Smartphones are daily use instruments that can serve as a powerful reminders to help individuals adhere to colonoscopy attendance and bowel preparation instructions.
Aims: The objective of this qualitative study was to better understand users' preferences for the content and features of a smartphone application that supports colonoscopy preparation.
Methods: Individuals aged 18 or over, English- or French-speaking, with recent colonoscopy and without colorectal cancer were invited to participate in one focus group session at the McGill University Health Centre. Participants were asked to discuss the kinds of Mobile health support tools they might use to help them carry out colonoscopy, the informational content needed to follow through with preparing for colonoscopy, and the information format that would make it easy to use the smartphone application. Discussions were 60-90 minutes, conducted by a trained facilitator using a standardized approach, and audiotaped for subsequent analysis.
Results: Nine individuals (2 women, 7 men) attended one of two focus groups. Seven themes were derived from the discussions: colonoscopy preparation, reminders & alerts, application features, information and instructions, data to input, ability to communicate with endoscopy staff, videos. Participants in both focus groups understood the benefits of a smartphone application that included: 1) it ensures patients do the right thing at the right time; 2) it eliminates conflicting and/or fear-inducing information; 3) it can be tailored to individuals' needs and expectations.
Conclusions: Focus groups were conducted to ensure that the smartphone application addresses users' needs and expectations for information to carry out the colonoscopy. Findings are being used to develop a smartphone application that supports patients prepare for and attend colonoscopy.

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CLINICAL PRACTICE

University and the Research Institute of the McGill University Health Centre

A73
SURVIVAL PREDICTORS IN PATIENTS UNDERGOING LIVER TRANSPLANT FOR NON-ALCOHOLIC STEATO-HEPATITIS: A POPULATION-BASED COHORT STUDY

C.F. Rueda-Clausen, F.S. Cardoso, N. Kneteman, C.D. Karvellas, S. Veldhuyzen van Zanten

University of Alberta, Edmonton, AB, Canada

Background: Non-alcoholic steatohepatitis is a recognized cause of cirrhosis affecting 12% of word population. The proportion of orthotopic liver transplants (OLT) for NASH cirrhosis increased 8-fold (1.2 to 9.7%) between 2001-2009 and is anticipated to become the leading indication for OLT in the next 20 years. Surprisingly, disease-specific indications and mortality predictors for OLT in NASH are lacking.

Aims: To develop a 5-years mortality prediction model applicable during the pre-surgical assessment of patients with NASH cirrhosis eligible for OLT.

Methods: This single center retrospective cohort study included subjects undergoing OLT at the University of Alberta between 2002-2012 for NASH/cryptogenic cirrhosis. Clinical information was extracted from a dedicated computerized database (OTTR) and audited. The primary outcome was all-cause mortality at 5 years. Prediction models were constructed using Cox proportional hazard regression techniques. Model assumptions and discrimination capacity were tested. Ethics approval was obtained from the local ethics board.

Results: Of 524 OLT patients, NASH cirrhosis was the main indication in 41 (8%) patients (NASH-OLT). Compared to those receiving an OLT for other indications, the NASH-OLT cohort had comparable follow-up times (2.7 vs. 3.2y. p=0.4), 5yrs-mortality rates (11/41; 27% vs. 106/483; 22%, p=0.4) and MELD scores (18 vs. 20, p=0.1); a greater BMI (28 vs. 25 p=0.0006), higher prevalence of diabetes (39 vs. 20%, p=0.004) and renal insufficiency (32 vs. 16%, p=0.004), donors with lower Donor Risk Indexes (1.37 vs. 1.49, p=0.05) longer hospital stays (34 vs. 30d, p=0.01) and received two times more blood products during transplant (p<0.03).

Previously published mortality estimation tools had poor discriminatory capacity in the NASH-OLT cohort: Charlson index for OLT [C-index = 0.54, p=0.6], United Network for Organ Sharing (UNOS) [C-index = 0.58, p=0.4] and Cardoso 2014 [C-index = 0.43, p=0.9].

We developed a 5yr mortality prediction model that included: extreme (<600 or >1200) **modified-BMI** (BMI kg/m^2 * albumin g/L) [coef=1.62; p=0.02], pre-operative **INR** [coef=-2.76; p=0.02) and receiving a **non-local transplant** [coef=2.49; p=0.02). This new model had better mortality prediction capacity than any previously reported model (X^2 = 16.4, C-index=0.84, p=0.0008).

Conclusions: Previously validated survival predictors for OLT perform very poorly in the NASH-OLT population. In this small cohort, 3 simple preoperative parameters (**modified BMI, INR and receiving a non-local transplant**) can be used to predict 5-yrs mortality in NASH-OLT recipients with excellent discriminatory capacity. Further validation of the proposed model needs to be done in a larger cohort.

A74
THE IMPACT OF SOFOSBUVIR-BASED THERAPY ON RENAL FUNCTION IN HEPATITIS C VIRUS PATIENTS WITH ADVANCED LIVER DISEASE

B.S. Thomas[5], B. Aljudaibi[2], P. Adams[4], P. Marotta[3], M. Levstik[1], K. Qumosani[6]

1. London Health Sciences Centre, London, ON, Canada; 2. Gastroenterology , London Health Sciences Centre , London, ON, Canada; 3. London heatlh sciences Center, University of Western Ontario, London, ON, Canada; 4. Gastroenterology, University Hospital, London, ON, Canada; 5. Medicine, Western University, London, ON, Canada; 6. London Health Sciences Centre, London, ON, Canada

Background: Management of Hepatitis C virus (HCV) in chronic liver disease patients has been evolving over the past decade with the adoption of newer treatment strategies given the tolerability of these agents. HCV patients treated with Sofosbuvir-based therapy have seen hepatic recovery albeit the degree and specific patient population in which this occurs is undetermined. It can be hypothesized that renal function would improve post treatment given hepatic recovery and reduced diuretic use. The effect of Sofosbuvir-based therapy on renal function in the advanced liver disease population currently remains unclear.

Aims: To assess the effect of Sofosbuvir-based therapy on renal function amongst HCV patients undergoing liver transplant assessment.

Methods: Analysis of prospectively collected data of a cohort of HCV patients who have undergone liver transplant assessment at London Health Sciences Centre from January 2014 to January 2015. Patients who had commenced or completed Sofosbuvir-based therapy were selected. Patient outcomes included sustained virologic response at 12 weeks (SVR12), glomerular filtration rate (GFR) pre and post treatment, MELD-Na score, Child-Pugh score and liver transplant status were analyzed.

Results: Interim analysis was performed on 44 patients. A total of 22 patients (52%), all genotype 1, had commenced Sofosbuvir-based therapy with all patients who completed therapy, 19/19 (100%), acheiving SVR12. The mean MELD-Na score of these patients was 20.2 and mean Child-Pugh score was 8.4. 3/22 patients on therapy died, 1 from small bowel

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ischemia after completing therapy and 2 deaths prior to completion of therapy, both patients died from sepsis. 9/19 who achieved SVR12 had confirmed HCC, 3/19 have underwent orthotopic liver transplantation and were excluded from GFR evaluation. 16 patients Pre/Post Treatment GFR were assessed. The mean GFR pre-treatment was 88.6 ml/min/1.73m2and the GFR post treatment mean was 79.5 ml/min/1.73 m2, there was no significant difference between the two groups (P=0.18). None of the patients discontinued therapy.

Conclusions: In this preliminary analysis, there was no clear difference in GFR post treatment with Sofosbuvir-based therapies. Sofosbuvir-based therapies were quite efficacious in this small sample size of the advanced liver disease population. Larger studies are needed to further evaluate the effect of Sofosbuvir-based therapy on renal function in patients with advanced liver disease.

HEPATOBILIARY NEOPLASIA

Poster of Distinction

A75
TARGETING THE WARBURG EFFECT IN HEPATOCELLULAR CARCINOMA CELLS

S. Cassim[1], V. Raymond[3], M. Bilodeau[2]

1. CRCHUM, Montreal, QC, Canada; 2. Liver Unit, CRCHUM, Montréal, QC, Canada; 3. CRCHUM, Montreal, QC, Canada

Background: The avid consumption of glucose (Glu) with concomitant lactate production by malignant cells is called the Warburg effect (WE). As most invasive tumours harbour this feature, this has proven of great clinical importance in detecting malignancies with PET scans. Unfortunately, in the liver, the detection of tumors is often compromised by the strong intrinsic Glu metabolic activity. Understanding the manner by which hepatocellular carcinoma (HCC) cells use Glu to proliferate is essential if we want to bypass the aforementionned difficulty.

Aims: Recently, targeting molecular mechanisms involved in the WE such as lactate dehydrogenase (LDH) has been advocated as a very promising anti-cancer target. We hypothesized that the modulation of LDH which catalyzes the conversion of pyruvate to lactate might have an impact on HCC cell tumorigenicity, since the production of lactate has been shown to increase tumor invasion.

Methods: We generated a mouse hepatoma cell line Dt81Hepa1-6 (Dt) derived from Hepa1-6 (H1-6) cells that displays greater tumorigenicity *in vivo*. We hypothesized that this increased tumorigenicity involved the WE. Cells were cultured in 25mM Glu over a period of

24-48h. Glu uptake was assessed using a fluorescent Glu analog, 2-NBDG. mRNA and metabolite quantification were respectively measured by qPCR and HPLC. Aerobic glycolysis was inhibited using increasing doses of sodium oxamate (SODOX), a classic inhibitor of LDH, to reduce lactate production. LDH activity was measured by the Biochemical core facility of CRCHUM. MTT assay was used to test the dose-response effects of SODOX on cell viability. Cell Doubling Time (CDT) was evaluated every 24h for 72h with SODOX (100 mM).

Results: Dt showed an increased ability to uptake Glu in low extracellular Glu in comparison with H1-6 (3±0.3 vs 1.4±0.1DO/µg prot, P<0.01). Increasing the extracellular Glu concentration led to an increase in Glu uptake only in Dt cells (P<0.001). qPCR and metabolite analysis showed that Dt displayed a higher glycolytic rate than H1-6, with greater ATP production (P<0.001). We then investigated the effect of SODOX on these cells. First, LDH acticvity was reduced in a dose-response manner after 24h with SODOX (100mM, P<0.01). MTT revealed that SODOX dose-dependently decreased cell viability of both H1-6 and Dt cells but that Dt were significantly more resistant at 100mM SODOX (43±1.5 *vs* 55±2.6, P<0.01). Finally, CDT revealed that SODOX significantly slowed Dt proliferation; this effect was even more pronounced on H1-6 (P<0.001).

Conclusions: These results suggest that the WE is effective in HCC cells and that increased tumorigenesis is associated with metabolic changes in glucose metabolism that favor ATP production. The WE represents a potentially remarkable new target to treat HCC. Our preliminary results suggest that decreasing LDH activity is one of the ways to achieve this goal.

A76
SINGLE OPERATOR PANCREATOSCOPY IN THE EVALUATION OF PANCREATIC NEOPLASMS: A CASE SERIES

T. Hansen[2], D.C. Moffatt[1]

1. Department of Medicine, University of Manitoba, Winnipeg, MB, Canada; 2. University of Manitoba, Winnipeg, MB, Canada

Background: Pancreatic neoplasms are most commonly diagnosed by endoscopic ultrasound (EUS), computed tomography (CT) scan and magnetic resonance cholangiopancreatography (MRCP). However, all these imaging modalities have limitations in their ability to diagnose small main duct intraductal papillary mucinous neoplasm (MD-IPMN) or early pancreatic neoplasms. Single operator pancreatoscopy (SOP) is a new modality to diagnose pancreatic neoplasia that is gaining popularity as case series and a retrospective single-center study have been published showing favorable efficacy.

Aims: This case-series was performed to evaluate our

centre's experience with SOP.

Methods: Patients who underwent SOP using the Spy-Glass Direct Visualization System (Boston Scientific, Natick, Mass) between June 2013 and July 2016 were identified. Main outcome measurements included efficacy and safety of pancreatoscopy.

Results: During the study period, 32 patients underwent SOP for evaluation of suspected IPMN or pancreatic duct neoplasia. Prior to SOP, all patients had either an EUS or MRCP. Twenty-two (68.8%) patients had an EUS while 29 (90.6%) had MRCPs with indeterminate features for MD-IPMN or pancreatic neoplasia. Twenty-one (65.6%) patients were female and the mean age was 64.9 $\pm$ 12.2 years at the time of procedure. Technical failure occurred in 6 (18.8%) patients. Samplings through biopsy or brushing, were performed in 8 (30.7%) of patients.

Overall, 13 (40.6%) patients had a pancreatic duct neoplasia, MD-IPMN, side branch IPMN or combined IPMN. In one patient, the pancreatoscope could not be introduced into the pancreatic duct.

High-risk patients (n=8) were considered to be individuals who were diagnosed with MD-IPMN with or without side branch involvement. One patient is currently awaiting surgery. Five patients (71.4%) were diagnosed with adenocarcinoma and 1 (14.2%) was diagnosed with a dysplastic cyst via surgical specimens. The last patient did not undergo surgery and is being followed with serial imaging that has yet to suggest malignancy. Of the 19 patients with a negative pancreatoscopy for IPMN, 0 have developed an IPMN or pancreatic neoplasm in mean follow up of 1.5 years (SD 0.67). In our series, if pancreatic duct cannulation is successful, SOP has a diagnostic accuracy, sensitivity and specificity of 92.3%, 100% and 90.4% respectively for determining high risk IPMN/pancreatic cancers at time of ERCP.

Complications occurred in 2 (7.6%) patients, 1 (3.8%) mild post-ERCP pancreatitis and 1 (3.8%) contained perforation related to sphincterotomy. Prophylactic pancreatic stents were placed in 27 (84.4%) patients and rectal indomethacin was used in 27 (84.4%) patients.

Conclusions: Our case-series suggests that SOP to evaluate for pancreatic neoplasia is safe and adds important information in the evaluation of pancreatic duct neoplasm that are not definitively diagnosed by EUS or MRCP.

Funding Agencies: None

A77

TRACKING WAIT TIMES AND OUTCOMES OF RADIOFREQUENCY ABLATION IN PATIENTS WITH HEPATOCELLULAR CARCINOMA: A QUALITY IMPROVEMENT INITIATIVE

O. Ahmed[4], M. Brahmania[5], M. Kelley[1], M. Kowgier[7], K. Khalili[6], R. Beecroft[4], E. Renner[4], D. Wong[4], H. Shah[4], J. Feld[3], H.L. Janssen[2], M. Sherman[4]

1. Queen's University, Kingston, ON, Canada; 2. Liver Clinic, Toronto Western Hospital, Toronto, ON, Canada; 3. Medicine, University Health Network University of Toronto, Toronto, ON, Canada; 4. University of Toronto, Toronto, ON, Canada; 5. Gastroenterology, University of Toronto, Toronto, ON, Canada; 6. University of Toronto, Toronto, ON, Canada; 7. University of Toronto, Toronto, ON, Canada

Background: Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third leading cause of cancer death worldwide.[1] Radiofrequency ablation (RFA) is the current recommended curative treatment option for non-surgical patients with early stage disease.[2] A recent report by Cancer Care Ontario shows the expected number of HCC cases requiring RFA will grow at a greater rate than RFA capacity estimates.[3] Currently, no recommended wait times exist for HCC.

Aims: In this study, we look at wait times for patients with HCC undergoing RFA and the development of adverse events. We also aimed to identify system gaps where quality improvement measures can be implemented.

Methods: This was a retrospective study conducted at the University Health Network looking at all patients diagnosed with HCC and referred for RFA between January 2010 until December 2013. Data on demographics and co-morbidities were obtained along with biochemistry, hematology and virology values. The time from diagnosis of HCC to presentation at Tumor Board rounds and the time from Tumor Board rounds to treatment were documented. Outcomes defined a priori were all-cause death and all-cause liver transplantation. Statistical analysis was performed with a help of a statistician. The study was approved by the UHN Research Ethics Board.

Results: 225 patients were included in the study. 72.4% percent were male and the median age was 63 years (SD+/-10.4). Median tumor size at diagnosis was 22 mm (SD +/-8.3), mean MELD was 8.7 (Range=7.2-11.3) and 55.6% had Barcelona stage 0. The cause of liver disease was viral hepatitis in 73% (Hepatitis B and C). The median time from HCC diagnosis to RFA treatment was 97 days (IQR 75-139). In multivariable analysis wait times per 30 days was associated with an increased risk of death (HR=1.16; 95% CI 1.08-1.25; p=<0.001).

Conclusions: Our study demonstrates increasing wait times for RFA in patients with HCC is associated with an increased risk of death. The high wait times along with increasing requirements for RFA will place a heavy burden on already limited RFA resources. By identifying potential barriers, we hope to develop a comprehensive strategy to reduce wait times and allocate resources for future RFA treatment at UHN.

Funding Agencies: None

A78
DIRECT-ACTING ANTIVIRALS ARE NOT ASSOCIATED WITH EARLY TUMOR RECURRENCE AFTER CURATIVE TREATMENTS IN HEPATITIS C-RELATED HEPATOCELLULAR CARCINOMA

Y. Chan, S. Macleannan, J. Wong, E. Dixon, C.S. Coffin, M. Swain, K.W. Burak

University of Calgary, Calgary, AB, Canada

Background: Interferon (IFN)-free regimens using new direct acting antivirals (DAA) have revolutionized the treatment of chronic hepatitis C (HCV) infection and demonstrate a sustained viral response (SVR) of over 90%. Recent publications have suggested an association between DAA therapy and early hepatocellular carcinoma (HCC) recurrence raising concerns about their safety.
Aims: Therefore, we conducted a retrospective study to investigate the impact of DAA initiation on early tumor recurrence after curative treatments in hepatitis C-related HCC.
Methods: From a combined surgery (January 2008-December 2015) and interventional radiology (January 2012-December 2015) database, 103 unique HCV infected patients with primary or recurrent HCC were identified. After excluding patients who failed to achieve complete radiological response (n=19), received transarterial chemoembolization (TACE) (n=17), received anti-viral therapy prior to HCC diagnosis or therapy (n=14), were lost to follow-up (n=7), died within 3 months of therapy (n=6), and received interferon containing DAA regimens (n=3), 37 HCV infected patients with complete response to their curative HCC therapy for at least 3 months, including 20 who subsequently received DAA therapy, were identified.
Results: With the exception of age (Control 64 years vs DAA 58 years, p<0.0133), baseline gender, total bilirubin, albumin, MELD score, alpha-feto protein levels, percentage of patients with primary HCC, and total tumor volume did not differ between the control and DAA group. Both groups were predominately infected with genotype 1 (Control 86% vs DAA 75%), while the remaining patients in the control and DAA group were infected with genotype 2 and 3, respectively. The overall median clinical remission period for the entire cohort was 26 months. Median interval between HCC treatment and the start of DAA treatment was 12.5 months, but ranged from 2 to 42 months. During a median observation time of 8 months that ranged from 2 to 20 month in the DAA group, 5 (25%) cases of recurrence were observed. Kaplan-Meier analysis showed improved probability of staying in clinical remission in the DAA group (<0.0001), even in subgroup analysis limiting the interval between HCC treatment and the start of antiviral therapy to less than 2 years. BCLC staging of recurrent disease was similar in both groups. (BCLC 0/A: Control 64% vs DAA 60%; BCLC B/C: Control 28% vs DAA 40%).
Conclusions: In this preliminary analysis, DAA treat-ment after curative HCC therapy was not associated with early recurrence. Future studies using a larger cohort and longer follow up period is needed to confirm these findings.

HORMONES, TRANSMITTERS, GROWTH FACTORS

A79
CHARACTERIZATION OF VIPOMA-MEDIATED INTESTINAL EPITHELIAL CELL SECRETION

G. Leung, A. Elkadri, R. Murchie, C.E. Thoeni, A. Muise

The Hospital for Sick Children, Toronto, ON, Canada

Background: A 3-year old female with a history of chronic watery diarrhea was diagnosed with a suprarenal vasoactive intestinal peptide (VIP)-secreting neuroblastoma ('VIPoma'). Neuroblastomas are one of the most common malignancies in children aged 0-5 years, while VIP is a gastrointestinal neuropeptide that can act upon epithelial cells, neurons, and immune cells. Secretory diarrhea and hypokalemia are classic symptoms of a VIPoma, however the precise mechanism remains unknown.
Aims: To define in the pathway of VIP-mediated ion secretion using intestinal organoids.
Methods: Prior to diagnosis, supplemental KCl was given (3 mmol/kg) to address the low potassium. Following this, serum and stool samples were collected daily for 8 days to measure electrolyte (Na^+, K^+, Cl^-) levels and stool osmolal gap. Intestinal organoids were cultured from a sigmoid colon biopsy of a non-inflamed control patient. Organoids were labelled with calcein AM dye and assessed every 12 min for 1-2 hrs by microscopy, with luminal ion secretion assessed by the increase in organoid size over time.
Results: The patient's serum potassium levels were consistently below the normal range and the stool osmolal gap was <50 mmol/L (indicative of secretory diarrhea). Supplemental KCl increased [K^+] in the blood but failed to improve the diarrhea. VIP levels at the time of diagnosis were 7.3X above the upper limit of the normal range. To test this in vitro, VIP was applied to intestinal organoids in vitro; concentrations above the normal range (10^{-10} and 10^{-9} M) but not within the normal limits (10^{-11} M) induced a swelling response in normal human enteroids. This swelling was completely abolished in isotonic K^+-deficient buffer, and dependent on Ca^+ for maximal effect. The use of the non-specific potassium channel blocker tetraethylammonium chloride (TEA; 1-10 mM) did not significantly reduce the organoid swelling response when applied 30 min prior to VIP stimulation.
Conclusions: Increased intake of potassium improved serum [K^+] levels but did not relieve the diarrheal symptoms. A significant swelling response occurs in

intestinal organoids when stimulated with VIP in the absence of a neural or immune network. More studies are needed to further characterize the signalling pathway and ion channels through which this secretory response occurs in the intestinal epithelium.

IMMUNOLOGY AND INFLAMMATORY BOWEL DISEASE

Poster of Distinction

A80
ENDOSCOPIC HEALING WITH USTEKINUMAB IN CROHN'S DISEASE: THE UNITI ENDOSCOPY SUB-STUDY

B.G. Feagan[1], W. Sandborn[3], C. Gasink[4], D. Chan[4], Y. Lang[5], P. Pollack[4], S. Hanauer[2], D. Wolf[6], D. Jacobstein[4], J. Johanns[7], P. Szapary[4], P. Rutgeerts[8]

1. Robarts Clinical Trials Inc, London, ON, Canada; 2. University of Chicago, Chicago, IL; 3. University of California San Diego, La Jolla, CA; 4. Janssen Research & Development, LLC, Spring House, PA; 5. Janssen Research & Development, LLC, Spring House, PA; 6. Atlanta Gastroenterology Associates, Atlanta, GA; 7. Janssen Research & Development, LLC, Spring House, PA; 8. University Hospital Gasthuisberg, Leuven, Belgium

Aims: To evaluate endoscopic healing in the ustekinumab (UST) induction (UNITI-1&2) & maintenance (IM-UNITI) phase 3 studies.
Methods: Substudy patients (pts) had colonoscopies at baseline (UNITI Wk0), then 8 & 52 weeks later (IM-UNITI Wk44). Video-endoscopies were centrally read by a single blinded reader for ulcerations & SES-CD. In UNITI, pts received one IV dose (UST 130mg, UST ~6mg/kg, or PBO). Pts with clinical response [CR] (CDAI drop≥100) in UNITI were re-randomized to subcutaneous (SC) PBO or UST 90mg (q12w or q8w) [primary randomized IM-UNITI population]. Non-randomized pts were added to the pooled IM-UNITI population: UST IV non-responders - SC UST 90mg, then SC UST 90mg q8w if in CR 8wks later; PBO IV non-responders - UST IV 130mg, then SC UST 90mg q12w if in CR 8wks later; PBO induction responders - PBO throughout. Pts required SES-CD ≥3 at UNITI Wk0 to be included. Primary outcome: Change in SES-CD at UNITI Wk8 (combined UST vs PBO). IM-UNITI Wk44 efficacy was evaluated for both the IM-UNITI populations.
Results: At wk8, UST reduced SES-CD significantly more vs PBO. Results were similar across UST doses, studies, & other endpoints (Table 1a). At IM-UNITI Wk44, in the primary randomized IM-UNITI population trends favoured UST vs PBO maintenance (especially UST 90mg q8w) but small sample sizes (UST n=46; PBO n=24) limited conclusions. In the post-hoc pooled IM-UNITI population (Table 1b), trends supporting UST

maintenance were favourable, especially 90mg q8w.
Conclusions: The endoscopy substudy primary endpoint was met: One IV UST dose significantly reduced SES-CD vs PBO, as early as Wk8. More pts receiving UST maintenance achieved wk44 endpoints vs PBO. These data support efficacy of UST in inducing & maintaining endoscopic healing in CD.

(Table 1a) Week 8 Results from UNITI-1/2

	PBO (N=97)	UST (N=155)
SES-CD Change from BL, mean (SD)§	-0.7 (4.97)	-2.8 (8.10)*
Clinically meaningful endoscopic improvement1	29.9%	47.7%*
Endoscopic Response2	13.4%	20.6%
Endoscopic Remission3	4.1%	7.7%
Mucosal Healing4	4.1%	9.0%

(Table 1b) IM-UNITI Week 44 Results

	PBO (N=51)	90mg q12w (N=47)	90mg q8w (N=74)
SES-CD Change from BL, mean (SD)	-2.0 (5.35)	-1.5 (4.22)	-3.8 (6.02)
Clinically meaningful endoscopic improvement1	27.5%	29.8%	48.6%*
Endoscopic Response2	4.2%	5.9%	24.1%*
Endoscopic Remission3	9.8%	12.8%	20.3%
Mucosal Healing4	9.8%	12.8%	21.6%

*P <0.05 §Primary endpoint
1SES-CD reduction ≥3 from UNITI BL
2SES-CD reduction ≥50% from UNITI BL
3SES-CD ≤2
4No ulcerations

Poster of Distinction

A81
POOLED SAFETY ANALYSIS FROM THE USTEKINUMAB CROHN'S DISEASE AND PSORIATIC DISEASES PHASE 2 AND 3 TRIALS

B.G. Feagan[2], B.E. Sands[3], W. de Villiers[4], E. Ott[5], C. Gasink[5], Y. Lang[6], P. Szapary[7], D. Jacobstein[8], S. Ghosh[1]

1. Gastrointestinal Section, Imperial College london, London, United Kingdom; 2. Robarts Clinical Trials Inc, London, ON, Canada; 3. Icahn School of Medicine at Mt Sinai, New York, NY; 4. U of Stellenbosch, Stellenbosch, South Africa; 5. Janssen Research & Development, LLC, Spring House, PA; 6. Janssen Research & Development, LLC, Spring House, PA; 7. Janssen Research & Development, LLC, Spring House, PA; 8. Janssen Research & Development, LLC, Spring House, PA

Background: Ustekinumab (UST) is well-established

in psoriasis (PsO) & psoriatic arthritis (PsA) with up to 5 years safety data from psoriasis clinical trials with 3117 pts & 8998 patient years (PY). However, limited safety data have been presented in Crohn's disease (CD). In CD, Phase 2/3 data show that UST is safe & effective.

Aims: Here we present CD safety data & compare it to safety from psoriatic diseases.

Methods: Safety data from 5 CD (2 Ph2/3Ph3) trials were analyzed with the previously reported PsO (1 Ph2/3Ph3) & PsA (1 Ph2/2 Ph3) trials. Psoriatic pts received UST 45 or 90mg SC; Ph3 CD pts received one IV UST dose (130mg or ~6 mg/kg) then 90mg SC q8w or q12w. Permitted concurrent treatments differed by indication: PsO – none; PsA – methotrexate; CD - immunosuppressives & corticosteroids. All pts who received ≥1 dose of UST were included. Outcomes are presented as events per 100 PY.

Results: In the PBO-control period, 3636 pts received UST (1582 PsO, 692 PsA & 1362 CD). Treated pts with ≥1 reported event PBO vs UST in pooled indications (events/100 PY): AEs 556.1 vs 594.3; SAEs 19.5 vs16.4; infections 135.8 vs138.1; serious infections 2.9 vs 3.3; MACE 0.26 vs 0.60; malignancies 0.26 vs 0.12; deaths 0 vs 0.12. Through 1 year, 5884 pts received UST (3117 PsO, 1018 PsA, & 1749 CD) over 4521 PY. Rates of AEs, SAEs, & infections were similar between UST & PBO (Table) across all groups. Event rates in the combined CD studies were also similar between groups with more frequent overall AEs, & infections in CD pts.

Conclusions: UST has a favorable safety profile in CD with one IV induction dose up to 6mg/kg & SC maintenance up to 90mg q8wks. Evaluation of the CD experience did not alter the safety profile of UST established in pts with psoriatic disease treated up to 5 years.

Key safety events through 1yr

	CD		PsA		PsO		Pooled	
	PBO	UST [b]	PBO	UST	PBO	UST	PBO	UST
Pts treated/PY of F/u	943/347	1749/1106	379/145	1018/850	733/182	3117/2566	2055/674	5884/4521
Pts D/c due to AE(%)	4.8	6.2	5.8	3.0	2.3	2.8	4.1	3.8
Events per 100 PY								
AE/SAE	712.2/43.8	641.6/35.4	343.4/13.8	254.2/9.3	414.8/8.8	390.6/8.8	552.4/27.9	426.4/15.4
Infection/Serious Infection [a]	145.1/6.9	134/6.4	102.8/0.7	78.0/0.9	120.7/1.7	137.4/1.4	129.4/4.2	125.4/2.5
MACE	0.00	0.09 [c]	0.69	0.71	0.55	0.55	0.30	0.46
Death	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.11
Malignancy (exc NMSC)	0.00	0.36d	0.00	0.12	0.55	0.43	0.15	0.35

aAssessed by investigator, b incl UST 1, 3, 4.5, or 6mg/kg IV; 130mg IV, SC 90mg; c1 MACE: subarachnoid hemorrhage due to aneurysm rupture; d4 events in 3 pts: 1 multiple myeloma, 1 adenocarcinoma & incidental carcinoid tumor; 1 prostate cancer

Poster of Distinction

A82
5-ASA & CHEMOPREVENTION IN IBD: A POPULATION-BASED ANALYSIS

A. Dorreen[1], S. Stewart[1], L. Lix[3], J. Jones[2]

1. Gastroenterology, Dalhousie University, Montreal, QC, Canada; 2. Medicine, QE II HSC, Dalhousie University, Halifax, NS, Canada; 3. University of Manitoba, Winnipeg, MB, Canada

Background: Inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), is a chronic, relapsing and remitting inflammatory disease of the gastrointestinal tract. Colorectal cancer (CRC) is a well-documented complication of IBD and is associated with IBD severity, extent and duration. Treatment with 5-aminosalicylic acid (5-ASA) reduces the risk of CRC in IBD.

Aims: Our objective was to test the association of cumulative exposure to 5-ASA on CRC risk.

Methods: A retrospective cohort study was performed using a population-based IBD cohort derived from administrative health data in Saskatchewan, Canada. Data were from 1979 to 2011. Exposure to 5-ASA and CRC diagnosis using ICD diagnoses during the study period were examined. CRC rates were compared between 5-ASA exposed/non-exposed groups using chi-square tests; exposure to 5-ASA was evaluated using survival analysis. To account for differences in 5-ASA exposure, propensity scores (PS) based on IBD duration, immunomodulator (IM) and anti-TNF exposure, number of endoscopies, and decade of IBD diagnosis were used to match non-exposed to exposed patients. In the propensity-matched cohorts, we controlled for gender, location (urban/sub-urban/rural), diagnosis and previous corticosteroid use. A dose response survival model was developed in an attempt to control for the duration of 5-ASA. We assumed a 5-ASA dose of 2000 mg/day, and subsequently marked subjects as being "off" treatment if they did not renew a prescription within 30 days of their last prescription. The Kaplan-Meier estimator was used to describe the time-to-event data and Cox

proportional hazards regression models were used to test the association of exposure with CRC diagnosis; hazard ratios (HRs) and 95% confidence intervals (95% CIs) were reported. Analyses were stratified by type of IBD (UC, CD).

Results: A total of 8821 IBD patients were included in the study, of which 289 (3.3%) developed CRC. In the CRC-free group, 73.9% (n=6307) of patients had exposure to 5-ASA, whereas 61.9% (n=179) had exposure in the CRC group. In the PS-matched cohort, the HR was 2.56 for exposed versus non-exposed individuals (95% CI:[1.9, 3.5]). The risk of CRC diagnosis was higher in the UC sub-group (HR=3.54, 95% CI:[2.3, 5.5]) when compared to the CD population (1.73, 95% CI:[1.1, 2.6]), controlling for gender, location and decade of diagnosis. In our adjusted dose-response model using truncated 5-ASA dosing, the risk of CRC diagnosis was higher in the UC sub-group (HR=2.83, 95% CI:[1.6, 5.1]) when compared to CD (HR=2.17, 95% CI:[1.1, 4.2]).

Conclusions: This population-based cohort study suggests a chemo-protective effect of 5-ASA exposure for CRC diagnosis amongst patients with IBD. A larger protective effect was observed amongst UC patients than CD patients. Further data are needed to elucidate the biologic mechanism of CRC reduction.

Funding Agencies: None

Poster of Distinction

A83
THE MUCOSA-ASSOCIATED-MICROBIOTA IS ASSOCIATED WITH RELAPSE IN CROHN'S DISEASE PATIENTS UNDERGOING ILEOCECAL RESECTION

M. Laffin[1], T. Perry[1], H. Park[1], P. Gillevet[3], M. Sikaroodi[3], G.G. Kaplan[2], R. Fedorak[1], K.I. Kroeker[1], L.A. Dieleman[1], B. Dicken[1], K. Madsen[1]

1. University of Alberta, Edmonton, AB, Canada; 2. Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada; 3. George Mason University, Fairfax, VA

Background: A large proportion of Crohn's disease patients require an intestinal resection at some point. The most common type of intestinal resection in CD patients is an ileocolonic resection (ICR). Unfortunately, following ICR, disease recurs at the anastomosis in up to 80% of subjects at one year. Evidence suggests that the fecal stream and its associated microbial contents play a central role in disease recurrence.

Aims: The aim of this study was to define the mucosal-associated microbiota at the time of ICR and 6 months post-operatively and to determine if microbial community structure at the time of surgery was predictive of future disease relapse.

Methods: Ileal biopsies were obtained at surgery and after 6 months from CD patients undergoing ICR (n=45). Composition and function of mucosal associated microbiota was assessed by 16S rRNA sequencing and PICRUSt analysis. Endoscopic recurrence was assessed using the Rutgeerts score. As a measurement of tissue disease activity, TNFα concentration was measured in ileal samples taken at the time of surgery using a Meso Scale discovery platform. To identify microbial composition and metabolic pathways with differentiating abundance in the different groups, the LDA (Linear Discriminant Analysis) Effect Size (LEfSe) algorithm was used with the online interface Galaxy.

Results: At 6 months, 30 patients remained in remission while 15 had recurrent disease. Demographic data between the two groups was similar. At the time of surgery, LEFse analysis of mucosal biopsies showed Clostridiales to predict maintenance of remission while Enterobacteriales predicted disease recurrence. In addition, a greater proportion of microbial genes associated with aerobic respiration were present in biopsy samples taken at surgery from patients which went on to have disease recurrence. An increase in Lachnospiraceae from surgery to 6 months post-ICR was associated with remission. At the time of surgery there was no difference in α-diversity or degree of inflammation as measured by TNFα levels between the patients which remained in remission or had disease recurrence at 6 months.

Conclusions: Specific mucosal-associated bacterial populations and gene content at the time of surgery are associated with maintenance of remission following ICR in subjects with CD, independent of inflammation. This identification of specific bacterial populations associated with maintenance of remission may enable the development of targeted therapies to alter gut ecology towards a specific profile and thus prevent post-operative recurrence of CD.

Funding Agencies: None

Poster of Distinction

A84
HIGH FECAL CALPROTECTIN LEVELS IN ULCERATIVE COLITIS PATIENTS IN CLINICAL REMISSION ARE ASSOCIATED WITH SPECIFIC CLINICAL AND DIETARY INTAKE PARAMETERS.

A.H. Keshteli, T. Hoevers, K. Madsen, N. Hotte, C. Nickurak, K.I. Kroeker, F. van Den Brand, R.S. Valcheva, R. Fedorak, L.A. Dieleman

Medicine, University of Alberta, Edmonton, AB, Canada

Background: Ulcerative colitis (UC) is a debilitating chronic inflammation with frequent relapses. Fecal calprotectin (FCP), a cytosolic protein of mucosal neutrophils, is the most promising non-invasive fecal marker of intestinal inflammation. We have previously shown that UC patients in clinical remission who had FCP>150 µg/g had a significantly higher chance of relapse within the next 12 months.

Aims: In this study we aimed to investigate which demographic, clinical, laboratory, dietary and lifestyle

related factors were associated with high FCP.
Methods: In this cross-sectional study, FCP was measured using ELISA on samples from adult UC patients who were in clinical remission (Partial Mayo score<3). Demographic (age, gender), clinical (e.g. disease subtype, medication, disease duration), laboratory (e.g. serum vit D, B12, iron status, liver function tests, C-reactive protein), and lifestyle related (e.g. physical activity, smoking, anthropometric measurements) measurements were collected. Health related quality of life was assessed using SIBDQ-10. Assessment of dietary intake during the past twelve months before enrollment in the study was performed using a validated food frequency questionnaire. Residual method was used to calculate energy-adjusted nutrients intake.
Results: Seventy-two patients were included in this study (mean age: 40.7±14.1 years, females: 60.7%). Interestingly, 41.0% of UC patients in clinical remission had FCP >150 µg/g, defined as "high FCP". The prevalence of high FCP in males and females was 54.2 and 32.4%, respectively (P=0.09). After adjusting for gender, age and BMI, patients with high FCP had a significantly higher carbohydrate (233.0±34.8 vs. 214.4±25.1 g/d, P=0.02) intake, but lower consumption of alcohol (2.1±3.8 vs. 4.4±5.1 g/d, P=0.05), monounsaturated (25.7±11.7 vs. 29.3±7.8 g/d, P=0.08), and polyunsaturated fatty acids (12.3±6.5 vs. 14.7±5.5g/d, P=0.06). The prevalence of high FCP in patients who had previous history of proctitis, left-sided colitis, and pancolitis was 0, 38, and 49%, respectively (P=0.02). Serum albumin level was higher in patients with normal FCP than in patients with high FCP (44.8±2.4 vs. 43.2±2.9 g/L, P=0.02). FCP was not related to vitamin D, B12, iron, obesity, physical activity, and quality of life status.
Conclusions: Increased fecal calprotectin as a marker of subclinical disease in UC patients is associated with high carbohydrate intake and low consumption of monounsaturated and polyunsaturated fatty acids in male patients with more extensive previous disease. These findings suggest that diet can be a significant determining factor in modulation of inflammation in UC patients who are in clinical remission.

Funding Agencies: Alberta Innovates - Bio Solutions

Poster of Distinction

A85
EFFICACY AND SAFETY OF DOSE ADJUSTMENT AND DELAYED RESPONSE TO USTEKINUMAB IN MODERATE–SEVERE CROHN'S DISEASE: RESULTS FROM THE IM-UNITI MAINTENANCE STUDY
B.E. Sands[1], C. Gasink[5], D. Jacobstein[6], L. Gao[7], J. Johanns[8], P. Szapary[9], J.F. Colombel[3], S. Targan[10], S. Ghosh[2], W. Sandborn[4]

1. Icahn School of Medicine at Mt Sinai, New York, NY; 2. Gastrointestinal Section, Imperial College london, London, United Kingdom; 3. School Of Medicine, Mount Sinai Medical Center , New York, NY; 4. University of California San Diego, La Jolla, CA; 5. Janssen Research & Development, LLC, Spring House, PA; 6. Janssen Research & Development, LLC, Spring House, PA; 7. Janssen Research & Development, LLC, Spring House, PA; 8. Janssen Research & Development, LLC, Spring House, PA; 9. Janssen Research & Development, LLC, Spring House, PA; 10. Cedars-Sinai Medical Center, Los Angeles, CA

Aims: Ustekinumab (UST) has been shown to induce and maintain clinical response and remission in moderate-severe Crohn's disease (CD) in 2 induction (UNITI-1 & 2) and 1 maintenance (IM-UNITI) randomized, PBO-controlled Phase 3 trials. We evaluated the efficacy of UST in 2 additional groups in IM-UNITI: patients (pts) who dose adjusted following loss of response (LOR) and pts who did not have a clinical response to IV UST during induction and had an additional subcutaneous (SC) dose.
Methods: Pts in clinical response [CR-100] (≥ 100 point decrease in CDAI) after single dose IV dose were randomized to SC PBO, UST 90mg q12w or q8w. Pts who met LOR criteria, defined as a CDAI score of ≥ 220 and a ≥ 100 point increase from the IM-UNITI baseline CDAI score, between wks8 and 32 of IM-UNITI could undergo a single dose adjustment as follows: PBO→q8w, q12w→q8w, and q8w→q8w (no adjustment) and were assessed for CR-100 and clinical remission (CDAI < 150) 16wks later. Separately, UST IV non-responders received SC UST 90mg, then continued SC UST 90mg q8w if in CR 8wks later.
Results: 51 (39%), 29 (23%), and 28 (22%) pts in the PBO, q12w and q8w groups, respectively, underwent dose adjustment after meeting LOR criteria. Among these pts, clinical remission and CR-100 were observed in 39% and 71% of pts adjusting PBO→q8w (a situation similar to a drug holiday), 41% and 55% in the q12w→q8w group, and 32% and 46% in the q8w→q8w group when assessed 16wks later (Table 1). Median change in CDAI after adjustment was -121, -141 and -78.5 in the PBO→q8w, q12w→q8w and q8w→q8w groups, respectively. Of 467 pts not in response to UST following IV induction in UNITI1&2, 50.5% and 28.9% were in clinical response and remission 8wks after one additional UST dose (90mg SC). Among the 251 of these pts continuing dosing at wk8 of maintenance, 68.1% were in CR-100 and 50.2% were in remission at wk44. No increases or changes in patterns of adverse events were seen among pts who dose adjusted.
Conclusions: In pts who met LOR criteria, dose adjustment from UST 90mg q12w to 90mg q8w provided some additional clinical benefit compared to pts who remained on UST 90mg q8w. Additionally, pts who were initial induction non-responders can benefit from continued treatment with at least 1 SC UST dose 8wks after IV induction.

Table 1: Proportion of pts achieving clinical response & remission 16 wks after dose adjustment

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

	CR-100	Clinical Remission
PBO→UST q8w	71%	39%
UST q12w→UST q8w	55%	41%
UST q8w → UST q8w	46%	32%

Poster of Distinction

A86
CHARACTERIZING THE POST-TRANSFER PERIOD AMONGST PATIENTS WITH PEDIATRIC ONSET IBD: THE IMPACT OF ACADEMIC VS. COMMUNITY ADULT CARE ON EMERGENT HEALTH RESOURCE UTILIZATION
N. Bollegala[4], A. Griffiths[1], A. Kovacs[5], H. Steinhart[2], G.C. Nguyen[3]

1. Hospital for Sick Children, Toronto, ON, Canada; 2. Mount Sinai Hospital, Toronto, ON, Canada; 3. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 4. GI, Women's College Hospital, Toronto, ON, Canada; 5. University Health Network, Toronto, ON, Canada

Background: Patients diagnosed with Inflammatory Bowel Disease (IBD) during childhood require transfer to an adult gastroenterologist, in Ontario usually just prior to their eighteenth birthday. Pediatric Onset IBD (PO-IBD) is a complex phenotype with demonstrated non-compliance risk that may require targeted measures to optimize healthcare outcomes in the adult care setting.
Aims: The purpose of this study was to determine the impact of post-transfer health care setting (academic vs. community gastroenterologist) on emergent health resource utilization.
Methods: This was a population-based retrospective cohort study using health care administrative data from Ontario, Canada. A cohort of patients with PO-IBD was identified and health resource utilization during a 2-year pre-transfer period, transfer of care period and 2-year post-transfer period was analyzed. Post-transfer healthcare setting was defined as academic (i.e. gastroenterologists providing care in a university affiliated tertiary care center) vs. community. A third comparator group, loss-to-follow-up, was also identified. The primary outcome of this study comprised Emergency Department (ED) utilization. Secondary outcomes included hospitalizations, surgeries, ambulatory visits, endoscopic investigations and radiological investigations.
Results: Overall, there were no significant differences found in ED use, ambulatory care visits (aside from the expected drop in the lost to follow-up group), hospitalizations, endoscopic procedures or radiological procedures between exposure groups.
Conclusions: Post-transfer healthcare setting does not appear to significantly impact emergent health resource utilization in the post-transfer period.
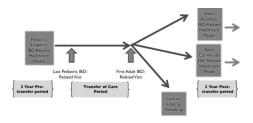
Univariable Analysis of Select Primary and Secondary Outcomes

Univariable Analysis: Outcomes in the Post-Transfer Period		Community (n=639)	Academic (n=1057)	Lost to adult GI follow-up (n=347)	p-value
ED visits	Mean (SD)	2.5 (2.4)	2.9 (3.3)	2.5 (2.1)	0.3
GI ambulatory visits	Mean (SD)	5.1 (3.8)	5.9 (3.9)	0 (0)	<0.0001 *
Admissions	Mean (SD)	1.4 (0.8)	2.2 (2.2)	1.7 (0.6)	0.09
Colonoscopy	Mean (SD)	1.4 (0.8)	1.4 (0.7)	1.5 (0.6)	0.3

ED = Emergency Department, GI = Gastroenterology, SD = Standard Deviation

Poster of Distinction

A87
DEVELOPMENT AND VALIDATION OF DIAGNOSTIC CRITERIA FOR IBD WITH AN EMPHASIS ON IBD-UCLASSIFIED IN CHILDREN: A MULTICENTER STUDY FROM THE PEDIATRIC IBD PORTO GROUP OF ESPGHAN
L. Birimberg Schwartz[1], D. Turner[2]

1. The Division of Gastroenterology, Hepatology and Nutrition, Sickkids childrens hospital, Toronto, ON, Canada; 2. Shaare Zedek Medical Center, Jerusalem, Israel
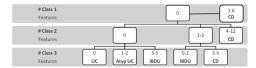
Background: The revised Porto criteria identify subtypes of pediatric inflammatory bowel diseases: ulcerative colitis (UC), atypical UC, Inflammatory Bowel Disease Unclassified (IBDU), and Crohn's disease (CD).

Aims: In continuation of the Porto criteria, we aimed to further derive and validate criteria for standardizing the diagnosis of the IBD subtypes with an emphasis on IBDU, the least well defined subtype.

Methods: This was a multicenter retrospective longitudinal study from 23 centers affiliated with the Porto-group of ESPGHAN. Both a hypothesis driven judgmental approach and mathematical CART modeling were utilized for creating a diagnostic algorithm. Since jejunal and ileal inflammation is easily recognized as CD, we focused here on colitis phenotype.

Results: 749 IBD children were enrolled- 236 (32%) Crohn's colitis (CD), 272 (36%) ulcerative colitis (UC) and 241 (32%(IBDU (age 10.9±3.6 years) with a median follow-up of 2.8 years (IQR 1.7-4.3). A set of 23 features were clustered in 3 classes according to their frequency in UC: 6 class-1 (0% prevalence in UC), 12 class-2 (<5% prevalence) and 5 class-3 (5-10% prevalence). According to the algorithm, UC should be diagnosed if no features exist in the three classes. Different combinations of the features classify atypical UC, IBDU and CD. The algorithm differentiated UC from CD and IBDU with 80% sensitivity (95% CI (71-88)) and 84% specificity (95% CI (77-89)), and CD from IBDU and UC with 78% sensitivity (95% CI (67-87)) and 94% specificity (95% CI (89-97)).

Conclusions: The validated algorithm can adequately classify children with IBD into CD, UC and IBDU.

Poster of Distinction

A88
A PROSPECTIVE STUDY OF MECHANISMS OF INTESTINAL INFLAMMATION AFTER ILEAL RESECTION IN CROHN'S DISEASE: PRELIMINARY ANALYSIS OF PHENOTYPIC PREDICTORS OF ENDOSCOPIC RECURRENCE
K. Boland[1], J. Stempak[2], M.S. Silverberg[1]

1. Zane Cohen Centre for Digestive Diseases, Mount Sinai Hospital, Univeristy of Toronto, Toronto, ON, Canada; 2. Zane Cohen Centre for Digestive Diseases, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

Background: Post-operative endoscopic recurrence of ileal Crohn's Disease (CD) is common, however the evolution of disease recurrence over time requires further analysis to identify mechanisms of intestinal inflammation.

Aims: The aim of this project is to study the complex interplay between genetic, microbial and gene expression as well as phenotypic features associated with post-operative ileal endoscopic recurrence. Here we present preliminary analysis of recruited subjects.

Methods: Patients with confirmed CD scheduled to undergo elective or emergent ileocolic resection with a primary anastomosis were recruited to this prospective study at a tertiary referral center. Clinical data, peripheral blood and serum collection was performed pre-operatively and at follow up for endoscopic assessment including activity scores and biopsies for microbiome analysis. Endoscopic recurrence was defined as Rutgeert's score of i2, i3 or i4 in the neo-terminal ileum.

Results: Forty-five patients were enrolled in this study. Thirteen patients withdrew from the study, and 3 await first endoscopy post ileal resection. Twenty-nine patients have completed at least 1 post-operative endoscopy, and 27/29 completed 2 post-operative colonoscopies with a median follow-up interval of 18 months (4-144 months). Forty-one per cent (n=12/29) of patients developed endoscopic recurrence in the neo-terminal ileum. There were no statistically significant differences in age, gender, age at diagnosis, history of smoking or Montreal Classification of CD in patients with endoscopic recurrence. There was no significant difference in history of previous surgery for IBD in patients with recurrence (P=0.66). However, shorter time to first abdominal surgery for CD predicted endoscopic recurrence (median 1 versus 8 years, P=0.017, Mann Whitney Analysis). Use of disease-modifying medication at the time of ileal resection including systemic steroids, antibiotics, immunomodulators and anti-TNF agents did not predict endoscopic recurrence at post-operative colonoscopies. Treatment with anti-TNF at the time of the first post-operative colonoscopy was associated with survival without endoscopic disease recurrence (n=5/29, P=0.0388, Log-rank [Mantel Cox] Test).

Conclusions: Preliminary phenotypic results of a prospective analysis of patients undergoing potentially curative resection for ileal CD demonstrate that a shorter time to first surgery for CD predicted endoscopic recurrence (P=0.017), indicating potentially more aggressive phenotype in these patients. Furthermore, use of anti-TNF post-operatively before colonoscopy assessment was also associated with a lower risk of endoscopic recurrence (P=0.388). These results will support ongoing investigation of the microbial and transcriptomic data to be evaluated in this group.

Poster of Distinction

A89
THE IBD SYMPTOM INVENTORY: MEASUREMENT CHARACTERISTICS AND VALIDITY IN A CLINIC SAMPLE
K. Sexton, J.R. Walker, L.E. Targownik, L.A. Graff, C. Haviva, B. Beatie, S.K. Petty, M.T. Bernstein, h. singh, N. Miller, C.N. Bernstein

University of Manitoba, Winnipeg, MB, Canada

Background: Most measures of IBD symptoms are cli-nician administered, and existing self-report measures suffer from narrow breadth, inadequate measurement properties, or burdensome length. The IBD Symptoms Inventory (IBDSI) was developed to assess a broader range of patient-reported IBD symptoms.
Aims: To evaluate the measurement properties of a new self-report measure of IBD symptoms.
Methods: Consecutive IBD patients attending an outpatient GI clinic were invited to participate while waiting for their appointment. Participants completed a survey which included the IBDSI, the IBD Ques-tionnaire (Guyatt et al., 1989), and the Manitoba IBD Index (Clara et al., 2009). The IBDSI was developed by adapting symptom items from existing clinician-rated or diary-format symptom inventories; following factor analytic work, 35 items were retained assessing symp-toms on 5 subscales: bowel symptoms, abdominal discomfort, fatigue, bowel complications, and systemic complications. As part of standard care, participants were administered the Harvey Bradshaw Index for Crohn's disease (HBI; Harvey & Bradshaw, 1980) or the Powell-Tuck Index for ulcerative colitis (PTI; Powell-Tuck et al., 1978) by a clinical nurse specialist with extensive experience in IBD. A gastroenterologist completed a global assessment of disease activity on a 4-point Likert scale (0=inactive to 3=severely active symptoms).
Results: 267 patients (58.1% female; CD n=142, UC n=125; ages 18-81 years, M=43.4, SD=14.6) provided informed consent and completed the surveys. The IBDSI showed excellent internal consistency (α=0.93 for the total score, 0.55-0.88 for subscale scores), correlated highly with low IBD-related quality of life on the IBDQ (r=-.89), symptom frequency on the MIBDI (r=.67), and clinician-rated global assessment (r=.70). ROC analyses found that a score ≥ 24 (in CD) or ≥ 17 (in UC) showed excellent sensitivity and specificity for the HBI and PTI cut offs of ≥ 5 for active disease (AUC = .93 and .95), respectively.
Conclusions: The IBDSI is a reliable and valid pa-tient-reported measure of a broad range of common IBD symptoms. The IBDSI showed strong measurement properties, with a supported factor structure, very good internal consistency, evidence of convergent validity, and excellent sensitivity and specificity to clinician-rated measures assessing active disease, and is thus recommended for use in either clinic or research

settings. A shorter version of the measure (24 items) with similar measurement characteristics is available. Use of the measure could allow clinicians to score and follow symptom reports as a means to quantify the impact of interventions.

Poster of Distinction

A90
EARLY LIFE INFECTION OF MICE WITH THE TAPEWORM PARASITE *HYMENOLEPIS DIMINUTA* PROTECTS AGAINST DNBS-INDUCED COLITIS
T. Arai, F. Lopes, A. Wang, D.M. McKay

Physiology & Pharmacology, Uni. Calgary, Calgary, AB, Canada

Background: According to the hygiene hypothesis, the lack of exposure to intestinal helminths in childhood could be an important environmental factor in the development of auto-inflammatory disease. In Canada there has been a significant increase in pediatric (early) and adult (later) onset IBD. We showed that infection with *H. diminuta* reduced the severity of di-nitroben-zene sulphonic acid (DNBS) in adult mice. Here we test the hypothesis that infection with this helminth will exert an anti-inflammatory benefit in young mice.
Aims: To define if three-week old (young) mice can expel *H. diminuta* and if they are protected from DNBS-induced colitis.
Methods: First, helminth infectivity was compared in three- and eight-week old Balb/c mice (bred at Univ. Calgary). Second, young mice were orally infected with 5 cysticercoids of *H. diminuta* and 8 or 10 days later received 1.5 mg of DNBS intra-rectally. Colitis was assessed 72h post-DNBS by: 1) loss of body weight, 2) colon length, 3) disease activity score, 4) histopa-thology, and 5) concanavalin-A stimulated cytokine production from spleen cells. In other experiments, the ability of re-challenge with helminth antigen to protect mice from DNBS-induced colitis in later life was tested.
Results: The young mice successfully rejected *H. diminuta*, although this was slightly delayed by ~3 days compared to adult mice. The young mice devel-oped DNBS-colitis as determined by all indicates of measurement. Mice infected with *H. diminuta* 8 days before administration of DNBS showed no amelioration of disease; however, adjusting the temporal aspect of the study, we found that mice infected 10 days prior to DNBS had substantially less severe colitis (this 10 day time-point corresponded with expulsion of the parasite). Furthermore, helminth antigen treatment after early life infection protected the mice from colitis in later life.
Conclusions: Young mice expel *H. diminuta* by a functional immune response and infected mice can

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be protected from DNBS-induced colitis. While the mechanism of the anti-colitic effect is likely to parallel that seen in adults (i.e. involves IL-4, IL-10 and IgG1). *H. diminuta* antigen treatment after early life infection protects against colitis in later life. We present these preliminary data in support of the consideration of helminth therapy in early onset IBD, and triggering of anti-helminth immunological memory to treat IBD later in life.

Poster of Distinction

A91
NOVEL TRIM22 INTERACTIONS REVEAL POTENTIAL CAUSATIVE MECHANISMS IN VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE (VEOIBD)

K. Hossain[1], Q. Li[2], J. Pan[2], C. Guo[2], N. Warner[2], A. Muise[2]

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

Background: The severe multi-systemic phenotype of VEOIBD is often difficult to treat with conventional therapies. Causative monogenic mutations have been identified, but the majority of VEOIBD patients present without any known defect. Our recently published whole exome sequencing (WES) of VEOIBD patients identified autosomal recessive variants in antiviral E3 ubiquitin ligase TRIM22, identifying its novel role in NOD2 signal regulation through interaction and ubiquitination of NOD2. TRIM22 patient variants caused aberrant NOD2 antiviral and pro-inflammatory signalling. TRIM22's role in these pathways, and roles TRIM proteins play in proliferation and apoptosis, inspires confidence in its critical role in VEOIBD. However, the complete range of pathways influenced by TRIM22 remains a mystery.
Aims: Our hypothesis that TRIM22 lies at a crossroad of multiple disease related pathways will be tested by uncovering binding partners and their clinical implications in VEOIBD.
Methods: Candidate binding partners were identified by BioID, a method by which TRIM22 is fused with a promiscuous biotin ligase. Biotin affinity capture and mass spectrometry identified proximal biotinylated proteins. Co-immunoprecipitation (co-IP) and immunofluorescence (IF) were used to validate interactions. Candidates were tested with ubiquitination assays for modification by TRIM22. TRIM22 patient samples were investigated by immunohistochemistry (IHC). The BioID list was cross-referenced with our WES database for potential disease causing variants.
Results: Co-IP shows TRIM22 interaction with HDAC1, a key component of the Mi-2/nucleosome remodeling and deacetylase (NuRD) complex involved in cell growth and apoptosis. Endogenous TRIM22 and HDAC1

show nuclear co-localization in CACO-2 colorectal adenocarcinoma and U-937 histiocytic lymphoma cell lines. TRIM22 patient variants show reduced HDAC1 binding in preliminary experiments. TRIM22 may affect HDAC1 ubiquitination state in preliminary assays. IHC of a colon sample from one TRIM22 variant patient exhibits ubiquitin aggregation occurring predominantly in the nucleus. TRIM22 BioID reveals 22 genes with potentially disease causing variants in our WES database.
Conclusions: BioID revealed multiple Mi-2/NuRD complex proteins, suggesting a role for TRIM22 in chromatin remodeling and gene regulation. TRIM22 variants' effects on HDAC1 binding, ubiquitination, and function could reveal a novel disease mechanism. Other candidates include associations with primary immune deficiency (e.g. cyclin T1 and associated CDK9), host-virus interaction sites, regulators of NOD2 signalling (e.g. PML), and genes within known IBD loci. The 22 potentially disease causing genes revealed by BioID can be verified by future studies, providing an example of causative gene discovery in VEOIBD with potential for personalized therapies.

Poster of Distinction

A92
ANTIBIOTICS FOR INDUCTION AND MAINTENANCE OF REMISSION IN CROHN'S DISEASE

C.M. Townsend[1], C.E. Parker[2], J. MacDonald[3], B.G. Feagan[1], V. Jairath[1], R. Khanna[1]

1. University of Western Ontario, London, ON, Canada; 2. Robarts Clinical Trials, London, ON, Canada; 3. Cochrane IBD Group, Robarts Clinical Trials, London, ON, Canada

Background: Trials of antibiotic therapy for Crohn's disease (CD) have produced conflicting results.
Aims: We performed a systematic review and meta-analysis to determine the efficacy and safety of antibiotics for induction and maintenance of remission in CD.
Methods: EMBASE, MEDLINE, the Cochrane Library and the Cochrane IBD Group Specialized Register were searched from inception to September 2016. Randomized controlled trials (RCTs) comparing antibiotics to placebo or an active comparator in CD patients were considered for inclusion. Data were analyzed based on intention-to-treat. Risk ratios (RR) and corresponding 95% confidence interval (95% CI) were calculated for dichotomous outcomes. The primary outcome was the number of patients who failed to achieve clinical remission. Methodological quality was assessed using the Cochrane risk of bias tool. GRADE was used to assess the overall quality of the evidence for the primary outcome.
Results: Fourteen RCTs (n = 1469 patients) were

eligible. Two trials were rated as high risk of bias (no blinding). Eight trials were rated as unclear risk of bias and 4 trials were rated as low risk of bias. Ciprofloxacin, metronidazole, clarithromycin, rifaximin and cotrimoxazole were evaluated at therapeutic doses. Comparisons included antibiotic vs. placebo, antibiotic vs. steroid, antibiotic vs. placebo in addition to usual therapy and antibiotic vs. placebo in addition to biologic therapy. A pooled analysis of 8 placebo-controlled RCTs (801 patients) showed no significant difference in clinical remission at 6 to 10 weeks. Fifty per cent (267/535) of antibiotic treated patients failed to enter remission compared to 59% (158/266) of placebo patients (RR 0.87, 95% CI 0.75-1.01; moderate quality evidence). A pooled analysis of two placebo-controlled studies (155 patients) showed no statistically significant difference in relapse rates at 52 weeks. Forty-five per cent (37/83) of antibiotic treated patients relapsed compared to 57% (41/72) of those assigned to placebo (RR 0.87, 95% CI 0.52-1.47; low quality evidence). There were no statistically significant differences between antibiotics and placebo in the proportion of patients with adverse events (RR 0.87, 95% CI 0.75-1.02; 9 studies; 852 patients), serious adverse events (RR 1.12, 95% CI 0.26-4.76; 4 studies; 555 patients), or withdrawal due to adverse events (RR 0.86, 95% CI 0.57-1.29; 9 studies; 858 patients).
Conclusions: Antibiotics are ineffective for induction or maintenance of remission in Crohn's disease.

Poster of Distinction

A93
POST-INDUCTION INFLIXIMAB TROUGH LEVELS VARY WIDELY AND AID IN INDIVIDUALIZING INFLIXIMAB MAINTENANCE THERAPY FOR PEDIATRIC IBD
C.M. Popalis, K. Frost, N.J. Carman, T.D. Walters, A. Griffiths, P.C. Church

Division of Gastroenterology, Hepatology and Nutrition, Department of Paediatrics, The Hospital for Sick Children and University of Toronto, Toronto, ON, Canada

Background: Clinical trial data in patients with IBD shows that infliximab (IFX) efficacy correlates with trough drug levels. Absence of drug predisposes to antibody formation and secondary loss of response.
Aims: We aimed to individualize IFX regimens through early post-induction drug levels in pediatric patients with Crohn's disease (CD) and ulcerative colitis (UC).
Methods: Starting September 2013 at SickKids Hospital, Toronto children/adolescents initiating IFX via a 3-dose induction regimen were given their first maintenance dose earlier than the conventional 8 weeks following 3rd induction dose. IFX trough levels, measured by ELISA at the time of first maintenance infusion were compared between CD and UC. The influence of baseline characteristics such as physician global assessment (PGA) of disease activity, albumin and hsCRP on trough levels pre-dose 4 was assessed.
Results: 125 patients with IBD (81 CD, 44 UC; 60% male) were identified (Table). CD and UC patients were similar in age, gender, disease duration, BMI, and hsCRP. However, UC patients had higher disease activity, lower albumin, and higher steroid use at baseline. 81 CD patients infused in standard fashion (weeks 0, 2, 6) had a median dose of 5.3 mg/kg (IQR 5.0-5.5) across 3 induction doses. They had median trough levels at week 12 of 9.3 mcg/mL (IQR 4.8-13.4). 65/81 (80%) received concomitant immunomodulator during induction. 22 (27%) CD patients had a week 12 trough level <5 mcg/mL, and 18 (22%) had a level <3 mcg/mL. 44 UC patients were induced more intensively, with many given 3 doses over 4-5 weeks. They also received higher doses (median 6.3 mg/kg over 3 induction doses) compared to CD (p<0.001). All UC patients were given their first maintenance dose 4 weeks following the 3rd induction dose. The median trough level of 10.2 mcg/mL (IQR 3.7-14.4) was similar to CD patients dosed 6 weeks after their 3rd infusion (Figure). Dose 4 trough levels were <7mcg/mL for 17 (37%) UC patients and <3mcg/mL for 9 (21%).
Conclusions: Post-induction trough levels are variable for pediatric IBD patients. For many patients, standard maintenance infusions beginning at week 14 would result in suboptimal trough levels. In this cohort, patients with UC cleared drug more rapidly, requiring more intensive dosing to achieve comparable drug levels post induction.

Baseline characteristics

Characteristic	Crohn's Disease (N= 81)	Ulcerative colitis (N=44)	p-value
Male, N (%)	50 (62%)	25 (57%)	0.28
Age at induction, yrs, median (IQR)	13.5 (12.0-15.2)	14.8 (12.1-16.3)	0.23
Disease duration, yrs, median (IQR)	0.23 (0.1-1.2)	0.61 (0.3-1.3)	0.19
PGA mod/severe disease, N (%)	39 (48%)	35 (80%)	<0.001
Steroid use at baseline, N (%)	27 (33%)	43 (98%)	<0.001
Body mass index, kg/m2, median (IQR)	18.2 (16.3-20.5)	18.5 (16.5-21.0)	0.57
Baseline serum albumin, median (IQR)	38.0 (33.0-42.0)	33.0 (29.0-39.0)	<0.001
Baseline serum hsCRP, median (IQR)	8.9 (2.5-37.6)	6.7 (1.9-19.8)	0.70

IBD

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

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A94
USE OF LOW-DOSE CTE IN PREDICTING ACTIVE IN-FLAMMATION IN CROHN'S PATIENTS WITH INTERME-DIATE FECAL CALPROTECTIN LEVELS
O. Gerami, J. Brown, P. Vos, J. Leipsic, T. Lee, R.A. Enns, B. Bressler, G. Rosenfeld

University of British Columbia, Vancouver, BC, Canada

Background: Crohn's disease (CD) is a condition that affects young individuals. Clinically assessed disease activity by a Gastroenterologist is the gold standard for identifying patients with active inflammation and relapse. Fecal Calprotectin (FC) is a biomarker that is an independent indicator of active inflammation. Bressler et al has shown that FC levels <100 µg/g strongly predict quiescent CD, and those >250 µg/g strongly predict active inflammation/relapse. FC levels between 100-250 µg/g is an indeterminate zone that warrants further testing to confirm the presence/absence of disease. Computed tomography enterography (CTE) is a proposed next test. Recent research has shown that low-dose CTE using model-based iterative reconstruction (MBIR) is non-inferior to standard dose CTE for identifying signs of small bowel inflammation.
Aims: To assess the utility of MBIR CTE signs, in patients with intermediate FC levels, for predicting those who would have active inflammation on clinical assesment.
Methods: A single-center, retrospective cohort study of 163 patients subjected to clinical assessment , FC measurement and low dose CTE to evaluate CD activity between November 2012 & February 2015. The CTE studies for each patient were reviewed by two radiologists for radiographic findings of small bowel CD

inflammation. Clinically assessed disease activity by a Gastroenterologist served as the reference standard. Multivariate logistic regression was used to build a scoring equation based on FC levels & radiographic signs to predict active disease in the reference standard.
Results: Of the 163 patients, 92 (56%) patients had active inflammation based on clinical assessment. Sixty-five (71%) of the 92 patients clinically diagnosed with active inflammation also had CTE that was deemed active by overall radiologist impression. Fifty (70%) of the 71 patients clinically diagnosed with inactive inflammation also had CTE that was deemed inactive by overall radiologist impression. Sensitivity, specificity, PPV & NPV of overall radiologic impression for CD activity was 0.70, 0.71, 0.75, 0.65, respectively.

138 patients had measured FC levels. Seventy-eight (57%) had clinically active disease & 60 (43%) had clinically inactive disease. In those with active disease, 16 (20%), 13(17%) & 49(63%) had FC levels <100 µg/g, 100-250 µg/g, >250 µg/g, respectively. In those with inactive disease, 53 (88%), 7(12%) & 0(0%) had FC levels <100 µg/g, 100-250 µg/g, >250 µg/g, respectively.

An equation based on mural stratification & FC level predicted active disease the best. This equation had a sensitivity, specificity, PPV, NPV & accuracy of 0.82, 0.90, 0.91, 0.79 & 0.85, respectively.
Conclusions: In patients with FC levels between 101-250, MBIR CTE is a reasonable further test to confirm the presence/absence of disease

Table 1. Relationship and diagnostic accuracy of radiologic variables and fecal calprotectin with the clinical reference standard.

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A95
THE EFFICACY OF SURVEILLANCE COLONOSCOPY ON SURVIVAL IN INFLAMMATORY BOWEL DISEASE ASSOCIATED COLORECTAL CANCER: A SYSTEMATIC REVIEW & META-ANALYSIS
S. Perera[1], A. Warner[2], R. Almotasen[1], G. Boldt[3], H. Matsuoka[4], B. Yan[1], M. Sey[1], A. Rahman[1], D.A. Palma[2], S. Asfaha[1]

1. Gastroenterology, Western University, London, ON, Canada; 2. Department of Radiation Oncology, London, ON, Canada; 3. London Health Sciences Centre, London, ON, Canada; 4. Nishiwaki Municipal Hospital, Nishiwaki, Japan

Background: Patients with inflammatory bowel disease (IBD) are at increased risk of developing colorectal cancer (CRC). This risk is related to disease extent, duration and severity. Current guidelines recommend routine colonoscopy 8-10 years after the initial onset of disease. However, no large controlled trials have investigated the efficacy of surveillance colonoscopy and the benefit remains unproven.
Aims: A systematic review and meta-analysis was performed to evaluate whether surveillance colonoscopy for CRC impacts the survival of patients with IBD.
Methods: A systematic review of MEDLINE and EMBASE databases was undertaken to identify studies that examined the impact of surveillance colonoscopy on overall survival of patients with IBD associated CRC. Three hundred and forty-five studies were screened by title and abstract, followed by a detailed review of twenty three studies. Only studies that included a control group of IBD patients (a surveillance versus a non-surveillance arm) were included in this analysis. Effect estimates (hazard ratios [HR]) and confidence intervals (CIs) were computed, with a fixed-effects model created to estimate the effects. Cochrane's Q and I^2-statistics were used to assess study heterogeneity. Additionally Dukes stage of the tumour was compared between the surveillance and non-surveillance groups using the Fisher's exact test.
Results: Four relevant studies were identified, and this included a total of 334 patients. Of these patients, 118 underwent surveillance colonoscopy, while 216 did not. Surveillance colonoscopy was associated with improved overall survival, with the HR of death being 0.354 in the surveillance group (95% CI 0.217-0.578; p<0.001). Furthermore, these studies were not found to be heterogeneous (Q = 1.727, P = 0.631, I^2 = 0. 000). Analysis of pathology data from two of the studies demonstrated that in the surveillance group tumours were more likely to be diagnosed at an earlier stage (Dukes A, P < 0.001), than in the group that did not undergo surveillance where tumours were more likely to be diagnosed at a later stage (Dukes C and D, P = 0.018 and P = 0.017).
Conclusions: Our systematic review and meta-analysis demonstrates that surveillance colonoscopy does in fact improve overall survival in patients with IBD and suggests that surveillance colonoscopy additionally provides the advantage of detecting earlier staged colorectal tumours than when no surveillance is performed.

A96
THE TRANSCRIPTION FACTOR HNF4A PLAYS A KEY ROLE IN REGULATING PANETH CELL SPECIFIC WNT3 EXPRESSION AND IS CRUCIAL FOR EPITHELIAL MAINTENANCE.
C. Jones, F. Boudreau

Université de Sherbrooke, Sherbrooke, QC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

A97
IMPACT OF MESENCHYMAL BMP SIGNALING IN ULCERATIVE COLITIS
V. Reyes-Nicolas, J.M. Allaire, V. Pomerleau, C. Ouellet, R. Servant, F. Boudreau, N. Perreault

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

NOT PUBLISHED AT AUTHOR'S REQUEST

A98
VASOACTIVE INTESTINAL PEPTIDE PROMOTES TH17 IMMUNE RESPONSES THEREBY PROTECTING AGAINST CITROBACTER RODENTIUM INDUCED COLITIS
H. YU[2], X. Wu[2], H. Yang[2], L.S. Celiberto[2], F.A. Graef[3], E.S. Bosman[4], C. Ma[2], T. Huang[2], G. Reid[2], B. Vallance[1], K. Jacobson[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Pediatrics, BC Children's Hospital Research Institute, Vancouver, BC, Canada; 3. Medicine, UBC, Vancouver, BC, Canada; 4. Experimental medicine, University of British Columbia, Vancouver, BC, Canada

Background: Vasoactive intestinal peptide (VIP), a 28 amino acid neuropeptide, exhibits potent anti-inflammatory effects in autoimmune and inflammatory diseases. Interestingly, recent *ex vivo* studies suggest that VIP can promote the production of proinflammatory Th17 cells (primarily secrete cytokine IL-17A). While Th17 cells likely aggravate inflammation in autoimmune diseases, they are known to be protective against *Citrobacter rodentium* induced colitis-a mouse model of colitis.
Aims: The aim of this study was to examine the *in vivo* significance of VIP-Th17 signaling axis during an enteric pathogen (*Citrobacter rodentium*) infection.
Methods: Wild type mice, VIP deficient ($Vip^{-/-}$) mice and VIP treated $Vip^{-/-}$ mice were infected with *C. rodentium* for 10 days. Body weight loss and survival rates were recorded daily. Bacterial counts in the intestinal and systemic sites were determined by an *in vivo* imaging system and plating method. Mucosal damages were analyzed by Haemotoxylin and Eosin staining. The production of cytokines (such as IL-1β, IL-6, IL-17A,

IL-22 and TNF-α) were quantified by quantitative PCR, ELISA and FACS.

Results: *Vip*^{-/-} mice infected with *C. rodentium* showed dramatic body weight loss, decreased survival rates, increased bacterial colonization in intestinal and systemic sites, worsened mucosal damages/inflammatory responses as well as reduced production of Th17 cell responses. Importantly, exogenous treatment of *Vip*^{-/-} mice with recombinant VIP ameliorated *C. rodentium*-induced colitis, accompanied by restoration of Th17 cell responses.

Conclusions: We provide the first *in vivo* evidence that VIP promotes Th17 immune responses thereby protecting against *C. rodentium* induced colitis.

Funding Agencies: CCC

A99
SYSTEMIC DELIVERY OF AN INHIBITOR OF MITO-CHONDRIAL FISSION REDUCES THE SEVRITY OF CHEMICALLY-INDUCED COLITIS IN MICE
N. Mancini[2], W. Xu[2], 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

Background: Mitochondria exist as a dynamic network that is continually remodelling by the controlled processes of fission and fusion that are critical to cell health, regulating metabolic activity, proliferation and apoptosis. Excessive mitochondrial fission can be a feature of neurological and metabolic diseases. Perturbed mitochondrial form and function can occur in IBD, yet nothing is known of mitochondrial dynamics in the context of these inflammatory conditions. The peptide drug P110 is an inhibitor of the Dynamin-Related Protein 1 (Drp1) fission-inducing protein. We hypothesized that mitochondrial fragmentation (i.e. fission) would contribute to enteric inflammatory disease and sought to test this using P110 in murine models of colitis.

Aims: Determine if systemic delivery of the inhibitor of mitochondrial fission, P110, would ameliorate, to any significant degree, disease severity and inflammation in chemically-induced colitis in mice.

Methods: Balb/c mice were treated with (i) 5% dextran-sodium sulfate (DSS) in drinking water for 5 days, followed by 3 days of water recovery or (ii) dinitrobenzene sulphonic acid (DNBS; 3 mg ir, 72h) ± daily P110 (ip., 3mg/kg/day). Disease was assessed by (a) colonic length, (b) weight change, and (c) macroscopic and histological damage scores.

Results: Both DSS and DNBS induced substantial disease in mice (n=8 and 4, respectively). Co-treatment with the inhibitor of mitochondrial fission, P110, significantly reduced the severity of DSS-induced colitis as gauged by colon length macroscopic disease score, although histopathology was not different from

DSS-only treated mice. In DNBS-induced colitis P110 co-treatment was also beneficial, with mice displaying less wasting, a longer colon and less macroscopic damage and colonic histopathology.

Conclusions: There is a re-emergence of interest in mitochondria in enteric inflammatory disease, where excessive fragmentation could be of pathophysiological significance. Use of a peptide engineered to inhibit pathological mitochondrial fission, reduced the severity of disease in two models of colitis. While the target cell for the P110 drug awaits identification, we speculate that suppression of mitochondrial fission is worthy of consideration as a new option to treat IBD.

Funding Agencies: CCC, CIHRUniversity of Calgary Eyes High Program

A100
THE UNFINISHED SYMPHONY: GOLIMUMAB IS EFFICIENT AS SALVAGE THERAPY IN PATIENTS WITH REFRACTORY CROHN'S DISEASE
T. Greener[2], G. Greenberg[3], H. Steinhart[1], M.S. Silverberg[1]

1. Mount Sinai Hospital, Toronto, ON, Canada; 2. Gastroenterology , Mount Sinai Hospital , Toronto, ON, Canada; 3. Medicine, Mt Sinai Hospital, Toronto, ON, Canada

Background: Golimumab is a fully human, IgG1k monoclonal antibody against anti–tumor necrosis factor (anti-TNF) agent approved for the treatment of moderate-to-severely active ulcerative colitis. However, there have been no formal trials to date to assess its utility in Crohn's disease (CD).

Aims: This study's aim was to assess the efficacy and safety of golimumab use in patients with anti–TNF refractory CD.

Methods: Consecutive patients with CD who were treated at a single IBD centre with golimumab between March 2010 and September 2016 were included in a retrospective observational study. Clinical response was defined as significant reduction in symptoms and biochemical markers of CD, with no requirement for surgery or introduction of immunomodulators. Outcome was assessed after 6 and 12 months and at last clinical follow-up.

Results: Forty-five patients were included, with a median follow-up of 22 months (interquartile range 12–34) following initiation of golimumab. Induction regimens were generally higher than the standard protocol with first month cumulative doses of 300 mg and greater in all patients and 400 mg and above in 75% of the patients. All patients had previously failed at least 2 anti-TNF agents. In 64% of patients, anti-TNF failure was due to loss of response and in 23% due to adverse effects. Clinical response at 6 months was achieved in 32/45 (71%) patients. The proportion of patients still in clinical response at 1 year and 3 years

were 79% and 65%. Throughout follow-up 59% remained on treatment.

Conclusions: This study demonstrates the efficacy of golimumab in CD patients who were previously refractory to at least 2 biologics. An initial response is successfully maintained in the majority of patients for up to 3 years. Future studies should be performed in CD to formally assess the efficacy of golimumab in a randomized controlled trial and to establish the optimal dosing regimen.

Funding Agencies: None

A101
NO ASSOCIATION WITH RISK OF INFECTION IN IBD WITH HIGH SERUM INFLIXIMAB LEVELS

T. Greener[2], B. Kabakchiev[3], M.S. Silverberg[1]

1. Mount Sinai Hospital, Toronto, ON, Canada; 2. Gastroenterology , Mount Sinai Hospital , Toronto, ON, Canada; 3. Lunenfeld research institute , Toronto, ON, Canada

Background: Improved rates of clinical outcome in IBD are associated with higher IFX levels and some patients are treated with higher than standard dosing due to suboptimal response. Data evaluating the correlation between IFX levels and toxicity is limited.
Aims: To evaluate the safety of IFX in IBD patients and compare the frequency of adverse events (AE's) in relation to their levels
Methods: We performed a retrospective analysis of 180 patients with at least one measurement of serum IFX from 2012 through 2016. The cohort was divided separately according to an IFX level cut-off of 15 ug/ml and into 3 groups based on IFX concentrations (<8; 8-20; >20). Frequencies of AE's were compared using logistic regression.
Results: The frequency of total AE's was significantly higher in patients with IFX levels less than 15 ug/ml (64% vs 34%; p=0.02). Infusion reactions were also more frequent in the NR group (10% vs 0% p=0.015). However, there were no significant associations between the rate of infections, skin manifestations or serious AE and IFX levels. No significant differences in rates of infections were demonstrated among the 3 groups of IFX levels.
Conclusions: Higher IFX levels were not associated with higher rates of infections. Clinicians and patients should be aware of the risks of AE with IFX therapy but higher dosing should not be avoided if clinically indicated.

Funding Agencies: None

A102
THIOPURINE METABOLITE LEVEL MONITORING LEADS TO INDIVIDUALIZED AND OPTIMIZED THIOPURINE THERAPY IN ADULT INFLAMMATORY BOWEL DISEASE (IBD)

J. Zhu[2], J. Abraldes[2], L.A. Dieleman[2], V. Huang[2], K.I. Kroeker[2], F. Peerani[2], K. Wong[2], D. LeGatt[1], R. Fedorak[2], B.P. Halloran[2]

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

Background: The thiopurine drugs (6-MP, azathioprine (AZA)) are purine anti-metabolites commonly used in IBD. About 55% of active IBD fail to respond to thiopurine weight based dosing. Studies suggest 6-thioguanine (6-TG) and 6-methylmercaptopurine (6-MMP) levels are better therapeutic targets than weight-based regimens. The therapeutic range of 6-TG is 400-750*. 6-TG levels >750*, 6-MMP levels >6600* increase risk of bone marrow, hepatic toxicity respectively. Xanthine oxidase inhibitor allopurinol (ALL) can decrease the shunting to 6-MMP and increase 6-TG levels in "shunters" (6-MMP/6-TG ratios >20).
Aims: To assess thiopurine metabolite levels in adult IBD patients, physician response to levels, how they altered therapy and patient outcomes.
Methods: Metabolite levels were obtained retrospectively from a chart review of 159 adult IBD patients between 2014 and 2015. All had levels measured for non-response or toxicity. Clinical outcomes were examined. Steady state metabolite levels were analyzed using the Dervieux-Boulieu method.
Results: Sub-therapeutic (subT) clinical response was the main indication for assessing levels (69.2%). Mean 6-TG and 6-MMP levels were 443.4*, 3690.5* respectively. SubT 6-TG and supra-target 6-MMP levels occurred in 95 (60%), 27 (17%) patients. Mean 6-MMP/6-TG ratio was 10.9 (95% CI 8.8-13.0). There were 25 shunters with mean ratio 35.1 (range 21.2-68.1). Overall physician responses to abnormal levels were dose alternation or initiating new therapy (89%), and to diagnosis of shunting was dose reduction with initiation of ALL (76% (19/25)). Highest concordance was seen in subT 6-TG levels and sub-clinical response (59%). AZA dose escalation did not lead to incremental change in 6-TG level; 6-MMP level was nonlinearly increased by higher AZA dose (Figure 1). Highest 6-TG levels (586.6*) were seen in AZA+5-ASA+anti-TNFα group (95% CI 429.8-734.4*, AZA 137.5mg) compared to thiopurine monotherapy group (474.1*,95% CI 361.7-586.6*, AZA 160.7mg). Lowest 6-TG level 392.4*(95% CI 303.5-481.3*, AZA 141.2mg) was seen in AZA+anti-TNFα group (NS ANOVA p= 0.32). There was no difference in AZA dose in these three groups (p=0.19). AZA dose was lowest in AZA+ALL group, and achieved comparable 6-TG levels (AZA 71.4mg, p<0.0002, 6-TG 453.3* p=0.66). In 5 patients, metabolite levels were re-measured; there were reduction of 6-MMP and increased 6-TG levels post ALL use and none developed side effects (Table 1).
Conclusions: This data suggests that weight based dosing is a suboptimal way to achieve therapeutic

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levels of 6-TG. The addition of ALL may be a safe alternative for those who do not response to standard dose escalation. The optimal interval of serial metabolite monitoring remains to be determined.

*pmol/8x10^8 RBC

Figure 1: Boxplot of 6-TG levels in relation to azathioprine doses.

Table 1. Drug Adjustment, Metabolite Levels Pre and Post Adjustment in 5 IBD Patients and Outcomes

		AZA (mg)	Allopurinol (mg)	Other Other IBD Drugs	6-TGN Level*	6-MMP Level*	mHBI/p Mayo	Outcome
Case 1: UC Pancolitis	Pre	100	0	Anti-TNFα+Pred	173	7942	5	
Sub-therapeutic response	Post	100	100	Anti-TNFα	451	350	0	Clinical remission
Case 2: CD Colonic Dz	Pre	200	0	None	221	10422	2	
Others	Post	50	100	None	152	350	0	Clinical remission
Case 3: CD Ileocolonic Dz	Pre	150	0	Anti-TNFα + 5-ASA	206	14023	0	
Transaminase elevation	Post	25	100	Anti-TNFα + 5-ASA	421	431	0	Normalized liver enzymes
Case 4: CD Ileal Dz	Pre	200	0	None	222	12904	6	
Sub-therapeutic response	Post	25	100	Anti-TNFα	281	350	0	Clinical remission
Case 5: UC Pancolitis	Pre	200	0	Anti-TNFα + 5-ASA	236	1810	0	
Others	Post	100	100	Anti-TNFα + 5-ASA	646	350	0	Clinical remission

A103
EARLY INITIATION OF ANTI-TNF THERAPY IS COST-SAVING COMPARED TO LATE INITIATION FOR PATIENTS WITH CROHN'S DISEASE

C.L. Beilman[1], E. Kirwin[3], C. Ma[2], C. McCabe[1], R. Fedorak[1], B.P. Halloran[1]

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

Background: Anti-TNF therapies are effective for the induction and maintenance of remission in patients with Crohn's disease (CD), and are generally prescribed when patients fail to respond to conventional, less-costly medical therapies including steroids and immunomodulators. Our recent retrospective study showed that early initiation (within two years of diagnosis) of anti-TNF therapies reduced rates of surgery and loss of response requiring dose escalation. However, the cost effectiveness of this strategy is unknown, given the expensive nature of these medications.

Aims: The aim of this study was to determine if early initiation of anti-TNF therapy is more cost-effective compared to delayed initiation for the management of CD.

Methods: A Markov model was constructed to simulate the progression of patients with CD after the initiation of either infliximab or adalimumab. Using this model, we compared the lifetime cost-effectiveness of early (≤2 years after diagnosis) versus late (>2 years after diagnosis) initiation of anti-TNF therapy using published loss of response rates. Transition probabilities were determined through a literature search and costs were obtained from the Alberta Disease Registry. Utility scores were obtained from published literature using the Standard Gamble Approach. Deterministic and probabilistic sensitivity analysis was used to characterize uncertainty related to input parameters.

Results: Over a patient's lifetime, early initiation of infliximab yielded an additional 1.02 quality-adjusted life years (QALYs) and saved $18,054 compared to late initiation of infliximab. Early initiation of adalimumab yielded an additional 0.74 QALYs and saved $18,526 compared to late initiation of adalimumab. At a willingness-to-pay threshold of $50,000 per QALY, early initiation of both infliximab and adalimumab had a 68% chance of being cost-effective, while late initiation had a 32% chance of being cost-effective.

Conclusions: Based on our current model, early initiation of either infliximab or adalimumab is cost-saving and dominates late initiation for patients with CD. These results may serve to support early treatment with anti-TNF therapy from both a cost and patient outcome perspective.
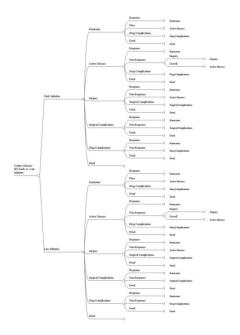
Figure 1. Model structure diagram.

A104
COST-EFFECTIVENESS OF INFLIXIMAB BIOSIMILAR 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. University of Alberta, Edmonton, AB, Canada; 2. University of Calgary, Calgary, AB, Canada

Background: Infliximab is an anti-TNF therapy with proven efficacy for the induction and maintenance of remission in patients with Crohn's disease (CD). An infliximab biosimilar, CT-P13 (marketed as Inflectra), has recently been introduced that could potentially result in large cost-savings for this patient population. However, the molecular complexity and sensitivity to changes in manufacturing of biologic agents makes it difficult to verify the similarity of biosimilars to their respective innovator biologics. Due to these challenges, it is important to assess the effect of biosimilars on patient outcomes while considering the cost-savings associated with these therapies.
Aims: The aim of this study was to provide an economic analysis comparing the cost-effectiveness of infliximab (Remicade) to its biosimilar (Inflectra) for the management of CD.
Methods: A Markov model was constructed to simulate the progression of patients with CD after initiating either infliximab or its biosimilar, Inflectra. Based on this model, we calculated the cost and effectiveness of each treatment strategy over a 5-year time horizon. Transition probabilities were obtained from a literature search, and loss of response rates were obtained from published centre data and observational studies. The cost of health states were accessed using the CIHI patient cost estimator, and the cost of infliximab (Remicade and Inflectra) was obtained from the Alberta Health and Wellness Drug Benefit List. Utility values were obtained from a literature search, and the Standard Gamble approach was used. Deterministic and probabilistic sensitivity analysis was executed to characterize uncertainty.
Results: Over a 5-year period, infliximab therapy costs $167,388 and yielded 3.91 quality-adjusted life years (QALYs). Infliximab's biosimilar costs patients $111,981 and yielded 3.61 QALYs over 5 years. At a willingness-to-pay threshold of $50,000 per QALY, infliximab's biosimilar had a 91% chance of being cost-effective, whereas infliximab therapy had a 9% chance of being cost-effective.
Conclusions: Infliximab's biosimilar Inflectra (CT-P13) resulted in large cost reductions despite similar effectiveness to its innovator biologic for patients with CD. Based on these results, the introduction and mainstream usage of Inflectra may help reduce the economic burden associated with CD.

A105
AN ONLINE EDUCATIONAL PORTAL IMPROVES CONCERNS OF INFLAMMATORY BOWEL DISEASE PATIENTS REGARDING PREGNANCY AND MEDICATION.
R.T. Sutton[1], K. Wierstra[2], L. Ambrosio[1], L.A. Dieleman[1], B.P. Halloran[1], K.I. Kroeker[1], R. Fedorak[1], K. Wong[1], K. Berga[2], V. Huang[1]
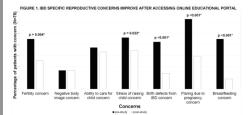
1. Division of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 2. MacEwan University, Edmonton, AB, Canada

Background: The impact of a mother's chronic disease on fetal development makes dealing with inflammatory bowel disease (IBD) during pregnancy complicated. Almost 50% of women with IBD have poor reproductive knowledge; this has been associated with unsubstantiated concerns toward pregnancy, and towards IBD medications. With the help of Pixel Designs Company, we developed an educational web portal to address these concerns.
Aims: To evaluate the educational web portal for effectiveness at improving pregnancy and medication concerns in IBD patients.
Methods: IBD patients aged 18-45 years were invited to participate in a study to evaluate the effectiveness of an educational web portal covering the topics of heritability, fertility, surgery, pregnancy outcomes, delivery, postpartum, and breastfeeding in the context of IBD and IBD medications. Patients completed pre- and post-study questionnaires about seven IBD-specific pregnancy concerns, and identified Likert scores for nine medication concerns from the Beliefs About Medicines Questionnaire (BMQ).The non-parametric McNemar's test was used to determine if the proportion of patients who had each pregnancy concern decreased post-intervention. For medication concerns, the Wilcoxon signed-rank test was used to compare median differences between Likert scores. 95% confidence intervals and SPSS Version 23 were used for all analysis.
Results: Seventy-eight of 111 patients (70.3%) completed pre and post-study questionnaires. Demographics for the 78 are as follows: median age 29.3 (IQR 25.6 - 32.9) years; 54 (69.2%) Crohn's disease; 21 (26.9%) ulcerative colitis; 63 (80.3%) females, 5 (7.9%) currently pregnant and 19 (30.2%) previously pregnant. Medication history: 10 (12.8%) sulfasalazine, 67 (85.9%) mesalamine/5-ASAs, 17 (21.8%) budesonide, 63 (80.8%) steroids, 12 (15.4%) methotrexate, 55 (70.5%) azathioprine/mercaptopurine, 42 (53.8%) biologics, and 38 (48.7%) antibiotics. The intervention significantly decreased the proportion of patients who reported reproductive concerns regarding: fertility, added stress of raising a child affecting IBD, birth defects from IBD, pregnancy causing a flare-up, and inability to breastfeed due to IBD or medications. The BMQ Likert scores significantly decreased post intervention for concerns about having to take IBD medication, becoming too dependent on IBD medication, and the long-term effects of IBD medication.

Conclusions: The educational web portal effectively reduced the proportion of patients who reported certain concerns about pregnancy in IBD, in addition to concerns regarding their IBD medications.

FIGURE 1. IBD SPECIFIC REPRODUCTIVE CONCERNS IMPROVE AFTER ACCESSING ONLINE EDUCATIONAL PORTAL

Funding Agencies: AIHS

A106
USTEKINUMAB IS EFFECTIVE FOR MAINTAINING CLINICAL RESPONSE IN REFRACTORY MODERATE-TO-SEVERE CROHN'S DISEASE: A MULTICENTRE COHORT STUDY

C. Ma[1], R. Fedorak[2], G.G. Kaplan[1], L.A. Dieleman[2], S. Devlin[1], N. Stern[2], K.I. Kroeker[2], C. Seow[1], Y. Leung[1], K.L. Novak[1], B.P. Halloran[2], V. Huang[2], K. Wong[2], S. Ghosh[1], R. Panaccione[1]

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

Background: Ustekinumab is a monoclonal antibody targeting interleukins 12 and 23. Ustekinumab has recently been approved for treatment of Crohn's disease by the United States Food and Drug Administration but long-term maintenance of clinical response in the real-world setting is unclear.
Aims: To assess the efficacy of ustekinumab for maintaining clinical response in CD
Methods: A retrospective multicentre cohort study was performed at two institutions (University of Calgary, University of Alberta). CD patients achieving clinical response to ustekinumab induction between 2011 and 2016 were eligible for inclusion. The primary outcome was loss of clinical response, defined as ustekinumab dose escalation, ustekinumab re-induction, rescue corticosteroids, surgery, or drug discontinuation. Multivariate Cox proportional hazards regression analysis was used to assess predictors of loss of response, expressed as hazard ratios (HR) with 95% confidence intervals (CI).
Results: We identified 98 CD patients responding to ustekinumab induction. Median follow-up was 56.1 weeks (IQR 31.6-105.0). 30 patients (30.6%) lost clinical response during maintenance therapy at a median time of 48.7 weeks (IQR 34.4-84.3). 15 patients (15.3%) required dose escalation, 7 patients (7.1%) required reinduction, 9 patients (9.2%) required rescue corticosteroids, and 7 patients (7.1%) underwent surgical resection. 10 patients (10.2%) discon-

tinued ustekinumab due to loss of response. In Cox proportional hazards regression, high dose induction at 6mg/kg (HR 0.16 [95% CI: 0.03-0.79]) and concurrent immunomodulator use were protective against loss of response (adjusted HR 0.35 [95% CI: 0.14-0.91])
Conclusions: In this large multicentre cohort of CD patients with initial response to induction therapy, ustekinumab was effective for maintaining clinical response in 70% of patients over long-term follow-up. Long-term maintenance may be improved in patients receiving higher dose induction regimens and using concomitant therapy.

Table 1 – Baseline patient demographic

	n = 98
Male, n (%)	41 (41.8)
Median age at ustekinumab induction (years, IQR)	44.7 (40.0 – 57.7)
Median disease duration prior to ustekinumab induction (years, IQR)	13.7 (9.0 – 22.5)
Median weight (kg, IQR)	73.0 (58.0 – 85.0)
Current smoker Former smoker Never smoker	22 (22.4) 14 (14.3) 62 (63.3)
Ileal disease Colonic disease Ileocolonic disease	20 (20.4) 24 (24.5) 54 (55.1)
Inflammatory disease Stricturing disease Penetrating disease	44 (44.9) 24 (24.5) 30 (30.6)
Previous intestinal resections, n (%)	62 (63.3)
Previous Anti-TNF Failure, n (%) Infliximab Adalimumab	90 (91.8) 85 (86.7) 72 (73.5)
Disease Activity Median CRP (mg/L, IQR) Median HBI (IQR) Concurrent IMM, n (%) Concurrent steroids, n (%)	- 7.5 (2.0 – 20.8) 8 (5 – 12) 41 (41.8) 39 (39.8)
Ustekinumab Dosing Median induction dose (mg/kg, IQR) Maintenance q8 weeks, n (%) Maintenance q12 weeks, n (%)	- 3.5 (2.6 – 5.0) 45 (78.9) 11 (19.3)
Median Follow-up Duration, weeks (IQR)	56.1 (31.6 – 105.0)
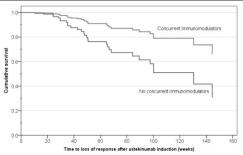
Figure 1 – Survival curves for the proportion of Crohn's disease patients experiencing loss of response to ustekinumab maintenance therapy, stratified by concurrent immunomodulator (red line) and no concurrent immunomodulator (blue line) therapy at ustekinumab induction

A107

POSTOPERATIVE OUTCOMES AMONG USTEKINUMAB TREATED CROHN'S DISEASE PATIENTS: A MULTI-CENTRE CANADIAN PROVINCIAL EXPERIENCE

H. Shim[6], C. Ma[2], H. Al-Farhan [6], A.K. Aldarmaki[6], J. Pang[2], C. Seow[7], R. Fedorak[1], S. Devlin[2], L.A. Dieleman[4], G.G. Kaplan[8], K.L. Novak[5], K.I. Kroeker[4], B.P. Halloran[3], R. Panaccione[2]

1. Los Alamos National Laboratory, Edmonton, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 4. Medicine, University of Alberta, Edmonton, AB, Canada; 5. Gastroenterology, University of Calgary, Calgary AB, AB, Canada; 6. Gastroenterology and Hepatology, University of Calgary, Calgary, AB, Canada; 7. Medicine, University of Calgary, Calgary, AB, Canada; 8. Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada

Background: Ustekinumab (UST), an anti IL12/23 inhibitor, has been recently approved for the treatment of moderate to severe Crohn's disease (CD) in Europe and the United States. In Canada, UST has been used off-label for CD patients failing anti-TNF therapy. **Aims:** We aim to review postoperative safety outcomes for UST-treated CD patients which has not been previously reported. **Methods:** A retrospective chart review of UST-treated CD patients at two tertiary care academic centres (University of Calgary, University of Alberta) who underwent abdominal surgery between April 1, 2013 and July 31, 2016 was performed. The primary outcome was occurrence of postoperative complications stratified by timing [early (<30 days) vs. late (≥30 days to 6 months) post surgery]. **Results:** Nineteen UST-treated CD patients underwent abdominal surgery. Patients was exposed to UST preoperatively [median 7 months (IQR 3-12 months)] and continued postoperatively. Median postoperative follow-up was 14 months (IQR 7-22 months). Seven patients (36.8%) had perioperative prednisone (≥20mg/day) with 5 patients (26.3%) used in combination with immunomodulator (azathioprine or methotrexate). No patient has diabetes mellitus. Bowel obstruction was the leading indication for surgery (12/19, 63.2%) and most surgeries occurred in the emergency setting (10/19, 52.6%) via open laparotomy (13/19, 68.4%). One patient experienced an early postoperative wound infection, following his index emergency laparotomy for bowel perforation while on combination prednisone, methotrexate and UST. No other patients experienced early or late postoperative anastomotic leakage, abscess or non-surgical site infections. Three patients (15.8%) reported postoperative ileus and all resolved with conservative treatment. There were no deaths. **Conclusions:** In this small series, pre-operative UST did not appear to be associated with an increase in postoperative complications.

Baseline patient demographics, n=19

Median age (years, IQR)	35 (26-53)
Male gender (n, %)	5 (26.3%)
Median BMI (IQR)	23 (20-27)
Median duration of CD prior to surgery (years, IQR)	14 (8-20)
Montreal classification Age:	
A1: less than 16 years A2: between 17 and 40 years A3: over 40 years	9 (47.4%) 7 (36.9%) 3 (15.8%)
Behaviour:	
B1: inflammatory B2: stricturing B3: penetrating P. perianal disease	1 (5.3%) 10 (52.6%) 8 (42.1%) 7 (36.8%)
Location:	
L1: ileal L2: colonic L3: ileocolonic L3/4: ileocolonic and upper digestive	5 (26.3%) 3 (15.8%) 9 (47.4%) 2 (10.5%)
Median preoperative serum albumin (g/L, IQR)	33 (29-42)
Perioperative immunosuppression (n, %)	
Corticosteroid ≥20mg/day Azathioprine Methotrexate	7 (36.8%) 4 (21.1%) 9 (47.4%)
Type of surgery:	

IBD

Ileal resection	
Ileocolonic resection	6 (31.6%)
Subtotal colectomy	7 (36.8%)
Proctocolectomy	4 (21.1%)
Ostomy	2 (10.5%)
Primary anastomosis	14 (73.7%)
Stricturoplasty	5 (26.3%)
Fistula repair (enteroenteric and enterocutaneous fistula)	1 (5.3%)
	2 (10.5%)
Hernia repair	1 (5.3%)

A108
USTEKINUMAB IS EFFECTIVE FOR INDUCING CLINI-CAL, ENDOSCOPIC, AND RADIOGRAPHIC RESPONSE IN REFRACTORY MODERATE-TO-SEVERE CROHN'S DISEASE: A MULTICENTRE COHORT STUDY

C. Ma[1], R. Fedorak[2], G.G. Kaplan[1], L.A. Dieleman[2], S. Devlin[1], N. Stern[2], K.I. Kroeker[2], C. Seow[1], Y. Leung[1], K.L. Novak[1], B.P. Halloran[2], V. Huang[2], K. Wong[2], S. Ghosh[3], R. Panaccione[1]

1. University of Calgary, Calgary, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. University of Birmingham, Birmingham, United Kingdom

Background: Ustekinumab is a monoclonal antibody targeting the p40 subunit of interleukins 12 and 23. Gastroenterologists have begun to prescribe usteki-numab off-label for treatment of Crohn's disease (CD) due to promising clinical trials but robust open label data is lacking
Aims: Assess the real-world efficacy of ustekinumab for inducing clinical, endoscopic, and radiographic response in CD
Methods: A retrospective multicentre cohort study was performed at two academic institutions (University of Calgary, University of Alberta) on CD patients receiving ustekinumab between 2011-2016. The primary outcome was achievement of clinical or objective re-sponse at 3, 6, and 12 months after induction. Clinical response was defined by symptom improvement and reduction in Harvey Bradshaw Index of >2 points with tapering off corticosteroids. Objective response was defined by improvement in endoscopic or radiographic CD, as assessed by ileocolonoscopy, contrast-en-hanced ultrasound, or CT/MR enterography
Results: We identified 167 CD patients treated with ustekinumab. Median follow-up was 39.0 weeks (IQR 23.3-87.1 weeks). 95.2% (159/167) had previously failed anti-TNF therapy. 63 patients (37.7%) had clinical response at 3 months. Among 143 patients followed for 6 months or discontinuing drug prior to 6 months, clinical response was achieved in 57.0% (85/149). At 12 months, clinical response was achieved in 54.2% (58/107) of patients. Endoscopic or radiographic response was demonstrated in 48.6% of patients (54/111) at 6 months and 46.9% of patients at 12 months (38/81). Fifty-three patients (31.1%)

experienced an adverse event: 8 patients discontinued therapy due to intolerable side effects (4.8%)
Conclusions: To the best of our knowledge, this multicentre cohort study is the largest reported open label experience with ustekinumab for CD. We found that ustekinumab was a safe and effective therapy for inducing steroid-free clinical and objective endoscopic and radiographic response

Table 1 – Baseline patient characteristics

	n = 167
Male, n (%)	73 (43.7)
Median age at ustekinumab induction (years, IQR)	44.6 (31.8 – 55.5)
Median weight (kg, IQR)	72.0 (58.4 – 83.5)
Current smoker, n (%)	46 (27.5)
Former smoker, n (%)	29 (17.4)
Never smoker, n (%)	92 (55.1)
Ileal disease	49 (29.3)
Colonic disease	35 (21.0)
Ileocolonic disease	83 (49.7)
Inflammatory disease	65 (38.9)
Stricturing disease	56 (33.5)
Penetrating disease	46 (27.5)
Previous intestinal resections, n (%)	111 (66.5)
Previous IMM therapy, n (%)	126 (75.4)
Azathioprine	113 (67.7)
Methotrexate	62 (37.1)
Previous biologic failure, n (%)	159 (95.2)
Primary non-response	46 (27.5)
Secondary non-response	116 (69.5)
Adverse effect	64 (38.3)
Failure of 1 biologic	42 (25.1)
Failure of 2 biologics	93 (55.7)
Failure of >2 biologics	24 (14.4)
Disease Activity	-
Median CRP (mg/L, IQR)	7.8 (2.2 – 23.0)
Median HBI (IQR)	8 (6 – 12)
Concurrent IMM, n (%)	73 (43.7)
Concurrent steroids, n (%)	72 (43.1)
Ustekinumab Dosing	-
Subcutaneous induction, n (%)	148 (88.6)
Intravenous induction, n (%)	19 (11.4)
Median induction dose (mg/kg, IQR)	3.6 (2.6 – 5.7)
3mg/kg induction dose, n (%)	105 (62.9)
6mg/kg induction dose, n (%)	62 (37.1)
Median follow-up, weeks (IQR)	39.0 (23.3 – 87.1)

Figure 1 – Steroid-free symptomatic and objective response to ustekinumab therapy

A109
BIOPSYCHOSOCIAL MODEL OF IBD: CHANGE IN PAIN PHENOTYPES AFFECTS PSYCHOLOGICAL VARIABLES
D.A. Tripp[2], P. Verreault[1], M. Ropeleski[1], M. Woo[1], A. Muere[1], M.J. Beyak[1]

1. Queen's University, Kingston, ON, Canada; 2. Psychology, Anesthesiology, and Urology, Queen's University , Kingston, ON, Canada

Background: IBD is a chronic disease in which patients often experience pain. This pain may be located in sites related to the gut, or regions outside the bowel. Comorbid pain may exacerbate the impact of the disease on QoL. Our previous work demonstrated an association between psychosocial variables (e.g., depression, catastrophizing, QoL) and different pain phenotypes.
Aims: The objective of this study was to evaluate the changes in pain phenotypes and how these changes related to levels of depression, catastrophizing and QoL across three time points (i.e., baseline, 6-month, and 1-year).
Methods: IBD patients seen in an outpatient clinic (n = 118) completed questionnaires including body pain map, demographics, pain, depression, catastrophizing, and QoL. Patients were pain phenotyped as IBD0 if they did not endorse any pain, IBD if they endorsed pain in any area associated with IBD only (i.e., lower abdomen, pelvis and buttocks), or as IBD+ if they endorsed pain in area associated with IBD along with any other area of the body. Change in pain phenotype group from baseline to 1-year follow-up was used to categorize patients (e.g. IBD0 to IBD, IBD0 to IBD+, etc. or stable within group). Repeated measures ANOVA was conducted for depression, catastrophizing and QoL with Change Groups as between subject factors.
Results: 118 participants completed the 3 time points, 17 participants reported pain only in areas not associated with IBD and were excluded. Patients were 64.4% female (M age = 45.07 [SD = 15.26]). 68/101 participants stayed in their respective pain phenotype groups (11 IBD0, 22 IBD, 35 IBD+). 3 transferred to more severe phenotype (IBD to IBD+), 7 transferred to less severe phenotype (IBD+ to IBD), 8 who experience no pain at baseline switched to a more severe phenotype (4 IBD, 4 IBD+), and 15 transferred from any pain phenotype to a no pain phenotype (IBD or IBD+ to IBD0). There were significant differences in depression and QoL scores across Change Groups, but not for catastrophizing. Less severe phenotypes displayed lower depression scores and higher QoL scores. Participants transferring to more severe phenotypes (i.e., IBD0 to IBD, IBD to IBD+) had higher depression and lower QoL scores. Participants transferring to a less severe phenotype (i.e., IBD+ to IBD, IBD to IBD0) had lower depression and higher QoL scores. There was a significant interaction of Change Group and time for QoL; switching from IBD to IBD+ did not impact QoL, but switching from IBD+ to IBD significantly improved participants' QoL.
Conclusions: This study demonstrates the negative impact of pain on patient depression and QoL in IBD over time. The findings suggest that clinicians should carefully consider comorbid pain in patients with IBD as it affects how a patient copes with the disease; change to a lower pain phenotype may improve patient depression and QoL.

A110
THE EFFECT OF SMOKING ON INDUCTION OF REMISSION OR RESPONSE TO ANTI-TUMOR NECROSIS FACTOR THERAPIES IN PATIENTS WITH CROHN'S DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS
S. Lee[1], Z. Zhang[1], E. Kuenzig[3], G.G. Kaplan[2], C. Seow[2]

1. Community Health Sciences , University of Calgary, Calgary, AB, Canada; 2. Medicine and Community Health Sciences, University of Calgary, Calgary, AB, Canada; 3. Children's Hospital of Eastern Ontario, Ottawa, ON, Canada

Background: Anti-tumour necrosis factor alpha (TNF) therapies including infliximab, adalimumab and certolizumab, have been proven to be effective for the induction of response and remission in patients with Crohn's disease. Smoking, a modifiable factor, has been demonstrated to have a negative influence on disease activity.
Aims: We conducted a systematic review and meta-analysis to examine the association between smoking status and clinical outcomes (remission and response) in individuals with Crohn's disease treated with anti-TNF therapies.
Methods: MEDLINE, EMBASE and PubMED were searched from inception to July 2016. References and conference abstracts were searched to identify additional studies. We included observational studies that reported smoking status and clinical outcomes (remission and response) related to the use of anti-TNF therapies in patients with Crohn's disease. Study selection and data extraction were performed by two independent reviewers. Methodological quality was assessed using modified version of the Newcastle Ottawa Scale. The primary outcome was remission and defined as less than 150 CDAI points or less than 4 HBI points. The secondary outcome was response and defined as a reduction of 70 CDAI points or decrease of 3 or more HBI points. Risk ratios (RR) and 95% confidence intervals (95% CI) were calculated. Meta-analysis was used to pool the relative risk from identified studies with a random effects model.
Results: Of the 1211 studies reviewed for eligibility

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and data extraction, we included fifteen observational studies in the final meta-analysis. There was no statistically significant association between smoking and induction of remission (RR: 0.77; 95% CI: 0.56 to 1.05) and response (RR: 0.96; 95% CI: 0.89 to 1.03) to infliximab and adalimumab. Subgroup analysis were conducted to determine the source of heterogeneity. Prior exposure to anti-TNF therapies, type of anti-TNF therapies (infliximab vs. adalimumab), and disease behaviour (luminal vs. fistulising) was not a source of heterogeneity.
Conclusions: Smoking did not have a significant effect on the induction of clinical response or remission in patients with Crohn's disease that were treated with anti-TNF therapies. Clinicians should therefore not base their decision to use anti-TNF therapies, such as infliximab and adalimumab, in patients with Crohn's disease solely on the individual's smoking status.
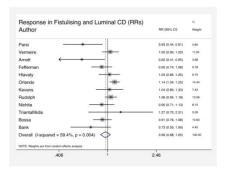
Figure 1. Relative risk ratio for response to anti-TNF therapies (infliximab or adalimumab) in smokers compared to non-smokers in twelve studies

A111
INFLIXIMAB FOR INDUCTION OF REMISSION IN CROHN'S DISEASE
N. Deol[1], T. Nguyen[2], C.E. Parker[3], R. Khanna[4], J. MacDonald[3], B.G. Feagan[4], V. Jairath[4]

1. Gastroenterology , Western University, London, ON, Canada; 2. Robarts Clinical Trials, London, ON, Canada; 3. Cochrane IBD Group, London, ON, Canada; 4. Department of Medicine, London, ON, Canada

Background: Crohn's disease (CD) is a chronic idiopathic disease characterized by transmural inflammation of the gastrointestinal tract.
Aims: To evaluate the efficacy and safety of infliximab (IFX) for induction of remission in CD.
Methods: MEDLINE, EMBASE, the Cochrane Library were searched from database inception to August 2016. Randomized controlled trials (RCTs) comparing IFX to placebo or an active treatment for induction of remission in CD were eligible for inclusion. Data were analyzed on an intention-to-treat basis. The risk ratio (RR) and corresponding 95% confidence interval (CI) were calculated for dichotomous outcomes. The primary outcome was failure to enter clinical remission. Methodological quality was assessed using the Cochrane risk of bias tool. GRADE was used to assess the overall quality of the evidence for the primary outcome.
Results: Five RCTs (total 956 patients) were included. All of the studies were judged to be at low risk of bias. Targan 1997 compared patients receiving a single 5, 10 or 20 mg/kg IFX infusion to placebo. At week 4, 67% (56/83) of IFX patients failed to enter remission (defined as a Crohn's Disease Activity Index <150) compared to 96% (24/25) of placebo patients (RR 0.70, 95% CI 0.59-0.83; moderate quality evidence). Lemann 2006 compared IFX 5 mg/kg to placebo. All patients received azathioprine (AZA) or 6-mercaptopurine. At week 24, the failure to enter corticosteroid-free clinical remission rate was lower in the IFX group (46%; 26/57) compared to placebo (73%; 41/56) (RR 0.62, 95% CI 0.45-86; moderate quality evidence). Colombel 2010 compared IFX 5 mg/kg monotherapy, AZA monotherapy, and a combination of these drugs. At week 26, 56% (94/169) of IFX patients failed to enter corticosteroid-free clinical remission compared to 70% (119/170) of AZA patients (0.79, 95% CI 0.67-0.94; moderate quality evidence). D'Haens 2008 compared patients receiving IFX 5 mg/kg and early immunosuppressive therapy with AZA to patients receiving conventional therapy. At week 26, 40% (26/65) of the IFX group failed to enter clinical remission compared to 64% (41/64) of the conventional therapy group (RR 0.62, 95% CI 0.44-0.89; moderate quality evidence). Present 1999 did not report remission or response rates but did include safety data. A pooled analysis and results from Colombel 2010 and D'Haens revealed no statistically significant difference in serious adverse events for IFX vs. placebo, IFX vs. AZA or IFX plus AZA vs. conventional therapy, respectively.
Conclusions: Moderate quality evidence from a limited number of RCTs indicates that IFX is effective for induction of remission in CD.

A112
EARLY USE OF THERAPEUTIC DRUG MONITORING TO INDIVIDUALIZE INFLIXIMAB THERAPY IN PAEDIATRIC IBD: A MULTICENTRE PROSPECTIVE COHORT STUDY
E. Crowley[10], N.J. Carman[10], V. Arpino[10], K. Frost[11], A. Ricciuto[10], M. Sherlock[4], J. Critch[5], D.R. Mack[8], E.I. Benchimol[2], K. Jacobson[1], S. Lawrence[1], J. deBruyn[6], W. EL-MATARY[7], A. Otley[3], H.Q. Huynh[9], P.C. Church[10], T.D. Walters[10], A. Griffiths[10]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Gastroenterology, Hepatology and Nutrition, Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 3.

Pediatrics, Dalhousie University, Halifax, NS, Canada; 4. Pediatric Gastroenterology, McMaster Children's Hospital, Hamilton, ON, Canada; 5. Memorial University, St. John's, , Canada; 6. Paediatrics , University of Calgary, Calgary, AB, Canada; 7. Pediatric Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 8. Pediatrics, University of Ottawa/CHEO, Ottawa, ON, Canada; 9. Pediatrics, University of alberta, Edmonton, AB, Canada; 10. The Hospital for Sick Children (SickKids), Toronto, ON, Canada; 11. The Hospital for Sick Children (SickKids), Toronto, ON, Canada

Background: Utilization of therapeutic drug monitoring (TDM) to individualize biologic therapy is a logical strategy, given the variable drug clearance and multiple factors influencing pharmacokinetics. Indeed, previously documented wide variability of infliximab levels have been observed early post induction in pediatric patients. However, a randomized controlled trial in adults did not demonstrate improved outcomes with TDM implemented following induction phase of infliximab treatment.
Aims: The aim of the study was to determine infliximab trough levels during induction therapy in children with IBD, with the goal to pre-emptively personalize maintenance dosing.
Methods: Beginning in May 2016, children with IBD at participating sites in the Canadian Children IBD Network, when prescribed 3-dose infliximab induction therapy via either standard or intensified regimen, had pre-infusion trough levels measured by ELISA at the time of 3rd dose. An algorithm incorporating this trough level and the interval between doses 2 and 3 was used to determine timing and dose of first maintenance infusion, aiming to provide a trough level of 5-10 ug/mL when tested before dose 4. Induction regimens were at the discretion of the treating physician, but often intensified among patients with severe UC. Influence of patient demographics and baseline clinical disease activity (physician global assessment and wPCDAI or PUCAI) on early trough levels were assessed.
Results: From May to October 2016 at 6 participating sites, 77 children (mean age 12.4 years, 57% male, 53% CD, 47% UC/IBD-U) received 3-dose infliximab induction. CD patients were infused in standard fashion at weeks 0, 2, 6 with a mean dose of 5.5mg/kg/dose and concomitant immunomodulation (93% methotrexate; 7 % azathioprine); median pre-dose 3 IFX level was 11.9ug/ml (IQR: 8.5-27.2).
UC/IBD-U patients (18% steroid-dependent, 82% steroid-refractory) received more drug (mean 6.8mg/kg/dose across 3 doses) and via an intensified regimen in 34%. Pre-dose 3 IFX levels (median 13.5ug/ml;IQR: 4.9-24.3) were comparable to CD despite higher dosing. 25% of UC/IBD-U patients *vs.* 11% of CD patients had infliximab trough level <5 ug/ml at time of dose 3.
Conclusions: Variability in infliximab exposure is evident during induction. Patients with UC cleared drug

more rapidly, requiring higher weight-based dosing and a more intensive regimen to achieve comparable drug levels post induction. Ongoing monitoring of trough levels measured prior to dose 4 in this cohort will determine whether early TDM with personalized dosing more consistently ensures adequate drug exposure with subsequent better clinical outcome.

Funding Agencies: None

A113
WHAT IS A FLARE OF IBD? THE MANITOBA LIVING WITH IBD STUDY
K. Witges[1], L.E. Targownik[1], C. Haviva[1], K. Sexton[1], J.R. Walker[1], L.A. Graff[2], L. Lix[1], N. Miller[1], C.N. Bernstein[1]

1. University of Manitoba, Winnipeg, MB, Canada; 2. Clinical Health Psychology, University of Manitoba, Winnipeg, MB, Canada

Background: Persons with IBD and their clinicians often use the term 'flare' to refer to a presumed disease worsening. Instruments used to identify a patient-defined IBD flare are limited.
Aims: A case-control design was used to assess the relationship between a 7-point indicator used to identify an IBD flare and alternative measures of disease activity and quality of life: fecal calprotectin (FCAL), a 2-point self-report scale defining IBD as inactive/active, a newly developed symptom index score (SIBDSI), and the short form IBDQ (SIBDQ).
Methods: Persons aged 18-75 living in Manitoba with a confirmed IBD diagnosis (n=71) were surveyed biweekly for 26 weeks (98% response rate), and provided periodic stool samples. A patient-defined IBD flare was identified using a score of 6 or 7 on the 7-point indicator; a dynamic measure assessing change in symptoms over time. Participants with self-defined flares were systematically matched to controls (participants who had never reported a flare) based on survey week, sex, and disease type. We compared the prevalence of active IBD symptoms using the SIBDSI and the SIBDQ. We also compared SIBDSI and SIBDQ scores for both flares and controls at the time and two weeks prior to the reported flare, to determine if the patient-identified flare reflected a change in symptom activity. A FCAL level ≥ 150 was indicative of intestinal inflammation.
Results: 38% of participants reported at least one IBD flare during the study period. 97.2% of persons reporting a flare described having active IBD compared with 32.4% of controls (p<0.001). 94.4% of persons reporting a flare vs 38.2% of controls had an SIBDSI score above the cut-off of 14 for CD; 13 for UC (p<0.001). The mean SIBDSI score was significantly different in flares versus controls (31.1±12.0 vs 11.9±7.5, p<0.001), as was the mean SIBDQ score (44.3±9.1 vs 57.0±9.1, p<0.001). There was a greater change in SIBDSI and SIBDQ scores among flares than among controls, comparing two weeks prior and the

time of the reported flare (SIBDSI Δ=8.61±8.37 vs 0.27±3.94; SIBDQ Δ=6.22±5.27 vs 0.45±3.36; p<0.001 for both. Participants in the flare group were no more likely than matched controls to have an elevated FCAL (52.9% vs. 47.1%, p=0.825) at the time of the reported flare.

Conclusions: The presence of a self-reported flare was associated with higher levels of symptom activity and lower health related quality of life. Changes in symptoms and quality of life concurrent with the report of a flare, provided confirmation of the patient experience. While FCAL levels did not differentiate those reporting a flare from those not, scores were elevated for approximately half of both groups, suggesting inflammation does not consistently translate to symptoms.

A114
ASSESSMENT OF INFLAMMATORY BURDEN IDENTIFIES CROHN'S DISEASE AND ULCERATIVE COLITIS PATIENT GROUPS WITH DIFFERENT DISEASE-DRIVING PATHWAYS AND THERAPEUTIC RESPONSE TO ANTI-TNF TREATMENT

S. Pavlides[1], M. Loza[2], P. Branigan[2], C. Monast[3], A. Rowe[1], F. Baribaud[2]

1. Janssen Research & Development Ltd, High Wycombe, United Kingdom; 2. Janssen Research & Development, LLC, Spring House, PA; 3. Janssen Research & Development, LLC, Spring House, PA

Background: CD and UC are thought to be driven by both common and distinct pathobiology. Heterogeneity in both diseases is underscored by variability in clinical responses to therapeutic interventions.
Aims: To explore this heterogeneity we aimed to classify individuals into subgroups based on their pathobiology and assess the relationship of these subgroups to clinical response to anti-TNF.
Methods: Colonic biopsies from healthy volunteers (HV), CD patients and UC patients were analyzed by performing hierarchical clustering on enrichment scores (ES) calculated from a library of gene signatures. These signatures represent various immunological processes and cell types. Biopsies were collected as part of a previously published study (GSE16879) and were taken at baseline (BL) or post anti-TNF treatment (PT) and patients were a mix of clinical responders (R) and non-responders (NR). Gene signatures that were significantly differentially enriched between groups of interest were identified using general linear models.
Results: Differential enrichment analysis identified 58 signatures that were significantly different from HV for CD and UC at BL. These signatures represented multiple conditions, including activated T cells, monocytes, macrophages or neutrophils and

stimulation with poly:IC or bleomycin. A baseline comparison of R and NR separately to HV common in CD and UC revealed 43 and 69 differentially enriched signatures, respectively, suggesting higher inflammation burden in NR. For both CD and UC, hierarchical clustering clearly separated diseased BL from HV and R from NR. PT samples from R were also shown to cluster with HV while PT NR samples clustered with the BL diseased samples suggesting that inflammation burden was reduced in R but not NR.
Conclusions: Our analysis identified common disease-driving pathways for CD and UC, supporting the notion of a disease continuum rather than two distinct diseases. However, within that continuum, distinct patient groups existed based on overall inflammatory burden which correlated with clinical response to anti-TNF. Our approach could facilitate better design of clinical studies testing novel therapeutics by concentrating on patient subsets that share similar disease-driving pathways which may increase the likelihood of clinical response.

A115
ROLE OF GUT SEROTONIN IN ANTIMICROBIAL PEPTIDE PRODUCTION

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

Farncombe Family Digestive Health Research Institute; Department of Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada

Background: Antimicrobial peptides (AMPs) constitute an armory of innate regulators of crucial importance in the gastrointestinal (GI) tract. It is becoming evident that AMPs, especially human β-defensins (hBDs) produced by colonocytes, shape the composition of the microbiota and help maintain gut homeostasis. Defective bacterial clearance and subsequent modulation of gut microbiota, due to abnormal defensin expression, is associated with pathogenesis of various GI diseases including Inflammatory Bowel Disease (IBD). Serotonin or 5-hydroxytrytophan (5-HT) is a neurotransmitter and hormone that contributes to the regulation of various physiological functions in GI tract. Changes in gut 5-HT signaling are observed in IBD as well as in experimental colitis. Enterochromaffin (EC) cells of the human GI tract are the largest producers of 5-HT, and 5-HT biosynthesis depends on the rate-limiting tryptophan hydroxylase 1 (Tph1). We have previously demonstrated Tph1-deficient ($Tph1^{-/-}$) mice, which have significantly lower gut 5-HT levels, exhibited reduced severity of colitis compared to their wild-type ($Tph1^{+/+}$) littermates; while replenishing 5-HT led to increased severity of colitis. As EC cells are situated in the epithelial layer and epithelial cells express 5-HT receptors, we hypothesize that 5-HT can influence β-defensin production directly by acting on

the adjoining epithelial cells in relation to innate defense in the GI tract.

Aims: To elucidate the role of 5-HT in β-defensin production from intestinal epithelial cells in the context of regulating innate immune response.

Methods: We utilized human colonic HT-29 cells to assess the level of hBD expression upon stimulation with 5-HT (10^{-3}, 10^{-7}, 10^{-11} M). Quantitative PCR (qPCR) and conventional ELISA were performed to measure gene expression and protein levels in culture supernatant, respectively. Additionally, we measured mouse β-defensin levels in colonic tissues of n*aïve Tph1$^{+/+}$* and *Tph1$^{-/-}$*.

Results: 5-HT, in a dose dependent manner, regulates hBD production by HT-29 cells, where higher 5-HT concentrations down-regulated both mRNA and protein levels. Moreover, we observed significantly higher levels of total mBD in the colonic tissues of *Tph1$^{-/-}$* compared to *Tph1$^{+/+}$*, suggesting an inhibitory role of 5-HT in defensin production.

Conclusions: Our results illustrate that 5-HT released from EC cells can modulate hBD production from intestinal epithelial cells. These results exemplify novel information on the interaction between 5-HT and hBD in relation to intestinal innate immune response and corroborate with previous findings of attenuated hBD expression in colonic CD patients.

Funding Agencies: CCC

A116
ABERRANT IMMUNE RESPONSE AGAINST INVADING BACTERIA INCREASES MORTALITY IN MUC2 MUCIN DEFICIENT MICE IN LPS INDUCED SEPSIS
M. Kumar, F. Moreau, K. Chadee

MIID, University of Calgary, Calgary, AB, Canada

Background: A physical barrier in the gut, formed mainly by the mucus bilayer, keeps gut microbiota and/or components away from translocating into host tissues. Perturbation of the mucus layer, as in inflammatory bowel diseases (IBD), leads microbial penetrants to initiate local and systemic inflammation. Unregulated inflammation can aggravate into sepsis, causing mortality due to multiple organ failure. IBD patients are at high risk for developing sepsis due to their defective gut barrier function, yet is poorly understood. *Muc2$^{-/-}$* mice without a mucus barrier have low-grade inflammation with bacterial penetrants and is an excellent model to study chronic colitis and ideal for IBD related studies.

Aims: To assess immune response in *Muc2$^{-/-}$* mice in lipopolysaccharide (LPS) induced sepsis.

Methods: LPS was administered in *Muc2$^{-/-}$* and WT littermates intra-peritoneally (i.p.) as 5mg/kg body weight (BW) and monitored for BW loss and mortality. Mice were euthanized at 24 or 48 h. Spleen and intestinal tissue were harvested for immunophenotyping and histology. Single cell suspension of splenocytes were prepared and stained with anti CD3, CD4, CD8, CD19 and CD49b antibodies for T-cells, B-cells and NK cells. Apoptotic and dead cells were determined by Annexin V and 7-AAD staining. Immunophenotyping was done using FACS Canto and data was analyzed by FlowJo software. Bacterial penetrance into distal ileum, cecum and colonic tissue was determined using fluorescence in situ hybridization (FISH) and real time RT-PCR.

Results: *Muc2$^{-/-}$* mice basally exhibited significantly larger numbers of splenic B-cells, CD8+ cells and NK cells than WT littermates suggesting ongoing elevated systemic inflammation. CD4+ cells were unchanged. Notably, *Muc2$^{-/-}$* mice exhibited increased apoptosis of splenic B-cells at baseline indicating systemic inflammation and immunosuppression. Following LPS induced sepsis, we observed increased bacterial penetrance through the distal ileum, cecum and colonic walls of *Muc2$^{-/-}$* mice at 24 and 48 h as compared to WT littermates. In WT littermates, LPS treatment led to massive accumulation and secretion of mucus (mucus plug) in the lumen that impaired bacterial translocation. Moreover, splenocytes in LPS induced sepsis showed significantly increased apoptosis of B-cells, decreased apoptosis of CD4+ and CD8+ cells in *Muc2$^{-/-}$* as compared to WT littermates. The aberrant immune response in *Muc2$^{-/-}$* mice was correlated with significantly increased bacterial burden in the liver and spleen resulting in rapid BW loss and mortality.

Conclusions: Our research suggests that during chronic IBD, host immune cells may become exhausted with continual exposure to microbial penetrants leaking through the altered and/or depleted intestinal mucus barrier. This can result in aberrant immune response against invading pathogens and increased susceptibility to sepsis.

Funding Agencies: CCC, CIHR

A117
IMPLICATION OF LRRK2 IN CROHN'S DISEASE PATHO-GENESIS.
j. rocha[2], M. Schlossmacher[3], D. Philpott[1]

1. University of Toronto, Toronto, ON, Canada; 2. Immunology, University of Toronto, TORONTO, ON, Canada; 3. University of Ottawa, Ottawa, 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). Studies using a murine colitis model have pointed to the involvement of LRRK2 in regulating an NFAT-dependent pathway that dampens the production of certain inflammatory cytokines. Also, recent work showed that LRRK2 interacts with NOD2 in Paneth cells in order to properly secrete antimicrobial peptides into the intestinal lumen and promote gut-microbiota homeostasis.

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 Crohn's disease (CD).

Methods: WT and LRRK2-deficient neutrophil and macrophages were infected with different Gram-negative and a Gram-positive Bacteria (*S. typhimurium* and *Listeria monocytogenes*) in a gentamicin protection assays and colony-forming unit assessment will determine the competence of LRRK2 deficient cells for bacterial phagocytosis (4h) and killing capacity (24h). We evaluate 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) phenotype after injection of different microbial stimuli including FK105 (NOD1 ligand), MDP (NOD2 ligand) and LPS (TLR4 ligand) in WT mice compared to LRRK2-KO and G2019S-KI mice.

Results: We found that LRRK2 KO mice have a defect in migration of immune cells (neutrophil and monocytes) to the peritoneal cavity after injection of different microbial stimuli including FK105 (NOD1 ligand), MDP (NOD2 ligand) and LPS (TLR4 ligand). In contrast, the G2019S knock-in mice show a higher rate of migration of immune cells compared to cells from wild-type animals. Neutrophils from LRRK2 mice were compromised in their ability to transmigrate in vitro in a transwell assay using fMLP as a chemattractant. In parallel, we designed experiments to examine reactive oxygen species (ROS) produced in response to infection of myeloid cells with bacteria. Neutrophils and bone marrow-derived macrophages from LRRK2 KO mice infected with *Listeria monocytogenes* or *Salmonella typhimurium* 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 are beginning 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 the mucosal barrier maintenance, including how its deficiency may predispose an individual to developing CD.

A118
EXPOSURE TO CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE E.COLI (AIEC) AT THE HEIGHT OF INFECTIOUS COLITIS IMPAIRS HOST-MEDIATED CLEARANCE OF AIEC
H. Law[1], B.K. Coombes[2]

1. McMaster, Hamilton, ON, Canada; 2. McMaster University, Hamilton, ON, Canada

Background: Prior exposure to foodborne pathogens causing acute gastroenteritis can have long lasting consequences, including an increased risk of Crohn's disease (CD). However, the underlying pathologic connection between the inciting event and CD, a chronic inflammatory condition, is not known. Adherent-invasive *E. coli* (AIEC) are enriched in the intestinal mucosa of CD patients though exactly how it contributes to this chronic illness is unclear. We recently demonstrated that AIEC-colonized mice exposed to acute infectious gastroenteritis drives the expansion of tissue-associated AIEC in regions of pronounced inflammation.

Aims: Since AIEC are associated with inflamed regions of the gut, we hypothesized that host inflammation could be a susceptibility factor that promotes *de novo* AIEC colonization.

Methods: We tested this in a conventional C57BL/6 mice that when exposed to AIEC develop a self-limited infection. C57BL/6 mice were infected with *Citrobacter rodentium* to initiate acute infectious colitis, or kept uninfected. Subsequently, *C. rodentium*-infected mice were exposed to AIEC at one of three distinct stages of colitis (peak *Citrobacter* load, peak inflammatory response, or during convalescence after *Citrobacter* clearance and mucosal restitution). Over the infectious period, bacterial load was measured in feces and tissues. Pathology was evaluated by ELISA and microscopically.

Results: We report that *Citrobacter*-colonized mice challenged with AIEC at either the peak of *Citrobacter* load or during the convalescence period resulted in clearance of AIEC within 2-3 weeks and without overt influence on overall pathology. Strikingly, *Citrobacter*-colonized mice infected with AIEC during peak period of colitis led to bacterial persistence and impaired clearance as mice remained AIEC-positive as late as day 59 after the acute infectious colitis resolved. In contrast, *Citrobacter*-naïve mice resolved the infection by day 19 and lacked the pronounced pathology observed in the co-infected group.

Conclusions: Together, our data suggests that the period of peak inflammation following infectious colitis is a time when host succeptitibilty to AIEC is greatest, leading to protracted AIEC colonization and greater immunopathology.

A119
THE MICROBIAL METABOLITE SENSOR PREGNANE X RECEPTOR (PXR) RESTRAINS FIBROBLASTS FROM PROMOTING INTESTINAL INFLAMMATION AND FIBROSIS IN MICE
K.L. Flannigan[1], L. Alston[1], S. Mani[2], S.A. Hirota[1]

1. Physiology & Pharmacology, University of Calgary, Calgary, AB, Canada; 2. Albert Einstein College of Medicine, Bronx, NY

Background: Fibrosis contributes to intestinal stricture and obstruction in 30-50% of Crohn's disease patients.

The pathogenesis of fibrosis is incompletely understood and has virtually no effective treatments. The pregnane X receptor (PXR), a xenobiotic receptor involved in detoxification responses, has been identified as a modulator of fibrosis in hepatic stellate cells. Of the number of foreign ligands for the PXR, the tryptophan metabolite indole-3-propionic acid (IPA) produced by the intestinal commensal *Clostridium sporogenes* can bind to the PXR to mediate signalling events that protect intestinal barrier function. The role of the PXR in intestinal fibrosis and if microbial metabolite sensing can affect intestinal fibrotic responses is unknown.
Aims: To examine the role of the PXR and its ability to sense microbial metabolites in the modulation of intestinal fibrosis.
Methods: Intestinal inflammation was induced using DSS (3.5%) for 5 days followed by healing for 25 days. Fibrosis was assessed using Masson's trichrome and Sirius Red staining of colonic sections. Mouse primary colonic fibroblasts were grown from wild type (WT) and PXR-/- mice and stimulated with cytomix (TNFα, IL1β, and IFNγ) for 24 hours to assess cytokine production by Luminex. Fibroblasts were also stimulated with cytomix in the presence of the PXR agonists PCN or IPA and assessed for gene expression via qPCR. NFkB activity was assessed by Western blot for phos-p65. To examine the microbiota's role in fibrosis, after the 5-day course of DSS the microbiota was depleted for 25 days with an antibiotic cocktail (vancomycin, neomycin, metronidazole, ampicillin). *C. sporogenes* DNA was detected in feces using qPCR.
Results: Following a 25-day recovery after DSS, WT mice demonstrated clear intestinal fibrosis. When compared to WT mice, PXR-/- mice demonstrated significantly greater levels of fibrosis. Mouse primary fibroblasts were found to express the PXR. Following stimulation with cytomix, PXR-/- fibroblasts produced dramatically higher levels of inflammatory cytokines including eotaxin, CXCL2, G-CSF, GM-CSF, IL-9, and IL-15. Importantly, PCN and the microbial metabolite IPA suppressed the expression of these cytokines. These effects in PXR-/- fibroblasts may be linked to the increased activity of NFkB that was observed both basally and after stimulation with cytomix compared to WT fibroblasts. Depletion of the microbiota supressed levels of *C. sporogenes* DNA in feces and exacerbated intestinal fibrosis.
Conclusions: PXR signaling in intestinal fibroblast appears to be required to restrain inflammation and fibrosis. Luminal sensing of bacterial derived indoles (i.e. IPA) via PXR may be involved in this process, highlighting a xenobiotic-microbiota axis that could be targeted to prevent the intestinal fibrosis observed in Crohn's disease.

A120
PREVALENCE OF ANXIETY AND DEPRESSION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
G. Byrne[3], B. Bressler[1], G. Rosenfeld[2]

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

Background: Inflammatory bowel disease (IBD) patients are not routinely screened for depression and anxiety despite knowledge of an increased prevalence in people with chronic disease and negative effects on quality of life.
Aims: We aim to determine the prevalence of anxiety and depression in IBD patients.
Methods: The prevalence of anxiety and depression was assessed in outpatients with IBD attending a clinic associated with a tertiary teaching hospital (St. Paul's Hospital, Vancouver, Canada) through retrospective chart review. The presence of anxiety and/or depression was determined using the Patient Health Questionnaire – 9 and Generalized Anxiety Disorder – 7 self-report questionnaires (administered routinely to patients attending the clinic), with a score above 10 considered a positive result. Patients were also considered to have depression or anxiety if diagnosed by psychiatric interview after referral to a psychiatrist. Information regarding patient demographics, disease characteristics and medications was also collected. Disease activity was defined using the Partial Mayo Score (UC) or Harvey- Bradshaw Index (CD) where patients with a score within the moderate or severe range were considered to have active disease. Multivariable analysis was used to determine associations between patient factors and depression and anxiety.
Results: 327 patient charts were reviewed. The study population was 49.8% female, 37.9% had Ulcerative Colitis and 62.1% Crohn's Disease, mean age was 38.72 +/- 14.44, and mean time since diagnosis 10.96 years +/- 8.64. The rates of depression and anxiety were found to be 25.8% and 21.2% respectively, with 30.3% of patients suffering from depression and/or anxiety. Three percent of patients were on steroids and 61% were previously or currently on biologics. Approximately 13% of patients had active disease at the time of assessment. Disease activity was found to be significantly associated with depression and/or anxiety (p=0.01). Females were more likely to have anxiety (p=0.01).
Conclusions: A significant proportion of IBD patients suffer from depression and/or anxiety. The rates of these mental illnesses would justify screening and referral for psychiatric treatment in clinics treating this population. Patients with active disease are particularly at risk for mental health sequelae and should therefore be paid extra attention in screening and treatment efforts.

IBD

A121
DESIGNER PROBIOTICS AS A NOVEL THERAPEUTIC AGAINST INFLAMMATORY BOWEL DISEASE.
S.K. Gill, A. Godovannyi, J.A. Barnett, C.S. Quin, D.L. Gibson

University of British Columbia Okanagan , Kelowna , BC, Canada

Background: Inflammatory bowel disease is a major health burden in developed countries. Current pharmaceutical therapies are risky or ineffective for long-term use and are associated with severe side effects. Therefore, new alternative therapies for IBD are needed. Probiotic therapy, which is the ingestion of non-pathogenic microorganisms to provide health benefits, is considered a potential treatment option. However, clinical trials using probiotics for IBD treatment have yielded very inconsistent and difficult to interpret data. There is a lack of evidence to support the use of probiotic supplementation in IBD manage-ment. We have created genetically engineered probiotics that we hypothesize are more efficacious than current commercial probiotics.
Aims: The overall aim is to determine if the novel designer probiotics will result in better efficacy of probiotic therapy against IBD.
Methods: Post-weaned female C57BL/6 mice (n=8) were given either of the two designer probiotics (007A or 007B) or the unmodified parent strains with $1x10^9$ CFU/ml via oral gavage for 1-3 days. The mice were challenged with 3.5% DSS via drinking water for 7 days to induce DSS-induced murine colitis. Weight change and clinical scores were assessed. Intestinal immune responses including histopathological scoring, immune cell infiltration, and cytokine analysis were performed.
Results: Both designer probiotics, 007A and 007B, were shown to be more efficacious during colitis compared to the unmodified parent strains. Macroscopic examination revealed modified designer probiotics have less bloody and loose stool in their colon and cecum compared to the unmodified parent strains. Both designer probiotic groups lost significantly less body weight and had lower clinical scores during the DSS-induced colitis period. The unmodified parent DSS group lost up to 15% of their initial starting body weight and had high clinical scores, indicating humane endpoint. Our designer probiotic supplementation showed significantly fewer gene expression levels of pro-inflammatory markers such as TNF-α, IFN-γ, IL-1β, and IL-17a. In contrast, the unmodified parent strains showed elevated expression of many pro-inflammatory markers, indicating no improvement during IBD.
Conclusions: Our proprietary designer probiotics control inflammation and associated symptoms during colitis. This research could result in genetically improved probiotics leading to better efficacy and a potential alternative therapeutic option for IBD patients.

A122
CANADIAN STUDY OF ADHERENCE OUTCOMES IN HUMIRA® (ADALIMUMAB) PATIENTS: THREE-YEAR RESULTS FROM THE COMPANION STUDY IN GASTROENTEROLOGY PATIENTS
J. Marshall[1], G. Lebovic[2], B. Millson[3], M. Sung[3], T. Gaetano[4], M. Latour[4], M. Laliberte[4]

1. McMaster University Medical Centre, Hamilton, ON, Canada; 2. Applied Health Research Centre, St. Michael's Hospital; Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, ON, Canada; 3. IMS Brogan, Kirkland, QC, Canada; 4. AbbVie, St.Laurent, QC, Canada

Background: HUMIRA® (adalimumab, ADA) is a TNF-alpha inhibitor indicated for inflammatory autoimmune diseases including Crohn's disease (CD) and ulcerative colitis (UC). Patients receiving ADA in Canada can enroll in the AbbVie Care patient support program (PSP) providing personalized services.
Aims: This retrospective study assessed the impact of specific factors, including PSP services and patient characteristics, on persistence and adherence to ADA over a 3-year period in the overall cohort (all indications) and in CD and UC patients specifically.
Methods: ADA PSP patients were linked to the IMS longitudinal pharmacy transaction database using a probabilistic matching algorithm. Patients starting ADA between July 2010 and August 2012 were indexed and tracked for 36 months to calculate days until end of persistence (>90 days without therapy), censored for persistence through month 36. Cox regressions and multivariable logistic regression models provided hazard ratios (HR) and adjusted odds ratios (OR) to measure the association between patient characteris-tics/PSP services and persistence and adherence, respectively. Adherence was measured using the medication possession ratio (MPR) (≥80% MPR). Additional analyses were done in patients who were persistent up to when specific PSP services were introduced in a separate cohort.
Results: A final sample of 4,772 patients (including 1,921 CD and 108 UC patients) was selected. In the overall cohort, older age groups had significantly greater odds of adherence (40-49, 50-59, 60-69, 70+; OR=1.3, 1.4, 1.4, 2.1; p<0.05 for all comparisons) relative to the 30-39 years age group. In a subset of patients (n=2,866) who were persistent when ongoing care coach calls were available, those receiving this service were 65% less likely to stop therapy (HR=0.35, p<0.01) and 38% more adherent (OR = 1.38, p<0.01) compared to those without it. Among this patient subset, CD and UC patients (n=1,321) who received this service were 53% more persistent (HR=0.47, p<0.01) and 45% more adherent (OR=1.45, p<0.05) compared

to those without it.

Conclusions: Ongoing care coach calls provided by the AbbVie Care PSP significantly correlate with greater patient persistence and adherence over 36 months. These results may help refine services that improve treatment adherence.

Funding Agencies: AbbVie

A123
INCREASING TIME ON TREATMENT IS PREDICTIVE OF IMPROVED LONG-TERM RETENTION FOR STABLE REMICADE® (INFLIXIMAB) INFLAMMATORY BOWEL DISEASE PATIENTS IN CANADA

J. Marshall[2], M. Marrache[1], E. Ewara[1]

1. Janssen Inc, Toronto, ON, Canada; 2. McMaster University and Farncombe Family Digestive Health Research Institute, Hamilton, ON, Canada

Background: Many patients treated with anti-TNF agents discontinue therapy.

Aims: The objective of this analysis was to determine the long-term retention patterns of stable Canadian IBD patients treated with REMICADE® (infliximab [IFX]).

Methods: Using IMS Brogan™ Canadian private and public insurance claims data, our analysis included IBD patients with: (1) first IFX claim between Jan 2008-May 2015; (2) no IFX claims 12 months prior to the initial claim; (3) ≥1 claim for any other drug 12 months after the initial IFX claim; and (4) ≥1 claim for any non-IFX drug 4 months after May 2015. Retention was measured at 12-month intervals and unadjusted odds ratios were determined. Within-group analyses compared 12 month retention by number of years on IFX and compared subgroups of patients according to age group, gender, prior biologic experience, region (private claims only) and insurance type.

Results: 4,360 patients had ≥2 years of claims history and had been on IFX for ≥1 year. Within-group comparisons showed that the probability of being retained on IFX in subsequent 12 month periods increased with cumulative time on IFX. Patients on IFX for 2-5 years showed significantly higher retention in the subsequent 12 months compared to patients on IFX for only 1 year (P<0.05). Similar trends were observed across when stratified by gender and insurance type, as well as in patients in Ontario, aged 19-64 years, and those who were biologic-naïve. Annual retention up to and including 5 years was significantly better for patients who were publicly insured, and lived in Ontario and Eastern Canada when compared to patients who were privately insured, and lived in British Columbia, respectively.

Conclusions: Real world patients treated with IFX have excellent long-term treatment retention. Previous duration of IFX treatment appears to predict better future retention, becoming statistically significant after 2 years. The results were robust and consistent amongst various subgroups of stable Canadian IBD patients.

Odds of Being Retained (Odds Ratio)

Retention Year vs Year	IBD Patients n=4,360	Male n=2,055	Female n=2,288	Bio-Naïve n=4,147	19-64 Years n=3,561	Public Claims n=1,290	Private Claims n=2,033	Ontario n=1,358
2 vs 1	1.3	1.2 p=0.06	1.4	1.3	1.2	1.2 p=0.09	1.4	1.4
3 vs 1	1.6	1.5	1.7	1.6	1.4	1.4	1.7	1.8
4 vs 1	1.8	1.9	1.7	1.8	1.7	1.8	1.6	1.8
5 vs 1	2.5	2.2	2.8	2.4	2.8	1.7	2.1	2.1

p value<0.05 unless noted otherwise

Funding Agencies: NoneJanssen Inc.

A124
THE DIAGNOSTIC ACCURACY OF BLOOD AND TISSUE-BASED TESTS FOR CYTOMEGALOVIRUS REACTIVATION IN INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

P. Tandon[2], T. Shukla[2], P.D. James[2], R. Mallick[1], J. McCurdy[2]

1. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 2. Department of Gastroenterology, The Ottawa Hospital, Ottawa, ON, Canada

Background: Several diagnostic techniques exist to detect cytomegalovirus (CMV) reactivation in inflammatory bowel disease (IBD). The accuracy of these tests compared to one another remains poorly defined.

Aims: As such, the aim of this study was to compare the sensitivity and specificity of diagnostic tests for CMV reactivation in IBD.

Methods: Multiple electronic databases were searched through July 2015 for cross-sectional and cohort studies comparing the accuracy (sensitivity and specificity) of at least two diagnostic tests for CMV reactivation in IBD. Initially, the accuracy of blood-based tests (whole blood PCR (bPCR) or pp65 antigenemia assay) was determined using tissue-based tests (tissue PCR (tPCR), immunohistochemistry (IHC) or hemotoxylin and eosin (H&E)) as the reference standard. Next the accuracy of individual tissue-based tests was assessed. Weighted summary estimates were determined by bivariate analysis, with random-effects or fixed-effects modelling when appropriate. Individual study quality was assessed by the QUADAS-2 tool.

Results: Twelve studies compared blood-based tests (6 by bPCR, 5 by pp65, 1 by both) with tissue-based

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tests. The overall sensitivity and specificity of blood-based tests was 65% (95% CI, 31-99%) and 92% (95% CI, 89-96%) respectively. The sensitivity of bPCR was 63% (95% CI, 51-76%), and the sensitivity of pp65 antigenemia was 39% (95% CI, 27-52%). Eight studies compared histopathology (5 by H&E and 4 by IHC) with tPCR. The sensitivity of H&E was 6.2% (95% CI, 2.2-16.3%), and the sensitivity of IHC was 28.3% (95% CI, 12.2-52.8%) when compared to tPCR as the reference standard. Specificity was high for H&E (98.1%; 95% CI, 94.2-99.4%), and IHC (98.0%; 95% CI, 92.2-99.5%). Studies were limited by low study quality and in the ability to compare clinically relevant CMV reactivation. **Conclusions:** Our study demonstrates that blood-based tests and H&E are insensitive markers for CMV reactivation in IBD and should not be used as sole diagnostic tests.

Funding Agencies: None

A125
CHARACTERIZATION OF RATES AND PREDICTORS OF VENOUS THROMBOEMBOLISM PROPHYLAXIS IN HOSPITALIZED INFLAMMATORY BOWEL DISEASE PATIENTS AT A TERTIARY CARE CENTRE IN NEW BRUNSWICK, CANADA.

A.M. Harrigan[1], C. Williams[2], G. Stoica[3]

1. Undergraduate Medical Program, Faculty of Medicine, Dalhousie Medicine New Brunswick, Saint John, NB, Canada; 2. Department of Medicine, Faculty of Medicine, Dalhousie University, Halifax, NS, Canada; 3. Horizon Health Network Research Services, Saint John, NB, Canada

Background: Inflammatory bowel disease (IBD) patients are at an increased risk for venous thromboembolisms (VTE), especially during hospitalization. Literature has shown that rates of VTE prophylaxis in hospitalized IBD patients are suboptimal.
Aims: The aim of this study is to characterize the rates and predictors of VTE prophylaxis in hospitalized IBD patients at the Saint John Regional Hospital, NB, Canada.
Methods: A retrospective chart review of 351 IBD patients hospitalized from June 2010 to June 2016 was conducted. Data pertaining to VTE prophylaxis and clinical characteristics of the patients were abstracted. A linear regression was performed to determine the service where hospitalized IBD patients were more likely to receive VTE prophylaxis. A multivariate log-Poisson regression and a multiple hierarchical multivariate logistic regression were conducted to identify the predictors of VTE prophylaxis.
Results: Hospitalized IBD patients admitted to the Internal Medicine or General Surgery service were more likely to receive pharmacological VTE prophylaxis (adjusted OR=2.36; 95% CI: 1.18-4.66; p <0.0001), and those admitted to the Family Medicine or other services were more likely to not receive pharmacological

VTE prophylaxis (adjusted OR=3.12; 95% CI: 1.80-6.60; p <0.0001). A strong positive association was demonstrated between the receipt of VTE prophylaxis and IBD patients presenting with rectal bleeding in combination with a high Charlson Comorbidity Index score (OR=2.9; 95% CI:1.67-4.57; p<0.001). A positive medium association was demonstrated between the receipt of VTE prophylaxis and IBD patients with a high risk designation from the Padua VTE Risk Assessment Tool in combination with a higher score on the Charlson Comorbidity Index (OR=1.7; 95% CI: 1.5-2.24; p<0.05) or the presence of a blood abnormality on the complete blood count at the time of admission (OR=2.2; 95% CI: 1.8-4.12; p <0.05). Yearly improvement in rates of VTE prophylaxis were appreciated in IBD patients with a combination of a high risk designation from the Padua VTE Risk Assessment Tool and a higher Charlson Comorbidity Index score.
Conclusions: Rates of VTE prophylaxis in hospitalized IBD patients were highest in patients admitted to General Surgery, where surgical procedures are a well-established risk of VTE. Patients with IBD admitted to the non-surgical services were less likely to receive VTE prophylaxis and discrepancies in awareness of the need for VTE prophylaxis in hospitalized IBD patients may account for these trends. Predictors of receiving VTE prophylaxis were a combination of more severe patient presentation and the presence of general VTE risk factors.

Funding Agencies: Dalhousie Medicine New Brunswick Research Program

A126
REAL WORLD CLINICAL EFFICACY OF LOW DOSE USTEKINUMAB INDUCTION IN CROHN'S PATIENTS REFRACTORY TO ANTI-TNF THERAPY

N. AL YATAMA[2], R. ROFAIEL[4], N. Chande[1], T. Ponich[3], J.C. Gregor[3]

1. The University of Western Ontario, London, ON, Canada; 2. GASTROENTEROLOGY, UNIVERSITY OF WESTERN ONTARIO , LONDON, ON, Canada; 3. LONDON HEALTH SCIENCES CENTRE, London , ON, Canada; 4. university of western ontario, LONDON, ON, Canada
Background: Patients with moderate to severe Crohn's disease refractory or intolerant to steroids, immunomodulators and anti-TNF therapy currently have few options for medical management outside of clinical trials. Ustekinumab, a monoclonal antibody, which inhibits interleukins 12 and 23 is currently being used safely and effectively to treat patients with psoriasis and recent studies suggest that it may be of value in treating moderate to severe Crohn's disease in patients both naive and refractory to anti-TNF therapy. Currently the intravenous formulation of ustekinumab used in these studies is unavailable for use outside of clinical trials.
Aims: The aim of this study was to examine the clinical efficacy of subcutaneously (sc) loaded ustekinumab in

patients with moderate to severe Crohn's disease who had failed at least one anti-TNF agent.

Methods: All patients given a loading dose of usteki-numab 270 mg sc over two weeks were included in this retrospective analysis. Baseline demographic data was collected. The primary outcome was the proportion of patients who achieved a Harvey-Bradshaw Index (HBI) </= 3 and who remained on ustekinumab at six months of therapy post loading dose, without requiring a change in ustekinumab dose nor the addition of any new agents to treat their Crohn's disease. Secondary outcome measures included the number of patients with serious adverse effects, the proportion of patents judged as improved (reduction of their HBI but not meeting the target of 3 or less) and the proportion of patients with a HBI </=3 regardless of whether or not their Crohn's medications were increased.

Results: 47 patients were started on sc ustekinum-ab, among which 30 (64%) were females. The age of patients ranged from 24 to 74 years old with a mean of 46.1 years of age. Twenty eight (60%) had failed two anti-TNF agents while the remainder had failed only one. The mean HBI at drug initiation was 9.7 (range 5 to 16). All patients were still on ustekinumab at six months with 2 patients (4 %) every 12 weeks, 43 patients (92%) every 8 weeks, 1 patient (2%) every 6 weeks, and 1 patient (2%) every 4 weeks). At six month follow up 24/47 patients (51%) had an improvement in HBI of at least 3 points and 10/47 (21%) met the primary outcome measure of HBI 3 or less. No serious adverse events (ie. infection, systemic allergic reactions or malignancies) were observed.

Conclusions: Loading doses of ustekinumab 270 mg sc administered over a two week period followed by maintenance doses at 4 or 12 week intervals appear to be clinically efficacious in the treatment of patients with moderate to severe Crohn's disease refractory to anti-TNF therapy. With further experience it will be determined whether higher loading and maintenance doses given either sc or intravenously will further improve the rates of response and remission.

A127
CROHN'S DISEASE DIAGNOSIS AFTER PROCTOCOLEC-TOMY AND ILEAL POUCH-ANAL ANASTOMOSIS FOR ULCERATIVE COLITIS: THERAPEUTIC APPROACH

J. Hercun[1], C. Richard[2], R. Lahaie[3], P. Poitras[1]

1. Université de Montréal, Montreal, QC, Canada; 2. Université de Montréal, Montreal, QC, Canada; 3. Université de Montréal, Montréal, QC, Canada

Aims: New onset Crohn's disease (CD) occurs in about 10% of patients having undergone total proctocolec-tomy and ileal pouch-anal anastomosis (IPAA) for the treatment of their ulcerative colitis (UC). Our objective was to review the treatment of CD developed in our patients with IPAA.

Methods: We reviewed files of 302 patients with an IPAA performed between 1985 and 2014 at the CHUM-Hôpital Saint Luc in Montreal. In patients with a minimal follow-up of 5 years postoperatively, 35 cases of CD were diagnosed. Patients were classified as having a diagnosis of CD through intestinal inflammation (proximal to the ileal pouch) (19 patients), fistulising (perineal) disease (11 patients), or a combination of both (5 patients).

Results: CD was diagnosed on average 88 months postoperatively (ranging from 2 to 244 months). Disease was controlled in 3 of 15 patients who received 5-ASA (20 %), in 7 of 19 patients treated with immu-nomodulators (37%), in 13 out of 17 patients receiving biologic TNF-inhibitors (76%). Surgical treatment was performed in 13 patients (7 patients needed pouch removal). Surgery was done in 9 out of 11 of cases with fistulising disease (82%); with pouch removal in 36% of cases, whereas in only 2 of the 19 patients in the intestinal inflammation group (11%). Pouch removal enabled discontinuation of medical therapy in 5 cases whereas the remaining 2 patients required long term therapy with TNF-inhibitors.

Conclusions: Therapeutic options for new onset CD of the ileal pouch are identical to the options available for treatment of typical CD. The approach can be tailored depending on the mode of presentation. Removal of the pouch enabled discontinuation of pharmacological therapy in a certain number of cases.

A128
CROHN'S DISEASE DIAGNOSIS AFTER PROCTOCOLEC-TOMY AND ILEAL POUCH-ANAL ANASTOMOSIS FOR ULCERATIVE COLITIS: PREDICTIVE FACTORS

J. Hercun, R. Wassef, R. Lahaie, P. Poitras

Université de Montréal, Montreal, QC, Canada

Aims: Total proctocolectomy and ileal pouch anal-anastomosis (IPAA) is considered a curative pro-cedure for ulcerative colitis (UC). However, symptoms of Crohn's disease (CD) can occur postoperatively in some cases. Having previously reviewed the postoper-ative prevalence of CD, our aim was to identify potential predictive factors present at time of surgery.

Methods: We reviewed the files of 302 patients with an IPAA performed between 1985 and 2014 at the CHUM Hôpital Saint Luc in Montreal. 163 patients with a min-imal follow-up of 5 years postoperatively were included in the analysis. The preoperative diagnosis was UC in 145 cases and indeterminate colitis (IC) in 18 cases. There were no cases of CD.

Results: New onset CD was diagnosed post-operatively in 35 cases. When comparing IPAA patients with or without CD, the following predictive factors for CD were identified: active tobacco smoking at time of surgery (5 % UC vs 22 % CD p=0.006), preoperative steroid treatment (86 vs 100% p=0.014), interrogation from the

clinician regarding a putative CD (7 vs 26 % p=0.004), mouth ulcers (12 vs 27% p=0.093). A past history of tobacco smoking was associated with UC (38 % UC vs 19 % CD p=0.058). No difference between endoscopic or histological appearance was noted between both groups. Pouchitis was observed more frequently in the CD group (63 vs 26 % p<0.001)

Conclusions: In our study, endoscopic and clinical characteristics at time of surgery failed to differentiate apparent UC patients later identified as CD. Some clinical points such as smoking history statistically correlated with a postoperative diagnosis of CD. In practice, clear predictive factors of clinical outcome remain to be determined.

A129
RATES AND CLINICAL PREDICTORS OF URGENT FINDINGS ON ABDOMINOPELVIC COMPUTED TOMOGRAPHY IN EMERGENCY DEPARTMENT PATIENTS WITH INFLAMMATORY BOWEL DISEASE

E. Wishart, R. Bryce, L. Worobetz

University of Saskatchewan, Saskatoon, SK, Canada

Background: Abdominopelvic computed tomography (APCT) has become a common imaging modality to investigate abdominal complaints, particularly in the emergency department (ED). Despite their clinical utility, APCTs carry a risk of cumulative radiation exposure. This risk is of particular concern in inflammatory bowel disease (IBD) patients given the chronic relapsing nature of the disease and repeated APCT scans. Therefore, attempts must be made to minimize the number of APCT scans in IBD patients by identifying those most likely to have urgent findings.

Aims: We aimed to quantify the rates of abdominopelvic computed tomography (APCT) in IBD patients presenting to the ED with gastrointestinal complaints and to examine clinical predictors of urgent findings in this population.

Methods: A retrospective cross-sectional study was performed among patients with IBD presenting to 3 EDs in Saskatoon between 2014-2015 with a gastrointestinal complaint. The primary outcomes were the rate of APCT, and the rates of obstruction, perforation, abscess or non-IBD related urgent findings (OPAN) on APCT. Clinical predictive variables analyzed were demographics, clinical symptoms, IBD medication use, physical exam findings, and laboratory values. Variables with a univariate P<0.2 were included in a multivariable logistic regression model.

Results: 181 patients presenting over 265 ED encounters met the inclusion criteria. 92 patients (50.8%) received a total of 104 APCTs. 40 patients had ulcerative colitis (UC). 11 (27.5%) of the UC patients received APCT. Only 1 of 12 APCTs in UC identified OPAN (8.3%) - a duodenal ulcer. 141 patients had Crohn's disease. 81 (57.4%) of the CD patients received APCT. 36 of 92

APCTs in CD identified OPAN (39.1%). The CT findings regarding OPAN for CD patients are shown in Table 1. Clinical variables retained in the final model were leukocyte count >11, diarrhea and BRBPR/hematochezia.

Conclusions: 39.1% of the APCTs performed in the ED among patients with CD showed urgent findings. Only 1 APCT performed on UC patients found non-IBD related urgent findings. To reduce unnecessary radiation exposure, the selection process for IBD patients referred for APCT must be improved. Using a clinical predictive model including leukocyte count >11, presence of diarrhea and presence of BRBPR/hematochezia may help in the selection of CD patients who should be investigated with APCT.

Frequency Distribution of OPAN Pathology on CT (N=92)

Pathology type	Number (%)
No Pathology	56 (60.9)
New/Worsening Obstruction	14 (15.2)
Perforation	6 (6.5)
Abscess	14 (15.2)
Non-Crohn's Disease	6. (6.5)

Subjects may have multiple types of pathology.

A130
TABLEAU DASHBOARD AS A QUALITY IMPROVEMENT AND STRATEGIC DRIVING TOOL IN THE IBD OUTPATIENT SETTING: EARLY EXPERIENCE FROM THE IBD CENTRE OF EXCELLENCE AT THE UNIVERSITY OF ALBERTA HOSPITAL

E. Lytvyak, L.A. Dieleman, B.P. Halloran, V. Huang, K.I. Kroeker, F. Peerani, K. Wong, R. Fedorak

University of Alberta, Edmonton, AB, Canada

Background: Prevalence of Crohn's disease (CD) and ulcerative colitis (UC), the two types of inflammatory bowel disease (IBD), is accelerating with over 230,000 Canadians and 30,000 Albertans living with this disease nowadays and over 1,500 new cases occurring annually in Alberta. IBD care is characterized by high utilization of health-care services, and IBD patients' outcomes have important implications for health, employment, quality of life and health care costs. Improving the efficiency of health care delivery in the IBD care is critical. Structure, process and outcome quality indicators (QIs) are commonly used measures to gain insight into health care organizations' performance regarding the quality of care provided. Transparency of quality is also of great importance for informed decision-making by IBD practitioners, various stakeholders and policy makers.
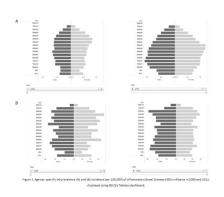
Aims: The aim of this project is to implement the IBD QIs Dashboard into real clinical settings that will

provide our IBD Unit with: (1) near real-time profile of structure, process and outcome Qis; (2) full spectrum of health and health care outcomes; (3) a visual display of evidence-practice gaps and barriers related to the Qis; (4) benchmarks to provide direction for IBD practice change based on evaluation of the provincial and zonal IBD prevalence and incidence rates.

Methods: The IBD practitioners in the IBD Unit (www.ibdunit.com) at the University of Alberta have developed a set of the QIs that are relevant, based on IBD practitioner's scope and domain of practice, and for which there is empirical evidence linking IBD practitioners' inputs and interventions to the outcomes. Data are extracted from the electronic health records, Discharge Abstract Database, National Ambulatory Care Reporting System and Interactive Health Data Application by the Alberta Government, and then displayed using interactive IBD QIs Dashboard utilizing Tableau software.

Results: A sample of the results obtainable using from the databases and displayed on the IBD QIs Dashboard is shown in Figure 1.

Conclusions: By adaptation of the IBD Qis Dashboard into real clinical settings as pragmatic and strategic driving tool we will now be able to pursue the following goals: (1) improve monitoring and reporting of IBD care system performance; (2) advance the IBD care experience for health care providers; (3) educate residents and fellows on various aspects of IBD care; (4) inform quality improvement and scale-up of IBD-related services; (5) reliably and accurately predict future health care needs in order to manage and distribute resources effectively; (6) improve long−term outcomes for IBD patients by generating evidence and capacity to enhance IBD care system performance.

Figure 1. Age-sex specific (A) prevalence (%) and (B) incidence (per 100,000) of Inflammatory Bowel Disease (IBD) in Alberta in 2000 and 2012, displayed using IBD Qis Tableau dashboard.

A131
ELECTRONIC HEALTH RECORD−BASED SMARTSETS INTEGRATE VARIOUS ASPECTS OF FLARE MANAGEMENT IN OUTPATIENTS WITH INFLAMMATORY BOWEL DISEASE THEREFORE ENSURING CONTINUITY OF CARE

E. Lytvyak[1], S. Devlin[2], L.A. Dieleman[1], B.P. Halloran[1], V. Huang[1], K.I. Kroeker[1], R. Panaccione[2], F. Peerani[1], K. Wong[1], R. Fedorak[1]
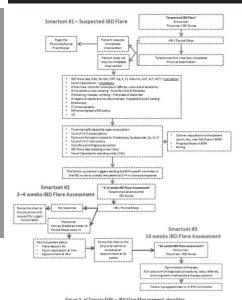
1. University of Alberta, Edmonton, AB, Canada; 2. University of Calgary, Calgary, AB, Canada

Background: Clinical course of inflammatory bowel disease (IBD) is characterized by periods of relapse (flares) and remission. Induction and maintenance of sustained endoscopic remission is the primary target in treatment of IBD resulting in improved quality of life, reduced complications rates, better health outcomes and less burden on the health care system.

Aims: The aim of this project is to implement the Electronic Health Record (EHR) based IBD "Flare management" algorithm that will ensure adherence to guidelines and continuity of IBD care over time warranting better health and health care outcomes.

Methods: In the IBD Unit at the University of Alberta Hospital (www.ibdunit.com) in collaboration with University of Calgary IBD specialists, we designed, developed and validated a set of the IBD Clinical Care Pathways (CCPs) (www.ibdclinic.ca/ibd-ccp/). These IBD CCPs are supported by systematic reviews of published evidence and are comprised of protocols, algorithms and checklists that help to harmonize clinical and administrative aspects, ensure stability of remission, and continuity of IBD care in outpatient setting.

Results: As a result of collaboration between the IBD Unit at the University of Alberta Hospital and Ambulatory Clinical Information Systems at the Alberta Health Services, the "Flare management" IBD CCPs have been successfully incorporated into eClinician® EHR system in a form of smartsets (documentation templates comprising of components relevant to the specific appointment and clinical situation).

The "Flare management" IBD CCPs encompass three subsequent smartsets representing comprehensive stepwise approach: (1) Suspected flare, (2) 2-4 weeks' Mid-flare, and (3) 16 weeks' Post-flare assessments. The complete algorithm is presented on the Figure 1. While using the smartsets, system prompts the IBD specialist to provide educational resources and instructions to the patient. One-time clicks lead to issuing and immediate printing of the requisitions, prescriptions, referral letters, progress notes, and after-visit summaries.

Conclusions: Implemented into real clinical settings, the "Flare management" IBD CCPs have many advantages including but not limited to: (1) maximizing compliance with up-to-date evidence-based guidelines; (2) streamlining the workflow by bridging various aspects of it; (3) helping to follow medication authorization more thoroughly to protect against misuse and overuse; (4) improving communication between IBD team members; (5) exercising "proactive care" by engaging patients into decision-making process, not just reacting to their needs; (6) accurately capturing data essential for measuring the process and outcome quality indicators and perform better reporting.

IBD

Figure 1. eClinician EHR – IBD Flare Management algorithm

A132
THREE QUARTERS OF INFLAMMATORY BOWEL DISEASE PATIENTS ON MAINTENANCE INFLIXIMAB THERAPY IN CLINICAL REMISSION SHOW EVIDENCE OF MUCOSAL INFLAMMATION WITH ELEVATED FECAL CALPROTECTIN

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

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: Fecal calprotectin (FCP) has been demonstrated to be a noninvasive marker of mucosal inflammation and when elevated, correlates with endoscopic mucosal disease activity in patients with Ulcerative Colitis (UC) and Crohn's Disease (CD). Endoscopic mucosal healing and normalization of FCP represents desired therapeutic results in these patients as it has shown to improve patient outcomes by reducing hospitalization and surgery.
Aims: To determine the proportion of patients with UC and CD in clinical remission on maintenance infliximab (IFX) therapy who had elevated FCP test results.
Methods: Sequential UC and CD patients over 18 years of age attending an IFX infusion clinic at the University of Alberta completed a Partial Mayo Score (pMS) or Harvey Bradshaw Index (HBI), as a determinant of clinical remission or disease activity, and were given a FCP test kit to voluntarily complete and return. FCP was determined using ELISA methodology.
Results: FCP test kits were given to 243 patients and 98 (40.3%) returned the kit for analysis (22 UC, 76 CD). Patients were separated by 4 categories: FCP ≥ 250 mcg/g, FCP ≥ 100 mcg/g, FCP < 250 mcg/g and FCP < 100 mcg/g. Twenty-three patients had FCP levels ≥ 250 (8 UC, 15 CD) of which, 78.3% were in remission, as indicated by pMS or HBI. Forty-one patients had FCP levels ≥ 100 (12 UC, 29 CD) of which, 73.2% were in clinical remission. Seventy-four patients had FCP levels < 250 (14 UC, 60 CD), of which, 79.7% were in clinical remission. Fifty-six patients had FCP levels < 100 (10 UC, 46 CD) of which, 83.9% were in clinical remission. Table 1 summarizes patient results for UC and CD.
Conclusions: Over 75% of patients on maintenance IFX therapy identified as being in clinical remission, as per disease activity scoring, yet show evidence of mucosal inflammation with elevated FCP tests. This suggests that to achieve a therapeutic outcome of mucosal healing with inflammatory bowel disease therapy, objective monitoring should be routinely conducted in all patients.

FCP concentrations for 98 IBD patients in clinical remission at the University of Alberta

	Crohn's Disease	Ulcerative Colitis
n (%)	76 (77.6)	22 (22.4)
FCP ≥ 250 (%) Clinical remission Clinically active	13 (86.7) 2 (13.3)	5 (62.5) 3 (37.5)
FCP ≥ 100 (%) Clinical remission Clinically active	22 (75.9) 7 (24.1)	8 (66.7) 4 (33.3)
FCP < 250 (%) Clinical remission Clinically active	46 (76.7) 14 (23.3)	13 (92.9) 1 (7.1)
FCP < 100 (%) Clinical remission Clinically active	37 (80.4) 9 (19.6)	10 (100.0) -

A133
EFFECTIVENESS AND SAFETY OF VEDOLIZUMAB INDUCTION THERAPY IN PATIENTS WITH ULCERATIVE COLITIS: REAL-WORLD EXPERIENCE IN A TERTIARY IBD CENTRE

P. Zezos[1], B. Kabakchiev[2], A.V. Weizman[1], G.C. Nguyen[1], N. Narula[1], K. Croitoru[1], H. Steinhart[1], M.S. Silverberg[1]

1. Mount Sinai Hospital, Toronto, Toronto, ON, Canada; 2. Lunenfeld Tannenbaum Research Institute, Toronto, ON, Canada

Background: Vedolizumab (VDZ) is a humanized monoclonal IgG1 antibody which inhibits leukocyte vascular adhesion and migration into the gastrointestinal tract through α4β7 integrin blockade. This agent became available in Canada in mid-2015 for the treatment of

moderate to severe ulcerative colitis (UC).

Aims: To investigate the real-world efficacy and safety of vedolizumab (VDZ) as induction therapy in UC patients at a tertiary IBD centre and to examine predictors of remission.

Methods: Demographic and clinical data for UC patients treated with 300mg VDZ infusions at weeks 0, 2, 6 and 14 was gathered retrospectively. Clinical remission (CR, partial Mayo score≤2) and steroid-free clinical remission (SFCR) after the first 3 infusions (induction phase) between weeks 8-12 were the primary endpoints. Secondary endpoints were CR and SFCR after 4 infusions (1st maintenance infusion) between weeks 16-20. Adverse events were also recorded.

Results: Data from 68 UC patients (63% male, median age 33 years, median disease duration 6 years, median pMayo 7) were analyzed. Anti-TNF naive were 31% and 69% had pancolitis. At the time of first infusion, 49% were on systemic steroids and 20% on an immunomodulator, while 44% patients were started on VDZ monotherapy. Median partial Mayo scores and median CRP levels improved significantly after 3 and 4 VDZ infusions compared to baseline (p<0.05). After 3 infusions (n=68), 37% and 31% of the patients achieved CR and SFCR respectively. After 4 infusions (n=53), 36% and 32% of the patients were in CR and SFCR respectively. Seventy percent of the non-responders after the 3rd infusion remained non-responders after the 4th infusion. Baseline characteristics including disease duration less than 5 years, no prior anti-TNF exposure, immunomodulator concurrent treatment, mild disease (p=0.025) and CRP less than 5mg/L (p=0.004) were associated with clinical remission after the first 3 infusions. Clinical remission after 3 VDZ infusions was significantly associated with sustained clinical remission after 4 infusions (p<0.001). Overall, 12% discontinued VDZ due to no response and 7% underwent elective proctocolectomy. There were no infusion reactions or serious side effects. The most common side effect was headache (7%).

Conclusions: VDZ is an effective, safe and well tolerated treatment option in refractory UC patients. Clinical remission and steroid-free clinical remission can be achieved in 1/3 of the patients after the induction phase. This real life series in a tertiary care centre demonstrates similar efficacy results as the other real-world clinical studies. Assessment of VDZ response after the 3rd infusion could be critical to determine treatment benefits and decide further management.

Patient characteristics	N=68
Gender	Male 63%
Age at start of vedolizumab, *median [IQR], years*	33 [26-43]
Disease duration, *median [IQR], years*	6 [4-10]
Disease extent	Ulcerative proctitis (E1)=1.5% Left-sided colitis (E2)=29.5% Extensive colitis/Pancolitis (E3)=69%
Extraintestinal manifestations	15%
Prior Immunomodulators	59%
Number of prior anti-TNF medications used	0=31%, 1=50%, 2=16%, 3=3%
Reason for anti-TNF discontinuation	Primary non response=43%, Secondary loss of response=47% Adverse events=10%
Vedolizumab monotherapy	44%
Concomitant corticosteroids	49%
Concomitant immunomodulators	19%
Treatment outcomes	*weeks 0 & 6, N=68 week 14, N= 53*
Clinical remission week 6, 14	37%, 36%
Steroid-free clinical remission week 6, 14	31%, 32%
On steroids week 0, 6, 14	49%, 37%, 24%
Median clinical Mayo Score week 0, 6, 14	7,4,4
Median CRP (mg/L) week 0, 6, 14	7.6, 5, 2.6
Adverse events (Side effects)	16% (11 pts-5 headache/migraines, 2 transient rash, 2 folliculitis, 1 gastroenteritis, 1 pruritus
Vedolizumab discontinuation Surgery (Colectomy)	12% (8 primary non response) 7% (N=5)

week 6= post 3rd infusion, week 14=post 4th infusion

Baseline characteristics and vedolizumab treatment outcomes in UC patients

A134
ANALYSIS OF POTENTIAL MICROBIAL-METABOLITE SENSORS IN THE BRAIN DURING EXPERIMENTAL COLITIS

F. Vicentini, N. Cluny, L. Griffin, Q. Pittman, M. Swain, S.A. Hirota, K.A. Sharkey

University of Calgary, Calgary, AB, Canada

Background: Patients with inflammatory bowel disease frequently show changes in behavior. Known as sickness behaviors, these alterations include anxiety, depression, fatigue and social withdrawal. The pathways by which inflammation in the gut leads to changes in the brain are yet to be fully elucidated. Recently it has been shown that the enteric microbiota plays a significant role in gut-brain communication. During gut inflammation, the microbiota are altered, possibly modifying the interactions established between bacterial metabolites and the brain. These changes could be related to the onset of the sickness behaviors. Furthermore, receptors in the brain that might sense the microbial metabolites are poorly described.

Aims: To investigate the presence of potential microbial-metabolite receptors in the brain: Pregnane X receptor (PXR), aryl hydrocarbon receptor (AhR), toll-like receptor 4 (TLR4), free-fatty acid receptor 2 and 3 (FFAR2 and FFAR3) - and their potential modulation during colonic inflammation.

Methods: Colitis was induced in male C57Bl/6 mice by administration of 2.5% dextran sulphate sodium (DSS) in the drinking water for 5 days. Controls were housed in the same room and received normal drinking water. On day 7, macroscopic damage of the colon was assessed and the brain was collected: sagittally divided in half, or by dissecting the hypothalamus, hippocampus, and amygdala. Bacterial receptors were assessed

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

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by RT-qPCR.
Results: DSS-treated mice presented with body weight loss (p=0.002) and increased macroscopic damage score (p<0.0001) compared to controls. Half brains from control mice were used to evaluate the presence of the receptors. AhR and TLR4 mRNA expression was found in half brain samples (Ct value < 30), whilst the PXR, FFAR2, and FFAR3 had low mRNA expression under baseline conditions (Ct value > 30). The expression of AhR and TLR4 in half brain samples was comparable between control and DSS-treated groups (p=0.79 for both receptors). The effect of DSS-induced colitis on AhR mRNA expression in the hippocampus, hypothalamus, and amygdala was examined. There was no effect of colitis on AhR receptor expression, though there was a trend for a reduction in the amygdala (p=0.06) compared to control. To evaluate the activation of AhR, we measured the expression of Cyp1a1 – an up-regulated AhR gene. Colitis did not alter Cyp1a1 mRNA expression in hippocampus, hypothalamus or amygdala.
Conclusions: Some types of microbial-metabolite receptor are present in the brain. Their expression levels appear unaffected by colitis. Further studies are required to identify if the activation of these receptors is a factor in the development of sickness behaviors in colitis.

A135
MICROBIOME IN CROHN'S DISEASE PATIENTS: A COMPILATION OF PUBLICLY AVAILABLE DATASETS
L. Bedrani[1], W. Turpin[1], M. Smith[2], D. Guttman[3], M.S. Silverberg[2], W. Xu[4], A. Paterson[5], K. Croitoru[2]

1. University of Toronto, Toronto, ON, Canada; 2. Mount Sinai Hospital, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada; 4. Princess Margaret Cancer Centre, Toronto, ON, Canada; 5. University of Toronto, Toronto, ON, Canada

Background: Crohn's disease (CD) is thought to be triggered by the interaction of the host immune response with environmental factors including the gut microbiome. The gut microboime of CD patients has been characterized as dysbiotic, but in spite of many studies the nature of that dysbiosis or its impact on disease pathogenesis is unclear. Several available systematic reviews compile the characteristics of CD dysbiosis but report contradicting results.
Aims: Assess the differences between CD and control microbiome by compiling previously published 16S rRNA sequencing data from publicly available databases.
Methods: A PubMed search was performed using the keywords 'Crohn Disease AND gut microbiota AND 16S' in articles titles and abstracts. A total of 26 studies wereidentified but only 6 fulfilled our two inclusion criteria, namely available 16S rRNA sequencing data,
and must include biopsies and/or fecal samples from controls and CD patients. Raw 16S sequencing data were downloaded, and processed using Qiime (v.1.9) classical pipeline and Operational Taxonomic Units (OTU) picked from GreenGenes v.13_8 (close reference OTU picking). Data from samples with a minimum of 1000 reads were analyzed using a logistic regression, with disease status (Control vs CD) as an outcome, taxa abundance as the main explanatory variable and study, age, gender and the sequencing depth as covariates. The raw p values were corrected by the number of independent taxa (n=162). The same regression model was applied to alpha diversity as assessed by chao1 and Shannon indices.
Results: In this study, 229 controls were compared to 201 CD patients. The analysis showed that the abundance of the Class *Clostridia* was significantly lower in CD patients (Q<0.01) due primarily to lower genus *Lachnospira* (Q < 0.01) and partially due to lower *Rosburia, Oscillospira* and *Coprococcus* (P<0.05, Q>0.05). Alpha diversity indices were also significantly lower in CD patients as compared to controls.
Conclusions: The combined analysis of 16S sequencing data from six previous studies allowed us to confirm two previously reported results in CD patients namely, a lower abundance of taxa from the *Clostridia* class, as well as a lower alpha diversity. On the other hand, we did not record any significant variations in *Enterobacteriaceae* family or *Faecalibacterium* genus, often described as altered in CD patients. Differences between this and prior analyses may reflect other parameters such as drug treatment or disease activity which were not captured in this analysis.

A136
THE ROLE OF KERATIN-19 POSITIVE STEM CELLS IN COLONIC REGENERATION POST COLITIS
E. Fazio[1], R. Nattiv[2], D. Castillo-Azofeifa[2], Y. Nusse[2], J. SCHANIN[2], O. Klein[2], S. Asfaha[1]

1. University of Western Ontario, London, ON, Canada; 2. UCSF, San Francisco, CA

Background: The intestinal and colonic epithelia are rapidly renewed every 3 to 5 days. In the intestine, at least two principal stem cell pools, comprised of rapidly cycling crypt based columnar (CBC) *Lgr5*^{+} cells and slower cycling *Bmi1*-expressing cells located above the crypt base, have been described. In the colon, however, we have recently identified an additional, spatially distinct, *Lgr5*-negative stem cell pool that is a subset of *Krt19*-positive cells. Recent studies have shown that colonic inflammation resulting from DSS-induced colitis leads to loss of distal colonic crypts associated with the rapid loss of Lgr5+ cells. Despite the transient loss of Lgr5+ stem cells, the colonic crypts regenerate and homeostasis is restored.
Aims:

The goal of this study was to determine whether the Krt19+ colonic stem cell pool is responsible for colonic crypt regeneration during colitis.

Methods: To examine whether *Lgr5* and/or *Krt19* mark normal colonic stem cells that contribute to epithelial regeneration upon colonic injury, we crossed *Lgr5*-GFP-IRES-CreER or *Krt19*-BAC-CreER transgenic mice to the ROSA26r-Tdtomato reporter line. Mice were then treated with tamoxifen followed by water (control) or DSS (in the drinking water x 7 days) to induce colitis. *Lgr5*+ and *Krt19*+ cells were then studied in the context of normal homeostasis or following colonic injury following DSS injury.

Results: Our results demonstrated that *Lgr5*+ stem cells are sensitive to DSS-induced colonic injury. Similar DSS-induced colitis injury experiments were also carried out using Notch1-CreER and Math1-CreER transgenic mice crossed to ROSA26r-Tdtomato mice and revealed little to no lineage tracing from absorptive or secretory cells, respectively. In contrast, *Krt19* marked long-lived cells above the crypt base that were resistant to DSS-induced colonic epithelial injury and gave rise to *Lgr5*^{+} cells in the newly regenerated crypts. Moreover, in separate experiments using Lgr5-DTR-GF-P;K19-BAC-CreER; ROSA26r-Tdtomato mice, diphtheria toxin induced ablation of *Lgr5*^{+} cells demonstrated that *Lgr5*^{+} stem cells are dispensable for colonic epithelial regeneration following DSS-induced colitis.

Conclusions:
Our data suggest that analogous to the small intestine, Krt19+ stem cells in the colon are similarly more resistant to epithelial injury than Lgr5+ stem cells.

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A137
PANCREASTATIN (PTS) EXACERBATES COLONIC INFLAMMATION
N. Eissa[1], L. Kermarrec[3], C.N. Bernstein[4], J. Ghia[2]

1. Immunology, Children's Hospital Research Institute of Manitoba, University of Manitoba, Winnipeg, MB, Canada; 2. Immunology and Internal Medicine Section of Gastroenterology, University of Manitoba, Winnipeg, MB, Canada; 3. Immunology, University of Manitoba, Winnipeg, MB, Canada; 4. Internal Medicine section of Gastroenterology, University of Manitoba, Winnipeg, MB, Canada

Background: Chromogranin-A (CgA) is elevated in inflammatory bowel disease (IBD) and in murine models of colitis. CgA produced by enteroendocrine cells can be cleaved in several peptides including the immunoregulatory pancreastatin (PTS: $CgA_{273-301}$). Macrophages (Mo) play a major role in IBD through an impaired transition from a pro-inflammatory (classical activated Mo (CAMs)) to anti-inflammatory (alternative activated Mo (AAMs)) phenotypes. Previously we demonstrated that in mouse, the lack of CgA (CgA$^{-/-}$)

induced a significant decrease of colitis associated to a decreases and an increase of CAM and AAM markers respectively

Aims: The aim of this study was to investigate the role of PTS in colitis using a pre-clinical and clinical approaches

Methods: Serum level of PTS and mRNA expression of CgA were quantified in active UC and healthy individuals & mice using ELISA & RT-qPCR. Colitis was induced in CgA$^{-/-}$ and wild type (WT) mice by administrating dextran sulfate sodium in drinking water (DSS 5%, 5 days), and PTS treatment (2.5mg/kg/day, 6 days) or vehicle started 1 day before induction. Disease activity index (DAI) was daily evaluated, and macro-scopic scores at sacrifice day. The serum level of CRP was quantified using ELISA. Colonic MPO, IL-1β, IL-6, TNF-α, MIP-1α, MIP-1β, ARG-1, YM1 & TGFβ were assessed using ELISA or RT-qPCR. Naïve peritoneal macrophages were isolated from CgA$^{-/-}$ and WT mice and treated with PTS (200ng/ml; 2, 24h) then exposed for 6 h to LPS (100 ng/ml) or to IL-4/IL-13 (20ng/ml) to promote CAMs or AAMs. CAMs markers (IL-6, IL-1β, TNF-α, MIP-1α, MIP-β) and AAMs markers (ARG-1, YM1, TGFβ) were quantified by using ELISA and/or RT-qPCR. *In vitro* chemotaxis activity of PTS (200 ng/ml) on naïve Mo was assessed by migration assay using MCP-1 (30ng/ml)

Results: CgA & PTS levels significantly increased in human active UC and WT colitic mice. In colitic CgA$^{-/-}$ mice, we confirmed a significant increase of colitis through the regulation of all the pro and anti-inflamma-tory markers. PTS treatment significantly increased the onset and severity of colitis in CgA$^{-/-}$ and in WT mice. Macroscopic score, CRP, colonic MPO, IL-1β, IL-6, TNF-α, MIP-1α and MIP-1β increased significantly, while ARG-1, YM1, TGFβ decreased in colitic WT & CgA$^{-/-}$ mice treated with PTS. IL-6, IL-1β, TNF-α, MIP-1α & MIP-β were significantly increased in PTS-conditioned CgA$^{-/-}$ CAMs but not in WT, however, a significant decrease of ARG-1, YM1, & TGFβ was demonstrated in both groups. Meanwhile, PTS-condi-tioned CgA$^{-/-}$ & WT AMS expressed significantly less ARG-1, YM1, & TGFβ when compared to IL-4/IL-13 control condition. In undifferentiated macrophages, PTS significantly increased macrophages migration

Conclusions: These findings suggest that PTS contributes to the pathogenesis of colitis and inflammatory process *via* the modulation of Mo phenotype and function. Targeting PTS may lead to novel therapeutic strategies in IBD

A138
DOES AN EXTRACT OF THE TAPEWORM HYMENOLEPIS DIMINUTA PROMOTE A REGULATORY NEUTROPHIL
N. Graves, F. Lopes, J. Gilleard, D.M. McKay

University of Calgary, Calgary, AB, Canada

IBD

Background: Data are emerging that neutrophils may play an overlooked role in the response to infection with helminths, perhaps early in the infection and particularly those species that cause tissue damage (e.g. *Nippostrongylus brasiliensis* - a gut nematode (roundworm)). We have noted an early recruitment of neutrophils into the peritoneal cavity following injection of a crude extract of the tapeworm *Hymenolepis diminuta* (HdE), and this HdE suppresses dinitroben-zene sulfonic acid (DNBS)-induced colitis. Thus we hypothesized that HdE induced an anti-inflammatory phenotype in murine neutrophils.

Aims: (1) to determine if HdE directly converts neutrophils to an anti-inflammatory phenotype *in vitro*, and (2) to determine if intraperitoneal (ip.) injection of HdE induces an anti-inflammatory phenotype in recruited neutrophils.

Methods: Neutrophils were isolated by a Percoll gradient from the bone marrow of healthy BALB/c mice and were treated with HdE (100-1000 μg/mL) and the following measures of activity assessed: (a) viability, (b) Ca^{2+} signaling, (c) chemotaxis, (d) cytokine production. HdE (1 mg) was injected ip. into BALB/c mice and 4h later, peritoneal exudate cells (PECs) were collected. These cells were then co-cultured with anti-CD3/anti-CD28 stimulated splenic $CD4^+$ T cells for 4 days, and IL-10 measured in the culture medium by ELISA.

Results: Direct application of HdE to neutrophils was not preferentially cytotoxic as assessed by trypan blue staining or LDH release, and elicited a slow increase in intracellular Ca^{2+} that was also observed in Ca^{2+}-free medium, suggesting the increased Ca^{2+}-detected was via release from intracellular stores. HdE did not induce neutrophil chemotaxis, nor did it directly stimulate the production of TNF-α, or IL-10 (n=3-9), but it did suppress LPS-driven neutrophil chemotaxis (n=4). The PECs retrieved 4h after injection of HdE (90-95% neutrophils based on nuclear morphology), but not LPS, evoked increased production of the anti-inflammatory cytokine IL-10 from co-cultures of activated murine splenic $CD4^+$ T cells. Co-culturing HdE-treated bone marrow derived neutrophils with activated $CD4^+$ T cells did not replicate this result.

Conclusions: Treatment with HdE induced a subtle Ca^{2+} mobilization in murine neutrophils and remarkably suppressed their movement in response to LPS. The PECs recruited in response to HdE promoted IL-10 production from T cells. If validated, this would represent a novel aspect of immunoregulation whereby neutrophils recruited in response to helminths can educate and enhance the 'differentiation' of a T cell into a regulatory phenotype characterized by IL-10 production (i.e. Tr1-like phenotype).

A139
ASYMPTOMATIC IBD IS A COMMON FINDING IN FIT POSITIVE INDIVIDUALS

J. Quinlan[2], M. Borgaonkar[2], S. Antle[1], D. Pace[2], J.S. McGrath[2]

1. Gastroenterology, Eastern Health, St. John's, , Canada; 2. Medicine, Memorial University, St. John's, , Canada

Background: Inflammatory Bowel Disease is often present for months and even years before a formal diagnosis is made. This time represents a missed opportunity for early intervention that may have a significant impact on disease course and prevent unnecessary surgeries.

Aims: The purpose of this study was to assess findings of undiagnosed IBD within Newfoundland and Labrador from the provincial colon cancer screening program.

Methods: Data for this study was obtained in a pro-spective fashion using the Newfoundland and Labrador Colon Cancer Screening Program. Those enrolled in the study were between the ages of 50-74 at average risk for colon cancer. Between July 1, 2012 and June 30, 2016, participants were provided with two FIT tests – if a minimum of one test was ≥100ng/mL, participants were further evaluated via colonoscopy. Data on the patient's age, gender, FIT value, presence of adenoma, pathology, and other variables were collected.

Results: Of the 21,371 FIT kits mailed out, 16,152 (75.6%) were returned, of which, 2694 (16.7%) had at least one FIT value ≥100ng/mL. At the time of analysis, 1831 participants had been further evaluated by colonoscopy. Colonoscopy identified 35 patients (1.9%) with undiagnosed inflammatory bowel disease, con-firmed by pathology. Of those found to have IBD, 57.1% were female, 42.9% were male, and 54.3% had two positive FIT values. The age of those with IBD ranged from 50-71 with a mean of 59.5. The highest FIT value of those with IBD ranged from 100.0 to 18877.0 with a mean of 2048.1, 25th percentile of 180, 50th percentile of 518, and 75th percentile of 1463. For comparison, the mean highest FIT value for those with colon cancer was 4219.8, for those with an adenoma was 1140.2 and for those with no finding was 580.4.

Conclusions: This study shows that undiagnosed inflammatory bowel disease in the fifth to seventh decade of life is not an uncommon occurrence. The prevalence of diagnosed IBD in Canada is estimated to be 0.428%, with 0.194% having ulcerative colitis and 0.234% having Crohn's disease. Of the 16,152 participants who returned their FIT test, 0.27% were found to have undiagnosed IBD. These findings suggest that there is a substantial burden of undiagnosed IBD in Newfoundland and Labrador.

A140
ADEQUACY OF PHARMACOLOGIC THROMBOPROPHY-LAXIS IN ADULTS HOSPITALIZED FOR ACTIVE INFLAMMATORY BOWEL DISEASE AT THE CIUSSS-CHUS
N. Clermont Dejean, S. Plamondon

Gastroenterology, Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

A141
DIFFERENT INDUCTION RESPONSE CRITERIA DO NOT INFLUENCE 1 YEAR RESPONSE AND REMISSION RATES OF USTEKINUMAB 90MG Q8W IN PHASE III PROGRAM
D. Naessens[1], J. Johanns[1], C. Gasink[2]

1. Janssen R&D, LLC, Spring House, PA; 2. Janssen R&D, LLC, Spring House, PA

Background: Crohn's disease Phase III maintenance clinical trials with biologics are typically randomized withdrawal trials, in which patients (pts) that responded after induction with a specific biologic are re-randomized to either maintenance therapy or placebo (PBO). Different response criteria have been used to qualify responders for these studies, such as CDAI70 at wk 2, 4 or 6 & CDAI 100 at wk8, but the influence of this criterion on remission results at year 1 has not been investigated.
Aims: In the IM-UNITI study, pts with a CDAI 100 response 8wks after ustekinumab (UST) induction were re-randomized to either PBO, UST 90mg Q12w or UST 90mg Q8w. Non-responders to UST induction, as well pts that received PBO for induction remained blinded in the trial. Non-responders to UST induction received UST 90mg SC Q8w at wk0 of IM-UNITI. Since both UST CDAI-100 responders & non-responders received 90mg Q8w, remission rates at 52wks of total treatment can be calculated for UST 90mg Q8w for pts with different induction response criteria.
Methods: Pre-specified analyses were conducted to evaluate the proportion of pts in remission & CDAI-100 response at 52wks of total treatment in the different arms of IM-UNITI for pts with a
70 point CDAI response to UST at wk6 of induction.
70 point CDAI response to UST at wk3 of induction
100 point CDAI response to UST at wk8 of induction (original response criterion)
The overall proportion of remitters & CDAI-100 responders at wk52 of total treatment were calculated for pts with a CDAI-70 response to UST respectively at wk3 or 6 of induction taking into account their relative distribution over the randomized or non-randomised arms receiving 90mg Q8w.
Results: Remission rates after 52wks of total treatment in pts receiving 90mg UST Q8w are summarized (see

Table). Similarly, CDAI-100 response rates after 52wks of total treatment in pts receiving 90mg UST Q8w were calculated for the different induction response categories. Rates were 60.8%, 58.3% & 59.4% for CDAI-70 responders at wk3, 6, & CDAI-100 responders at wk8 respectively.
Conclusions: The majority of pts with CDAI-70 response at either wk3 or 6 after induction also had a CDAI-100 response at wk8. Using different qualifiers for response to UST induction did not result in different response or remission rates after 1 year of treatment in pts treated with UST 90mg Q8w.

Response criterion	Randomized group (CDAI-100 responders at wk8)		Non-randomized group (no CDAI-100 at wk8)		Overall wk 52 remission rate in responders
	# pt randomized	Wk52 remission rate in 90mg Q8w arm	# pts at start of maintenance	Wk52 remission rate (90mg Q8w)	
CDAI 70 responder wk 6	347	55.0%	127	42.5%	51.7%
CDAI 70 responder wk 3	283	60.7%	102	41.2%	55.5%
CDAI 100 responder wk 8 (original response criterion)	388	53.1%			53.1%

A142
INTER-OBSERVER AGREEMENT AND THE ROLE OF EDUCATIONAL TRAINING ON THE ENDOSCOPIC SCORING OF CROHN'S DISEASE
J.M. Tessolini[2], E. Zittan[1], M.S. Silverberg[1]

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

Background: As the management of inflammatory bowel disease (IBD) focuses on the importance of mucosal healing, endoscopic scoring systems such as the Simple Endoscopic Score for Crohn's Disease (SES-CD) are becoming important tools in the objective measurement of inflammation. Concern regarding inter-observer variability and feasibility has limited use of the SES-CD in the clinical setting.

IBD

IBD

Aims: The study goal is to determine whether an educational program teaching endscopic scoring will improve performance and inter-observer agreement among trainees.
Methods: Gastroenterology residents were provided with videos of seven ileocolonoscopies representative of a range of ileal and colonic Crohn's disease severity. Participants individually scored the videos using the SES-CD. The residents then participated in a 1-hour educational session involving a didactic lecture with examples using the SES-CD led by a faculty member with expertise in IBD. Participants then re-scored the same videos. Five videos chosen randomly were also scored by IBD experts. Inter-observer agreement among gastroenterology trainees and expert scorers was calculated using the intra-class correlation coeffi-cient (ICC) obtained from the total SES-CD scores.
Results: Six gastroenterology residents completed the pre-training SES-CD scoring, attended the training session, and completed the post-training re-scoring. Three IBD expert scorers completed the scoring. The table below shows the inter-observer agreement among the different groups for the pre- and post-train-ing scenarios. There was no change in inter-observer agreement among trainees or all scorers after the educational session.
Conclusions: Among gastroenterology trainees and between trainees and expert scorers, there was good inter-observer agreement for SES-CD scores. There was very good inter-observer agreement among expert scorers. A 1-hour training session on endoscopic scoring did not improve inter-observer agreement. This study supports routine use of the SES-CD in the clinical setting to improve reporting consistency and aid in clinical evaluation however, a more intensive educa-tional program to improve endoscopic scoring accuracy among trainees should be developed.

Intra-class correlation coefficients and inter-observer agreement among gastroenterology trainees and IBD experts using the SES-CD

Group	ICC	95% confidence interval	Agreement
Trainees, pre-train-ing	.700	.394-.926	Good
Experts	.938	.735-.993	Very good
Trainees, post-training	.674	.384-.917	Good
Trainees + experts, pre-training	.749	.462-.963	Good
Trainees + experts, post-training	.731	.437-.959	Good

ICC: intra-class correlation coefficients

Funding Agencies: University of Toronto Gastroenterol-ogy Training Program

A143

FOOD AVOIDANCE IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: WHAT, WHEN AND WHO?
F. Bergeron[1], N. Presse[2], L. D'Aoust[3], M. Lemoyne[4], M. Bouin[5]

1. Internal Medecine, Université de Montréal, Montreal, QC, Canada; 2. Univeristé de Montreal, Montreal, QC, Canada; 3. Univeristé de Montreal, Montreal, QC, Canada; 4. Univeristé de Montreal, Montreal, QC, Canada; 5. Université de Montreal, Montreal, QC, Canada

Background: Patients with inflammatory bowel diseases are known to avoid a variety of foods. However, it remains unclear how this behavior varies across patients.
Aims: This cross-sectional study aimed to describe food avoidance in these patients and investigate whether it varied according to disease's activity, disease's subtype, Crohn's location, and prior history of bowel resection, strictures, and fistulae.
Methods: Outpatients with Crohn's disease (n=173) and ulcerative colitis (n=72) reported which food they avoid during remission and active disease using a list of 82 food items classified in 10 food categories. Medical charts were reviewed for patients' characteris-tics. Linear regression analyses were used to compare food exclusion rates between inflammatory bowel disease subgroups and food categories.
Results: In total, 75% of patients reported food avoidance behavior during remission. Food exclusion rates varied from 1 to 39%. Most avoided foods were those with capsaicin, meat alternatives, and raw vegetables. Overall, food exclusion rates were 69% higher in active disease than in remission (P<0.001), 38% higher in Crohn's disease than ulcerative colitis (P<0.001), and 50% higher in stricturing than non-stricturing Crohn's disease (P<0.001). No association was found with other disease characteris-tics. The avoided foods were very similar across patients except for alcoholic beverages and foods rich in dietary fibers/residue, which were avoided more specifically in active disease and Crohn's disease, respectively.
Conclusions: Food avoidance is common in inflamma-tory bowel disease but varies according to disease characteristics. Future nutrition research should consider that inflammatory bowel disease patients may respond differently to diet modification.

Funding Agencies: None

A144
THE EFFICACY OF COLONOSCOPIC BALLOON DILATION IN STRICTURING CROHN'S DISEASE
W. Alghamdi, N. Chande, J.C. Gregor

London Health Sciences Centre, Western University, London, ON, Canada

Background: Stricture formation is one of the most common complications of Crohn's disease. Management options include medical therapy and surgical resection or strictureplasty. An increasingly more common middle ground approach is colonoscopic balloon dilation (BD).
Aims: The aim of this study was to examine the efficacy and complication rate of BD in a population of patients with symptomatic strictures.
Methods: Retrospectively, all patients in our local IBD practice who underwent colonoscopic balloon dilation with a diagnosis of a symptomatic Crohn's stricture between January 2006 and March 2016 were reviewed. Demographic data were collected and technical and clinical success determined to compare the results between primary and anastomotic strictures. Technical success was defined as subjective improvement in the stricture and the ability to pass the scope through it. Clinical success was defined as subjective clinical improvement at follow up 3 months or more after the procedure. *Pearson's chi-squared* test was used to compare relative efficacy.
Results: 98 patients were identified with a total of 108 strictures dilated. The mean age of the patients was 45.2 years (range 20-79). 64.3% of the patients were females. 51.9% of the strictures were anastomotic. 32.4% were on immunomodulators (methotrexate, azathioprine or 6-mercaptopurine) and 25.9% on anti-TNF therapy at the time of the dilation. 30.6% were on steroids. An adult Olympus colonoscope (diameter 13.2 mm) was used in 86.1% of cases. 31.5% of strictures were estimated to be less than 10 mm in diameter. 82.4% of the strictures were impassable prior to dilation. The most common balloon diameter was 15 mm (24.1%) with a median dilation diameter of 16.5 mm. Technical success was achieved in 62%. Clinical success was achieved in 84.3%. Complications were observed in one patient (post colonoscopy bleeding requiring hospitalization for supportive measures and blood transfusion). Comparison of primary and anastomotic strictures demonstrated a statistically significant difference in technical success (73.1% vs 51.8%, p=0.023) but not clinical success (86.5% vs 82.1% p=0.531).
Conclusions: Colonoscopic balloon dilation of both primary and anastomotic strictures is feasible and appears to be clinically efficacious in a majority of patients with symptomatic primary and anastomotic Crohn's strictures. Complication rates, though not insignificant, appear to be acceptably low.

A145
"REAL WORLD" SAFETY AND EFFECTIVENESS OF VEDOLIZUMAB FOR ULCERATIVE COLITIS: RETROSPECTIVE STUDY FROM A TERTIARY CARE CANADIAN CENTRE
L. Kwapisz, V. Jairath, V. Karthik, M.D. Beaton, J.C. Gregor, R. Khanna, T. Ponich, M. Sey, B. Yan, N. Chande
UWO, London , ON, Canada

Background: Vedolizumab (VDZ), a humanized monoclonal antibody which targets the α4β7 integrin and prevents homing of lymphocytes to the gut, was approved by Health Canada in 2015 for treatment of moderate to severe ulcerative colitis (UC). Its gut selective mode of action offers potential for a lower risk of systemic infection while achieving similar or greater efficacy compared to conventional treatments.
Aims: To assess clinical response and safety of VDZ.
Methods: Retrospective cohort study from a tertiary care Canadian centre between May 2015 to August 2016. Adult patients with UC treated with VDZ, with follow-up after initiation of therapy, were eligible. Patients were identified through infusion center listings and data abstracted from electronic medical records, review of clinic records, endoscopy reports and infusion centre reports. Clinical response - defined as normalization of stool frequency and absence of rectal bleeding, as well as physician global assessment, and serious adverse events were assessed. Patients were eligible for safety analysis as long as at least one dose was received.
Results: Eighty-eight patients were included, with a median age of 47 years (range 18-85), 58% (51/88) male, 53% (47/88) tumor necrosis factor (TNF)-antagonist exposed with a median follow up of 17 weeks (range 0-61 weeks). The median disease duration was 7 years (range 0-46), 61% (54/88) had a history of disease extension beyond the splenic flexure and 23% (20/88) had a history or prior/active smoking. Patients received a median of 5 VDZ doses (range 1-13) and 47% (41/88) were receiving concomitant treatment with prednisone at the initiation of VDZ. 51% (29/57) of patients achieved clinical response by the end of their induction period (week 6) and 56% (20/36) achieved clinical response at 6 months and 64% (44/69) of patients overall achieved clinical response at some point during the study period. 24 patients underwent endoscopic evaluation after starting VDZ of which 7/24 patients (29%) were reported to have mucosal healing or improved mucosa. No infusion reactions were reported. In 7% (6/88) of patients there were reports of an infection which required antibiotics, of which four had an upper respiratory tract infection and only one patient was admitted for treatment of pneumonia. One patient discontinued VDZ secondary to arthralgia and lethargy after their initial dose.
Conclusions: VDZ is a safe and effective treatment for UC in routine clinical practice. In this study, clinical response after induction was achieved in over half of patients by week 6 and close to 2/3 overall achieved clinical remission. Only one patient discontinued treatment due to reports of arthralgia and lethargy after the infusion.

IBD

A146
ASSESSMENT OF THE USE OF THERAPEUTIC DRUG MONITORING OF INFLIXIMAB DURING MAINTENANCE IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

M. Chavannes[1], F. Gervais[1], R. Robitaille[2], V. Marchand[1], C. Deslandres[1], P. Jantchou[1]

1. Service de gastro-entérologie, CHU Sainte-Justine, Montréal, QC, Canada; 2. Biochemistry, Maison-neuve-Rosemont Hospital, Montreal, QC, Canada

Background: Infliximab (IFX) was proven effective in the induction and maintenance of remission in inflammatory bowel diseases (IBD) in both children and adults. There is a significant number of individual who lose response to the medication. Measurable IFX drug levels correlate with clinical response and mucosal healing. Few studies demonstrate that proactive monitoring in children improves drug levels and correlates with clinical response.
Aims: To assess the blood level of IFX in children during the maintenance period while on a proactive therapeutic drug monitoring management. The primary goal was to correlate improvement in infliximab levels with a proactive dose adjustment approach. The secondary objectives were to correlate the levels with clinical response and to assess the effect of combination therapy.
Methods: This was a retrospective cohort study. Patients were included if they had at least one serum level of IFX drawn between June 2014 and July 2016, and had a follow-up of at least 3 months following the level. We collected all trough levels drawn during maintenance phase. Levels were analyzed using the progenika promotor-IFX ELISA kit. We collected biochemical markers drawn a maximum of two weeks prior to the IFX level. We also collected clinical assessments at the time of IFX infusion as reported by the patient. This outcome was graded on a three-point scale (well, moderately well and unwell). The physician global assessment (PGA) was also recorded if it was done within 4 weeks of the IFX level.
Results: During the study period a total of 301 Children were receiving IFX. Among them, 155 children had at least one IFX serum level. After exclusion of patients with indeterminate colitis, induction levels and non trough levels, there were 146 patients (79.4% CD; 59.6 % boys; 357 IFX levels) evaluated, with a median of 2 levels (1-13) per patient. Thirty six percent were on combination therapy with the majority on methotrexate (65.3%). Patients with CD had a mean IFX level of 3.85 mcg/mL while those with UC had a mean of 5.43 mcg/mL. Levels were subtherapeutic in 40.9% and supratherapeutic in 26.3%. Clinical status as reported by patients and PGA did not correlate with IFX levels. In the patients on combination therapy, we found a statistical significant improvement in infliximab levels post initiation of treatment (p<0.0001). Twenty two percent of patient discontinued infliximab over the study period.

Conclusions: Despite dose adjustments, 40% of serum IFX levels were sub-therapeutic. We did not find a correlation between levels and clinical status. Combination therapy did improve levels. TDM may contribute in maintaining longevity of this therapy as compared to reports in the litterature. We feel that TDM is therefore a useful tool in the management of pediatric IBD.

A147
COMBINING INFLIXIMAB TROUGH LEVELS AND FECAL CALPROTECTIN LEVELS WITH CLINICAL DATA HAS THE POTENTIAL TO GUIDE CLINICAL DECISION-MAKING IN IMPROVING OUTCOMES FOR INFLAMMATORY BOWEL DISEASE PATIENTS ON MAINTENANCE INFLIXIMAB.

A. Amin[3], C. Prosser[7], K.I. Kroeker[8], H. Wang[6], C. Shalapay[9], N. Dhami[10], D.K. Fedorak[4], B.P. Halloran[2], L.A. Dieleman[5], K. Goodman[11], R. Fedorak[1], V. Huang[7]

1. Los Alamos National Laboratory, Edmonton, AB, Canada; 2. Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada; 3. (Core) Internal Medicine Program, University of Alberta, Edmonton, AB, Canada; 4. Divison of Gastroenterolgy , University of Alberta, Edmonton, AB, Canada; 5. Medicine, University of Alberta, Edmonton, AB, Canada; 6. Surgery, University of Alberta, Edmonton, AB, Canada; 7. University of Alberta, Edmonton, AB, Canada; 8. University of Alberta, Edmonton, AB, Canada; 9. University of Alberta, Edmonton, AB, Canada; 10. University of Alberta, Edmonton, AB, Canada; 11. University of Alberta, Edmonton, AB, Canada

Background: Infliximab (IFX) induces and maintains remission in Crohn's Disease (CD) and Ulcerative Colitis (UC). Secondary loss of response occurs in up to 45% of CD and 60% of UC patients on maintenance IFX. Studies are inconclusive on ideal IFX trough levels (ITLs) to prevent loss of response; recommendations range from "detectable" up to 10μg/mL. Patients with adequate ITLs still lose response, suggesting they still have gastrointestinal (GI) inflammation. Fecal Calprotectin (FCP), a marker of neutrophilic infiltration into the GI tract, when elevated predicts loss of response to maintenance IFX (sensitivity 0.80, specificity 0.82). We previously showed clinicians would alter decisions based on ITLs and FCP levels. There are no studies on using ITLs and FCP levels in conjunction with clinical presentation.
Aims: To determine if 6 month outcomes in IBD outpatients on IFX maintenance could be improved if clinicians had knowledge of both ITLs and FCP levels in addition to clinical data.
Methods: This was a pilot, retrospective case series of adult IBD outpatients on maintenance IFX, who prior to having levels drawn were in clinical remission. Actual clinical decisions were based on clinical presentation

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and standard labs. All subjects had blood ITLs drawn. A subset (Group 2) provided stools for FCP levels. An expert clinician panel made hypothetical clinical decisions with ITLs and FCP levels. Interval (between ITL and 6-months) and final 6-month outcomes were recorded. Comparisons were made between: actual clinical decisions and what ITLs should prompt (Group 1); and actual clinical decisions, what ITLs and FCP levels should prompt, and hypothetical clinical decisions (Group 2). Statistical analyses included: medians with interquartile ranges (IQRs); proportions; percentages; chi-squared and non-parametric analyses.

Results: Table 1 captures baseline demographics. There were no statistically significant differences in demographics between the two groups.

Table 2 highlights patients in (a) Group 1 and (b) Group 2 in whom ITL and/or FCP levels could have impacted clinical decision making. Of note, 2 out of the 6 patients (Group 2) had "adequate" ITLs but elevated FCP. Table 2 further summarizes what could have been done to prevent the clinical outcomes that occurred without these levels.

Conclusions: While previous studies have explored the use of ITLs and FCP levels in isolation, the results of this study demonstrate that knowledge of ITLs and FCP levels together, in addition to the patient's clinical presentation, can aid clinicians to optimize management and improve outcomes of IBD outpatients on IFX maintenance.

A148
SMARTPHONE APPS FOR IBD DISEASE MANAGEMENT: A QUANTITATIVE EVALUATION

E.Y. Liu[2], J. Crawford[1], L. Worobetz[2], S. Bhasin[2]

1. Regina Qu'Appelle Health Region, Regina, SK, Canada; 2. University of Saskatchewan, Saskatoon, SK, Canada

Background: Smartphone Apps for inflammatory bowel disease (IBD) are becoming increasingly popular. However, there is paucity of data on the function and quality of these applications. The lack of systemic investigation on IBD Apps prevents further comparative analysis with clinically validated scoring systems. This makes it difficult for patients to choose and for physicians to recommend the most appropriate App to help manage their disease.

Aims: To identify and quantitatively evaluate smartphone Apps for patient management of IBD.

Methods: Systematic search of smartphone Apps were carried out in Apple App Store for iOS operating system and Google Play Store for Android operating system using the following keywords: "IBD", "inflammatory bowel disease", "colitis", "ulcerative colitis" and "crohn's". Title inclusion (relating to management of Inflammatory Bowel Disease and in English) and exclusion criteria (only offers educational information or Conference App) were applied to all results. Apps that passed title screening were review independently by two reviewers using the validated Mobile Application Rating Scale. An App's quality was assessed based on engagement, functionality, aesthetics and information quality. Each item in MARS scoring tool was rated on a 5 point Likert scale. Each subcategory was averaged, then added to give an overall 5 point rating for the App. The two raters' data were presented as aggregated means and standard deviations. Spearman's bivariate analyses were used to assess correlation between overall rating and other App characteristics. App features were represented in a table format.

Results: Fifteen smartphone Apps for IBD management were included in the analysis. The top 3 Apps were IBD Health Storylines (4.9±0.53), GutCheckTM (4.78±0.18), and MyGiHealth (4.63±0). The information quality score of an App was most strongly correlated with the overall score (Spearman's rho=0.87, p=0.012), while functionality score, engagement score and aesthetics scores were less correlated with the overall score (Spearman's rho=0.61, 0.59 and 0.53 respectively). Number of features offered by an App was strongly correlated with the overall score (Spearman's rho=0.74, p=0.012) while cost and user ratings were poorly correlated with the overall score (Spearman's rho=0.06, 0.04 respectively).

Conclusions: This study provides a list of IBD disease management smartphone Apps with their associated features, ranked by order of quality by a validated scoring system. Information quality and features offered by an App appear to be most closely related to the overall quality of an App. This will allow physicians to recommend and patients to choose high quality Apps to support IBD management. Future studies will explore correlation between clinical validated scoring systems and information collected by high quality IBD management Apps identified in this study.

A149
DEVELOPING, EVALUATING, AND DISSEMINATING KNOWLEDGE TRANSLATION RESOURCES TO ANSWER PATIENT QUESTIONS ABOUT IBD AND ITS MANAGEMENT

J.R. Walker[2], L.E. Targownik[3], M.T. Bernstein[2], C. Haviva[5], L.A. Graff[2], G. Restall[4], h. singh[2], w. El-Matary[7], K. Vagianos[6], P. Thomson[6], 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; 5. University of Manitoba, Winnipeg, MB, Canada; 6. Health Sciences Centre, Winnipeg, MB, Canada; 7. University of Manitoba, Winnipeg, MB, Canada

Background: Previous research by our team indicates that patients and their families have many questions about IBD that are not fully answered by existing resources.
Aims: To describe the development, evaluation, and dissemination of education resources for persons with IBD.
Methods: Previous research identified questions that are important to persons with IBD – close to the time of diagnosis or after having the condition for many years. We developed a patient and family advisory committee to assist us in developing resources. Individual fact sheets were created to address specific questions using existing research evidence and language that can be understood by patients and family members.
Results: A wide range of concise fact sheets were developed covering important topics such as: new diagnosis of IBD, diagnostics in IBD, risk factors, common treatments (fact sheets for major classes – 5 ASA, thioprines, corticosteroids, biologics), managing cost of medications, insurance coverage for IBD medication, nutrition and IBD, antibiotics, probiotics, herbal medicines, marijuana and IBD, IBD and pregnancy, and IBD in childhood and adolescence. In addition to evaluation by the Patient and Family Advisory Committee, we collaborated with Crohn's and Colitis Canada to evaluate the fact sheets through contacts with members of their organization and web-based surveys. The surveys evaluated each fact sheet a section at a time and participants rated the degree to which fact sheets had enough (vs. not enough or too much) information, offered familiar or unfamiliar information, were trustworthy, and clear and understandable. Survey participants were also provided space to suggest improvements. Additional fact sheets will be developed in the future using a similar development and evaluation approach.
Conclusions: The fact sheets provide information in a convenient, understandable and accessible format that can be viewed electronically or downloaded for print. The fact sheets will be disseminated by Crohn's and Colitis Canada through their website and educational activities and have a Creative Commons copyright so they may be widely distributed in English and French versions. They will also be helpful to clinicians in providing clear information to their patients. Additional fact sheets on emerging topics will be developed following a similar approach. Involving the knowledge users in the development and assessment of education tools is key to optimizing knowledge translation. Samples of the fact sheets will be provided.

A150
IBD PATIENTS TRANSITIONING FROM PEDIATRIC TO ADULT CARE LACK THE NECESSARY TRANSITION SKILLS
T.A. Cookson[1], N.R. Klostermann[2], E. Wine[3], K.I. Kroeker[4]

1. Department of Gastroenterology, University of Alberta, Edmonton, AB, Canada; 2. Department of Medicine, University of Alberta, Edmonton, AB, Canada; 3. Pediatrics, University of Alberta, Edmonton, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada

Background: With the rise of inflammatory bowel disease (IBD) in pediatric patients, transition is a process that occurs more every day. In a prior study, we identified that an interactive IBD transition website was needed to assist pediatric patients with IBD make the transition from pediatric to adult gastroenterology care. This interactive website can be used to assess the transition skills of patients around the time of transfer of care.
Aims: To assess the transition skills of young adults with IBD around the time of transfer of care, before and after using the newly developed IBD Transition Website.
Methods: Participants between the ages of 16-18 years were recruited in the pediatric and adult IBD clinics at the Stollery and University of Alberta Hospitals. Written consent was obtained and participants were directed to the transition.ibdclinic.ca website and instructed to complete a short website assessment. After the participants complete the assessment, they are prompted to re-take the assessment after 30 days to assess if there is any change in these transition skills. Transition skills assessed include: 1) knowledge (IBD-Kid), 2) medication adherence, and 3) transition readiness (TRAQ).
Results: To date, 21 patients recruited and 8 have completed the initial assessment. Demographic data of those completing the initial assessment: 75% female; 75% have Crohn's Disease; median age of 17.5. Results of the baseline transition skills assessments are shown in Table 1; scores are compared to results to literature values. 30-day post-website access scores are not yet available.
Conclusions: In IBD patients transitioning from pediatric to adult care in Edmonton appear to have good knowledge and medication adherence, however show significant deficits in transition readiness skills. It is not yet known, if an IBD website intervention is able to improve these deficits.

Table 1. Participant assessment scores compared to previous study values.

Measure	Participant Score	Literature Value
IBD-KID (Disease Knowledge)	15.5(7)*	15.5(5)*
Medication Adherence	0% scored <4 (low adherence)	35% scored <6¥ (low adherence)

TRAQ (Transition Readiness Assessment Questionnaire)	0% scored ≥ 20.7/23 (≥90% mastery of skills)	5.3% scored ≥18/20 (≥90% mastery of skills)

* Median (IQR); measured by ¥Morisky Medication Adherence Scale-8

Funding Agencies: CEGIIR

A151
MEDICATION INDUCED INTERSTITIAL LUNG DISEASE IN A PATIENT WITH ULCERATIVE COLITIS
V. Dong[1], L.A. Dieleman[2]

1. University of Alberta, Edmonton, AB, Canada; 2. Medicine, University of Alberta, Edmonton, AB, Canada
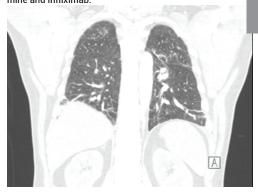
Background: Non-infectious pulmonary complications in ulcerative colitis (UC) are rare and can be an extra-intestinal manifestation or a consequence of medications. Medications known to cause pulmonary complications include mesalamine, sulfasalazine, methotrexate, azathioprine, and tumor necrosis factor alpha (TNF-α) inhibitors.
Aims: We present a case of interstitial lung disease development in a patient with UC who was treated with mesalamine and infliximab.
Methods: A 43 year old previously healthy male was diagnosed with UC in February. He was started on mesalamine at a dose of 4 grams a day as well as infliximab 5 mg/kg induction and maintenance every 8 weeks. In April, he reported abdominal symptoms and was found to have low infliximab levels. He was given another 5 mg/kg induction dose and his maintenance interval changed to every 4 weeks. He then presented to hospital in August with increasing shortness of breath and pleuritic chest pain. CT scan revealed ground-glass opacities in both lungs, particularly in the upper lobes. Infectious workup including a bronchoscopy was negative. However, he was treated empirically with a 5 day course of levofloxacin but did not return to baseline. At the time of discharge, pulmonary function testing (PFT) revealed a TLC of 44% and a DLCO of 50%. This patient was diagnosed with interstitial lung process. Mesalamine and infliximab were stopped as possible causative agents. A few weeks later this patient presented with a UC flare requiring IV steroids and prednisone taper. His bowel symptoms improved as did his respiratory symptoms. Follow up PFT at the end of September showed an improved TLC of 73% and DLCO of 83%.
Results: UC has various extra-intestinal manifestations including uveitis, arthritis, and rarely pulmonary disease. Besides complications of the disease itself, mesalamine and infliximab can both induce interstitial lung disease. Literature review has revealed mesalamine-induced lung toxicity to be rare, presenting as interstitial lung disease, alveolitis, eosinophilic pneumonia, or bronchiolitis obliterans with organiz-

ing pneumonia usually 2-6 months after medication start. Cases of infliximab-induced lung disease have also been reported mainly in the rheumatoid arthritis population presenting as an interstitial lung disease. The onset of toxicity is quite variable, usually after the 2nd and 5th infusions. Possible mechanisms include increased pro-inflammatory cytokines with inhibition of TNF-α and release of proteolytic enzymes upon interaction of infliximab with T-cells and macrophages. In both mesalamine and infliximab-induced pulmonary toxicity, steroid therapy results in clinical improvement.
Conclusions: In our patient, pulmonary toxicity can be due to mesalamine, infliximab, or a combination of both. This is the first case of interstitial lung disease as a drug-induced toxicity in a UC patient on both mesalamine and infliximab.

Ground-glass opacities in the upper lobes of both lungs

Funding Agencies: None

A152
TREATMENT SEQUENCE NETWORK-META ANALYSIS IN CROHN'S DISEASE
A. Varu[2], S. Palimaka[1], B. Hutton[2], F.R. Wilson[2], P. Dyrda[1], D. Naessens[3], C. Cameron[2]

1. Janssen Inc, Toronto, ON, Canada; 2. Cornerstone Research Group, Burlington, ON, Canada; 3. Janssen Pharmaceutica, Beerse, Belgium

Background: Crohn's disease (CD) is a chronic inflammatory condition of the intestinal tract. There are various treatments available for CD, including a recently developed treatment – ustekinumab (Stelara®).
Aims: The objective of this network meta-analysis (NMA) was to assess the comparative efficacy of ustekinumab and vedolizumab in the maintenance of clinical response and remission, after 1 year of treatment.
Methods: A systematic literature search was performed to identify RCTs published in English comparing biologic therapies for patients with moderate-to-severe CD. Key outcomes of interest were clinical response (CD activity index [CDAI] reduction of 100 points; CDAI-

100) and remission (CDAI<150), during maintenance treatment. A Treatment Sequence Bayesian NMA was conducted in order to account for re-randomization after induction of patients based on different clinical definitions (CDAI-70/100 response), the lack of similarity of the common comparator (placebo) in maintenance due to different induction treatment, and the full treatment pathway from induction.

Results: A total of thirteen RCTs were identified. Overall, ustekinumab 90 mg q8w was associated with statistically significant maintenance of clinical response (OR [95% CrI]: 1.66 [1.05; 2.62]) and clinical remission (OR 1.74 [1.05; 2.88]) relative to vedolizumab 300 mg q8w. Additionally, ustekinumab 90 mg q12w was associated with statistically significant maintenance of clinical response (OR [95% CrI]: 1.60 [1.01; 2.54]) relative to vedolizumab 300mg q8w. Findings for failed conventional and failed anti-tumor necrosis factor sub-populations are similar to those in the overall population but were not statistically significant, likely due to small sample sizes.

Conclusions: The results of the current NMA suggest that ustekinumab is associated with the highest likelihood of maintaining response or remission at 1 year compared with vedolizumab. Results should be interpreted with caution due to methodological limitations; however, the treatment sequence analysis may be the most methodologically sound analysis to derive estimates of comparative efficacy in CD in the absence of head-to-head evidence.

Results of Treatment Sequence Analysis in Overall Population

UST q8w	OR	Clinical Response 95% CrI	Pr	OR	Clinical Remission 95% CrI	Pr	UST q12w	OR	Clinical Response 95% CrI	Pr	OR	Clinical Remission 95% CrI	Pr
VDZ q8w	1.66	[1.05; 2.62]	85%	1.74	[1.05; 2.88]	85%	VDZ q8w	1.60	[1.01; 2.54]	83%	1.38	[0.83; 2.25]	68%

UST: ustekinumab; CrI: Credible Interval; Pr: Bayesian Probability; VDZ: vedolizumab

A153
MEASURING QUALITY OF LIFE AND DISEASE ACTIVITY IN PEDIATRIC PATIENTS RECEIVING INDUCTION THERAPY OF EXCLUSIVE ENTERAL NUTRITION OR CORTICOSTEROIDS FOR ACTIVE INFLAMMATORY BOWEL DISEASE

L. Hart[1], Y. Farbod[2], C.R. Halgren[4], L. Mbuagbaw[3], M. Zachos[1], N. Pai[1]

1. McMaster Children's Hospital, Etobicoke, ON, Canada; 2. McMaster University, Hamilton , ON, Canada; 3. McMaster University, Hamilton, ON, Canada; 4. McMaster University, Hamilton, ON, Canada

Background: Inflammatory bowel disease (IBD) is a chronic illness that can affect a child's physical, social and psychological well-being. Studies have shown that active IBD is associated with lower quality of life (QOL) scores in children. Exclusive enteral nutrition (EEN) and corticosteroids (CS) are effective treatment options for induction of remission in pediatric Crohn's disease (CD), while CS is effective for ulcerative colitis (UC). EEN, however, is often poorly utilized due to perceived increased treatment burden. Two studies have shown that QOL in children receiving EEN is significantly better at the end of therapy compared to baseline. However, no studies have assessed the effects of EEN therapy on QOL longitudinally during treatment, or against other IBD treatment options.

Aims: To determine if there is a difference in longitudinal QOL scores in pediatric CD and UC patients receiving an 8-week course of EEN versus CS therapy.

Methods: This prospective cohort study involved patients 5-18 years old with IBD, followed up at Mc-Master Children's Hospital (Hamilton, Ontario). Patients were included if they received EEN (Peptamen® 1.5) or CS therapy for induction of remission of moderate to severe CD or UC. All patients received 8 weeks of treatment. QOL was assessed using the KIDSCREEN-10 index. Clinical outcomes were assessed using the Pediatric UC Activity Index (PUCAI), or the modified Pediatric CD Activity Index (PCDAI). QOL and disease activity indices were assessed weekly during induction therapy, and 4 weeks after completion of therapy. Disease activity markers (albumin, CRP, fecal calprotectin) were also assessed during the course of induction therapy.

Results: 31 patients were enrolled. 17 patients received induction therapy with EEN and 14 with CS. In CD patients, as PCDAI decreased, QOL significantly increased (R=-0.41; p<0.001). Similar significant trends were seen in UC patients (R=-0.345; p=0.042). There was a small, but significant difference in QOL between the children on CS (higher QOL) and those on EEN of 2.24 points using the KIDSCREEN 10 index (95% CI 0.34-4.15; p=0.021). For the children on EEN or CS, an increase in QOL significantly correlated with a decrease in CRP levels (R=-0.271; p=0.041), however, such a correlation was not seen with albumin or fecal calprotectin.

Conclusions: Pediatric IBD patients receiving treatment for induction of remission experience an increase in quality of life as disease activity and CRP decreased. While there is a significantly higher QOL in patients on CS compared to EEN, the difference is small, and physicians and families should still consider the benefits of EEN therapy and its superior side-effect profile when

choosing therapy for induction of remission.

A154
PROPERDIN DEFICIENCY DOES NOT IMPACT THE MOUSE RESPONSE TO DSS-INDUCED COLITIS DESPITE DIFFERENCES IN COLONIC MICROBIOME
A.W. Stadnyk[2], G. Douglas[2], A. Comeau[2], U. Jain[1], W. Schwaeble[3], C. Stover[3], R. Bieko[1], M. Langille[2]

1. Microbiology and immunology, Dalhousie University, Halifax, NS, Canada; 2. Pediatrics, Dalhousie University, Halifax, NS, Canada; 3. University of Leicester, Leicester, United Kingdom

Background: The role of complement in colitis is only beginning to be understood. We reported that properdin deficient mice (P^{KO}) have increased susceptibility to infectious colitis and to piroxicam-provoked colitis when combined with IL-10 deficiency. Here we examined the PKO strain's response to chemical colitis, including their colon microbiome.
Aims: The aim was to determine whether properdin deficiency impacted the intestinal microbiome and response to DSS.
Methods: Second generation offspring from P^{KO} X C57BL/6 wildtype (WT) matings were used. Dextran sulfate sodium (DSS) was added to their water for 5 days, then groups of mice were killed either 1 (acute) or up to 5 days (recovery) later. The animals' weights were recorded and stool collected and frozen. At necropsy their colons were extracted, measured, a scraping collected, and the remainder prepared for histology or cultured overnight for secreted mediators. DNA was isolated from stool and mucosal scrapes and the 16S rRNA gene was amplified and sequenced for microbiome analysis.
Results: All mice lost weight and became inflamed with no significant difference between strains in any measure of pathology or anaphylatoxin levels. This was despite a significant difference in the colon microbiome of healthy mice of the two strains, and the colitis resulting in significant changes in the microbiome of both strains. Interestingly, a greater change was detected in mucosal scrapes but not feces of WT compared to P^{KO} mice.
Conclusions: We conclude that properdin does not play a role in chemical-induced colitis despite the mice hosting a different microbiome. Moreover, our results underscore how models of colitis may have different mechanisms including the relationship between complement and the microbiome.

A155
MOLECULAR LANDSCAPE OF ULCERATIVE COLITIS AND CROHN'S DISEASE IS CONSERVED
V. Jovanovic, J. Venner, J. Chang, P. Halloran, R. Fedorak, B.P. Halloran
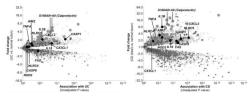
Medicine, Divison of Gastroenterology, University Of Alberta , Edmonton, AB, Canada

Aims: While disease-specific differences between IBD phenotypes are important, it is also of interest to see the conserved elements that reflect the response to injury shared by the phenotypes.
Methods: To map the elements conserved between Ulcerative Colitis (UC) and ileal Crohn's Disease (CD) we used microarrays to study the molecular landscape of 63 UC biopsies compared to 16 control colon biopsies, and 37 ileal CD biopsies compared to 7 control ileal biopsies. These comparisons were expressed as "molecular landscapes" using volcano plots of molecular association strength via p-value (x-axis) versus fold change (y-axis). The landscape of UC (Fig 1) was compared to that of ileal CD (Fig 2) for all 13709 interquartile-range filtered probe sets. We labeled transcripts of interest, including TNFalpha, calprotectin (S100A8 and S100A9), TNFalpha-inducible transcripts, inflammasome associated transcripts, IFNG-inducible transcripts, transcripts representing the response to injury (increased in UC and CD), and transcripts decreased in injured tissue (conserved epithelial genes associated with parenchymal function and metabolism).
Results: There was striking conservation between the molecular landscape of the two disease processes. In both UC and CD, TNF-alpha was interestingly only mildly increased in UC (Fold change= 1.2, P=NS) and CD (Fold change=2.4, P=0.02) compared to controls; however calprotectin (S100A8 and S100A9) was strongly induced in both UC (P=0.0006) and ileal CD (P=0.0001) but the fold change increase in CD was higher than that induced in UC (14x vs 4x). TNFalpha-inducible and inflammasome-associated transcripts were highly conserved across both UC and ileal CD. As expected, expression of inflammasome transcript NOD2 was only associated with CD (Fold change=2.7, P=0.003), but not in UC (P=NS). Epithelial transcripts were variably downregulated in both diseases, indicating the stereotyped dedifferentiation of the parenchyma. Analyses of specific differences between UC and ileal CD and of the most significantly up- and downregulated signals are currently being undertaken.
Conclusions: We conclude that although one might expect UC and ileal CD would have different inflammatory profiles as they present with markedly different phenotypes and in different epithelia, the large-scale molecular changes are strikingly conserved. Calprotectin expression was high in UC and CD in keeping with its current use a fecal biomarker in both diseases.

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A156
A HELMINTH EXTRACT DOES NOT ALTER THE ABILITY OF HUMAN IL-4 STIMULATED MACROPHAGES TO ENHANCE EPITHELIAL WOUND REPAIR

T.S. Jayme, J.L. Reyes, A. Wang, E.T. Thomson, P. Beck, D.M. McKay

University of Calgary, Calgary, AB, Canada

Background: Infection with parasitic helminths can reduce inflammation in animal models of colitis. A component of this anti-inflammatory effect may be induction of IL-4 driven anti-inflammatory/pro-resolution macrophages (M(IL4)) that have been implicated in wound repair. Infection with helminth parasites or exposure to worm extracts may elicit unique macrophage phenotypes. We hypothesized that macrophages co-treated with IL-4 and a crude extract of the rat tapeworm, *Hymenolepis diminuta* (HdE), would have an enhanced ability to promote repair in wounded epithelial monolayers.
Aims: To assess the impact of HdE on the development of human and murine M(IL4)s using canonical markers and assess the role of these cells in epithelial wound repair.
Methods: Human (THP-1 cell line, blood-derived) and murine (bone marrow-derived) macrophages were exposed to IL-4 (10 ng/ml; 48h), HdE (100 mg/ml; 48h), IL4+HdE, or left unstimulated (controls). The expression of M(IL4) markers were assessed by qPCR, immunoblotting or ELISA (human: CD206, CCL18, CD14; murine: arginase-1, Ym1). Caco2 epithelial cells were seeded, grown to confluence in 6-well plates (48h), and wounded with a razor blade. Supernatants collected from the different human macrophage populations were applied and total area of epithelial migration was measured (in mm^2) 24h later. TGFb levels in the macrophage supernatants were measured by ELISA.
Results: The development of human M(IL4)s was not affected by HdE co-treatment as assessed by any of the markers examined, whereas HdE did reduce protein expression of arginase-1 and Ym1 in murine M(IL4)s (n=4-6). Exposure of wounded epithelial monolayers to supernatants from M(IL4)s increased epithelial migration by 36% ± 14% (n=6, p<0.05) compared to baseline, with HdE neither enhancing nor inhibiting the epithelial wound repair. TGFb levels were increased in M(IL4) supernatants compared to those from non-stimulated macrophages: 353 ± 78* vs. 204 ± 71 pg/ml (n=11; *p<0.05 (paired t test)).

Conclusions: HdE has negligible effects on the induction of a human M(IL4) and does not inhibit its ability to promote epithelial wound repair, that could be TGFb-dependent. Thus, (1) M(IL4)s elicited in humans following infection with helminths will not be adversely affected by the release of worm antigen, and (2) if an anti-colitic effect of systemic delivery of helminth antigens to humans results in mobilization of an IL-4-type alternatively activated macrophage, this would be an indirect effect of the worm antigen.

A157
INCIDENCE OF VENOUS THROMBOEMBOLIC EVENTS IN PATIENTS WITH ULCERTIVE COLITIS DURING HOSPITALIZED AND POST-DISCHARGE SETTINGS

A. Israel[1], S. Murthy[1], A. Bollu[2], S. Parlow[1], J. McCurdy[1]

1. University of Ottawa, Ottawa, ON, Canada; 2. The University of British Columbia, Vancouver, BC, Canada

Background: Patients with inflammatory bowel disease (IBD) are at increased risk of venous thromboembolism (VTE) events. Hospitalized patients carry a higher risk for VTE events and as such guidelines recommend thromboprophylaxis for all admitted IBD patients. Risk of VTE in the post-discharge setting has not been as well defined; therefore, it remains unknown if extended thromboprophylaxis is warranted.
Aims: To compare the incidence of VTE events in patients with ulcerative colitis (UC) during hospitalized and post-discharge settings.
Methods: A retrospective observational study was conducted on consecutive UC patients admitted to The Ottawa Hospital with a disease flare between April 1 2006 and April 30 2012. Symptomatic VTE events were assessed during hospitalization and up to 1-year post-discharge through chart review.
Results: Of the 184 patients included, average length of stay was 12.3 days. Ninety four (51%) patients were male, with a median age of 41 years and 23% were current or ex-smokers. Thirty eight percent of all patients received prophylactic or full dose anticoagulation during admission. Overall 17 patients (9%) developed a VTE; 13 (7%) of inpatients and 4 (2%) of outpatients. The median time to diagnosis of outpatient VTE was 4 days (range 4-9 days). Of all VTE patients, 35% received thromboprophylaxis; 45% of inpatients and 25% of outpatients. Of all VTE patients, 82% received corticosteroids, 15% received biologics and 12% underwent colectomy during hospitalization. Of the patients who developed outpatient VTE, all were treated with corticosteroids and 1 (25%) with biologics. None of these patients underwent colectomy. Table 1 describes the individual outpatient VTE events.
Conclusions: In this small retrospective study VTE events were rare in patients with UC following discharge from hospital. Future studies with larger sample sizes are required to confirm these findings and

to identify predictors of high-risk patients who may benefit from extended thromboprophylaxis.

Table 1.

	1	2	3	4
Type of VTE	DVT	DVT and PE	Sigmoid sinus thrombus	DVT
Prophylaxis	No	*Yes	No	No
Length of Stay (d)	13	13	1	9
Age (y)	71	60	25	21
Smoking status	Ex-smoker	Ex-smoker	Ex-smoker	Non-smoker
Medications pre admission	Oral 5-ASA	None	None	Oral 5-ASA Steroids
Medications during admission	Steroids	Steroids	Steroids	Steroids Biologic
Colectomy	No	No	No	No
Duration between discharge and VTE event (d)	4	4	4	9

*Yes: therapeutic fragmin given history of VTE

Funding Agencies: None

A158
THE WAITING GAME: A SYSTEMATIC REVIEW OF ACCESS TO INFLAMMATORY BOWEL DISEASE CARE AND ITS IMPACT ON PATIENT OUTCOMES IN CANADA AND NOVA SCOTIA
H. Mathias, J. Jones

Digestive Care and Endoscopy, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada

Background: Inflammatory Bowel Disease (IBD), including Crohn's Disease (CD) and Ulcerative Colitis (UC), is a chronic early onset disease with debilitating lifelong effects on patients' physical and mental health. IBD is also associated with significant financial and social ramifications. Canada is reported as having the highest prevalence rate of IBD in the world. Within Canada, the province of Nova Scotia (NS) has the highest incidence rates of IBD. Appropriate access to timely and quality care is essential for disease management but very little is known about the impact of access to IBD care on disease related outcomes.
Aims: How does access to IBD care inform patient outcomes in Canada, and more specifically, in Nova Scotia?
Methods: A systematic review of literature pertaining to access to IBD care in Canada was conducted in July 2016. Summon and NovaNet databases were used in conjunction with an internet search engine being used to find relevant gray literature. The search terms "Access" + "Care" + "IBD" + "Canada" + "Nova Scotia" were used. Results were refined for "full texts online" and limited to peer reviewed journals published in English between 2006 and 2016. Search results were sorted by relevance. Exclusion criteria were articles not focused on both IBD and Nova Scotia. A secondary search was conducted using Novanet using the search terms "IBD" + "Nova Scotia."
Results: After the initial search, Summon produced 19 results, while Novanet could not find any matching results. After screening, only 2 results were included in the synthesis (Figure 1). The secondary search yielded 2 articles; however, after screening, none of the articles were included. Included articles and relevant grey literature were analyzed using the patient-centered Five 'A's of Access framework (approachability, acceptability, availability & accommodation, affordability and appropriateness) created by Levesque, Harris and Russell (2013).
Conclusions: Despite an increasing focus on access to health care and patient-centered evidence based medicine, and a notably high incidence rate of IBD in Nova Scotia, this systematic review uncovered large gaps in literature concerning access to IBD care in Canada and Nova Scotia. While some innovative work is being done in the province to address issues of access, the lack of available research in the field of IBD means that actual and perceived access is not adequately understood. Increased patient-centered research in the field of IBD would benefit the availability of accessible patient-centered care through evidence-based systems planning.
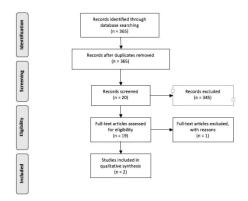
Figure 1. PRISMA flowchart of systematic review using Summon and Novanet databases for search terms "Access" + "Care" + "IBD" + "Canada" + "Nova Scotia"

Funding Agencies: None

A159
A SURVEY FOR THE USE OF PROBIOTICS, PREBIOTICS

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AND DIETARY FIBRE SUPPLEMENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

M. Silva[2], R. Chibbar[2], J. Walter[2], K. Goodman[2], A. Hassanzadeh Keshteli[1], R.S. Valcheva[2], L.A. Dieleman[2]

1. Centre of Excellence for Gastrointestinal Inflammation and Immunity Research, University of Alberta, Edmonton, AB, Canada; 2. Medicine, University of Alberta, Edmonton, AB, Canada

Background: Inflammatory bowel diseases (IBD) are chronic inflammatory conditions of the intestines that are believed to be induced by abnormal activation of the immune cells in 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. Unlike the current standard medications for IBD, these supplements are relatively safe. As such they are suggested as promising novel adjuvant modalities in the treatment of IBD. Although the role of these compounds in the prevention and treatment of IBD is understudied, there seems to be a widespread, undocumented use of these supplements by patients. Identification of usage of probiotics and prebiotics in IBD patients, will allow for optimization of therapy, and improved clinical outcomes.
Aims: To assess the intake of probiotics, prebiotics and dietary fibre supplements in patients with IBD in Edmonton, Alberta.
Methods: A cross-sectional, observational study using a 20-item survey questionnaire was used in patients with a diagnosis of IBD in the IBD Clinic at the University of Alberta. Data regarding demographics, disease characteristics, use and knowledge of probiotics, prebiotics and dietary fibre supplements was collected and analyzed using Fisher's exact test.
Results: In this pilot study, 23 participants with a known diagnosis of IBD (57% ulcerative colitis, 39% Crohn's disease, 4% indeterminate colitis) completed survey questionnaires. Statistical analysis demonstrated that a large number of participants were knowledgeable about probiotics and dietary fibres, but less about prebiotics (87% probiotics, 74% fibres, 43% prebiotics, P < 0.38). Sixty five per cent of surveyed patients have used these products in the past. However, regular usage (in the last year), was much lower (48% probiotics, 28% fibres, 4% prebiotics). Of those who used these alternative treatments in the past, 31% of patients experienced an increase in quality of life (QoL). Those without a university degree were more likely to use these products (67%, P < 0.37). The effect of gender on usage was negligible (53% males, 47% females, P < 1.0). Preliminary results did not reach statistical significance.
Conclusions: This pilot study shows that a large proportion of IBD patients have used probiotics, prebiotics and dietary fibre supplements in the past despite the lack of well-proven efficacy. Since these microbiota targeting strategies have a great potential to improve disease outcomes, it is important that clinicians and researchers document their use.

VIRAL HEPATITIS

Poster of Distinction

A160
ESTIMATION OF FIBROSIS PROGRESSION RATES FOR CHRONIC HEPATITIS C: UPDATED META-ANALYSIS AND META-REGRESSION

A. Erman[2], T. Hansen[3], J.M. Bielecki[4], J. Feld[1], M.D. Krahn[4], R. Thein[5]

1. Toronto Centre for Liver Disease, Sandra Rotman Centre for Global Health, University of Toronto, Toronto, ON, Canada; 2. Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada; 4. Toronto Health Economics and Technology Assessment Collaborative (THETA), University of Toronto, , Toronto, ON, Canada; 5. Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

Background: Chronic Hepatitis C viral infection (HCV) is a leading cause of cirrhosis, liver failure, and transplantation. The accurate estimation of HCV-disease progression is essential for evaluating the cost effectiveness of treatment and determining treatment prioritization.
Aims: The purpose of this study was to obtain updated progression rate estimates (FPRs; i.e., pooled annual transition probabilities) of hepatic fibrosis in individuals with chronic HCV infection and to evaluate the impact of covariates on disease progression though an updated systematic review of the evidence, meta-analysis and meta-regression.
Methods: A literature search was conducted using MEDLINE, EMBASE, and PubMed databases. The search covered a period of January 1990 to August 2014 with no language limit and was supplemented by reference and citation searches. In general, the review included peer-reviewed studies which examine hepatic fibrosis progression in HCV-infected individuals. Stage-specific annual transition probabilities ($F_{0\to1}$, $F_{1\to2}$ $F_{2\to3}$, $F_{3\to4}$) were estimated using the Markov Maximum Likelihood estimation method. Random-effects meta-analyses were used to pool FPRs. The impact of covariates on FPRs was explored through random effects meta-regression analyses. Time-to-cirrhosis was estimated using the pooled FPRs.
Results: Overall, the systematic review included a total of 130 studies involving 160 groups of HCV-infected individuals (N=55,581). The update contributed more subjects from non-clinical settings, injection drug users (IDUs), blood donor populations and genotype-1 and -3 infected groups. The pooled stage-specific FPRs were

$F_{0\to1}$: 0.113 (95%CI, 0.103-0.123); $F_{1\to2}$: 0.087 (95%CI, 0.079-0.096); $F_{2\to3}$:0.120 (95%CI, 0.110-0.131); $F_{3\to4}$: 0.116 (95%CI, 0.105-0.128). Based on meta-regression analyses (**Table 1**), a longer duration of infection, and genotype-1 infection were independently associated with a slower progression, whereas male gender and blood transfusion were associated with faster progression with at least one FPR. Relative to liver clinic populations, pediatric and IDU populations also displayed a faster rate of progression for at least one transition rate. The estimated unadjusted time-to-cirrhosis was 37 years for all groups, 36 for patients identified in a clinical setting, 48 for non-clinical settings, 59 for genotype-1 and 30 years for genotype-3 groups.
Conclusions: The current study provides updated estimates of FPRs associated with chronic HCV, explores covariates associated with progression and provides more precise progression estimates for specific patient populations. These estimates should allow for more accurate estimation of the cost-effectiveness of new HCV antivirals and alternative prevention strategies targeting different groups of patients.

	F0→F1*				F1→F2*				F2→F3*				F3→F4*			
Covariates	β	SE	P-value	RR	β	SE	P-value	RR	β	SE	P-value	RR	β	SE	P-value	RR
Intercept	-1.890	0.429	<.0001		-3.045	0.512	<.0001		-1.396	0.440	0.002		-1.802	0.550	0.001	
Study design																
Cross-sectional/Retrospective (ref)			1.00				1.00				1.00				1.00	
Retrospective-Prospective	-0.075	0.080	0.304	0.93	0.048	0.106	0.653	1.05	-0.045	0.067	0.506	0.96	-0.028	0.111	0.801	0.97
Study population																
Liver clinic (ref)			1.00				1.00				1.00				1.00	
Blood donors	-0.343	0.218	0.116	0.71	-0.148	0.274	0.596	0.86	-0.099	0.233	0.672	0.91	-0.017	0.290	0.954	0.97
Community	0.194	0.189	0.305	1.21	0.133	0.231	0.566	1.14	0.295	0.190	0.122	1.34	0.081	0.213	0.670	1.10
Dialysis patients	-0.094	0.175	0.591	0.91	0.109	0.216	0.616	1.11	0.105	0.202	0.603	1.11	-0.053	0.274	0.840	0.93
Females	0.002	0.287	0.995	1.00	0.501	0.354	0.159	1.65	0.045	0.291	0.877	1.05	-0.554	0.378	0.145	0.57
Haematological diseases	-0.267	0.256	0.229	0.75	0.246	0.297	0.405	1.28	0.335	0.243	0.170	1.40	0.323	0.344	1.02	
Injecting drug users	0.117	0.197	0.550	1.12	-0.240	0.240	0.314	0.78	0.048	0.201	0.813	1.05	0.699	0.245	0.004	1.84
Pediatric patients	-0.157	0.361	0.663	0.85	1.394	0.444	0.002	3.99	0.086	0.371	0.818	1.09	-0.049	0.489	0.921	0.95
Post-transfusion	-0.348	0.267	0.196	0.71	0.106	0.329	0.749	1.11	0.034	0.278	0.904	1.03	-0.170	0.355	0.633	0.84
Renal transplant recipients	-0.204	0.212	0.336	0.82	0.041	0.266	0.876	1.04	0.143	0.252	0.571	1.15	-0.242	0.381	0.527	0.79
Publication year																
<2000 (ref)			1.00				1.00				1.00				1.00	
2000 to <2005	-0.051	0.132	0.699	0.95	-0.016	0.168	0.921	0.98	-0.009	0.137	0.915	0.93	-0.234	0.170	0.169	0.79
2005 to <2010	0.045	0.146	0.751	1.05	0.101	0.181	0.391	1.22	-0.045	0.151	0.767	0.96	-0.255	0.187	0.175	0.78
≥2010	0.086	0.155	0.571	1.07	0.127	0.194	0.515	1.14	0.108	0.164	0.513	1.11	-0.175	0.205	0.393	0.84
Gender – male†	1.065	0.340	**0.002**	**2.90**	1.071	0.417	**0.011**	**2.92**	0.519	0.342	0.130	1.68	0.284	0.401	0.433	0.81
Age at HCV infection (years)	0.004	0.010	0.714	1.00	0.049	0.012	**0.001**	**1.04**	0.010	0.010	0.308	1.01	0.019	0.012	0.136	1.02
Duration of infection (years)	-0.090	0.008	**<.0001**	**0.94**	-0.034	0.011	**0.001**	**0.97**	-0.044	0.009	**<.0001**	**0.96**	-0.029	0.011	**0.009**	**0.97**
Injecting drug use†	-0.200	0.215	0.354	0.82	0.071	0.264	0.789	1.07	-0.218	0.217	0.316	0.80	0.196	0.271	0.995	1.11
Blood transfusion†	0.412	0.200	**0.004**	1.51	0.132	0.235	0.625	1.14	0.196	0.217	0.361	1.22	0.704	0.270	**0.010**	**2.02**
Excess alcohol use†	-0.400	0.239	0.091	0.67	0.533	0.292	0.070	1.70	0.093	0.234	0.692	1.10	0.262	0.289	0.313	1.34
HIV positive†	-0.290	0.277	0.741	0.75	0.580	1.077	0.591	1.79	1.395	0.564	0.25	0.25	-1.177	1.196	0.314	0.31
Genotype-1†	0.266	0.166	0.155	1.31	-0.351	0.230	0.130	0.70	-0.536	0.184	**0.006**	**0.58**	-0.411	0.227	0.072	0.66
Genotype-3†	0.221	0.268	0.411	1.25	0.004	0.328	0.990	1.00	0.370	0.260	0.157	0.68	0.296	0.317	0.458	1.27
I^2		84.84%				86.88%				85.45%				77.88%		
Adjusted R^2		46.62%				30.03%				43.01%				34.06%		

Table 1. Random-effects meta-regression of covariates associated with hepatic fibrosis progression. Linear mixed model-maximum likelihood method. *Log stage-specific transition probabilities. †Proportion. Values in bold indicate statistical significance. Abbreviations: β: coefficient; SE: standard error; CHC: chronic hepatitis C; HIV: human immunodeficiency virus; RNA: ribonucleic acid. I2: the proportion of variability in transition probabilities due to heterogeneity vs. sampling error; R2: the proportion of heterogeneity explained by covariates in the model.

Poster of Distinction

A161
ONGOING INCIDENT HEPATITIC C VIRUS INFECTION AMONG PEOPLE WITH A HISTORY OF INJECTING DRUG USE IN AN AUSTRALIAN PRISON SETTING

E.B. Cunningham[1], B. Hajarizadeh[1], J. Amin[1], B. Betz-Stablein[2], G.J. Dore[1], F. Luciani[1], S. Teutsch[2], N.A. Bretana[1], K. Dolan[3], A.R. Lloyd[1], J. Grebely[1]

1. The Kirby Institute, UNSW Australia, Sydney, New South Wales, Australia; 2. Inflammation and Infection Research Centre, UNSW Australia, Sydney, New South Wales, Australia; 3. National Drug and Alcohol Research Centre, UNSW Australia, Sydney, New South Wales, Australia

Background: There are close ties between injecting drug use and incarceration as a result of imprisonment for drug-related crimes and therefore Hepatitis C virus (HCV) transmission in prisons is high. The most effective strategies to prevent HCV transmission, including needle-syringe exchange (NSP) and opiate substitution therapies (OST) are commonly unavailable in the prisons. Understanding trends in incidence and associated factors in prisons is crucial for developing and improving HCV prevention and treatment programs in the prison setting.
Aims: This study investigated trends in HCV incidence and associated factors among a cohort of prisoners in New South Wales (NSW), Australia.
Methods: Data were available from the Hepatitis C Incidence and Transmission Study in prisons (HITS-p) from 2005-2014. Temporal trends in HCV incidence were evaluated. Factors associated with time to HCV seroconversion were assessed using Cox proportional hazards regression.
Results: Among 590 participants enrolled, 320 were eligible for inclusion (≥1 follow-up visit, lifetime history of injecting drugs, and HCV antibody/RNA negative at enrolment). The mean age was 26 years, 72% (n=229) were male, 33% (n=104) reported recent injecting drug use, 11% (n=35) reported greater than or equal to weekly injecting since entering prison, and 25% (n=81) reported syringe sharing during follow-up. 93 seroconversions were observed in the overall sample [815 person-years (py) of follow-up] while 32 seroconversions were seen in the continuously imprisoned population (507 py of follow-up). HCV incidence was 11.4/100 p-yrs (95% CI: 9.3-14.0/100 p-yrs) in the overall sample and 6.3/100 p-yrs (95% CI: 4.5-8.9/100 p-yrs) among the continually imprisoned sample. A stable trend in incidence was observed over the study period (Figure 1). In adjusted analyses among the overall sample, greater than or equal to weekly injecting was independently associated with time to HCV seroconversion. In adjusted analyses among the continuously imprisoned population, syringe sharing was independently associated with time to HCV seroconversion.
Conclusions: This study demonstrates that current prevention strategies have failed to reduce the incidence of HCV in the Australian prison setting between 2005 and 2014. This study also highlights the need for clean injecting equipment in prison given that needle and syringe sharing was associated with HCV infection among continually imprisoned participants, irrespective of frequency of injecting or the type of drug injected. Prison remains a high risk environment for acquisition of HCV infection and highlights the need for improved harm reduction strategies including NSP and evaluation of interferon-free HCV treatment as prevention strate-

gies in prisons.
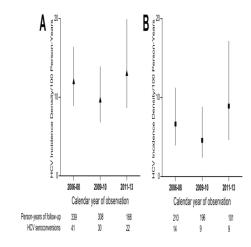
Figure 2: Incidence density of HCV infection among participants in the HITS-p cohort by year of study enrolment in: A) the overall population; and B) those participants continually in prison during follow-up.

Funding Agencies: NHMRC

Poster of Distinction

A162
SHIFT IN DISPARITIES IN HCV TREATMENT FROM INTERFERON TO DAA ERA: A POPULATION BASED COHORT STUDY

N.Z. Janjua[1], N. Islam[3], J. Wong [1], E.M. Yoshida[3], A. Ramji[2], H. Samji[1], Z. Butt [1], M. Chong [1], M. Alvarez[1], D. Cook[1], M. Tyndall[1], M. Krajden[1]

1. BC Centre for Disease Control, Vancouver, BC, Canada; 2. Gastrointestinal Research Institute, Vancouver, BC, Canada; 3. Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada

NOT PUBLISHED AT AUTHOR'S REQUEST

Funding Agencies: CIHR

Poster of Distinction

A163
DIRECT ACTING ANTIVIRAL UPTAKE DISPARITIES IN HIV-HEPATITIS C CO-INFECTED POPULATIONS IN CANADA

S. Saeed[1], E. Strumpf[2], S. Walmsley[3], C. Cooper[4], B. Conway[5], V. Laferriere[7], N. Pick[8], A. Wong[9], M.B. Klein[6]

1. Epidemiology, McGill University, Montreal, QC, Canada; 2. McGill University , Montreal, QC, Canada; 3. University Health Network , Toronto, ON, Canada; 4. Ottawa General Research Institute , Ottawa, ON, Canada; 5. Vancouver Infectious Diseases Centre, Vancouver, BC, Canada; 6. McGill University Health Centre Research Institute , Montreal, QC, Canada; 7. Centre Hospitalier de l'Universitee de Montreal, Montreal, QC, Canada; 8. Oak Tree Clinic, Vancouver, BC, Canada; 9. Regina Qu'Appelle Health Region, Regina, BC, Canada

Background: Direct acting antivirals (DAAs) have revolutionized hepatitis C (HCV) treatment with nearly 100% cure rates even in real-world studies, giving hope that HCV can be eliminated. Historically, HCV treatment initiation rates have been low, particularly among people who inject drugs (PWID) an important group to target if the goal is to reduce incident HCV infections.
Aims: In a publically funded health care setting, we investigated DAA treatment uptake disparities among HIV-HCV co-infected key populations.
Methods: The Canadian Co-Infection Cohort Study prospectively follows 1625 HIV/HCV co-infected participants from 19 centers, representing approximately a quarter of the total Canadian co-infected population in care. Among HCV RNA+ participants, we determined the incidence of HCV treatment initiation per year and stratified by different risk profiles (Aboriginals, women, PWID and men who have sex with men (MSM)). Multivariate Cox models were used to estimate adjusted hazard ratios (aHR) for DAA initiation accounting for age, sex, Aboriginal status, active (within 6 months) and past PWID, MSM, alcohol use, advanced fibrosis, HCV genotype, undetectable HIV RNA, province and income (a priori predictors of treatment initiation).
Results: Overall, HCV treatment initiations rose more than four times between 2013 and 2015, from 6 (95% CI: 5- 9) to 24 (95% CI: 20-29) per 100 person-years. After stratifying initiation by risk profiles, uptake was markedly lower among Aboriginals, women and active PWID. Among 854 HCV RNA+ participants, 195 initiated DAAs [128=ledipasvir/sofosbuvir (SOF); 28=SOF/ribavirin; 19=SOF/simeprevir; 13=SOF/ribavirin/interferon; 7=other all-oral regimens]. After adjustment (aHR, 95% CI), Aboriginals (0.56, 0.34-0.94), active PWID (0.54, 0.36-0.84) remained less likely to initiate HCV treatment. Women and past PWID tended to have lower treatment rates (0.80, 0.55, 1.15) and 0.73 (0.53, 1.02). Conversely, MSM were more likely to initiate DAAs (1.89, 1.41- 2.46). SVR rates were high in all sub-groups regardless of uptake: 100% in women and Aboriginals, 95% in active PWID and 91% in MSM compared to 93% for the cohort overall.
Conclusions: Treatment uptake has increased dramatically with the availability of all oral DAAs, but marginalized populations are still failing to access treatment. Barriers to treating these subgroups, who can obtain high SVR rates, need to be addressed if DAAs are to impact HCV incidence and the overall burden of chronic liver disease.

Poster of Distinction

A164
RAPID INTRAHEPATIC AND PERIPHERAL BLOOD HCV RNA DECLINE AND HCV-SPECIFIC IMMUNE RESPONSE INCREASE DURING IFN-FREE DAA THERAPY IN HCV TREATMENT-NAÏVE PATIENTS

S.A. MacParland[1], v. Cherepanov[2], L. Vijgen[3], M. Gamil[3], M. Beumont[3], S. Yoon[1], A. Rahman[1], C. Capraru[2], M.A. Ostrowski[1], M. Brahmania[4], D. Wong[5], R. Harrigan[6], H.L. Janssen[5], M.S. Sulkowski[7], J. Feld[5]

1. University of Toronto, Toronto, ON, Canada; 2. University Health Network, Toronto, ON, Canada; 3. Janssen Infectious Diseases BVBA, Beerse, Belgium; 4. Mt. Sinai Hospital, Toronto, ON, Canada; 5. Toronto Centre for Liver Disease, Toronto, ON, Canada; 6. University of British Columbia, Vancouver, BC, Canada; 7. Johns Hopkins University School of Medicine, Bethesda, MD

Background: Interferon (IFN)-free HCV direct-acting antiviral (DAA) treatment regimens lead to rapid HCV RNA decline and high rates of sustained virologic response (SVR).
Aims: This study examined the impact of IFN-free DAA treatment on HCV-specific T cell responses and immunophenotypic effects in peripheral blood and in the liver of patients.
Methods: Nine treatment-naïve patients with HCV genotype 1 and fibrosis stage 0-2 (defined by FibroSure ≤0.48 and APRI score ≤1) were treated for 6 weeks with sofosbuvir (nucleotide polymerase inhibitor), simeprevir (NS3/4A protease inhibitor) and daclatasvir (NS5A inhibitor). Peripheral blood mononuclear cells (PBMC) and fine needle aspiration liver biopsies (FNAB) were collected at baseline, day 2, week 1, end of treatment (EOT) and post-treatment follow-up week 24. HCV RNA was quantitatively measured at all time points in plasma using the Roche Cobas Taqman HCV assay v2.0 (lower limit of quantification [LLOQ]=15 IU/mL) and in blood and liver samples using the Abbott RealTime HCV assay (LLOQ=12 IU/mL). HCV-specific immune responses were evaluated by Enzyme-Linked ImmunoSpot (ELISPOT) assay with pools of overlapping peptides spanning the HCV genome. Cell quantities available from FNAB samples for assessment of HCV-specific T cell responses were low. PBMC and intrahepatic T cell phenotype and exhaustion were evaluated by flow cytometry with markers for CD3, CD4, CD8, CD127, Tim-3 and PD-1.
Results: Plasma HCV RNA rapidly declined and was <15 IU/mL undetectable in all 9 patients at EOT. All 9 patients achieved SVR12 and SVR24. HCV RNA also declined in liver tissue but was still detected in all 9 patients at EOT (low-level detectable in all 9 patients, <LLOQ of 12 IU/mL detectable in 3 patients). IFN-gamma producing HCV-specific T cell responses were detected by ELISPOT in blood and liver. Immunophenotyping demonstrated weaker hepatic T cell responses

during and after treatment compared to baseline. This was not associated with increased expression of markers of T cell exhaustion, although some patients showed decreased numbers of viable CD8 T cells. Meanwhile peripheral blood HCV-specific T cell responses were generally weak at baseline and became stronger and broader as treatment progressed.
Conclusions: With this potent DAA combination, all 9 patients achieved SVR with 6 weeks of therapy. However, trace amounts of virus remained detectable in the liver at the EOT in these patients who achieved SVR. Viral suppression was associated with increased HCV-specific T cell responses in the peripheral blood with a concurrent loss of HCV-specific responses in the liver, possibly due to loss of antigenic stimulation.

Poster of Distinction

A165
SHORT INJECTION CESSATION EPISODES AS OPPORTUNITIES FOR HEPATITIS C PREVENTION

E. Fortier[1], A. Artenie[1], D. Jutras-Aswad[2], É. Roy[3], J. Grebely[4], J. Bruneau[2]

1. Université de Montréal, Montréal, QC, Canada; 2. CHUM Research Center, Montréal, QC, Canada; 3. Université de Sherbrooke, Longueuil, QC, Canada; 4. The Kirby Institute, UNSW Australia, Sydney, New South Wales, Australia

Background: In Canada, the majority of new and existing cases of hepatitis C virus (HCV) infection occur among people who inject drugs (PWID), mostly through receptive sharing of injection material. Injecting drug use has been shown to be a dynamic process characterized by transitions in and out of injection. We have previously shown that short injection cessations are associated with a reduced risk of receptive sharing of injection material when resuming injection.
Aims: This investigation aimed to assess the association between HCV infection and intermittent injecting drug use, when considering one-month injection cessation episodes.
Methods: The HEPCO study is an observational cohort of PWID recruited and followed longitudinally in Montréal (QC). At 3-month intervals, uninfected participants (HCV RNA-negative) enrolled between March 2011 and December 2014 were tested for HCV, and completed an interviewer-administered questionnaire eliciting information on sociodemographics, drug use, and related behaviors and treatments. Participants were at-risk of either primary HCV infection (anti-HCV-negative participants), or reinfection/recurrence (anti-HCV-positive participants). Injecting drug use in the past 3 months was categorized as follows: injecting within 0 (no use), 1 or 2 (intermittent use), or 3 months (continuous use). HCV infection was estimated to occur at the midpoint between two visits. Cox regression analyses with

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time-dependent covariates were performed, and Ka-plan–Meier failure curves for multiple-record-per-sub-ject data were estimated.

Results: 311 participants with ≥1 follow-up visit (mean age 40 years, 82% male, 47% anti-HCV positive) contributed 1,689 visits. HCV incidence was 11.3 per 100 person-years [95% confidence interval (CI), 8.8-14.4]. At baseline, 188 (60%), 79 (25%) and 44 (14%) participants reported continuous, intermittent and no injecting drug use in the past 3 months, respectively. In univariate Cox models, intermittent and no injecting drug use were significantly associated with a reduced risk of HCV infection [intermittent use: hazard ratio (HR) 0.36, 95%CI 0.17-0.77; no use: HR 0.23, 95%CI 0.09-0.58] compared to continuous use. In models adjusted for age, gender and opioid substitution treat-ment, associations remained statistically significant for both intermittent (HR 0.40, 95%CI 0.19-0.86) and no injecting drug use (HR 0.30, 95%CI 0.12-0.77). There was no evidence of effect modification by anti-HCV status at baseline.

Conclusions: Intermittent injecting drug use was as-sociated with a reduced risk of HCV infection. Findings bring new perspectives regarding injecting profiles and their relation to HCV risk, and for improving PWID's ac-cess to clinical care and harm reduction interventions. Further work is needed to contextualize intermittent injecting drug use in the injecting drug use trajectory.
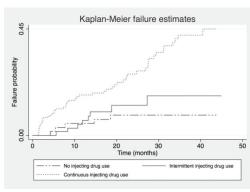
Figure 1. Kaplan-Meier failure estimates for HCV infection (n=311).

A166
SOFOSBUVIR-BASED THERAPY IN THE PRE-LIVER TRANSPLANT SETTING: THE CANADIAN NATIONAL EXPERIENCE

B. Aljudaibi[3], K.W. Burak[6], E.M. Yoshida[7], M. Bilodeau[1], P. Wong[4], A. Benmassaoud[5], T. Hussaini [9], B.S. Thomas[8], J. Chen[7], A. Teriaky[3], P. Marotta[2]

1. Liver Unit, CRCHUM, Montréal, QC, Canada; 2. London heatlh sciences Center, University of Western Ontario, London, ON, Canada; 3. Gastroenterology , London Health Sciences Centre , London, ON, Canada; 4. Gastroenterology, McGill University, Brossard, QC, Canada; 5. McGill University Health Center, Montreal, QC, Canada; 6. Liver Unit, Univ Calgary, Calgary, AB, Canada; 7. Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 8. Medicine, Western University, London, ON, Canada; 9. University of British Columbia, Vancouver , BC, Canada

Aims: To assess the efficacy of SOF-based therapy in HCV infected transplant eligible patients and to evalu-ate decompensated liver disease patients with respect to changes that occur in liver function in the short term and the resultant effect on their liver transplant status
Methods: A retrospective multicentre Canadian study of liver transplant candidates with advanced HCV cirrho-sis treated with SOF-based therapy. Outcomes included sustained virologic response (SVR), changes in MELD-Na score, Child-Pugh score and liver transplant status
Results: 96 liver transplant candidates with advance liver disease due to HCV were evaluated. 69 (71%) of patients have genotype 1, SVR was 88.3% (94% for G1, 68 % for non- G1). 49 patients were treated in the pre-assessment period and 47 patients were treated while awaiting transplantation. Of the 49 treated in the pre-assessment period, no significant difference in their average MELD-Na score (12 vs 12, p=ns) nor Child-Pugh score (7 vs 6 p=ns) occurred from baseline to SVR 12 date. However, among patients treated while wait listed for transplant, 14/47 (30%) remained active on the liver transplant list at the time of SVR12, 9/47 (19%) patients were delisted, 16/47 (34%) underwent liver transplantation. Progression of HCC lead to del-isting of 1 and 8 deaths (1 after transplant) occurred. Among delisted patients, the average MELD-Na changed from 15 to 12
Conclusions: SOF-based therapy for patients progress-ing to liver transplantation leads to high SVR rates, short term stability in liver function, and in a sizable portion leads to delisting. These improvements may increase over time. Longer term follow up and further analysis is needed to understand the overall impact this will have on wait list deaths, number of transplants required for HCV and survival of non-HCV recipients.

A167
AN ANALYSIS OF TREATMENT UPTAKE AND EFFICACY USING ALL-ORAL DIRECT-ACTING ANTIVIRAL (DAA) THERAPY IN HCV-INFECTED PEOPLE WHO INJECT DRUGS (PWID)

R. Shahi, G. Kiani, A. Alimohammadi, T. Raycraft, A. Singh, B. Conway

Vancouver Infectious Diseases Centre, Vancouver, BC, Canada

Background: Approximately 300,000 Canadians are infected with Hepatitis C (HCV), including over 60,000 British Columbians. People who inject drugs (PWID) account for over 50% of HCV infection cases in Canada. Historically, many medical professionals have considered PWID unsuitable candidates for HCV therapy due to concerns about adherence and reinfection after successful treatment. However, the availability of all-oral regimens has led to increased efficacy with improved tolerability and shorter treatment duration. This may represent a unique opportunity to engage HCV-infected PWID more effectively than was possible with interferon-based regimens. This study seeks to assess the efficacy of all-oral HCV therapies among PWID and provide a rationale for enhanced programs in this key population.

Aims: Our study seeks to assess the efficacy of all-oral HCV therapies among PWID and provide a rationale for enhanced programs in this key population.

Methods: A retrospective cohort analysis was performed on all HCV-infected patients who were treated at a tertiary clinic in downtown Vancouver and had a history of recent and ongoing injection drug use. HCV therapy was administered in the context of a program to address relevant medical, social, psychologic and addiction-related concerns. Appropriate HCV treatment regimens were chosen and follow-up visits (at weeks 2, 4, 6, 8, 10, 12, and/or 24 weeks) were scheduled. The primary outcome of the analysis was achievement of a sustained virologic response (SVR).

Results: To date, 50 active PWID received and completed all-oral HCV regimens. Key demographic variables include: mean age 52.4 (34-75) years, 74% male, 40% on opiate substitution therapy, 62%/66%/46% using heroin/cocaine/other stimulants. SVR was achieved in 44 (88%) cases; 4 patients (8%) exhibited virologic relapse and 0 (0%) were re-infected after a median 18 month follow-up period. The 4 patients with virologic relapse were on Sofosbuvir-based regimens - 1 patient with genotype 2a/2c (with Ribavirin), 2 patients with genotype 3a (with NS5A Inhibitor), and 1 patient with genotype 1a (with NS5A Inhibitor).

Conclusions: Although barriers to care exist among PWID, the availability of all-oral regimens represents an important advance to address them. High efficacy can be achieved in this vulnerable population, and it may be that post-treatment re-infection rates will be lower than might have been expected, especially with delivery of care and long-term follow-up within multidisciplinary programs such as ours. There is a need to establish a national cohort of HCV-infected PWID to optimize the parameters of engagement in medical care, provision of HCV therapy and long-term follow-up in this population.

A168

USE OF LEDIPASVIR/SOFOSBUVIR (LDV/SOF) WITH OR WITHOUT RIBAVIRIN (RBV) IN GENOTYPE 1 (GT 1) HCV-INFECTED PATIENTS POST LIVER TRANSPLANT (LT): EVALUATION OF SEVERAL REAL-WORLD DATA-SETS (RWD)

M. Bourliere[1], M. Charlton[11], M. Manns[12], M. Prieto[4], I. Fernandez[5], M. Londoño [7], R. Kwok[2], C. Smith[3], H. Ngo[8], S. Lee[6], J. Zhang[6], S. Arterburn[6], A. Copans[6], L. Rosarro[6], M. Curry[9], S. Flamm[10]

1. Hopital Saint-Joseph, Marseille, France; 2. Walter Reed National Military Medical Center , Bethesda, MD; 3. Medstar Georgetown University Hospital, Washington, ; 4. Unidad de Hepatología, Servicio de Medicina Digestiva, Hospital Universitari i Politècnic La Fe, Spain, Valencia, Spain; 5. Service of Gastroenterology Hospital Universitario , Madrid, Spain; 6. Gilead Sciences, Inc., Foster City, CA; 7. Hospital Clinic Barcelona, Barcelona, Spain; 8. Gilead Sciences Canada, Inc., Mississauga, ON, Canada; 9. Beth Israel Deaconess Medical Center, Boston, MA; 10. Northwestern University Feinberg School of Medicine, Chicago, IL; 11. Intermountain Medical Center , Murray, UT; 12. Hannover Medical School, Hannover, Germany

Aims: Post LT patients infected with HCV are considered a hard-to-treat population. The FDA and Health Canada have recently approved treatment with LDV/SOF+RBV in GT1 LT recipients ± compensated liver disease based on SOLAR-1 & -2 data. Recent reports have shown that SVR rates achieved in HCV monoinfected patients in clinical trials are similar to that observed in real world cohorts, however this is yet to be demonstrated in post-LT patients. The goal of this analysis was to compare efficacy rates in real world cohorts to clinical trial data in this population.

Methods: Integrated data on patients without cirrhosis or compensated cirrhosis who had undergone liver transplantation from 2 open-label phase-2 trials (SOLAR-1 and -2) was compared to 4 real-world datasets. Real-world cohorts included data from academic institutions, community medical centers and specialty pharmacies. Cohorts with less than 50 GT1 patients treated with LDV/SOF+RBV were excluded. Demographics, clinical characteristics, and SVR rates will be presented.

Results: In SOLAR-1 & -2, patients were assigned to receive LDV/SOF+RBV for 12 or 24 weeks, with SVR 12 rates of 95% to 98%. There were no viral breakthroughs and 3 patients relapsed. Patients from 4 real-world cohorts received LDV/SOF+RBV for 8, 12 or 24 weeks. SVR 12 in the 4 real-world cohorts in patients treated with LDV/SOF+RBV for 8, 12 or 24 weeks ranged from 94-100%. RWD showed patients who received LDV/SOF without RBV had SVR rates of 94% - 96%, while those who received LDV/SOF with RBV had SVR12 rates of 96% - 100%. Viral relapse rates were low, ranging from 1-2% across all the RW cohorts.

Conclusions: Evaluation of several heterogenous RWD shows comparable SVR12 rates to clinical trials.

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Patients with compensated liver disease post LT experience high cure rates of HCV with LDV/SOF+RBV. In addition, RWD showed GT1 patients who did not receive RBV had comparable SVR 12 rates to those did receive RBV with LDV/SOF.

SVR12 Rates for GT 1 Patients Post Liver Transplant

Regimens, % (n/N)	SOLAR-1,-2	Prieto et al.	HCV-TAR-GET	TRIO	Kwok et al.
LDV/SOF x 8, 12 or 24 wks	'	'	94% (90/96)		96% (111/115)
LDV/SOF+RBV x 8, 12 or 24 wks	'	96% (224/234)	'	95% (62/65)	'
LDV/SOF+RBV x 8, 12 or 24 wks	97% (299/308)	'	96% (109/114)	'	100% (41/41)
Viral Relapse, % (n/N)	1% (3/308)	2% (5/234)	'	2% (1/67)	<1% (1/156)

A169
FLUORESCENT LABELING OF THE HCV HELICASE TO MONITOR NUCLEIC ACID UNWINDING BY FRET
C. Ablenas[1], M. Powdrill[2], T. Shaw[2], G. Cosa[1], M. Gotte[3]

1. McGill University, Montreal, QC, Canada; 2. University of Ottawa, Ottawa, ON, Canada; 3. University of Alberta, Edmonton, AB, Canada

Background: The hepatitis C virus (HCV) non-structural protein 3 (NS3) contains a helicase activity essential for viral replication. The helicase binds to single-stranded (ss) regions of nucleic acids and unwinds duplexes in an ATP-dependent manner. The mechanism by which the helicase disrupts RNA secondary structure in the viral genome to make way for the replication machinery remains elusive. Several mechanisms have been proposed, which include an active mechanism whereby the helicase actively engages the ss/double-stranded (ds) junction of the substrate to unwind the duplex, and a passive mechanism where the helicase binds and translocates along a ss nucleic acid overhang, taking advantage of transient melting at the ss/ds junction.
Aims: To generate site-specific fluorescently labeled HCV helicase as a tool to track the movement of the enzyme during unwinding and monitor the dynamics of this process.
Methods: The unnatural amino acid p-azido phenylala-nine was incorporated in the recombinant HCV helicase during protein expression in *E. coli*. Using a strain-promoted azide-alkyne click reaction we developed a one-step process to screen for both protein expression and reactivity of the azido group from the incorporated unnatural amino acid. After successfully identifying a position in the helicase for incorporation of the unnatural amino acid and fluorescent labeling with a Cy5 fluorophore, we used the site-specific fluorescently labeled enzyme to monitor the location of binding by Förster Resonance Energy Transfer (FRET) to DNA substrates modified with an appropriate Cy3 donor fluorophore.
Results: Using our approach to simultaneously screen for protein expression with the unnatural amino acid as well as reactivity of the incorporated unnatural amino acid, we identified a position in the HCV helicase suitable for incorporation of p-azido phenylalanine and fluorescent labeling with a Cy5 fluorescent dye. We then developed a plate-based FRET assay to confirm that we could detect the location of binding on a DNA substrate in a distance-dependent manner. Finally, using single molecule fluorescence microscopy we were able to detect binding by FRET for individual enzyme-substrate complexes.
Conclusions: The FRET-based assay has the potential to monitor distinct steps of the unwinding process. Single molecule FRET experiments will provide a deeper understanding of the mechanism by which the helicase interacts with its substrate during unwinding and the dynamics involved in this process.

A170
MACROPHAGE SUBSET PHENOTYPE IS ALTERED IN CHRONIC HCV INFECTION & MAY CONTRIBUTE TO GENERALIZED CD8+T-CELL DYSFUNCTION
F. Ahmed[2], A. Kumar[1], C. Cooper[4], A.M. Crawley[3]

1. Children's Hospital of Eastern Ontario, Ottawa, ON, Canada; 2. University of Ottawa, Ottawa, ON, Canada; 3. Ottawa Hospital Research Institute, Ottawa, ON, Canada; 4. The Ottawa Hospital, Ottawa , ON, Canada

Background: It has been previously shown that chronic HCV infection causes generalized CD8+T-cell impairment, not limited to HCV-specific CD8+T-cell populations. In such an inflammatory hepatic disease, infiltrating monocyte-derived macrophages (MDM) contribute to a micro-environment that could influence cells trafficking through the liver, including CD8+T-cells. These MDM can differentiate into M1 (classically-activated) and M2a, M2b, M2c (alternatively-activated) with pro- and anti-inflammatory functions, respectively. Whether MDM subset generation in chronic HCV infection is altered in the liver is unknown. Furthermore, how these subsets influence CD8+ T-cell function needs investigation. We hypothesize that MDM
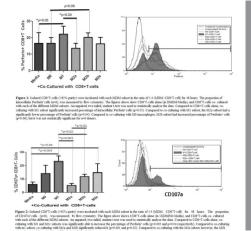
subset phenotypes are altered in chronic HCV infection, thereby contributing to CD8+T-cell dysfunction.

Aims: Aim 1: Assess the phenotypic differences between macrophage subsets in health and chronic HCV infection.

Aim 2: Examine the role of polarized macrophage subsets in altering CD8+T-cell function.

Methods: MDM subsets were generated from blood collected from healthy controls and HCV-infected individuals. Phenotypes were confirmed using surface receptors (CD163, CD206 and CD86) and quantification of secreted cytokines (IL-6, IL-10, IL-12, IFN-y and TNF-α). Autologous co-culture of MDM subsets and isolated CD8+T-cells in health enabled the assessment of CD8+T-cell functions.

Results: MDM subset phenotyping in chronic HCV infection suggests M2a cells have a higher percentage of CD206+ than M0 subset whereas in health, they showed no significant difference. In HCV infection, the concentration of IL-6 in M2a subset supernatants was significantly higher than healthy controls. In chronic infection, TNF-α release by any MDM subset was undetectable, whereas in health, M1 cells produced significantly higher amounts of TNF-α compared to M0 and M2a subsets. No differences were observed in the concentration of IL-10, IL-12p70, IFN-y, CD86 and CD163 between the subject groups. In uninfected controls, co-culturing CD8+ T-cells with M1 macrophages significantly increased the percentage of perforin+, CD107a+ and IFN-y+ CD8+ T-cells, compared to CD8+T-cells alone and M2a subset.

Conclusions: Phenotypic alterations in health and chronic HCV infection are evident both in terms of surface receptors and secreted cytokines suggesting impairment of MDM subsets. The importance of an M1 phenotype, in being able to prime CD8+T-cells and induce perforin and CD107a is evident. How the altered phenotype of MDM subsets in chronic HCV infection will influence the CD8+T-cell function, needs to be further investigated.

Figure 1: Isolated CD8+T-cells (>92% purity) were incubated with each MDM subset in the ratio of 1:4 (MDM: CD8+T-cell) for 48 hours. The proportion of intracellular Perforin+ cells (n=6) was measured by flow cytometry. The figures above show CD8+T-cells alone (in DMEM Media), and CD8+T-cells co-cultured with each of the different MDM subsets. An unpaired, two-tailed, student t-test was used to statistically analyse the data. Compared to CD8+T-cells alone, co-culturing with M1 subset significantly increased percentage of intracellular Perforin+ cells (p=0.05). Compared to co-culturing with M1 subset, the M2a subset had a significantly lower percentage of Perforin+ cells (p=0.04). Compared to co-culturing with M0 macrophages, M2b subset had increased percentage of Perforin+ cells (p=0.06), but it was not statistically significant for n=6 donors.

Figure 2: Isolated CD8+T-cells (>92% purity) were incubated with each MDM subset in the ratio of 1:4 (MDM: CD8+T-cell) for 48 hours. The proportion of CD107a+ cells (n=6), was measured by flow cytometry. The figure above shows CD8+T-cells alone (in DMEM Media), and CD8+T-cells co-cultured with each of the different MDM subsets. An unpaired, two-tailed, student t-test was used to statistically analyse the data. Compared to CD8+T-cells alone, co-culturing with M1 and M2c subsets was significantly able to increase the percentage of Perforin+ cells (p=0.003 and p=0.04 respectively). Compared to co-culturing with m1 subset, co-culturing with M2a and M2b significantly reduced it (p=0.001 and p=0.02). Compared to co-culturing with the M2a subset, however, the M2b subset increased the percentage of Perforin+ cells (n=0.01).

Role of MDM Subsets in CD8+T-cell function in health

A171
MINIMAL CHANGES IN URINE MARKERS OF TUBULAR DYSFUNCTION IN CHB PATIENTS RECEIVING TAF COMPARED WITH TDF

E. Tam[2], M. Khan[1], T. ide[3], S. Strasser[4], K. Yoon[5], S. Paik[6], J. Flaherty[7], K. Kim[7]

1. Gilead Sciences Canada, Inc, Mississauga, ON, Canada; 2. LAIR Centre, Vancouver, BC, Canada; 3. Kurume University Hospital, Kurume-shi, Japan; 4. Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia; 5. Pusan National University Hospital , Yangsan, Korea (the Republic of); 6. Samsung Medical Center, Seoul, Korea (the Republic of); 7. Gilead Sciences, Inc., Foster City, CA

Background: The use of Tenofovir (TDF) for the treatment of CHB results in high rates of viral suppression with no described resistance, but has been associated with small declines in renal function over time. Tenofovir alafenamide (TAF), a novel prodrug of tenofovir (TFV), is more stable in plasma and more efficiently delivers TFV into lymphoid cells and hepatocytes. Phase 3 studies of TAF in CHB demonstrated less renal effects vs TDF with a mean reduction of eGFR from baseline of 0.6 ml/min after 48 wks TAF, and 4.7 ml/min after 48 wks TDF .

Aims: Here, we explore changes in urine renal biomarkers in patients treated with TAF versus TDF.

Methods: In two identically-designed Phase 3 studies of TAF (Study 110, HBeAg+ and Study 108, HBeAg-), patients were randomized 2:1 to TAF 25 mg QD or TDF 300 mg QD, with matching placebo, and treated for 96

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wks. After wk 96, patients receive open label TAF for 48 wks. Biomarkers for renal glomerular dysfunction and tubular dysfunction and beta-2 microglobulin (B2M) were measured throughout the study and ratios to urine creatinine were calculated. Correlations between bio-markers were calculated using Spearman Correlation coefficients.

Results: Baseline correlations were highest for urine albumin/creatinine and protein/creatinine (correlation coefficient 0.57; p<0.001) as well as for RBP/creati-nine and b2M/creatinine (correlation coefficient 0.44; p<0.001). Week 48 change in markers also showed similar correlation coefficients among tubular and glo-merular markers. These correlations were strengthened when evaluating the TDF patients alone. At Week 48, changes in all 4 renal biomarkers were less in the TAF arm than in the TDF arm. Evaluating biomarker changes by baseline renal risk factors (older age, lower baseline GFR, pre-existing hypertension) demonstrated greater changes with TDF than with TAF which was accen-tuated in the high risk groups. The differences were greatest for RBP and B2M which are more sensitive markers for tubular dysfunction.

Conclusions: Baseline correlations were highest for urine albumin/creatinine and protein/creatinine (cor-relation coefficient 0.57; p<0.001) as well as for RBP/creatinine and b2M/creatinine (correlation coefficient 0.44; p<0.001). Week 48 change in markers also showed similar correlation coefficients among tubular and glomerular markers. These correlations were strengthened when evaluating the TDF patients alone. At Week 48, changes in all 4 renal biomarkers were less in the TAF arm than in the TDF arm. Evaluating biomarker changes by baseline renal risk factors (older age, lower baseline GFR, pre-existing hypertension) demonstrated greater changes with TDF than with TAF which was accentuated in the high risk groups. The differences were greatest for RBP and B2M which are more sensitive markers for tubular dysfunction.

A172
C-EDGE CO-STAR: RISK OF REINFECTION FOLLOWING SUCCESSFUL THERAPY WITH ELBASVIR (EBR) AND GRAZOPREVIR (GZR) IN PERSONS WHO INJECT DRUGS (PWID) RECEIVING OPIOD AGONIST THERAPY (OAT)
B. Conway[1], G.J. Dore[2], F. Altice[3], A. Litwin[4], J. Grebely[2], O. Dalgard[5], E.J. Gane[6], O. Shibolet[7], A. Luetkemeyer[8], R. Nahass[11], C. Peng[9], I. Gendrano[10], H. Huang[10], E. Chen[10], B. Nguyen[10], J. Wahl[10], E. Barr[10], M. Robertson[10], H. Platt[10]

1. Vancouver Infectious Diseases Centre, Vancouver, BC, Canada; 2. Kirby Institute , Sydney , New South Wales, Australia; 3. Yale School of Medicine, New Haven , CT; 4. Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY; 5. Institute of Clinical Medicine, Oslo, Norway; 6. Auckland Clinical Studies, Auckland, New Zealand; 7. Tel-Aviv Medical Center, Tel-Aviv, Israel; 8. UCSF School of Medicine, San-Francisco, CA; 9. China Medical University Hospi-tal, Taiwan, Taiwan; 10. Merck & Co., Inc., Kenilworth, NJ; 11. ID Care, Hillsborough Township, NJ

Background:
The fixed-dose combination of EBR 50 mg, an NS5A inhibitor, and GZR 100 mg, an NS3/4 protease inhibitor (EBR/GZR), is a highly effective and well-tolerated all-oral, once-daily regimen in diverse populations of hepatitis C virus (HCV) genotype (GT)1-, 4-, or 6-infect-ed patients, including PWID on OAT. However, data on HCV reinfection rates after successful treatment are limited.

Aims: To determing the rate of reinfections following sucessful HCV therapy with EBR and GZR in PWID receiving OAT

Methods: The double-blind, placebo-controlled CO-STAR study evaluated the efficacy of EBR/GZR for 12 weeks in treatment-naïve HCV GT1-/4-/6-infected patients receiving OAT. Patients were randomized 2:1 to an immediate treatment group (ITG) or a deferred treatment group. HCV reinfection was evaluated among ITG patients with undetectable HCV RNA at end of treatment (EOT). In patients with recurrent viremia following EOT, population sequencing and phylogenetic analysis were performed on baseline and post-treat-ment samples to distinguish relapse from reinfection.

Results: Three hundred one patients were randomized, with 201 in the ITG (76% GT1a; 20% cirrhotic; 8% HIV+). Baseline OAT included methadone (81%) and buprenorphine (19%), and 46% had detectable illicit drugs, excluding marijuana. Post-treatment viremia was detected in 18 patients, with 12 virologic failures and 6 probable reinfections (5 through follow-up week (FW)12 and 1 at FW24). Three patients identified as reinfections had subsequent clearance of HCV RNA. Estimated reinfection incidence per 100 person-years from EOT through FW12 is 10.5 (95% CI: 3.42, 24.6), and from EOT through FW24 is 3.4 (95% CI: 1.3,7.5). Follow-up analysis to determine if any probable rein-fections were due to relapse of nondominant baseline variants rather than reinfection will be presented.

Conclusions: Several HCV reinfection cases were detected among PWID on OAT following successful EBR/GZR therapy. Further follow-up is required to determine the natural course of HCV reinfection in the setting of interferon-free HCV treatment and the impact of viral persistence following reinfection on long-term response rates in this population.

A173
EVALUATION OF LIVER FIBROSIS SCORES POST-HCV SVR IN PEOPLE WHO INJECT DRUGS
T. Raycraft[1], A. Singh[1], A. Alimohammadi[1], R. Shahi[2], G. Kiani[1], D. Truong[1], B. Conway[1]

1. Vancouver Infectious Diseases Centre, Vancouver,

BC, Canada; 2. Vancouver Infectious Diseases Research & Care Centre Society, Vancouver Infectious Diseases Centre, Vancouver, BC, Canada

Background: In the developed world, people who inject drugs (PWID) constitute the majority of prevalent and incident Hepatitis C (HCV) infections. Treatment is often withheld due to concerns surrounding reduced efficacy related to poor adherence and a higher risk of re-infection after successful treatment. Current guidelines favour increasingly widespread access to highly effective direct-acting antiviral regimens within this population, with a view to curing HCV infection but also preventing HCV transmission. An additional ratio-nale for treatment may be to prevent the liver-related morbidity and mortality increasingly prominent among PWID. Data on the impact of HCV cure on liver fibrosis scores among PWID have not yet been generated in a systematic way.
Aims: The aim of this study is to assess the regression of fibrosis in people who inject drugs after achievement of HCV SVR.
Methods: We performed a retrospective observational study utilizing records of PWID successfully treated for HCV infection at our centre. HCV-infected PWID with ongoing recreational drug use, having achieved and maintained a sustained virologic response (SVR) and engaged in long-term medical follow-up were included. Fasting transient elastography (TE) scores post-SVR were compared to pre-treatment values. If such scores were unavailable, APRI scores were considered.
Results: A cohort of 57 subjects were included in this analysis. Of these, 45 (79%) actively injected drugs during treatment and 12 (21%) did so intermittently before and after HCV treatment. The median age was 53 (27-73) years, 47 (82%) were male, 52 (91%) were Caucasian, 42 (74%) were infected with HCV genotype 1, and 12 (21%) were genotype 3. In addition, 77% were HCV treatment-naïve and 10 (18%) were HIV co-infected, 9 (90%) of whom demonstrated complete virologic suppression (HIV viral load <40 copies/mL). The mean follow-up period was 472 (128-1247) days. Based on TE evaluations, the mean pre-treatment fibrosis scores of 11.9 (3-45) kPa (3-45) significantly decreased post-treatment to a mean of 9.6 (2-27) kPa (p=0.03). Mean APRI scores decreased from 0.91 to 0.40 (p=0.0001). Among 12 patients that initially suffered from cirrhosis (TE score >12.5 kPa), 11 (92%) had improved fibrosis scores after treatment, including 5 (42%) who decreased to a lower fibrosis category (F3 or less).
Conclusions: This data set shows significant, rapid improvement in liver fibrosis among PWID success-fully treated for HCV infection. In a population where liver-related morbidity and mortality is becoming a common clinical concern, this provides additional and strong rationale for the development of strategies to increase HCV treatment uptake.

Funding Agencies: Canadian Network on Hepatitis C

A174
A RETROSPECTIVE REVIEW OF CO-PRESCRIBING DIF-ECT ACTING ANTIVIRALS WITH HMG-COA REDUCTASE INHIBITORS IN HEPATITIS C INFECTED PATIENTS IN A VIRAL HEPATITIS CLINIC
L. DeVreese, P. Giguère, C. Cooper

The Ottawa Hospital, Ottawa, ON, Canada
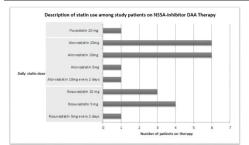
Background: Direct Acting Antiviral (DAA) therapy for the treatment of hepatitis C virus (HCV) has led to improvements in the efficacy, safety and tolerability of HCV management. However, managing drug-drug interactions between NS5A inhibitors and HMG-CoA reductase inhibitors (statins) remains a challenge in clinical practice.
Aims: The aim of this study was to assess the safety and tolerability of either continuing or discontinu-ing statins while on NS5A-based DAA therapy. By retrospectively evaluating statin use in our HCV clinic patients, we aspired to gain a better appreciation of how to safely manage patients presenting on concom-itant therapy.
Methods: A retrospective chart review at The Ottawa Hospital Viral Hepatitis Program's clinic was performed to 1) assess the number of statin-treated patients on NS5A inhibitor based HCV treatment and 2) to assess the safety and tolerability of either continuing or dis-continuing statins while on NS5A inhibitor DAA therapy, measured by the incidence of statin related myopathies and vascular events.
Results: 29/165 (17.8%) of patients pursing NS5A inhibitor therapy presented on a statin at baseline. Six out of 29 (20.7%) discontinued their statin prior to treatment, 10/29 (34.5%) continued on baseline doses and 13/29 (44.8%) were on a decreased dose. All pa-tients on co-therapy were on low doses of statins with none exceeding 25% of the suggested maximum daily statin dose. During co-therapy, one patient experienced stomach cramping and no patients discontinued their statin during DAA therapy. Of those discontinuing statins prior to starting treatment, no patients devel-oped vascular complications. One patient remaining on statin therapy suffered a myocardial infarction.
Conclusions: Although prescribing practices were not uniform, the majority of patients on a baseline statin were continued on statin therapy throughout NS5A inhibitor-based HCV therapy. Co-administration of low-dose statins with NS5A inhibitors appeared to be well tolerated resulting in no apparent or serious statin-re-lated adverse effects, despite the theoretical risk for DDIs. While co-therapy was reassuringly well tolerated, practitioners must continue to weigh the benefits and risks of co-administering statin therapy on a case-by-case basis. The addition of larger, prospective studies may help to better characterize the implications of pursuing co-therapy and provide further guidance to clinicians managing these complex patients.

VIRAL HEPATITIS

Description of statin use among study patients on NS5A-inhibitor DAA Therapy

A175
CAN HCV CORE ANTIGEN REPLACE HCV RNA TESTING IN THE ERA OF DIRECT-ACTING ANTIVIRALS?

S. Almarzooqi[3], M. van Tilborg[4], R. Maan[4], J. Vermehren[5], B. Maasoumy[6], T. Mazzulli[3], A. Duarte-Rojo[7], M. Kowgier[3], H.L. Janssen[3], R. de Knegt[4], J. Pawlotsky[1], G. Cloherty[8], C. Sarrazin[5], H. Wedemeyer[6], J. Feld[2]

1. Hôpital Henri Mondor, National Reference Center for Viral Hepatitis B, C and Delta, Créteil, France; 2. Medicine, University Health Network University of Toronto, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada; 4. Erasmus MC University Medical Center Rotterdam, Rotterdam, Netherlands; 5. Department of Gastroenterology and Hepatology, Goethe-University Hospital Frankfurt, Franfurt, Germany; 6. Department of Gastroenterology, Hepatology and Endocrinology, Hannover Medical School, Hannover, Germany; 7. University of Arkansas Medical Sciences, Arkansas, AR; 8. Abbott Molecular, Des Plaines, IL

Background: Potent direct-acting antivirals (DAAs) for treatment of chronic hepatitis C virus (HCV) infection have reduced the need for on-treatment monitoring. Currently, on-treatment response and outcome are determined by HCV RNA testing. A less expensive alternative to verify viral replication is HCV core antigen (HCV Ag).

Aims: The aim of this study was to determine if HCV Ag can be used for initial confirmation of viremia, on-treatment monitoring and determination of SVR in patients with chronic HCV infection receiving DAA treatment.

Methods: To evaluate the role of HCV Ag in confirming SVR, patients treated with DAAs ±Peg-interferon (IFN)/RBV were included, for the purpose of assessing HCV Ag to determine relapse, patients treated with any regimen (including Peg-IFN/RBV) were included. Serum HCV RNA and HCV Ag levels were assessed at baseline (BL), on-treatment (OT), end of treatment (EOT) and week 12 and/or 24 of follow up (FU). HCV RNA was considered the gold standard.

Results: In total, 181 patients were included, 112 (62%) of whom achieved SVR. Mean age was 54 years (19-79), 115 (64%) patients were male. The majority of patients was infected with genotype 1 (68%) and treated with a sofosbuvir-based regimen (58%). Median HCV RNA level at BL was 6.1 Log10 IU/mL (2.7-7.4) and HCV Ag level was 2409 fmol/L (0.85-20000). At BL, 165 out of 167 (98.8%) viremic patients tested positive for HCV Ag. Of the two patients who tested HCV Ag negative, one patient had a low RNA level (2.67 log10 IU/mL), whereas in the second patient HCV RNA level was high (6.38 log10 IU/mL). Baseline HCV Ag and HCV RNA levels were significantly correlated (R=0.87, p<0.001). At treatment week 4, HCV Ag levels had declined in all patients compared to baseline and were negative in 73%. HCV Ag at EOT was positive in 3 (2.7%) patients, all of whom achieved SVR; all were grey zone reactive (3-10 fmol/L). At week 12 FU, in one out of 68 patients (1.5%) who relapsed according to HCV RNA testing (3.11 log10 IU/mL) HCV Ag was not detected. This patient was therefore misdiagnosed as having an SVR by HCV Ag testing.

Conclusions: Our data support an algorithm of testing anti-HCV antibody (Ab) positive patients with HCV Ag, reserving HCV RNA for those who are Ab positive but Ag negative. HCV Ag can be used to confirm treatment adherence but may not be adequate for confirmation of SVR, which should still be done by HCV RNA. EOT testing with either test was of little clinical benefit. Assuming current practice involves HCV RNA testing at BL, OT, EOT and SVR, use of HCV Ag could eliminate 75% of HCV RNA tests.

A177
BIRTH COHORT SCREENING FOR HEPATITIS C IN AN OUTPATIENT ENDOSCOPY UNIT: A PILOT STUDY

M. Rai, C. Lowe, J. McKay, L. Joyce, L. Hookey, J.A. Flemming

Queen's University, Kingston, ON, Canada

Background: Chronic hepatitis C (HCV) is a curable asymptomatic infection that can progress to liver failure and hepatocellular carcinoma if left untreated. The Canadian Liver Foundation (CLF) recommends one-time HCV screening in all Canadians born from 1945-1975. A large proportion of outpatient endoscopic procedures are for colon cancer screening in this birth cohort providing an opportunity for HCV screening and linkage to HCV care.

Aims: We aimed to assess the feasibility of developing a targeted birth-cohort HCV screening program in the outpatient endoscopy setting.

Methods: This is a cross-sectional study of patients born from 1945-1975 presenting to the outpatient endoscopy unit at Hotel Dieu Hospital in Kingston, Ontario in September, 2016. Patients were scheduled for upper endoscopy, colonoscopy, and/or sigmoidoscopy. All patients were given written information on HCV and the CLF recommendation of birth-cohort screening. Patients were then asked to complete a

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short survey regarding previous HCV screening and acceptance of being screened during their endoscopy visit.

Results: During a 30 day period, 95% (223/235) of eligible patients completed the survey. The cohort was 53% female with a median age of 59 years (IQR 52-66 years). 83% had either never been screened or were unaware of their HCV status. Overall, 87% of participants would be accepting of HCV screening during their endoscopy visit, 9% would not accept screening and 4% stated they were unsure. These results suggest that almost 2,000 patients could be targeted for HCV screening in the endoscopy unit annually.

Conclusions: Most patients born from 1945-1975 presenting for outpatient endoscopy have not been screened for HCV but are accepting of screening during their procedural visit. This identifies a target population for the development of an HCV screening program to increase HCV identification and facilitate linkage to HCV care.

Funding Agencies: None

A178
ARGONAUTE 2 IS DISPENSABLE FOR EFFICIENT HEPATITIS C VIRUS REPLICATION IN HUH 7.5 CELLS.
Y. Amador, J.A. Wilson

Microbiology and Immunology, University of Saskatch-ewan, Saskatoon, SK, Canada

Background: A liver-specific microRNA, miR-122, protects the Hepatitis C virus (HCV) genome from degradation and promotes its replication. Therefore, the virus is deemed highly dependent on this miRNA. This makes it a very attractive therapeutic target that has shown promise in the clinical setting. Nevertheless, the underlying mechanism and the potential role of other host factors are still poorly understood. Argonaute (Ago) proteins are host multifunctional proteins that can be found at the heart of the RNA-Induced Silencing Complex. Humans express 4 Ago isoforms (Ago1-4) and Ago2, the only human Ago capable of endonucleo-lytic cleavage, has generally been viewed as the primary Ago involved in the HCV life cycle.
Aims: This work aimed to investigate the specific role of Ago2 and to determine the impact of the other Ago isoforms in the HCV life cycle.
Methods: To fulfill this objective we made use of the CRISPR/Cas9 technology to generate hepatoma-de-rived Ago2 knockout Huh7.5 cells.
Results: We have generated two cell lines with confirmed biallelic indel mutations in the Ago2 gene and both showed undetectable levels of Ago2 expression by Western blot. We also confirmed that the Ago2 knockout cells were devoid of knockdown activity by assaying for small interfering RNA (siRNA) directed

cleavage activity. Somewhat unexpectedly, Ago2 knockout cells are able to support HCV replication, albeit to lower levels (50-70%) than the wild-type cells. Importantly, in the absence of Ago2, two siRNAs targeting miR-122 binding site 1 rescue HCV replication that had been inhibited by blocking the activity of miR-122.
Conclusions: These results indicate that the other human Ago isoforms (Ago1, 3 and/or 4) are able to sustain HCV replication in the absence of Ago2, and that at least one, but potentially all, of the other Ago proteins can mediate miR-122 promotion of the HCV life cycle. Additionally, our data suggest that Ago2's endonucleolytic cleavage activity is not required for miR-122 promotion of HCV replication. At present, we are generating cell lines in which combinations of all 4 Ago isoforms are knocked out in order to assess the roles of each Ago isoform in the HCV life cycle, and generate an Ago null cell line to be used for trans-com-plementation assays to investigate the mechanism by which Ago and miR-122 promote the HCV life cycle. These novel cell lines constitute valuable tools in the field of HCV research. They will allow the identification of other host factors for the design of multi-target therapeutic approaches, with potentially reduced long-term side effects and higher barriers to resistance compared to single target approaches.

Funding Agencies: Saskatchewan Health Research Foundation and the Canadian Network on Hepatitis C

A179
FEATURES OF THE METABOLIC SYNDROME ARE ASSOCIATED WITH LACK OF SERUM ALT NORMALIZA-TION DURING THERAPY FOR CHRONIC HEPATITIS B
S. Fung[2], M. Khan[1], H. Yatsuhashi[3], W. Tak[4], M. Celen[5], J. Flaherty[6], K. Kim[6], R.P. Myers[6]

1. Gilead Sciences Canada, Inc, Mississauga, ON, Canada; 2. Toronto General Hospital, Toronto, ON, Canada; 3. National Hospital Organization Nagasaki Medical Center, Omura, Japan; 4. Kyungpook National University Hospital, Daegu, Japan; 5. Dicle University, Diyarbakir, Turkey; 6. Gilead Sciences, Inc, Foster City, CA

Background: Despite complete suppression of HBV DNA with antiviral agents, serum alanine aminotrans-ferase (ALT) levels fail to normalize in some patients with chronic hepatitis B (CHB).
Aims: Our objective was to evaluate factors associated with persistent ALT elevation during treatment with tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate(TDF).
Methods: Adults with CHB enrolled in two Phase 3 studies of TAF 25 mg QD vs. TDF 300 mg QD (Study GS-US-320-0108 in HBeAg- and GS-US-320-0110 in HBeAg+ subjects) were included. Rates of ALT normalization at Weeks 12 and 48 were determined using reference ranges recommended by AASLD (≤19

U/L for women, ≤30 for men). A sensitivity analysis examined ALT normalization according to central laboratory (Covance) criteria (<69 yrs:≤34 U/L for women, ≤43 for men; ≥69 yrs: ≤32 U/L for women, ≤35 for men). Associations between host, viral and treatment-related factors, including virologic suppression (HBV DNA <29 IU/mL; Roche COBAS Taqman), with persistent ALT elevation at Week 48 were determined using logistic regression.
Results: Based on AASLD criteria, 1,276 of 1,301 subjects (98%) had abnormal baseline (BL) ALT. Median BL ALT and HBV DNA were 82 U/L (IQR 56-126) and 7.4 log10 IU/mL (IQR 5.8-8.3), respectively. Compared with patients treated with TDF, ALT normalization by AASLD criteria at Week 12 (11% vs. 18%; P=0.003) and Week 48 (36% vs. 49%; P<0.001) were more common among patients treated with TAF. Similarly, ALT normalization by central laboratory criteria was greater in TAF vs. TDF-treated subjects at Week 12 (43% vs. 35%; P=0.015) and Week 48 (78% vs. 72%; P=0.012). Patients with elevated ALT at Week 48 had a higher prevalence of overweight (45% vs. 29%; P<0.001), hypertension (15% vs. 10%; P=0.007), dyslipidemia (11% vs. 6%; P=0.003), and diabetes (8% vs. 5%; P=0.062) compared with those with normal ALT. In a multivariate analysis, TAF treatment (odds ratio [OR] 0.60; 95% CI 0.44-0.82; P=0.002) and virologic suppression (OR 0.33; 0.22-0.49; P<0.001) were associated with a lower likelihood of ALT elevation at Week 48. Additional independent predictors of ALT elevation included female sex (OR 1.79; 1.29-2.47; P<0.001), higher BMI (OR 1.14; 95% CI 1.09-1.19; P<0.001), diabetes (OR 2.27; 1.11-4.63; P=0.024), cirrhosis (OR 2.64; 1.53-4.57; P<0.001), and lower BL ALT (OR 0.995; 95% CI 0.993-0.997; P<0.001).
Conclusions: In patients with CHB, treatment with TAF compared with TDF is associated with a greater likelihood of ALT normalization independent of virologic suppression. Patients with metabolic risk factors are less likely to normalize ALT, which could occur due to underlying hepatic steatosis.

A180
IMPROVED RENAL LABORATORY PARAMETERS IN CHB PATIENTS TREATED WITH TAF COMPARED WITH TDF
F. Wong[1], M. Khan[2], K. Agarwal[3], N. Furusyo[4], . Byun[5], J. Hwang[6], J. Flaherty[7], K. Kim[7]

1. Medicine, 9N/983 Toronto General Hospital, Toronto, ON, Canada; 2. Gilead Sciences Canada, Inc, Mississauga, ON, Canada; 3. Kings College Hospital NHS Trust, London, United Kingdom; 4. Kyushu Medical Center, Fukuoka, Japan; 5. Korea University, Seoul, Korea (the Republic of); 6. Keimyung University Dongsan Medical Center, Daegu, Korea (the Republic of); 7. Gilead Sciences, Inc., Foster City, CA

Background: Tenofovir Disoproxil Fumarate (TDF)

treatment results in high rates of viral suppression with no described resistance; however its use has been associated with a deterioration in bone mineral density and eGFR over time. TAF, a novel prodrug of tenofovir (TFV), has better stability in plasma resulting in lower systemic TFV exposures than TDF. Phase 3 studies of TAF in CHB demonstrated lower declines in eGFR compared to TDF over 48 weeks of treatment.
Aims: Here, we further characterize the clinical renal benefits of TAF compared to TDF.
Methods: In two identically-designed Phase 3 studies of TAF (Study 110 in HBeAg positive and Study 108 in HBeAg negative patients), patients were randomized 2:1 to TAF 25 mg QD or TDF 300 mg QD, each with matching placebo, and treated for 96 weeks. After Week 96, patients receive open label TAF for 48 weeks. Renal parameters including eGFR calculated by Cockcroft-Gault and CKD-EPI were evaluated throughout the study period. Chronic kidney disease (CKD) staging was categorized according to the NKF KDOQI guidelines (Stage 1: eGFR ≥ 90ml/min; Stage 2: eGFR 60-90 ml/min; Stage 3 eGFR 30-59 ml/min). Evaluated risk factors for kidney disease included older age and comorbidities of hypertension, cardiovascular disease and diabetes. Multivariate analysis was performed using backwards stepwise approach.
Results: Baseline demographics between TAF and TDF groups in both studies were generally balanced for risk factors for kidney disease. At week 48 , patients treated with TAF had smaller changes in creatinine (median change 0.01 mg/dL for TAF and 0.02 mgdL for TDF; p=0.012) and eGFRCG (median change -1.2 mL/min for TAF and -5.4 mL/min for TDF; p<0.001) during 48 weeks of treatment. The number of patients who had >25% creatinine clearance reductions was also greater in the TDF arm versus the TAF arm (14.5% vs 8.7%, p=0.002). Using the stages of CKD, a higher percentage of patients treated with TDF had one or more stage worsening in renal function at Week 48 (10.2% vs 6.5%; p=0.06). Among patients at highest risk for kidney disease (older age and comorbidities of hypertension, cardiovascular disease or diabetes), significantly more patients had worsening of renal function in TDF treated patients compared to TAF treated patients.Multivariate analysis of worsening renal function by CKD stage identified higher baseline eGFR, male gender, and Age > 50 as Independent predictors.
Conclusions: In patients with CHB, TAF therapy is associated with improvement of renal safety versus TDF. The benefits of TAF may be particularly evident in patients at higher risk of GFR decline.

A181
REAL-LIFE EFFICACY OF ELBASVIR/GRAZOPREVIR (EBV/GZV) FOR THE TREATMENT OF CHRONIC HCV GENOTYPE 1 AND 3 INFECTION
A. Alimohammadi, G. Kiani, T. Raycraft, R. Shahi, A. Singh, B. Conway

Vancouver Infectious Diseases Centre, Vancouver, BC, Canada

Background: The introduction of all-oral direct acting antiviral (DAA) regimens has allowed for better tolerated, shorter, and more effective courses of therapy for HCV infection. Elbasvir (EBV, NS5A inhibitor) and grazoprevir (GZV, NS3/4A protease inhibitor) is a new fixed dose combination that has demonstrated sustained virologic response (SVR) rates above 90% in a broad range of treatment-naïve and experienced populations, including people who inject drugs (PWID).
Aims: We sought to evaluate the efficacy of EBV/GZV in a clinical setting serving HCV-infected PWID.
Methods: An observational evaluation was conducted among HCV-infected patients seen at the Vancouver Infectious Diseases Centre (VIDC), where they had access to a multidisciplinary model of care to address medical, psychiatric, social and addiction-related needs prior to, during and after HCV therapy. All individuals that received EBV/GZV did so according to current clinical guidelines. At the time of the current analysis, the primary endpoint was defined as SVR-4, an undetectable HCV RNA four weeks post-treatment. Demographic and clinical correlates of success were also evaluated.
Results: To date, 13 individuals have received EBV/GZV in our program, 7 genotype 1a, 2 genotype 1b, and 4 genotype 3a (EBV/GZV administered in combination with sofosbuvir). Key demographic information includes: mean age 49.5 years, 23% female, 15% cirrhotic, 15% HIV co-infect and 85% current PWID. Adherence rates are high, with all patients having missed 0-2 doses. To date, six patients have reached the primary endpoint and 100% have achieved SVR-4, including 4/4 individuals with genotype 3a infection. Data will be presented on 20 patients with the SVR12 endpoint having been achieved.
Conclusions: The combination of EBV/GZV (with or without sofosbuvir) appears highly effective in clinical practice in a population similar to that enrolled in the C-EDGE CO-STAR protocol. If these preliminary data are confirmed, EBV/GZV will become another highly potent therapeutic option available for the treatment of HCV infection in diverse populations, including PWID

Funding Agencies: None

A182
HEPATOCELLULAR CARCINOMA (HCC) SCREENING PRACTICES IN CHRONIC HEPATITIS B (HBV) AMONG CANADIAN GASTROENTEROLOGISTS AND HEPATOLOGISTS: AN ONLINE SURVEY
A. Yau[2], C. Galorport[1], H. Ko[2], C.S. Coffin[3]
1. Medicine, Div. of Gastroenterology, St. Paul's Hospital , Vancouver, BC, Canada; 2. Medicine, University of British Columbia, Vancouver, BC, Canada; 3. Medicine, University of Calgary, Calgary, AB, Canada

Background: Current guidelines recommend HCC

surveillance in certain chronic HBV carriers: Asian male age > 40, Asian female age > 50, African/Non-African blacks, family history of HCC and cirrhosis.
Aims: To determine the HCC screening practices among Canadian gastroenterologists and hepatologists.
Methods: An online survey was performed.
Results: At this point, 22 responded (5 hepatologists, 17 gastroenterologists) and their years in practice were: < 5 (18.2%), 6-10 (22.7%), 11-15 (13.6%), 16-20 (4.5%), and > 21 (40.9%). The number of HBV patients seen per year was: < 10 (31.8%), 10-100 (36.4%), 100-200 (18.2%), 200-500 (4.5%), and > 500 (9.1%). All hepatologists and 12 (70.6%) gastroenterologists treat HBV.
77.3% (17/22) order US about every 6 months at the time of clinic visits, while 13.6% (3/22) have an automatic recall system and 9.1% (2/22) refer back to primary care physicians. 54.5% (12/22) include alpha-fetoprotein (AFP) with ultrasound.
For non-Asian, non-African HBV patients, 36.4% (8/22) screen them the same way as in Asians, 31.8% (7/22) screen with US every 6 months starting at an older age, 13.6% (3/22) screen with annual US at the same age, 9.1% (2/22) screen with annual US at an older age, and 9.1% (2/22) screen only cirrhotic.
For young (age < 40) non-African HBV patients with a family history of HCC, 36.4% (8/22) screen with US every 6 months regardless of age, 27.3% (6/22) screen with US and AFP every 6 months regardless of age, 18.2% (4/22) screen with annual US regardless of age, and 18.2% (4/22) screen the same way as those without a family history.
For HBV patients with non-alcoholic fatty liver disease (NAFLD): 50% (11/22) screen the same way as those without NAFLD, 31.8% (7/22) start screening with US every 6 months regardless of age if advanced liver fibrosis ($\geq$F3) is present, 9.1% (2/22) screen with MRI every 6 months regardless of age if advanced fibrosis ($\geq$F3) is present, and 9.1% (2/22) screen with US every 6 months regardless of age and stage of fibrosis.
Obstacles to HCC screening reported: lack of an automatic recall system (54.5%; 12), patient non-compliance (31.8%; 7), and limited access to US/MRI (13.6%; 3).
Conclusions: HCC screening practice vary widely among gastroenterologists and hepatologists for HBV patients with non-Asian, non-African descent, family history of HCC, and NAFLD. Incidence of HCC in these populations is unknown and HCC screening guidelines are desperately needed for these patients. Implementation of an automatic recall system could potentially facilitate HCC screening.

Funding Agencies: None

A183
SOFOSBUVIR-BASED ALL-ORAL REGIMENS FOR PATIENTS WITH CHRONIC HEPATITIS C GENOTYPE 3 INFECTION: INTEGRATED ANALYSIS OF FIVE CLINICAL STUDIES

G.R. Foster[1], S. Zeuzem[4], E.J. Gane[5], C. Stedman[6], J. Feld[3], A. Mangia[7], K. Agarwal[8], M. Swain[2], H. Mir[9], P. Troke[9], J. Llewellyn[9], M. Natha[9], B. Kreter[9], J. Zhang[9], J. McNally[9], D. Brainard[9], S. Strasser[10], S. Pianko[11]

1. Queen Mary University, London, United Kingdom; 2. Univ Calgary, Calgary, AB, Canada; 3. Medicine, University Health Network University of Toronto, Toronto, ON, Canada; 4. Johann Wolfgang goethe University Medical Center, Frankfurt, Germany; 5. Auckland Clinical Studies, Auckland, New Zealand; 6. Christchurch Hospital, Christchurch, New Zealand; 7. Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy; 8. Institute of Liver Studies, Kings College Hospital, London, United Kingdom; 9. Gilead Sciences, Inc., Foster City, CA; 10. Royal Prince Alfred Hospital, Sydney, Queensland, Australia; 11. Monash Health, Melbourne, Queensland, Australia

Aims: Hepatitis C virus (HCV) genotype 3 (GT3) infection represents the second most common genotype worldwide and is currently considered the most difficult genotype to treat. AASLD and EASL guidelines recommend sofosbuvir (SOF) based regimens for the treatment of patients with HCV GT3. This analysis evaluated the efficacy and safety of various 12-week SOF-based all-oral regimens for HCV GT3 from Phase 2 and 3 clinical studies
Methods: In the phase 2 ELECTRON-2 study, 26 treatment-naïve (TN) and 50 treatment-experienced (TE) HCV GT3 patients received 12 weeks of ledipasvir 90 mg (LDV)/SOF 400 mg daily + weight-based ribavirin (RBV) 1000 or 1200 mg divided twice daily. In the phase 2 CANADA study, 111 TN HCV GT3 patients received 12 weeks of LDV/SOF+RBV. In the phase 3 ALLY-3 study, 101 TN and 51 TE HCV GT3 patients received 12 weeks of SOF 400mg + daclatasvir 60 mg (DCV) daily. In the phase 3 ALLY-3+ study, 6 TN and 18 TE HCV GT3 patients received 12 weeks of SOF+D-CV+RBV. In the phase 3 ASTRAL-3 study, 206 TN and 71 TE HCV GT3 patients received 12 weeks of SOF 400 mg/velpatasvir 100 mg (VEL) daily, compared to 275 patients who received 24 weeks of SOF+RBV. Patients with compensated cirrhosis were allowed to enroll in all studies.
Results: 640 patients with HCV GT3 were enrolled in 5 clinical studies in North America, Europe, Australia, and New Zealand. Overall in all studies, the patients were male (62%), white (86%), and had IL28B non-CC genotype (61%). 190 patients (30%) were TE and 197 patients (31%) had compensated cirrhosis. Treatment responses will be reported. Therapy was well-tolerated with no patients discontinuing all treatment due to an adverse event.
Conclusions: SOF/VEL for 12 weeks achieved the highest SVR12 and lowest relapse rates seen among the 5 studies, including in compensated cirrhotic patients, and was superior to 24 weeks of SOF+RBV. It offers a fixed-duration, IFN- and RBV-free, well-tolerated, and highly effective therapy, even for difficult-to-treat GT3 patients.

Funding Agencies: Gilead Sciences Inc.

A184
DISSECTING THE ROLE OF THE POLY(C)-BINDING PROTEIN 2 IN THE HEPATITIS C VIRUS LIFE CYCLE
S. Cousineau, S. Sagan

Microbiology & Immunology, McGill University, Montreal, QC, Canada

Background: We currently know that the hepatitis C virus (HCV) uses a number of cellular elements - including proteins and microRNAs - to promote its own replication and to protect itself from cellular molecular defenses against viruses. One particular cellular RNA-binding protein, the poly(C)-binding protein 2 (PCBP2), is known to mediate the stability and expression of a number of cellular transcripts, and is also known to be co-opted by several positive-strand RNA viruses to promote their replication. Six PCBP2 binding sites have been identified on the HCV genome, including in areas of the 5' and 3' untranslated regions which are known to play important roles in HCV translation and RNA replication. However, the exact mechanism by which PCBP2 affects HCV replication still remains to be elucidated.
Aims: We aim to clarify the role of PCBP2 in the HCV life cycle, and to identify the specific step(s) of viral replication that are affected by PCBP2.
Methods: We are using the HCV cell culture system (specifically the JFH-1T strain) in Huh-7.5 cells to assess how viral protein synthesis, viral RNA accumulation, and the production of infectious viral particles is affected by knockdown of endogenous PCBP2 or the overexpression of a FLAG-tagged PCBP2 construct. We are further examining the effect of PCBP2 depletion on viral IRES-mediated translation as measured using a dual-reporter luciferase assay system.
Results: We will show that siRNA-mediated PCBP2 knockdown inhibits HCV protein expression, RNA accumulation, and infectious particle production. We will also show preliminary results that try to tease apart whether this effect is due to a defect in viral translation, RNA replication, or both.
Conclusions: We anticipate that investigating PCBP2-HCV interactions will help clarify the role of this host protein in the viral life cycle, and will provide a model for the regulation of viral RNA accumulation, and/or the switch from translation to replication. These mechanisms may also be applicable to other important human pathogens related to HCV, such as the Dengue or Zika viruses.

Funding Agencies: CIHRCanHepC

A185
IMPACT OF HEPATITIS C ERADICATION USING DIRECT ACTING ANTIVIRALS ON CONCURRENT PRIMARY BILI-

ARY CHOLANGITIS AND ASSOCIATED AUTOIMMUNITY.

H.H. Nguyen[2], A. Khathlan[2], M.J. Fritzler[2], M. Swain[1]

1. Univ Calgary, Calgary, AB, Canada; 2. Gastroenterology and Hepatology , University of Calgary, Calgary, AB, Canada

Background: Chronic Hepatitis C Virus infection has been commonly linked to the development of autoimmunity, in part through activation of B cells. As well, B cells have been shown to play an important pathogenic role in Primary Biliary Cholangitis (PBC). Patients with concurrent HCV infection and PBC have an increased risk of more rapidly progressive disease, although the mechanism underlying this effect is poorly understood. However, it seemed plausible that HCV infection could enhance PBC-associated autoimmunity thereby worsening disease.
Aims: Therefore, the aim of our study was to determine the impact of HCV eradication upon serological markers of autoimmunity (ie. autoantibody production) and liver biochemistry in PBC patients infected with HCV.
Methods: We identified 3 HCV-infected patients who also had significant serum AMA titers, and were followed in the University of Calgary Liver Unit. All 3 patients were treated with non-interferon based direct-acting antiviral (DAA) therapies. One patient was on UDCA therapy (13 mg/kg/day) during the treatment period (elevated serum alkaline phosphatase levels). The remaining two patients were not on UDCA therapy due to intolerance in one, and normal serum alkaline phosphatase levels in the other. Virological response to DAA's was assessed during and after therapy in all patients using a HCV Quantitative Nucleic Acid Test (Abbott), and serum liver biochemistries measured by Calgary Laboratory Services. Autoantibodies associated with autoimmune liver diseases, including PBC specifically, were measured before, during and after DAA treatment (Mitogen Advanced Diagnostics Laboratory, Calgary AB, Canada).
Results: All patients achieved a sustained virological response (SVR), as determined by a negative HCV RNA test 12 weeks post-DAA therapy. Titres of antimitochondrial antibodies (AMA-M2), anti- branched-chain 2-oxo-acid dehydrogenase complex and 2-oxo glutarate dehydrogenase complex (anti-3E-BPO), and anti- tripartite motif-containing protein 21 (TRIM21/Ro52) remained unchanged despite successful HCV eradication. Two of three patients exhibited a transient decrease in some autoantibody titres during DAA treatment, but these returned to baseline levels post-DAA therapy.
Conclusions: Our results suggest that ongoing HCV infection is not a significant driver of PBC-related autoimmunity/autoantibody production.

A186

INVESTIGATION OF THE PROTECTIVE ROLE OF MIR-122 AGAINST CELLULAR SENSORS OF RNA AT THE 5′ TERMINUS OF HEPATITIS C VIRUS GENOME

A. Bernier[1], Y. Amador[2], S. Sagan[1], J.A. Wilson[2]

1. Microbiology and Immunology, McGill University, Montreal, QC, Canada; 2. Microbiology and Immunology, University of Saskatchewan, Saskatoon, SK, Canada

Background: Approximately 200 million individuals worldwide are infected by hepatitis C virus (HCV). MicroRNA-122 (miR-122) is a highly abundant liver-specific miRNA shown to interact at two miR-NA-binding sites in the 5′ end of the HCV genome. This unusual interaction promotes HCV RNA accumulation in both HCV-infected cells and the livers of infected patients. Previous investigation of the stabilization of HCV RNA by miR-122 shows a slowed rate of decay in cells supplemented with miR-122 duplexes. Recent findings demonstrate that miR-122 protects HCV RNA from degradation by exoribonucleases. These results support a model whereby miR-122 acts to shield the 5′ terminus of the viral RNA, preventing its degradation or recognition by nucleases or cellular sensors of RNA. Protein kinase R (PKR) is activated mainly by long dsRNA, but short RNA stem-loops can activate PKR in a 5′ triphosphate-dependent manner, suggesting that the 3′ overhang created by miR-122 binding to the HCV 5′ end may also prevent recognition of HCV by PKR. In addition, the LGP2 protein is another RIG-I-like receptor that binds to dsRNA and acts as an on/off switch for RIG-I signaling.
Aims: We hypothesize that miR-122 forms a distinct complex with host and/or viral proteins that together protect the HCV 5′ terminus from recognition by cellular sensors of RNA, such as PKR and LGP2. Herein, we are investigating a protective role for miR-122 against these cellular sensors of RNA.
Methods: We are inhibiting PKR and LGP2 expression by siRNA knockdown in Huh7.5 cells, in the presence or absence of miR-122. To investigate the stabilization of the viral RNA in this context, we are montitoring viral RNA accumulation by luciferase assay and northern blot analyses. To investigate the contribution of miR-122, we are using miR-122 site mutants or sequestering miR-122 using an antisense locked nucleic acid inhibitor.
Results: We demonstrate that LGP2 expression is increased early during HCV infection in Huh7.5 cells. Knockdown of PKR or LGP2 in the presence of miR-122 has no significant effect on HCV RNA accumulation. Our current focus is on elucidating the effect of PKR and LGP2 knockdown on HCV RNA accumulation in miR-122 site mutants under limited miR-122 conditions or during miR-122 sequestration.
Conclusions: We expect that the results will reveal whether miR-122 binding to the 5′ terminus of HCV is protective against recognition by the cellular sensors of RNA, PKR and LGP2 and together with our collaborators in the Wilson lab, we are investigating the role of

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several other sensors of RNA, including IFIT-1, IFIT-5, RIG-I and MAVS. These results will provide insights into whether miR-122 binding to the HCV genome protects the viral RNA from recognition by cellular sensors of RNA and has implications for the mechanisms of miR-122 mediated promotion of HCV RNA accumulation.

A187
OBSERVATIONAL RETROSPECTIVE ANALYSIS OF PATIENTS IN THE CANADIAN ABBVIECARE (AC) HCV PATIENT SUPPORT PROGRAM

N. Ackad[1], P. Landry[2], R. El Marazi[1]

1. Abbvie Corporation, Montreal, QC, Canada; 2. Abbvie Corporation, St-Laurent, QC, Canada

Background: Recently developed hepatitis C virus (HCV) medications are much better tolerated and require much shorter treatment courses than those pre-viously available. Furthermore, they are more effective at controlling and eradicating HCV. HCV epidemiology in Canada is well documented but not for patients being treated with the newly available medications.
Aims: Analysis of the Canadian AC HCV database was undertaken to characterize enrolled patients, to tabulate reported treatment outcomes and to identify variables that may be associated with those outcomes, including patient-reported cure rates, treatment com-pletion and treatment initiation.
Methods: An observational retrospective study design was used to query the data in the AC HCV database. Data was anonymized, screened and validated. De-scriptive analyses were performed and logistic regres-sion employed to identify determinants of treatment initiation.
Results: Of 1,919 patients enrolled, 1,332 reported initiating treatment, 1,073 completing treatment and 519 reported viral response. Patients averaged 56 years old and 2/3 were male. Most were covered under Provincial drug plans. Only 2% of patients initiating treatment reported discontinuation. Not quite half of patients completing treatment reported virological response, but with only 9 treatment failures, a 98.3% cure rate among patients with complete data was computed (G1a:97.9%, 287/293, G1b: 98.9%, 183/185, G4: 100%, 21/21). Regression analysis performed to explore associations with treatment initiation showed that province of residence (BC, QC & SK vs. ON), fibrosis score >1 and ribavirin co-prescription were sig-nificantly associated with greater likelihood to initiate treatment. Patients covered by public insurance were 37% less likely to initiate treatment than those covered by private insurance (p=.007). Regression analysis to explore associations between patient characteristics and either failure to complete treatment or treatment success could not be reliably performed because patients reporting discontinuation or treatment failure were too few.

Conclusions: The AC population reflected the Canadian population in its distribution except that PEI was overrepresented in the database, likely reflecting the success of that province's unique HCV management strategy. Patient reported treatment result (cure/failure), recorded by 48.4% of those who completed treatment, was 98.3% positive, to be treated with caution because of incomplete reporting but consistent with clinical trial results (≥90% cured at 12 weeks). The present study successfully described many attributes of the patient population participating in the AC HCV program. Based on patient initiation, completion and patient activation model scores, the program may promote patients' engagement in their treatment.

A188
REAL-LIFE MANAGEMENT OF CHRONIC HEPATITIS C VIRUS INFECTION IN CANADA: DESCRIPTION OF PATIENT PROFILE, PROGNOSTIC FACTORS AND TREATMENT STRATEGIES

S. Borgia[3], M. Elkhashab[7], P. Ghali[8], K. Kaita[6], S. Lee[5], S. Shafran[4], E. Tam[9], B. Trottier[10], D. Webster[11], C. Pinson-nault[1], N. Ackad[2]

1. Medical, Abbvie Corporation, Saint-Laurent, QC, Canada; 2. Medical Affairs, Abbvie Corporation, Mon-treal, QC, Canada; 3. Osler Hepatitis Centre, Brampton, ON, Canada; 4. University of Alberta, Edmonton, AB, Canada; 5. University of Calgary, Calgary, AB, Canada; 6. University of Manitoba, Winnipeg, MB, Canada; 7. Toronto Liver Centre, Toronto, ON, Canada; 8. McGill University Health Centre, Montreal, QC, Canada; 9. Lair Centre, Vancouver, BC, Canada; 10. Clinique Medicale L'Actuel, Montreal, QC, Canada; 11. St John Regional Hospital, St John, NB, Canada

Background: Most recent major treatment guidelines recommend considering the patient profile and baseline prognostic factors (genotype, fibrosis level, treatment history) in the management of chronic hepatitis C virus (HCV) infections (CHC). There is, therefore, a need to better characterize clinician decision-making in real-life CHC management in Canada.
Aims: To describe the patient profile, prognostic factors and treatment strategies used in Canadian real-life CHC management.
Methods: Multicenter chart review of CHC patients diagnosed from 2005 to 2012. Patient data were ex-tracted for a minimum of 2 years after CHC diagnosis.
Results: 250 patients were included with a mean (SD) follow-up after diagnosis of 5.9 (2.3) years. Table1 summarizes the patient/disease characteristics at CHC diagnosis and the mode of management. A majority of patients (70.4%) received some antiviral treatment, with a lower proportion of treated G1 patients vs. non-G1 patients (64% vs. 76.7%). The most common initial treatments were IFN/RBV dual therapy (68.4%)

and NS3/4-containing IFN/RBV therapy (19.3%); Among non-G1 patients, 92.4% were treated with IFN/RBV dual therapy. SVR was achieved by 51.5% of patients (G1: 44.7%; non-G1: 62.2%), 19.3% relapsed and 11.1% were non-responders with initial treatment. The majority of treated patients (72.2%) experienced AEs, the most common ones being fatigue (33%), anemia (27.3%), insomnia (21.6%), neutropenia (18.8%). Two deaths were reported.

Conclusions: Despite the majority of HCV patients having mild fibrosis and being treated, most frequently with dual IFN/RBV therapy, SVR rates were low prior to the all-oral DAA era, highlighting the need for more efficacious treatments and suggesting that recommendations to still use IFN are not justifiable.

Patient/Disease Characteristics at HCV Diagnosis

Age, years, mean (SD)	46.5 (12.1)
Male gender, %	68
Risk factors*, %	
History of IV drug use	50
Blood transfusion	13.6
Tattoo	11.2
Comorbidities, %*	
Liver disease	21.2
Anemia	7.6
Neutropenia	4.8
HCV Genotype, %	
1	65.6
2	6
3	22.8
4	4.8
5	0.8
Fibrosis, %	
F0/F1	50.3
F2	22.7
F3/F4	27
Untreated, %	29.6
Initial treatment era, %‡	
2006-11	39.8
2012-13	44.3
2014-15	15.9
Initial treatment, %‡	
IFN/RBV	68.4
NS3/4 + IFN/RBV	19.3
NS5A and/or NS5B inhibitors w/o IFN	5.9
NS5A and/or NS5B inhibitors + IFN	1.2
NS3/4-NS5 w/o IFN	4.7
NS3/4-NS5 + IFN	0.6

*Most common
‡% of treated patients

A189
TREATMENT OF CHORNIC HEPATITIS C GENOTYPE 1 IN CANADA: REAL WORLD EXPERIENCE WITH OMBITASVIR/PARITAPREVIR/R AND DASABUVIR WITH OR WITHOUT RIBAVIRIN

S. Lee[3], C. Pinsonnault[1], N. Ackad[2], P. Landry[1]

1. Medical, Abbvie Corporation, Saint-Laurent, QC, Canada; 2. Medical Affairs, Abbvie Corporation, Montreal, QC, Canada; 3. University of Calgary, Calgary, AB, Canada

Background: The 3-direct-acting antiviral regimen of ombitasvir/paritaprevir/ritonavir + dasabuvir (3D) +/- ribavirin (RBV) has been shown to be safe and effective for the treatment of chronic hepatitis C (CHC) in randomized controlled trials. However, data on real world treatment experience is limited. In Canada, the 3D regimen is approved to treat patients with CHC genotype (GT) 1 including compensated cirrhosis.

Aims: The aim of this non-interventional study is to provide evidence of the effectiveness of the 3D regimen in a real world setting across broader clinical practice patient populations.

Methods: The Canadian AMBER study is an ongoing, prospective, multi-center, observational cohort study aiming at enrolling 600 treatment-naïve and -experienced GT1 patients with and without compensated cirrhosis. The treatment course was at the discretion of the treating physician, according to the standard of care of the institution. All patients who started therapy from October 2015 up to March 31st, 2016 and for whom a treatment duration of 12 weeks was intended were included in this interim analysis. Effectiveness was defined as having achieved sustained virological response 12 weeks post-treatment (SVR12).

Results: The inclusion criteria for this analysis were met by 115 patients. <u>Demographics:</u> 70% male, mean age 55 (SD 10.7), 81% Caucasian, 7% Asian. <u>Disease characteristics:</u> Mode of HCV infection was i.v. drug use in 41%, blood transfusion in 17%, contaminated medical device in 6% and unknown in 28% of patients; GT1a 54%, GT1b 43%, GT1 subtype unknown 3%; 12% had failed previous therapy; 23% had cirrhosis, 8% transition to cirrhosis, Child Pugh B was present in 2 patients. <u>Treatment:</u> 74 (64%) patients had RBV added to their 12 week 3D regimen (96% of GT1a), 41 (36%) patients did not receive RBV (78% of GT1b). See table for <u>co-morbidities</u>.

Conclusions: The data from this study may aid in better describing the medical profile of patients seeking care for CHC in real world. In contrast to development trials a broader population including patients with psychoactive substance dependency was enrolled. The effectiveness of new interferon-free regimens in such subpopulations is of particular interest. SVR12 data will be detailed in the poster.

Patients (total n=115) with co-morbidities (n/%)

Patients with ≥1 co-morbidity	90/78
HIV co-infection	7/6
HBV co-infection	2/2
Cardiovascular	25/22
Diabetes	13/11
Renal impairment	7/6
Creatinine Clearance <30 mL/min	4/4
Dialysis	2/2

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Psychiatric disease	21/18
Depression	18/16
Psychoactive substance dependency	36/31
Active injection drug users	6/5
Inhaled cocaine	5/4
Marihuana/cannabis	11/10
Opiate substitution therapy	27/24

A190
REGRESSION OF LIVER FIBROSIS AFTER SUCCESSFUL ALL ORAL ANTIVIRAL THERAPY IN HCV CIRRHOSIS: A PILOT STUDY EMPLOYING TRANSIENT ELASTOGRA-PHY AND CONTROLLED ATTENUATION PARAMETER (CAP)

J. Rayes[1], G. Sebastiani[2]

1. Internal medicine, McGill University, Saint-laurent, QC, Canada; 2. Royal Victoria Hospital, McGill University Health Center, Montreal, QC, Canada

Background: Studies on the regression of liver fibrosis after SVR are limited. Until the advent of accurate non-invasive tests for fibrosis, paired biopsy studies were limited by patient compliance and small sampling biases. Early studies comparing non-oral regimens using mostly paired liver biopsies showed a 62% regression in liver fibrosis after achieving SVR. Only four studies at the time of this publication have used the non-invasive FibroScan to measure fibrosis regression. A meta-analysis of these 4 studies predicts an 82% regression in fibrosis. Most recently a well-designed prospective study by the ANRS CO13 HEPAVIH study group looked at fibrosis regression using the FibroScan in patients co-infected with HIV and HCV who achieved SVR via oral or non-oral antiviral agents. This study showed at least 30% fibrosis regression in 74% of all patients at 2 years.

The landscape of HCV management continues to rapidly evolve with the combined advent of new all oral antivirals and new noninvasive measurements of liver fibrosis with the FibroScan. In this context no study to date has directly looked at fibrosis regression using FibroScan in HCV patients receiving an all oral antiviral regiment.

Aims: Primary objective: To elucidate the dynamics of liver fibrosis regression in patients who achieve SVR with an oral only antiviral regiment.

Secondary objective: To identify negative predictors for fibrosis regression including HIV status, IV drug use, hepatic steatosis, cirrhosis and history of hepatic decompensation.

Methods: The Chronic Viral Illness Service (CVIS) is a university-based clinic which has served over 3000 HCV-infected patients in 24 months. The CVIS is part of the McGill University Health Centre (MUHC) network located in Montreal, Quebec. A computerized database has been prospectively maintained to include all patients who have undergone HCV treatment. This data-

base will be combined with information obtained from the MUHC electronic medical records (Oacis system) to provide the researchers with the required data.

Results: Percentage reduction in fibrosis with 95% confidence intervals (all patients): 20.04 +/- 9.68 %.

Conclusions: There is a statistically significant reduction in liver fibrosis after treatment with DAAs. The study included only 18 patients; however, it still managed to achieve statistical significance. An extended database is under analysis to add more patients to the study and achieve better results.

98%
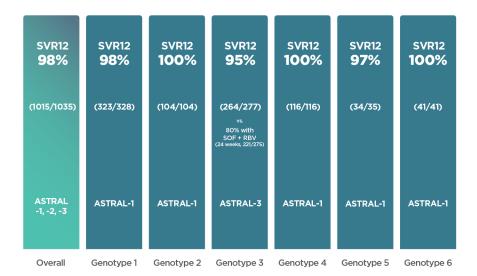
OVERALL SVR12 (VIROLOGIC CURE)'
DEMONSTRATED ACROSS THREE TRIALS (ASTRAL-1,-2 AND-3) AND ACROSS ALL STUDIED GENOTYPES# IN PATIENTS WITHOUT CIRRHOSIS AND WITH COMPENSATED CIRRHOSIS (1015/1035)'**

Overall	Genotype 1	Genotype 2	Genotype 3	Genotype 4	Genotype 5	Genotype 6
SVR12 **98%**	SVR12 **98%**	SVR12 **100%**	SVR12 **95%**	SVR12 **100%**	SVR12 **97%**	SVR12 **100%**
(1015/1035)	(323/328)	(104/104)	(264/277) vs. 80% with SOF + RBV (24 weeks, 221/275)	(116/116)	(34/35)	(41/41)
ASTRAL -1, -2, -3	ASTRAL-1	ASTRAL-1	ASTRAL-3	ASTRAL-1	ASTRAL-1	ASTRAL-1

SVR12* RATES IN PATIENTS TREATED WITH EPCLUSA (12 WEEKS) IN ASTRAL-1 (GENOTYPES 1, 2, 4, 5, 6) AND ASTRAL-3 (GENOTYPE 3)[1]

Adapted from EPCLUSA Product Monograph[1] GT=genotype; SOF=sofosbuvir; RBV=ribavirin

EPCLUSA (sofosbuvir/velpatasvir) is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults without cirrhosis or with compensated cirrhosis. EPCLUSA is also indicated in combination with ribavirin for the treatment of chronic HCV infection in adults with decompensated cirrhosis.

Refer to the page in the bottom-right icon for additional safety information and for a web link to the product monograph discussing:

• Contraindications in patients taking EPLUCSA in combination with ribavirin – the contraindications to ribavirin are applicable to the combination

• Relevant warnings and precautions regarding use with ribavirin, use in patients with decompensated cirrhosis who are infected with HCV genotype 2 or genotype 4, concurrent use with other medicinal products containing sofosbuvir, use with potent P-glycoprotein (P-gp) inducers and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4, coadministration with amiodarone (not recommended due to risk of serious symptomatic bradycardia), use in patients with severe hepatic impairment (Child-Pugh Class C), use in patients with severe renal impairment (eGFR < 30 mL/min/1.73m²) or end stage renal disease requiring hemodialysis, use in patients who have previously failed treatment with other regimens that include an NS5A inhibitor, use in pregnancy and breastfeeding, coadministration with ribavirin during pregnancy, use in patients with recurrent HCV infection after liver transplant, use in HCV patients co-infected with hepatitis B virus (HBV) or human immunodeficiency virus (HIV), concomitant use with tenofovir DF, particularly in those at increased risk for renal dysfunction, co-administration with an efavirenz-containing regimen, and monitoring of liver function including direct bilirubin is recommended in patients with decompensated cirrhosis

• Conditions of clinical use, adverse reactions, drug interaction and dosing information

In addition, the page contains the study parameters and reference list relating to this advertisement.

¶ SVR12=sustained virologic response, defined as HCV RNA <LLOQ at 12 weeks after the end of treatment. # Genotypes 1-6

POSTER SESSION 2
SUNDAY MARCH 5, 18H00-19H30

CHRONIC LIVER DISEASE INCLUDING ALCOHOLIC, CHOLESTATIC, AND METABOLIC DISEASE

Poster of Distinction

A191
NEXT GENERATION SEQUENCING IN THE INVESTIGATION OF HYPERFERRITINEMIA
P. Adams, A. Levstik, B. Sadikovic
Western University, London, ON, Canada

Background:
Hyperferritinemia is common and often suggests the diagnosis of iron overload. However, many times it is elevated secondary to inflammation, obesity, alcohol use, or unknown causes. Most Caucasian patients with iron overload are homozygotes for the C282Y mutation of the *HFE* gene. There are a growing number of iron related genes that may contribute to an elevated ferritin and iron overload.
Aims:
To design a next generation sequencing platform to assess for genetic mutations in 15 iron genes as a diagnostic tool in the investigation of hyperferritinema.
Methods:
Libraries were sequenced using the MiSeq v2 reagent kit to generate 2 x 150 bp paired-end reads using the MiSeq fastq generation mode (Illumina, San Diego, CA), with 24 different patient samples multiplexed per run. Sequence analysis for variant identification, alignment and coverage distribution was performed with NextGene software v2.4.1 (SoftGenetics, LLC, State College, PA) using standard alignment settings (allowable mismatch bases: 1; allowable ambiguous alignments: 50; seeds bases: 30; move step bases: 5; allowable alignments: 100; matching base percentage > 85%). BAM and VCF files were imported into Geneticist Assistant v1.1.5 (SoftGenetics, LLC; State College, PA) for quality control assessment (minimum base coverage; mean exon coverage). The methodology also will assess copy number variation and does not require MLPA confirmation. Genes analyzed included HFE, HJV, HAMP,TfR2,FTL,CP,SLC40A1. Patients were selected from the referral practice at a tertiary care hospital with elevations in serum ferritin > 1000 ug/L who were not typical C282Y homozygotes.
Results:
There were 120 patients selected for analysis. There were 6 patients homozygous for HJV mutations (G320V in 2 unrelated, and Leu366Ter in 4 related). There were 3 FTL mutations detected in patients with cataracts and heterozygous mutations found in HAMP, CP, TfR2, and TF genes.
Conclusions: Next generation sequencing provides a

platform to rapidly test for *HFE* and many other mutations in selected cases. Funding has been requested to provide this analysis for selected Ontario cases similar to funded genetic panels for other rare genetic diseases.

Poster of Distinction

A192
PRIMARY SCLEROSING CHOLANGITIS WITH CHOLELITHIASIS IS A DISTINCT PHENOTYPE WITH WORSE SYMPTOMS, DECOMPENSATION-FREE & TRANSPLANT-FREE SURVIVAL
R. Almeida[2], A. Arif[1], A. Cheung[1]
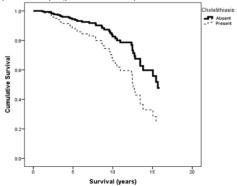
1. University of Toronto , Toronto, ON, Canada; 2. Gastroenterology, University of Toronto, Toronto, ON, Canada

Background: Primary sclerosing cholangitis (PSC) is a chronic cholestatic disease characterized by inflammation and fibrosis of the intrahepatic and/or extrahepatic biliary tree which can lead to cirrhosis and transplant after a median of 18 years. Approximately 26%-38% of patients with PSC may have cholelithiasis but classically, the presence of cholelithiasis favors a diagnosis of secondary rather than PSC.There is scant and conflicting data on the effect of biliary calculi on the clinical presentation and outcomes in PSC.
Aims: To determine if PSC patients with and without cholelithiasis are distinct entities characterized by differences in epidemiology, presentation, biochemistry, and differences in outcomes (ie. cirrhosis, decompensation, death or transplant).
Methods: A retrospective cohort study included patients with large-duct PSC from January 1990 to February 2016 at the Toronto Center for Liver Disease, Canada. Cholelithiasis & disease distribution were determined with baseline & follow-up imaging. Differences in continuous and categorical variables were evaluated with Students t-test and chi-square test, respectively. Cox regression was used to determine predictors of poor composite outcome (decompensation, liver-related death or transplant).
Results: 169/198 charts were included (126 no cholelithiasis [NCL]; 43 cholelithiasis [CL]). Less women had CL (p=.03); there were no other differences in baseline parameters (ie. disease distribution (p=.76), IgG4 level (p=.27), inflammatory bowel disease (IBD) (p=.76), type of IBD (p=.49). By the end, the CL group was more likely to be cirrhotic (65% vs 43%, p=.02), with intermediate/high Mayo Risk Scores (64% vs 36%, p=.04) & worse symptoms (jaundice, fatigue, pruritus, cholangitis), & worse outcome (p=.007), but similar rates of hepatobiliary cancer. The presence of cholelithiasis was an independent predictor of the composite outcome of decompensation, liver-related death or transplant when adjusting for a) age, cirrhosis, & ALP

CHRONIC LIVER DISEASE

(HR 2.45, 95%CI 1.17-5.13, p=.02) and b) sex, ethnicity & ursodeoxycholic acid (UDCA) use (similar HRs).
Conclusions: The presence of cholethiasis may partly explain the variability in the natural history of PSC across different studies. Modification of bile lithogenicity with therapies such as UDCA may alter symptom profile and prognosis in certain patients with PSC.

Funding Agencies: None

Poster of Distinction

A193
COGNITIVE DYSFUNCTION IS PRESENT IN HALF OF STABLE OUTPATIENTS WITH CIRRHOSIS AND IS STRONGLY ASSOCIATED WITH THE POTENTIALLY MODIFICABLE FACTORS, DEPRESSION AND LOW MUSCLE STRENGTH

M. Ney[4], P. Bhardwaj[2], B. Dobbs[2], F. Safari[2], S. Kalainy[2], M. Ma[2], R. Bailey[1], J. Abraldes[3], D. Rolfson[2], P. Tandon[2]

1. Royal Alexandra Hospital, Edmonton, AB, Canada; 2. University of Alberta, Edmonton, AB, Canada; 3. Liver Unit, University of Alberta, Edmonton, AB, Canada; 4. University of Calgary, Calgary, AB, Canada

Background: Impaired cognitive function is a key prognostic factor in patients with cirrhosis. This is often, but not always, attributable to hepatic encephalopathy (HE). The Montreal Cognitive assessment (MOCA) is a sensitive measure of mild cognitive impairment, yet has been sparingly reported in the literature in cirrhotic populations.
Aims: In a cohort of stable cirrhosis outpatients without overt HE, we aimed to: i) characterize baseline MOCA scores, ii) determine the domains of MOCA that are most commonly affected and iii) determine the predictors of a low MOCA score (<26).
Methods: Consecutive adults with cirrhosis assessed prospectively in one of two Edmonton cirrhosis clinics between May 2013 and June 2016 were screened for enrolment. Exclusion criteria included active malignancy, dementia, HCC outside of Alberta liver transplant criteria, end-stage renal disease and overt HE (as defined by lack of orientation (person, place, time) or asterixis). Multivariable logistic regression analysis was used to determine independent predictors of a MOCA <26.
Results: Fifty-three patients were excluded because they were disoriented to person, place or time. Of 390 included patients, the mean age was 55.6 ± 9.8, 62% were male and the etiology of cirrhosis was alcohol or hepatitis C in 54%. Thirty-two percent scored positive for depression. Forty-one percent had an abnormal handgrip as defined by BMI and sex cut-offs. The mean MOCA score was 25.2 ± 3.2 and 45% had a score of <26. Abnormalities were most commonly seen in the following MOCA subdomains – delayed recall (81%), visuospatial/executive (70%), attention (48%) and language (46%) and least commonly seen in abstraction (19%) and naming (7%). Depression was the only independent predictor of a MOCA <26, with increasing age trending to significance (Table 1).
Conclusions: In a large cohort of stable cirrhosis outpatients, 45% of them have MOCA scores below the accepted lower limits of normal. Depression and low muscle strength are associated with lower cognitive function scores. These potentially modifiable variable needs to be screened for and treated to determine if they may positively impact cognitive function. Ongoing work will associate MOCA total scores and subdomains with clinical outcomes including unplanned hospitalization, death and HE related hospitalizations.

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CAN NOVEL SEROLOGICAL MARKERS BE USED TO BETTER DEFINE PRIMARY BILIARY CHOLANGITIS (PBC)-AUTOIMMUNE HEPATITIS (AIH) OVERLAP SYNDROME

H.H. Nguyen[3], A.M. Shaheen[2], S. Urbanski[2], M.J. Fritzler[2], A.L. Mason[4], M. Swain[1]
1. Univ Calgary, Calgary, AB, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. Gastroenterology and Hepatology , University of Calgary, Calgary, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada

Background: It is estimated that up to 18% of patients with Primary Biliary Cholangitis (PBC) can be classified as having overlap features with Autoimmune Hepatitis (AIH). Patients with PBC-AIH overlap syndrome (OS) have been reported to exhibit suboptimal responses to Ursodeoxycholic acid therapy, and are more likely to progress to cirrhosis and its' complications. Serological markers, including anti-double stranded DNA (anti-dsDNA) and anti-P53, have been suggested to be robust markers for identifying patients with PBC-AIH OS. The identification of serological markers that can be confidently used to identify patients with PBC-AIH OS would be useful for the clinical management of PBC-AIH OS.
Aims: In our well defined PBC patient cohorts, various serological markers were evaluated for their potential utility for identifying PBC-AIH OS patients.

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

Methods: Blood samples from 214 patients from University of Calgary Liver Unit and University of Alberta biobanks were analyzed by Mitogen Diagnostic Laboratory (Calgary, AB Canada) for various classical and novel autoantibodies. Anti-dsDNA was measured by either the Crithidia luciliae immunofluorescence (CLIFT) assay (1:20 dilution) or a chemiluminescent immunoassay (CIA; Inova Diagnostics, SanDiego). Anti-P53, anti-Ro52/TRIM21, anti-YB 1, anti-MPP1, anti-GW182, anti-Ge-1, and anti-Ago 2 were measured by either an Addressable Laser Bead Immunoassay (ALBIA) or Line Immunoassay (LIA). Frequency of autoantibodies were compared between study groups using non-parametric statistical methods. The performance of patient serum biochemistry and autoantibody profiles to predict OS was determined using multivariate analysis. PBC-AIH OS was diagnosed according to the Paris criteria (Chazouilleres *et al*) and PBC was diagnosed as per European Association for the Study of the Liver guidelines.
Results: Of the 214 patients assessed, 16 (7.5%) had a diagnosis of OS. Compared to PBC patients, OS patients had similar age (median: 59 vs. 63, P=0.21) and female predominance (94% vs. 89%, P=1.00). Anti-dsDNA measured by CLIFT (37.5% in OS vs. 9.1% in PBC, P=<0.01), elevated serum ALT (62 IU/L in OS vs. 35 IU/L in PBC, P<0.01), and an elevated serum IgG (17.6 g/L in OS vs. 12.1 g/L in PBC, P<0.01) were associated with OS. In a multivariate model, Anti-dsDNA-by CLIFT, ALT and IgG were significant predictors of OS with area under the receiver operator curve (AUROC) value of 0.84.
Conclusions: The combination of presence of anti-dsD-NA, elevated serum ALT, and elevated serum IgG can be used to identify patients with PBC-AIH OS. Contrary to previous reports, anti-P53 was not associated with OS. In addition, other autoantibodies including anti-dsDNA (measured via CIA), anti-Ro52/TRIM21, anti-YB 1, anti-MPP1, anti-GW182, anti-Ge-1, and anti-Ago 2 were not associated with OS.

A195
GLUTAMINE SYNTHETASE IN ENDOTHELIAL CELLS OF THE BLOOD-BRAIN BARRIER: NEW TARGET FOR THE TREATMENT OF HEPATIC ENCEPHALOPATHY?
M.M. Oliveira, M. Tremblay, C.F. Rose

CRCHUM, Université de Montréal, Montreal, QC, Canada

Background: The liver plays a major role in regulating ammonia levels in the blood. Therefore, in liver disease the loss of hepatic function leads to hyperammonemia and increased brain ammonia and consequently hepatic encephalopathy (HE). Ammonia-lowering strategies remain the mainstay therapeutic strategy. Ammonia, both as an ion (NH^{4+}) and gas (NH_3), easily crosses all plasma membranes, including the blood brain barrier (BBB); the interface between the blood and the brain. Glutamine synthetase (GS), an enzyme which in the process of amidating glutamate to glutamine removes ammonia, plays an important compensatory role during liver disease. GS is expressed in muscle and brain (primarily in astrocytes) but has never been thoroughly explored in the BBB.
Aims: Therefore, the aim is to evaluate GS expression in endothelial cells of the BBB.
Methods: Using primary rat brain microvascular endothelial cells (ECs), the presence of GS was assessed using rtPCR, western blot, immunohistochemistry and activity assay. Furthermore, we isolated cerebral microvessels (CMV) from the frontal cortex of naïve rats and measured GS expression by western blot using brain lysates as positive control and by immunohistochemistry (co-localized with caveolin-1, a marker for ECs). In addition, to understand the effect of ammonia on GS, ECs were exposed to 1mM of ammonia chloride for 48h. Finally, ECs were subjected to plasma from bile-duct ligated (BDL) rats (model of chronic liver disease) or sham-operated controls. We have characterized this BDL model and found both systemic oxidative stress and inflammation, in addition to hyperammonemia.
Results: ECs expressed GS mRNA, protein and activity. However, expression of GS was lower compared to brain lysate control samples (p<0.05). GS expression in CMV showed similar results to brain but GS activity was less (p<0.05). Using immunohistochemistry, GS was detected in ECs and in vessels of brain from naïve rats. When cells were submitted to ammonia, an increase in GS activity was demonstrated (p<0.05). However, when exposed to conditioned medium from BDL rats, GS was decreased when compared to sham-operated controls (p<0.01).
Conclusions: These results demonstrate for the first time that GS is present in ECs in both *in vivo* and *in vitro*. The lower expression of the enzyme compared to that found in the brain, could explain why GS has never been reported in these cells. Interestingly, ammonia stimulates GS in ECs, but its activity is decreased in the presence of other pathogenic factors in plasma from cirrhotic rats such as oxidative stress and inflammation. We speculate that a downregulation of GS allows for a faster and easier entry of ammonia into the brain and therefore may be implicated in the pathogenesis of HE. We anticipate increasing GS in ECs of the BBB could become a new therapeutic target for HE.

A196
IDENTIFICATION OF AN IMMUNOSUPPRESSIVE DOMAIN IN HUMAN BETARETROVIRUS
M. Rahbari[1], D. Sharon[2], M. Houghton[2], A. Mason[1]

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

CHRONIC LIVER DISEASE
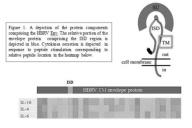
Background: Primary biliary cholangitis (PBC) is a slowly progressing autoimmune liver disease characterized by immune destruction of the interlobular bile ducts. While the etiology of PBC is unknown, it is thought to involve an environmental trigger in a genetically susceptible individual. Among environmental factors studied to date, only the human betaretrovirus (HBRV) has been reproducibly detected in PBC patients' biliary epithelium. Recent studies have shown that the majority of PBC patients as well as proportion of patients with AIH and cryptogenic cirrhosis have evidence of HBRV RNA and proviral integrations in their biliary epithelium

Aims: Previous studies suggest that PBC patiens make proinflammatory responses to HBRV proteins. Using overlapping peptides of the HBRV Gag and Env, we have found that 38% of PBC patients had memory CD8^{+} T-cell responses to HBRV Gag with intracellular IFN-γ and TNF-α production. Whereas only 7% of patients demonstrated proinflammtory responses by T-cells to HBRV Env stimulation in identical experiments. The finding of significant diminished proinflammatory T-cell response to HBRV Env versus HBRV Gag in PBC patients and our prior experience of finding diminished humoral responses to HBRV Env suggested a hypothesis that the HBRV Env may contain an immunosuppressive domain (ISD), a highly conserved sequence in transmembrane (TM) protein of retroviruses (such as HIV-1, MuLV and HERV-K) that induces immunoregulatory effect on the immune system

Methods: In order to determine whether HBRV Env contains an ISD, we used 85 overlapping 18-mer individual HBRV peptides corresponding to SU and TM proteins to stimulate healthy PBMC. We examined whether individual peptides induced IL-10, IL-4, and IL-6 secretion. PBMCs (3×10^5 cells/well) from a healthy donor were incubated with individual HBRV SU and TM peptides for 24 hrs prior to collection of the supernatants. IL-10, IL-4, and IL-6 levels were then measured by Mesoscale analysis

Results: We identified a single peptide homologous to other retroviral ISDs located in HBRV TM protein that lead to IL-10, IL-4, and IL-6 production. In order to validate the identification of the HBRV ISD we repeated the experiment using HBRV ISD sequences with a single AA difference. The mutations were selected based on the homology of the potential HBRV ISD with known conserved ISDs in other retroviruses. Accordingly, we were able to identify the functionally important AAs in the ISD within the HBRV TM that triggered IL-10, IL-4, and IL-6 production by selectively altering the AAs in the HBRV ISD sequence

Conclusions: These studies are important because they show how HBRV potentially avoids the immune attack to HBRV Env and tolerizes the host to viral infection. Further studies will be required to determine its other functional properties as well as the implications of this finding surrounding the pathophysiology underlying PBC

Figure 1. A depiction of the protein components comprising the HBRV Env. The relative portion of the envelope protein comprising the ISD region is depicted in blue. Cytokines secretion is depicted in response to peptide stimulation corresponding to relative peptide location in the heatmap below.

A197
PREVALENCE OF PRIMARY BILIARY CHOLANGITIS IN CANADA: FIRST NATIONAL STUDY

E.M. Yoshida[1], A. Fischer[2], A. Mason[3], H. Shah[4], K.M. Peltekian[5], M. Hux[2], S.L. Thiele[2], R. Borrelli[2]

1. Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada; 2. QuintilesIMS, Toronto, ON, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. University of Toronto, Toronto, ON, Canada; 5. Dalhousie University, Halifax, NS, Canada

Background: Primary biliary cholangitis (PBC) is a rare, progressive autoimmune liver disease that can result in significant morbidity, need for liver transplant, and premature mortality. Prevalence of PBC has been found to vary by geography and to be increasing over time. The only recent Canadian estimate is for Alberta where prevalence in 2001 was reported to be 227 cases per million.

Aims: Based on gaps in the existing PBC literature, we undertook this study to provide the first national and regional prevalence estimate of PBC in Canada.

Methods: The 2015 prevalence of PBC in Canada was estimated using longitudinal patient-level records of the Discharge Abstract Database and National Ambulatory Care Reporting System from the Canadian Institute for Health Information. Cases were identified using a PBC diagnosis (International Classification of Diseases Version 10 - Canadian Edition K74.3) between 2007 – 2015 at any hospital visit (acute care admission, same-day surgery, emergency department or hospital-based specialty clinic). Cases deceased prior to 2015 were excluded. Quebec records were not available for study. Although all Canadian hospitals report acute care admissions, as the proportions reporting other hospital-based services differ by province, crude case counts were projected to complete coverage. Prevalence estimates were age and gender adjusted to the 2015 Canadian population. The 2013 prevalence was estimated using the same methodology. Persons with late stage PBC were identified using late stage-related diagnoses.

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Results: The Canadian 2015 annual prevalence of PBC managed in a specialty clinic or visiting hospital was 318 (95%CI 309-327) cases per million. By region, prevalence per million estimates were: British Columbia 327 (95%CI 302-352); Alberta 292 (95%CI 275- 309); Prairie provinces 399 (95%CI 360-438); Ontario 283 (95%CI 269-297); and the highest prevalence of 465 (95%CI: 426, 504) was seen in Maritime provinces. PBC cases were predominantly female (78%), and the majority were aged 40 to 64 (54%), or over 65 years of age (39%). The 2013 prevalence of PBC was estimated to be 256 (95%CI: 248, 264) cases per million. PBC was classified as advanced stage for 29% (95%CI: 26%, 32%) of patients.
Conclusions: This study reports the first national prevalence for Canada and geographic regions, and provides an important basis for understanding the magnitude of disease in Canada. From 2013 to 2015, the prevalence of PBC remains increasing. Atlantic Canada appears to have the highest burden of PBC in the country.

A198
PHARMACODYNAMIC EFFECTS OF THE ORAL, NON-STEROIDAL FARNESOID X RECEPTOR AGONIST GS-9674 IN HEALTHY VOLUNTEERS
R.P. Myers[2], C. Djedjos[2], B. Kirby[3], A. Bilin[2], M. Khan[1], J. Gosink[2], Q. Song[2], R. Srihari[2]

1. Gilead Sciences Canada, Inc, Mississauga, ON, Canada; 2. GIlead Sciences, Inc., Foster City, CA; 3. GIlead Sciences, Inc., Foster City, CA

Background: GS-9674 is a non-steroidal Farnesoid X Receptor (FXR) agonist in development for the treatment of nonalcoholic steatohepatitis (NASH) and cholestatic liver disorders. Oral GS-9674 increased plasma fibroblast growth factor 19 (FGF19), decreased 7-α-hydroxy-4-cholesten-3-one (C4), and improved liver histology in rodent and primate models of NASH.
Aims: This first-in-human study evaluated the safety, pharmacokinetics (PK), and pharmacodynamic (PD) effects of GS-9674 in healthy volunteers. Data on PD markers (FGF19 and C4), PK/PD and PD/PD relationships, and the effects of GS-9674 on serum cholesterol are presented herein.
Methods: In this randomized, double-blind, placebo-controlled study, subjects received single and multiple doses (QD, 14 days) of GS-9674 (10, 30, 100, or 300 mg while fasting [N=12/cohort]) or matching placebo (N=3/cohort) with a 6-day washout between the single and multiple dose periods. Plasma FGF19 (by ELISA) and serum C4 (by LC-MS/MS) were measured over 24 hours pre-dose (Day -1) and after single (Day 1) and multiple dose administration (Day 20). PD parameters for FGF19 and C4 (AUC_{2-8hr} and C_{max} or C_{min}) were calculated and normalized to Day -1 values. Changes in serum cholesterol were also assessed.
Results: PD responses to GS-9674 observed on Day 1

and Day 20 were comparable. GS-9674 doses $\geq$30 mg significantly increased FGF19 and reduced C4 exposure compared to placebo (Table). Changes in FGF19 and C4 AUC_{2-8hr} were inversely correlated (r= -0.335 p =0.02). While FGF19 exposure did not show dose-dependent changes, changes in C4 AUC_{2-8hr} were inversely associated with GS-9674 AUCtau (r= -0.45 p <0.01). Effects of GS-9674 on serum cholesterol at Day 20 were mild and not significantly different from placebo.
Conclusions: Oral GS-9674 administration results in increased levels of FGF19 and decreased C4 confirming its biological activity. These data support the evaluation of GS-9674 in patients with NASH and cholestatic liver disorders.

A199
SCREENING FOR NONALCOHOLIC FATTY LIVER DISEASE BY TRANSIENT ELASTOGRAPHY WITH CONTROLLED ATTENUATION PARAMETER IN UNSELECTED PATIENTS WITH INFLAMMATORY BOWEL DISEASE
C. Saroli Palumbo[2], S. Restellini[1], C. Chao[1], A. Aruljothy[1], G. Sebastiani[4], T. Bessissow[3]

1. McGill University, Montreal, QC, Canada; 2. Gastroenterology, McGill University, Montreal, QC, Canada; 3. Gastroenterology, McGill University Health Center, Montreal, QC, Canada; 4. Royal Victoria Hospital, McGill University Health Center, Montreal, QC, Canada

Background: Nonalcoholic fatty liver disease (NAFLD) is the most frequent liver disease in North America. Patients with inflammatory bowel disease (IBD) are at risk for NAFLD due to chronic inflammation, hepatotoxic drugs, and alteration of gut microbiota. However, prospective data in unselected patients by means of validated and accurate diagnostic methods are lacking.
Aims: We prospectively investigated prevalence and predictors of NAFLD and liver fibrosis by transient elastography (TE) with associated controlled attenuation parameter (CAP) in unselected IBD patients free of liver disease as part of a routine screening program.
Methods: Any grade (involving >10% of hepatocytes), moderate (>30%) and severe (>60%) steatosis were defined as CAP $\geq$238, CAP $\geq$260 and CAP $\geq$292 dB/m, respectively. Significant liver fibrosis and cirrhosis (stage 2 and 4 out of 4, respectively) were defined as TE measurement $\geq$8 and $\geq$13 kPa. Active IBD was defined as partial Mayo score ≥3 and Harvey Bradshaw Index ≥5 for ulcerative colitis and Crohn's disease, respectively. Predictors of any grade NAFLD and significant liver fibrosis were determined by logistic regression analysis.
Results: 317 patients (mean age 42.9, 48.8% male) were included; 65.9% had Crohn's disease, and 28% had active disease at time of recruitment. Prevalence of any grade, moderate and severe steatosis was as follows: 39.7%, 32.6% and 19.8%, respectively. The prevalence of significant liver fibrosis and cirrhosis

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was 9.5% and 1.9%, respectively. Main predictors of NAFLD were older age, being overweight (BMI >25) and methotrexate use (Table1). The main predictors of significant liver fibrosis were prior IBD-related surgery, being overweight, dyslipidemic and on methotrexate. **Conclusions:** NAFLD diagnosed by TE with CAP is a major comorbidity in unselected IBD patients without known liver disease. These patients may also have significant liver fibrosis and cirrhosis, likely suggesting the coexistence of non-alcoholic steatohepatitis. Non-invasive screening strategies can help early diagnosis and initiation of interventions in this population, including weight loss, treatment of dyslipidemia and potentially drug regimen modification.

Table 1. Multivariate analysis of predictors of NAFLD and fibrosis

Variable	NAFLD		Significant liver fibrosis	
	aOR (95%CI)	P value	aOR (95%CI)	P value
Age	1.03 (1.01-1.06)	<0.001	1.00 (0.97-1.04)	0.84
BMI >25kg/m2	4.10 (2.28-7.37)	<0.001	3.44 (1.23-9.61)	0.02
Dyslipidemia	2.43 (0.67-8.73)	0.18	5.73 (1.47-22.3)	0.01
Disease duration	1.02 (0.99-1.05)	0.18	1.02 (0.97-1.07)	0.54
Prior IBD-related surgery	0.76 (0.37-1.56)	0.46	3.10 (1.06-9.06)	0.04
Methotrexate use	18.04 (1.75-185.99)	0.02	9.18 (1.68-50.05)	0.01
ALT	1.02 (0.99-1.04)	0.08	1.02 (0.99-1.05)	0.14

A200
AN INTEGRATED ANALYSIS OF EFFICACY OF OBETI-CHOLIC ACID IN CANADIAN PATIENTS
A. Mason[1], C. Vincent[2], A. Aspinall[3], M. Swain[3], G.M. Hirschfield[4], G. Minuk[5], H. Shah[6], J. Owens-Grillo[7], E. Smoot Malecha[7], L. MacConell[7]

1. University of Alberta, Edmonton, AB, Canada; 2. Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada; 3. University of Calgary, Calgary, AB, Canada; 4. University of Birmingham, Birmingham, United Kingdom; 5. University of Manitoba, Canada, Winnipeg, MB, Canada; 6. University of Toronto, Toronto, ON, Canada; 7. Intercept Pharmaceuticals, San Diego, CA

Background: Obeticholic acid (OCA) is a potent FXR agonist investigated for the treatment of primary biliary cholangitis (PBC) in 3 randomized, double-blind (DB), placebo (PBO)-controlled trials ± UDCA.
Aims: This analysis pools data from all 3 trials to investigate the efficacy and safety of OCA in patients treated in Canada.
Methods: Key Entry Criteria: ALP 1.5 to 10x ULN and conjugated bilirubin ≤2x ULN (Phase 2 trials, DB phase=3 months); ALP ≥1.67x ULN or total bilirubin >ULN but <2x ULN (Phase 3 trial, DB phase=12 months). Data were pooled and assessed at the end of DB treatment (EOT) for each trial. Patients receiving 5 or 10 mg OCA were pooled into a single group: ≤10 mg OCA.
Results: Baseline (BL) biochemistry values were elevated in the ≤10 mg OCA group compared to the PBO group (Table 1). In patients receiving concomitant UDCA, there were significant reductions in ALP, ALT, and GGT at EOT compared to PBO. Total bilirubin and AST were reduced but not significant. Efficacy was similar in patients receiving OCA monotherapy. Pruritus was the most common adverse event, which occurred in 32% of PBO patients and 61% of patients receiving ≤10 mg OCA.
Conclusions: Reductions in markers of cholestasis and hepatic damage with OCA treatment in Canadian patients were generally comparable to the global OCA treated population. Improvements in many of these markers have been associated with improved long-term outcomes in PBC.

Table 1. Improvements in Biochemistry with Obeticholic Acid

	Concomitant UDCA		Monotherapy	
	Placebo (n=15)	≤10 mg OCA (n=15)	Placebo (n=4)	≤10 mg OCA (n=3)
BL ALP (U/L)	277.0 (108.3)	321.7 (156.6)	527.6 (243.3)	1029.0 (227.0)
Δ EOT	-39.7 (25.2)	-106.2 (25.6)*	-16.6 (84.5)	-570.8 (176.2)
BL Total Bilirubin (µmol/L)	12.3 (4.4)	15.6 (8.5)	13.9 (7.4)	20.5 (4.7)
Δ EOT	-1.3 (1.8)	-3.9 (2.4)	-2.3 (1.0)	-9.9 (1.9)*
BL AST (U/L)	40.2 (10.4)	52.2 (39.2)	81.5 (51.0)	96.2 (45.3)
Δ EOT	9.7 (15.1)	-12.2 (20.7)	-19.8 (6.6)	-35.8 (8.4)
BL ALT (U/L)	45.7 (20.0)	62.8 (55.2)	95.4 (66.8)	124.7 (59.9)
Δ EOT	-5.8 (6.8)	-25.1 (7.5)**	-30.8 (6.8)	-55.9 (8.9)
BL GGT(U/L)	246.0 (141.8)	281.4 (212.2)	418.5 (246.2)	1085.3 (433.5)
Δ EOT	17.3 (35.1)	-146.4 (40.8)**	-52.2 (102.0)	-770.6 (160.8)*

BL values are Mean (SD).
Change from BL values are LS Mean (SE).
*p<0.05, **p<0.01. P-value for comparing OCA to PBO is obtained using an ANCOVA model with BL value as a covariate and fixed effects for treatment, DB UDCA usage and DB BL total bilirubin.

A201
PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE IN A COHORT OF HEALTHY CHILDREN IN ONTARIO
J. Dhaliwal[1], G. Chavhan[1], P. Wales[2], M. Mouzaki[3]

1. Hospital for Sick Children, Toronto , Toronto, ON, Canada; 2. The Hospital for Sick Children, Toronto, ON, Canada; 3. Gastroenterology, Toronto General Hospital , Georgetown, ON, Canada
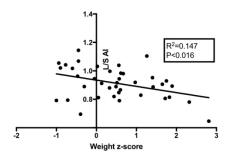
Aims: To determine the prevalence of hepatic steatosis in a cohort of previously healthy children and adolescents, with the use of abdominal computer tomography (CT).

Methods: Retrospective review of the Sickkids trauma database from (year 2004 to 2015). <u>Inclusion criteria</u>: previously healthy children ages 1-17yr having undergone an abdominal CT scan as a part of routine trauma assessment. <u>Exclusion criteria</u>: Involvement of spleen and/or liver in the injury, known metabolic condition, concurrent use of medications that could predispose to hepatic steatosis. Steatosis was defined as a liver spleen attenuation index (L/S AI) of <0.8. Anthropometrics and baseline demographics were collected. Statistical analyses were performed using Graphpad Prism 7.

Results: A total of 143 children were included in the analyses with a mean (SD) age of 7.12(4.26) years. 88 children were male (7.10(4.24) years old). The mean (SD) weight z score was 0.48 (0.97). Fifteen percent of the 137 children with a weight z-score between -2 to 2 had evidence of hepatic steatosis on imaging (using liver/spleen index <0.8). Twenty seven percent (6/22) of children with weight z-scores less than the 33rd percentile had L/S AI <0.8. An inverse correlation between weight z-scores and L/S AI was found in children >10 years ($P<0.016$) (Fig 1); however there was no correlation in pre-pubertal children ($P<0.374$).

Conclusions: Hepatic steatosis is highly prevalent in this cohort of healthy children in Ontario. Larger population based studies are needed to investigate the prevalence of hepatic steatosis in children across Canada.

Fig 1: Relationship between weight z score and liver/spleen attenuation index in children > 10 yrs of age

A202
BIOCHEMICAL PROFILE IN 68 PRIMARY BILIARY CHOLANGITIS (PBC) SUBJECTS HAVING AN INADEQUATE RESPONSE TO URSODEOXYCHOLIC ACID

P.F. Boudes[1], B. Bacon[3], M. Varga[1], Y. Choi[4], A. Steinberg[5], T. Turner[6], M. Swain[2]

1. CymaBay Therapeutics, Newark, CA; 2. Univ Calgary, Calgary, AB, Canada; 3. Saint Louis University School of Medicine, St Louis, MO; 4. CymaBay Therapeutics, Newark, CA; 5. CymaBay Therapeutics, Newark, CA; 6. Medpace Reference Laboratories, Cincinnati, OH

Background: Ursodexoxycholic acid (UDCA) is the first line treatment for PBC. However, up to 40% of subjects have an inadequate response characterized by a persistent elevation of Alkaline Phosphatases (AP).

Aims: Herein, we describe a number of additional biochemical abnormalities in PBC subjects having an inadequate response to UDCA.

Methods: Sixty-eight subjects with a confirmed diagnosis of PBC and a persistent elevation of AP (>1.67xULN) despite treatment with UDCA for at least a year were screened for a phase 2 intervention study (NCT02609048/EudraCT2015-002698-39). The mean age was 55 years old and 65 subjects were females (96%). The % of subjects with abnormal values and mean parameters values relative to the upper limit of normal (ULN) were assessed for the following: AP, γ-glutamyl transferase (GGT), 5' nucleotidase (5'N), transaminases (AST/ALT), Bone specific AP (BSAP), total-cholesterol (TC), LDL-C, HDL-C, total protein, total bilirubin (TB) and its fraction (direct and indirect), and albumin. The presence of lipoprotein X (LpX) in serum was assessed and a complete blood count was performed. Multiple linear correlations were explored.

Results: In addition to AP elevation, the most frequently elevated parameters in these subjects were GGT (97%), BSAP (90%), 5'N (76%), TC (75%), HDL-C (71%), AST (54%), ALT (47%), LDL-C (44%), direct bilirubin (35%), total protein (19%), and TB (16%). No subjects had LpX detected despite some having HDL-C cholesterol that reached 3-fold ULN.

There were strong correlations between AP and BSAP, AST, GGT and 5'N (all correlation coefficients ≥0.6 and p< 0.001). There was no correlation between AP and HDL-C.

Conclusions: The frequency of BSAP elevation and its strong correlation with AP were unexpected and could indicate that osteopenia is more prevalent in this population. The elevation of direct bilirubin was twice more frequent than the elevation of TB and could constitute a more sensitive prognostic marker. GGT was quantitatively more elevated than AP. The HDL-C elevation, which is known in PBC, can however reach unusual levels that are rarely seen in other conditions. The HDL-C increase did not correlate with the other markers of cholestasis, and it mechanism is unclear. LpX was not detected in any patients. The frequent increase in total protein is probably a consequence of the polyclonal increase in immunoglobulin M.

Mean values and fold ULN for selected parameters

	AP	GGT	BSAP	5'N	TC	HDL-C
Mean (SD)	273 (122)	204 (170)	45 (18)	27 (21)	237 (55)	82 (29)

CHRONIC LIVER DISEASE

	37-116 U/L	7-38 U/L	5.5-24.6 micromole/L	0-15 U/L	100-200 mg/dL	35-60 mg/dL
LLN-ULN						
Fold ULN	2.4	5.3	1.8	1.8	1.2	1.4

A203
ACTIVITY OF MBX-8025, A POTENT AND SELECTIVE PPAR-δ AGONIST, ON BIOCHEMICAL MARKERS OF CHOLESTASIS

A. Steinberg, Y. Choi, C.A. McWherter, P.F. Boudes

CymaBay Therapeutics, Newark, CA

Background: MBX-8025 is a potent and selective PPAR-delta agonist that decreases LDL-Cholesterol in subjects with mixed dyslipidemia and subjects with homozygous familial hypercholesterolemia (HoFH).
Aims: Herein, we describe the activity of MBX-8025 to decrease biochemical markers of cholestasis.
Methods: Alkaline phosphatases (AP), gamma glutamyl transferase (GGT), and total bilirubin (TB) were measured in three clinical studies: a 3-week parallel groups, placebo-controlled study in healthy volunteers; an 8-week parallel groups, placebo- and atorvastatin-controlled study in mixed dyslipidemia; and a 12-week dose escalating, non-controlled study in HoFH. MBX-8025 was administered orally, daily, at doses of 50, 100 and 200 mg. None of the subjects had a medical diagnosis of cholestasis and AP levels were considered within the normal range.
Results: Rapid onset (within 4 days) and consistent decreases in AP were observed in all three studies. Decreases were sustained during MBX-8025 treatment, reversible within a week upon discontinuation of MBX-8025, and AP values were not seen below the lower reference limit. The AP decrease was not consistently dose-dependent and was associated with a concomitant decrease in GGT of similar amplitude. Decreases (between -20% and -40%) in TB were also observed in healthy volunteers and patients with HoFH.
Conclusions: MBX-8025 significantly decreases biochemical markers of cholestasis in three different populations. A recent study in primary biliary cholangitis (NCT02609048) confirmed that this activity was translated in patients with cholestasis and was associated with a decrease in bile acid synthesis.

Mean Change (%) From Baseline in AP

Treatment	Healthy Volunteers		Mixed Dyslipidemia		HoFH	
	N	Mean % Change	N	Mean % Change	N	Mean % Change
Placebo	9	6	28	-4		NA
MBX-8025 50 mg	9	-28	28	-34	12	-25
MBX-8025 100 mg	9	-20	32	-43	10	-29
MBX-8025 200 mg	9	-26		NA	7	-40
Atorvastatin 20 mg		NA	28	7		NA

NA = Not Applicable

A204
FIBRINOGEN STORAGE DISEASE:A CASE SERIES AND LITERATURE REVIEW

M. Kehar[1], L. Brandao[2], S. Bowdin[2], E. Cutz[2], S.C. Ling[2], V. Ng[3]

1. Pediatric gastroenterology,hepatology and nutrition, Hospital for sick children, Toronto, ON, Canada; 2. The Hospital for Sick Children, Toronto, ON, Canada; 3. Division of Pediatric GI/Hepatology/Nutrition, The Hospital for Sick Children, Toronto, ON, Canada

Background: Fibrinogen Storage Disease (FSD) is characterized by hypofibrinogenemia and hepatic inclusions due to impaired release of mutant fibrinogen causing aggregation in the hepatic endoplasmic reticulum.
Aims: Review of clinical, laboratory,histopathological findings of 2 children with FSD **and a systematic review of the literature on FSD.**
Methods: Medical charts of two cases were reviewed. Pubmed, Medline and Cochrane databases were searched. Search term: fibrinogen storage disease, FSD, FGG.
Results: A 5 yr old male (Patient A) and 17 month old female (Patient B) were referred to The Hospital for Sick Children for consultation of asymptomatic elevation of liver enzymes. History and physical examination were non-contributory, key lab results provided in Table 1. Work-up for other causes of liver disease was unremarkable. Liver biopsy demonstrated hepatocytes with cytoplasmic eosinophilic inclusions on H&E stain, with mild portal fibrosis (Patient A) and lobular distortion, bridging fibrosis and nodule formation with some portal inflammation (Patient B) noted. Electron microscopy showed fingerprint-like structures in the dilated cisternae of the rough ER. Genetic testing for both patients revealed **Aquadilla** mutation in FGG gene. Patient B received ursodeoxycholic acid (UDCA), with modest improvement in liver enzymes. At last follow-up, both are asymptomatic with persistent elevation of liver transaminases and INR, and hypofibrinogenemia. Since the first published case of FSD in 1981, there have been no deaths or liver transplants reported in the subsequent total of 19 reported cases identified (9 males, mean age15.7 yrs, range 2-64yrs from year 1981-2016).

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Of 6 reported mutations in FGG gene, **Aguadilla** was most commonly seen (9/19 cases). Severity of disease varies, with cirrhosis present in 5/19 cases. Reported treatments include UDCA (n=3), vitamin E (n=1). Carbamazepine (n=4) provides a potential autophagy-enhancing therapy based on understanding of disease mechanism. Very limited outcome data is reported with survival reported for a mean of 6.3 years in 4 cases.
Conclusions: FSD-1 is a rare liver disease in children and adults, but important because potentially treatable. We add 2 cases to the very limited published experience. We suggest that affected patients should be monitored for development of fibrosis. Treatment with carbamazepine can be considered for those with progressive disease.

Table 1: Trends in labs and TE. CB – Conjugated Bili , UCB - Unconjugated Bilirubin , TE – transient elastography

Patient A	Time	CB (Umol/l)	UCB (umol/l)	Albumin (g/l)	ALT (IU/l)	AST (IU/l)	INR	Fibrinogen (g/l)	TE
A	Baseline	0	0	42	261	159	1.4	0.7	-
A	1yr	0	0	38	144	99	1.5	0.9	3.7
A	30m	0	6	38	118	103	1.3	1.3	4.6
Patient B	Baseline	0	0	40	117	209	1.6	0.6	-
B	3m	0	0	41	250	416	1.6	0.6	-
B	1y	0	0	42	126	93	1.4	0.9	-

Funding Agencies: None

A205
CONGENITAL ABSENCE OF THE PORTAL VEIN: DOES IT REALLY EXIST?
N. LAVERDURE, M. Lallier, J. Dubois, M. Paganelli

CHU Ste Justine, Montreal, QC, Canada

Background: Congenital portosystemic shunts are rare vascular malformation that can lead to pulmonary hypertension, encephalopathy and liver tumors. They were classified as type I(end-to-side portocaval fistula with no visible portal flow in the liver) and type II(side-to-side portocaval fistula)shunts.Type I shunts are often referred to a congenital absence of the portal vein(CAPV), and are still considered an indication for liver transplantation, whereas surgical or percutaneous closure is usually feasible for type II shunts.
Aims: Through a case report and a review of all published patients, we show that what is initially diagnosed as CAPV may conceal a hypoplasic portal vein that can successfully be closed by surgical ligation.
Methods: A 2-year-old girl was referred for liver transplantation in the context of recent diagnosis of CAPV. At presentation she was asymptomatic and showed a hypertrophic left liver lobe, without any complications. Her blood tests were normal excepted for moderately elevated serum ammonia levels. MRI confirmed the diagnosis of a type Ib portosystemic shunt(with superior mesenteric and splenic veins joining to form a short portal trunk ending into the inferior vena cava). Percutaneous venogram confirmed the absence of the portal vein. Nevertheless, a second direct catheterization of the shunt with temporary shunt occlusion allowed us to visualize an hypoplasic portal vein arising from the posterior face of the shunt. Pressure was measured at 12mmHg in standard conditions and 36mmHg upon temporary occlusion. We decided for a two-step occlusion. A partial banding was carried out without significant complications(normal liver tests, minimal transient ascites). The shunt was permeable, with a measurable portal flow, at follow-up Doppler ultrasound. 2 months later, moderate elevation of liver enzymes(3xULN) and mild ascites were detected, but resolved spontaneously within a few weeks. The shunt was not detected anymore, and the Doppler study showed a normal portal flow. A percutaneous venogram confirmed the total closure of the shunt and the permeability of the portal vein. The child is asymptomatic at 6-month follow-up.
Results: 202 cases of extrahepatic shunts were reported since 1979, of which 134 were described as CAPV. 38 patients(19%) had percutaneous or surgical shunt closure(12 &26, respectively), whereas 25 patients(12%) received a liver transplantation. Among all transplanted patients, only 4% had a preoperative percutaneous venogram with temporary shunt occlusion.
Conclusions: Overall, the case reported here exemplifies what emerges from published literature: a precise evaluation of the shunt with percutanous venogram and temporary occlusion is warranted in all patients with suspected CAPV. It allows detecting otherwise invisible hypoplasic portal veins that allow tore establish a physiological hepatic circulation and avoid liver transplantation.

Funding Agencies: None

A206
PREDICTORS OF HOSPITAL READMISSION FOLLOWING LIVER TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE
I. Alqalami, M. Al Ghanem, M. Sey, A. Teriaky, B. Aljudaibi

Gastroenterology , London Health Sciences Centre , London, ON, Canada

Background: Liver transplantation is a life saving procedure for patients with end stage liver disease or

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hepatocellular carcinoma. Morbidity and mortality rates have dramatically declined with the evolution of the procedure. However, hospital readmission after discharge is still common and increases healthcare costs. **Aims:** The purpose of this study is to determine predictors of hospital readmission in patients that underwent liver transplantation.

Methods: This is a retrospective study conducted at London Health Sciences Centre, a tertiary care centre, in London, Ontario, Canada. All patient who underwent liver transplantation between 2012 and 2016 were included in this study. Charts were reviewed to collect patient demographics, donor organ variables, readmission rates, and post-operative complications. Statistical analysis was performed with multivariable logistic regression. A p value <0.05 was statistically significant.

Results: There were 255 patients that underwent liver transplantation with a median age of 60 years old and 31% were female. The most common cause of liver disease was hepatitis C and alcohol. The median MELD score was 21. Of the liver transplants performed, 83% were from brain dead donors, 15% were from donors after cardiac death, and 2% were from living donors. The mean donor risk index was 1.68. Patients required readmission in 17% of cases after being discharged post-liver transplant. The most common cause of readmission was elevated liver enzymes in 6%, graft failure in 5%, and infection in 3%. The most common post-operative complications were surgical in 72%, infection in 20% and nutrition in 10%. Death occurred in 9% during the follow up period. On multivariable logistic regression the only significant predictor of readmission within 90 days of liver transplant was surgical complications with an odds ratio of 3.0 (95% confidence interval of 1.2-7.5, p-value of 0.02).
Conclusions: Hospital readmission post-liver transplantation is common which leads to increased healthcare utilization. Post-operative surgical complications were the only clinical predictor of readmission within 90 days of discharge.

Funding Agencies: None

A207
SCLEROSING CHOLANGITIS SECONDARY TO DISSEMINATED VARICELLA ZOSTER VIRUS: A CASE REPORT
J. Charette[1], R. Mohamed[1], C.N. Andrews[2], S. Vaughan[1], O. Larios[1], S. Jayakumar[3]

1. University of Calgary, Calgary, AB, Canada; 2. Gastroenterology, University of Calgary, Calgary, AB, Canada; 3. Medicine, University of Calgary, Calgary, AB, Canada

Background: Sclerosing cholangitis represents a spectrum of chronic and progressive diseases of the intrahepatic and extrahepatic biliary ducts. The condition is characterized by multifocal inflammation, fibrosis, and stricturing, resulting in biliary cirrhosis and eventual hepatic failure. While PSC accounts for the majority of cases, a small proportion can arise secondary to known causes including biliary surgery, obstruction, malignancy, bacterial cholangitis, trauma, ischemia, and infiltrative diseases.
Aims: Here we present a case of sclerosing cholangitis secondary to disseminated Varicella Zoster Virus.
Methods: A 70-year old female on Rituximab therapy for follicular lymphoma presented with abdominal pain, anorexia and a diffuse vesicular rash. EGD revealed severe esophagitis and a large, erosive mass in the fundus of the stomach. PCR studies of the skin and gastric mucosa confirmed the presence of disseminated Varicella Zoster Virus, which was treated with IV acyclovir. The patient presented soon after discharge with new symptoms of pruritus and fatigue, with elevated cholestatic liver enzymes. MRCP revealed multifocal strictures throughout the intrahepatic bile ducts with mild extrahepatic duct involvement. Liver biopsy was suggestive of a cholangiopathy of uncertain etiology without the classic "onion skin" pattern of PSC. Biopsies were negative for malignancy, and for viral PCR and immune serologic tests, including for autoimmune cholangiopathy. The patient showed improvement in both her symptoms and liver enzymes and repeat liver biopsy and MRCP confirmed stable disease. An endoscopic ultrasound revealed the presence of multifocal stricturing of the pancreatic duct with a normal common bile duct free of stones or sludge and normal pancreatic parenchyma.
Results: The diagnosis of disseminated VZV with GI involvement, and strong temporal relationship between the appearance of biliary disease and VZV infection suggest a VZV-induced SSC. The patient showed symptomatic and biochemical improvement following treatment with acyclovir. There are many features of this presentation including the patient's age, gender, rapid onset, and clinical improvement, which are very atypical for PSC. The patient does not have a history of inflammatory bowel disease and all autoimmune markers are negative. The pancreatic duct strictures are suggestive of a secondary cause affecting both the hepatic bile ducts and pancreatic duct. There was no evidence to suggest that another known secondary cause could have contributed to this patient's presentation. Serial liver biopsies were repeatedly negative for lymphoma. Obstructive and ischemic causes of SSC were ruled out via ERCP and MRCP.
Conclusions: In this case the most likely etiology of the sclerosing cholangitis is the disseminated VZV. This is the first reported case of VZV-induced SSC.

Funding Agencies: None

CYTOKINES AND INTRACELLULAR SIGNALS

Poster of Distinction

A208
SHP-2 PHOSPHATASE PREVENTS SENESCENCE IN NORMAL AND TUMOR INTESTINAL EPITHELIAL CELLS

V. Vaillancourt-Lavigueur[2], J. Gagné Sansfaçon[3], M. Langlois[2], N. Rivard[1]

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

Background: The protein tyrosine phosphatase SHP-2 is known to regulate many cellular functions including growth, differentiation and survival. Interestingly, a gain-of-function mutation (residue E76K) in the gene encoding SHP-2 has been found in some colorectal cancers. Importantly, intestinal epithelial cell (IEC)-specific expression of SHP-2^{E76K} mutant in mice was not sufficient to induce tumorigenesis but markedly promoted tumor growth under the *Apc*$^{Min/+}$ background. Conversely, SHP-2 silencing inhibited anchorage-independent growth of human CRC cells (Gagné-Sansfaçon *et al*., Oncotarget 2016). However, the molecular mechanisms involved in the pro-oncogenic action of SHP-2 remained to be identified.
Aims: To determine a possible role of the protein tyrosine phosphatase SHP-2 in the development of senescence.
Methods: Non immortalized human intestinal epithelial cells (HIEC) and human colorectal cancer cells (HCT116) were infected with lentiviruses encoding a shRNA directed against SHP-2. The impact on growth was assessed by BrdU incorporation, SA-β-galactosidase staining and qPCR or immunoblot analyses of regulatory proteins and signaling pathways regulating the cell cycle. SHP-2 deletion was induced *ex vivo* in intestinal organoids and the impact on organoid development was analyzed.
Results: SHP-2 silencing in HIEC changes cell morphology and results in the activation of the Wnt/β-catenin pathway and in the decreased activation of ERK1/2 MAP Kinases. Few days after silencing, the number of cells in S phase is significantly decreased and senescence (SA-β-galactosidase staining) as well as DNA damage (γH2AX) are observed. Western blot and qPCR analyses demonstrate increased expression of the cell cycle inhibitor p27 and increased phosphorylation of p53 on serine 15. Finally, deletion of SHP-2 in enteroids clearly limits their proliferative capacity and development ; notably, few days after, organoids loose their integrity and degenerate in contrast to control organoids that continue to develop.
Conclusions: In summary, our results suggest that SHP-2 protects intestinal epithelial cells against an oncogenic stress leading to senescence.

A209
XENOBIOTIC RECEPTOR REGULATION OF CLOSTRID-IUM DIFFICILE-ASSOCIATED TISSUE DAMAGE AND INFLAMMATION

S.L. Erickson, K.L. Flannigan, L. Alston, S.A. Hirota

Physiology & Pharmacology, University of Calgary, Calgary, AB, Canada

Background: The current treatments available for *C. difficile* infections (CDI) target the bacteria, however they do nothing to treat the damaging inflammation triggered by the virulence factors, TcdA and TcdB. Indeed, enhanced chemokine/cytokine expression during CDI is associated with poor clinical outcomes. Interestingly, a number of rifamycin antibiotics have been shown to have potent activity against *C. difficile*, while also exhibiting anti-inflammatory effects through their ability to activate the pregnane X receptor (PXR) and inhibit NFκB signaling. In the current study, we sought to test the hypothesis that targeting the PXR could prove to be an effective strategy to reduce *C. difficile* toxin-induced inflammation and tissue damage.
Aims: 1) To assess the ability of PXR agonists to attenuate TcdB-induced CXCL8/IL-8 production *in vitro*
2) To test whether PXR activation can attenuate TcdA/B-induced damage and inflammation in an *in vivo* model of *C. difficile* toxin exposure
3) Determine the mechanism by which activation of the PXR attenuates TcdA/B-induced damage and inflammation
Methods: We first assessed the ability of the PXR to modulate the production of the neutrophil chemokine CXCL8/IL-8 from human colonic intestinal epithelial cells (IECs;Caco-2), a mediator highly expressed during CDI. Caco-2 IECs were treated for 16 hours with purified *C. difficile* TcdB (2.5μg/mL) in the presence of PXR agonists at various concentrations (rifampicin, SR12813). In addition to culture supernatants, cell lysates were used to evaluate cell death and toxin function by immunoblot for caspase-3 and glucosylated RAC1, respectively. We then assessed whether PXR activation could attenuate toxin-induced inflammation and tissue damage *in vivo*. Mice were administered TcdA/B (25μg;intrarectal administration) in the presence of PCN(25mg/kg), a rodent specific PXR agonist. After 4 hours of TcdA/B exposure, colonic tissues were harvested and the expression of IL-17A, CXCL1, CXCL2 and CXCL10 were assessed by qPCR and neutrophil infiltration assessed by flow cytometry.
Results: Activation of the PXR with known agonists attenuated *C. difficile* TcdB-induced CXCL8/IL-8 release in Caco-2 IECs. This effect was not due to alterations in IEC survival, nor due to a direct inhibition of TcdB function by PXR agonists. In our *in vivo* studies, we found that PXR activation with PCN attenuated TcdA/B induced expression of the pro-inflammatory cytokines IL-17A, CXCL1, CXCL2, CXCL10 and significantly reduced neutrophil infiltration in the colon.
Conclusions: Although there are many emerging treatments for CDI, drug tolerability, disease recurrence, resistance and dosing remain problematic. Taken together, these data will help us expand our knowledge

CYTOKKINES

of the PXR's role in host-pathogen interactions, and its potential to be modulated for the treatment of inflammation and tissue damage in CDI.

A210
NEONATAL INFLAMMATORY SKIN AND BOWEL DISEASE CAUSED BY A HOMOZYGOUS EGFR MUTATION: A CASE REPORT AND REVIEW OF THE MEDICAL LITERATURE.
M. Alruwaithi[1], M. Sherlock[2]

1. McMaster Children's Hospital , Hamilton, ON, Canada; 2. Pediatric Gastroenterology, McMaster Children's Hospital, Hamilton, ON, Canada

Background: Epidermal growth factor receptor (EGFR) and its ligands are cell signaling molecules involved in diverse cellular functions, including cell proliferation, differentiation, motility, and cell survival. EGFR overexpression or over activity has been frequently described in association with a number of malignancies, most commonly lung carcinoma; however inherited loss of function mutations in the EGFR gene are extremely rare.
Aims: To describe a 5-year old child with a complex medical history in whom a homozygous mutation in the EGFR gene was identified.
Methods: Case report and literature review
Results: A now 5 year-old girl, born to non-consanguineous parents, was delivered following preterm labor at 27 weeks gestation. She weighed 890g. The pregnancy was complicated by polyhydramnios. Shortly after birth she was noted to have fragile skin with widespread erythema along with papules and pustules over her trunk and extremities. Clinical features included the following: downslanting palpebral fissures, thick eyebrows, no scalp hair, arachnodactyly, large feet with cavus and short sternum. She had a large ventriculoseptal defect and mitral valve regurgitation. Skin biopsy at 3 months of age found no histomorphologic alterations. There were no features of any inflammatory process. Testing for an interleukin 1 receptor antagonist deficiency was negative. Her skin has been persistently problematic with frequent Staphylococcal infections. Her scalp hair is sparse and coarse. She subsequently developed Fanconi syndrome and polycystic kidney disease. She has had frequent hospital admissions with skin and GI infections, including recurrent Clostridium difficile. She has had failure to thrive and chronic watery diarrhea since the age of 4 years. Upper endoscopy and colonoscopy revealed an antral gastritis and mild, non-specific chronic inflammation on colonic biopsies. She has hepatomegaly and mild elevation of transaminases. Whole exome sequencing revealed that she is homozygous for Gly428Asp, a loss-of-function missense mutation in the EGFR gene.

Literature Review
There have been only 3 reported cases of this mutation. Tow children were siblings from consanguineous parents of Roma descent. The third patient was also of Roma descent. All had similar characteristics to the patient presented here including sparse scalp hair, recurrent skin infections, failure to thrive, chronic diarrhea and nephromegaly. All were born prematurely and had IUGR. No patient survived beyond 2.5 years. To date, there is no known effective therapy for the condition.
Conclusions: EGFR signaling abnormalities affect multiple organ systems and have a severe phenotype. We report the clinical presentation and oldest living .patient with this condition, highlighting the role for whole exome sequencing in patients where a diagnosis is elusive

A211
PROTEOLYTIC CLEAVAGE OF E-CADHERIN BY INFLAMMATORY PROTEASES PRODUCES BIOACTIVE PEPTIDES THAT MODIFY EPITHELIAL FUNCTION
M. Gordon[2], W. MacNaughton[1]

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

Background: The inflammatory microenvironment in the gut contains a variety of proteases from numerous sources including inflammatory cells. 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. EMT involves the degradation of junctional proteins such as E-cadherin [Ecad], but the mechanisms by which Ecad is lost and the functional consequences of Ecad degradation remain incompletely understood.
Aims: To test the hypothesis that inflammatory proteases cleave Ecad to produce peptides that alter epithelial homeostasis by altering cell migration, proliferation, or cell death.
Methods: Ecad cleavage *in vitro* was determined using Western blot. Recombinant Ecad was incubated with neutrophil elastase [NE] in a cell-free system and 24 peptides identified by mass spectrometry were chosen for high-throughput screening based on frequency of occurrence, p-value scoring, and accessibility of cleavage sites. Peptides were synthesized and tested for biological activity including proliferation, cell death, and cell migration. Murine CMT-93 intestinal epithelial cells were cultured in 96 well plates and wounded 5 days post-confluency using the EssenBio WoundMaker™ tool. Wells were imaged simultaneously with the IncuCyte™ live-cell imaging system for 24-48 hours following exposure to 1, 10, or 100 µg/mL concentrations

of peptides. Cells were transfected with a GFP marker to allow automated cell number tracking to measure proliferation. Cytotoxicity was determined using Cytotox dye which binds cells undergoing membrane degradation. All analysis was done using the IncuCyte™ ZOOM platform in conjunction with ImageJ software.
Results: Basolateral stimulation of human Caco2 and murine CMT93 cells with NE confirmed the ability of NE to produce C- and N-terminal Ecad fragments in vitro. Of the 24 synthesized Ecad peptides, we identified 10 that significantly influenced wound closure rates both positively and negatively. Two peptides significantly inhibited wound healing rate by 13-26% compared to vehicle controls at a concentration of 100 μg/mL. Six peptides (100 μg/mL) significantly increased wound healing rates by 7-11% and three peptides (10 μg/mL) significantly increased wound healing rates by 6-13% compared to vehicle controls. Preliminary results suggest several of these peptides may also have cytostatic or pro-proliferative activity.
Conclusions: Our results suggest that degradation of cell junction proteins by inflammatory proteases can create bioactive peptides that alter epithelial homeostasis and alter cell migration. Our data reveal a novel pathway whereby epithelia respond to inflammatory tissue damage at the cellular level to alter a barrier phenotype to a more dynamic epithelium.

A212
EXPRESSION AND CHARACTERIZATION OF SOLUBLE PEKIN DUCK PROGRAMMED DEATH-1
Q. Yao[1], K.P. Fischer[1], L. Tyrrell[2], K.S. Gutfreund[3]

1. University of Alberta, Edmonton, AB, Canada; 2. Medical Microbiology and Immunology, University of Alberta, Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada

Background: Programmed death 1 (PD-1, CD279) negatively regulates TCR complex-initiated signaling by interacting with its cognate ligands PD-L1 (B7-H1, CD274) and PD-L2 (B7-DC, CD 273). Recently, therapeutic targeting aimed at abrogation of co-inhibition through PD-1 has led to breakthroughs in the treatment of cancer and has shown potential for the treatment of chronic viral infections. We have identified the duck PD-1, PD-L1 and PD-L2 proteins that have a sequence identity of 31%, 45% and 36% with human PD-1, PD-L1 and PD-L2, respectively.
Aims: The aim of this study was to express soluble duck PD-1 (duPD-1) for functional characterization in the duck hepatitis B model.
Methods: The duPD-1 ectodomain (501 bp) was inserted into pZeo2B in frame with a polyHis tag and expressed in 293T cells. Culture supernatants were assessed immunoblot and soluble duPD-1 was affinity purified and conjugated with RPE. Full-length PD-L1 and PD-L2 fused in frame with eGFP were inserted in

pZeo2B and expressed in 293T cells, respectively. Binding of soluble duPD-1 to duPD-L1 and duPD-L2 were assessed by FACS in PD-L1-eGFP-, PD-L2-eGFP- and eGFP-transfected 293T cells.
Results: Soluble duPD-1 could be expressed as a secreted protein in 293T cells. Affinity purified soluble duPD-1 conjugated with RPE could bind to duPD-L1 and duPD-L2 expressed on 293T cells.
Conclusions: Soluble duPD-1 can be expressed as a secreted protein and retains binding affinity to duPD-L1 and duPD-L2 that can be used to study the role of PD-1 co-inhibition in the duck hepatitis B infection model.

EPIDEMIOLOGY AND THE BURDEN OF ILLNESS

A213
A SURVEY OF WORKPLACE ACCOMMODATIONS AMONG PERSONS WITH IBD.
T. Chhibba[2], J.R. Walker[2], L. Shafer[2], K. Sexton[2], M. Ivekovic[2], G. Restall[2], h. singh[2], L.E. Targownik[2], C.N. Bernstein[1]

1. University of Manitoba, Winnipeg, MB, Canada; 2. University of Manitoba, Winnipeg, MB, Canada

Background: IBD can threaten performance in the workplace with periods of decreased function and possibly periods of absence due to illness. Little is known about the accommodations that may help maintain persons with IBD in the workplace during periods of increased symptoms.
Aims: To identify the experiences with workplace accommodations among persons with IBD when ill.
Methods: Participants were recruited from the population-based University of Manitoba Research Registry. Those 18 to 65 years were invited to complete a survey with a section assessing experiences with workplace accommodations in 6 areas identified in earlier qualitative research as important for persons with IBD.
Results: 1143 individuals responded to the survey (46% response rate) and 881 (77%) had experienced IBD symptoms in the workplace at some point in their life. The mean age was 49.7 years 61% were female. Mean IBD duration was 20.6 years.
Most respondents (73%) described IBD symptoms experienced in the workplace as severe to very severe. The accommodations considered needed when they were ill (% reporting): time to go to medical appointments during regular working hours (81%), easy access to a suitable toilet (71%), a chance to take a 30 to 60 minute break when not feeling well (54%), flexible or reduced hours of work each day (47%), flexible start time and work hours (44%), and reduced days of work each week (35%). Most arranged for the accommodations

either by themselves or through informal arrangements with a supervisor; formal requests for accommodation were much less common. Some found required accommodations somewhat or very difficult to arrange with the most difficult accommodation to arrange being reduced days of work each week (35%).

Bivariate and multivariate analysis was conducted on three outcome variables. Requirement for two or more accommodations was most impacted by sex (female, OR=1.75 95%CI=1.18-2.60), having high levels of current emotional distress (OR=1.86 95%CI=1.19-2.89) and those with higher reported disease severity OR=2.45 95%CI=1.63-3.68). Not asking for required accommodations was most impacted by age (>53 years {median split}, OR=1.47 95%CI=1.05-2.06), having high levels of current emotional distress (OR=1.65 95%CI=1.19-2.28) and having higher reported disease severity (1.78 95%CI=1.24-2.55). Having increased difficulty in arranging for accommodations was most impacted by sex (female, OR=1.77 95%CI=1.19-2.63), those with higher reported disease severity (OR=1.86 95%CI=1.16-2.99) and those with high levels of current emotional distress (OR=2.29 95%CI=1.58-3.33).

Conclusions: The knowledge of accommodations required by persons with IBD and areas where there may be difficulty arranging them will assist in educating persons with IBD and their employers. This in turn could result in better support in the workplace.

A214
AN ANALYSIS OF FIT RESULTS AND NEOPLASTIC FINDINGS FROM THE NEWFOUNDLAND AND LABRADOR COLON CANCER SCREENING PROGRAM
J. Quinlan[2], M. Borgaonkar[2], S. Antle[1], D. Pace[2], J.S. McGrath[2]

1. Gastroenterology, Eastern Health, St. John's, , Canada; 2. Medicine, Memorial University, St. John's, , Canada

Background: Fecal Immunochemical Testing (FIT) is currently used in a number of Canadian provinces to screen for colorectal cancer. The Canadian Partnership Against Cancer (CPAC) recommends a FIT positive predictive value for neoplasia be >50%. Newfoundland and Labrador currently does not triage its colonoscopy waitlist for colorectal cancer screening beyond having one FIT value ≥100ng/mL.
Aims: The aim of this study is to assess the effectiveness of different FIT cut-offs and combinations of FIT cut-offs in predicting adenomas and colorectal cancer.
Methods: Data for this study was obtained in a prospective fashion using the Newfoundland and Labrador Colon Cancer Screening Program. Those enrolled in the study were between the ages of 50-74 at average risk for colon cancer. Between July 1, 2012 and June 30, 2016, participants were provided with two FIT tests – if a minimum of one test was ≥100ng/mL, participants

were further evaluated via colonoscopy. Data on the patient's age, gender, FIT value, presence of adenoma, pathology, and other variables were collected.
Results: Of the 21,371 FIT kits mailed out, 16,152 (75.6%) were returned, of which, 2694 (16.7%) had at least one FIT value ≥100ng/mL. The highest positive FIT values ranged from 100 to 54,017, with a mean of 942.3, 25th percentile of 145, 50th percentile of 260, and 75th percentile of 576. At the time of analysis, 1831 participants had been further evaluated by colonoscopy. Of those who had a colonoscopy, 73 (4.0%) were found to have colorectal cancer and 1092 (59.6%) were found to have an adenoma. The positive predictive value for both adenomas and colorectal cancer increased with increasing FIT values and serial positive values. Those with two FIT values ≥5000ng/mL had the highest adenoma detection rate (100.0%) and highest rate of colorectal cancer (53.8%), which was significantly higher than those with one FIT value ≥100ng/mL (p-values 0.002 and ≤0.001, respectively).
Conclusions: There is a limited amount of Canadian research evaluating the performance of FIT testing within colorectal cancer screening programs. This research suggests that by increasing the FIT cut-off there is an improvement in adenoma detection rate. Patients with two FIT positive results are more likely to have colon cancer or an adenoma compared to patients with only one FIT positive result. Further triaging of colonoscopy wait lists could be considered based on quantitative FIT values and number of positive tests thus reducing the time to diagnosis for patients most likely to have colorectal cancer.

Table 1. Colonoscopy Results by FIT Cutoff

	1 FIT ≥ 100	2 FIT ≥ 100	1 FIT ≥ 200	2 FIT ≥ 200	1 FIT ≥ 1000	2 FIT ≥ 1000	1 FIT ≥ 5000	2 FIT ≥ 5000
Colonoscopy	1831	748	1106	289	290	84	62	12
Colorectal Cancer	73 (4.0%)	61 (8.2%)	66 (6.0%)	45 (15.6%)	40 (13.8%)	20 (23.8%)	15 (24.2%)	7 (58.3%)
Adenoma	1092 (59.6%)	538 (71.9%)	740 (66.9%)	228 (78.9%)	208 (71.7%)	68 (81.0%)	48 (77.4%)	12 (100.0%)

A215
CHANGING INCIDENCE OF INFLAMMATORY BOWEL DISEASE IN THE PEDIATRIC POPULATION OF BRITISH COLUMBIA
J.M. Chan[3], M.W. Carroll[2], M. Smyth[2], Z. Hamilton[2], R. Prosser[2], D. Evans[2], G. Rosenfeld[3], K. Jacobson[1]

1. BC Children's Hospital, Vancouver, BC, Canada; 2. Divison of Gastroenterology, Hepatology & Nutrition, BC Children's Hospital, Vancouver, BC, Canada; 3. University of British Columbia, Vancouver, BC, Canada
Background: Inflammatory Bowel Disease (IBD) is a chronic relapsing intestinal inflammatory disease that manifests most often early in life. Though rarely fatal, there is no cure thereby requiring life-long management with significant health care burden. Canada presents a robust platform for administrative health database study with its single payer health care system and high prevalence of IBD . The incidence rate of childhood onset of IBD has been increasing worldwide and increases in pediatric IBD have been found in Ontario but no study has been undertaken in British Columbia (BC). Our group obtained an IBD cohort from the BC Ministry of Health with full hospitalization, physician services and drug dispensation databases between 1991 and 2011.
Aims: Applying an Ontario-derived validated case definition of IBD, we aimed to determine the province-wide epidemiology of pediatric IBD in BC and impact on health care utilization, comparing the results with the established BC Children's Hospital (BCCH) IBD registry. We **hypothesized** that pediatric IBD is increasing and associated with increased health utilization and burden.
Methods: All patients registered as being entitled to receive health related services in BC between 1994 and 2008 were eligible for study. IBD cases were identified using a combination of IBD-coded physician encounters and hospitalizations. Age and gender standardized incidence and prevalence rates were calculated and fitted to Poisson regression models. Trends of utilization outcomes such as rates of utilization of specialist, general practitioner, hospital IBD-related services and IBD-related medications were determined over time using bootstrap resampling.
Results: The overall incidence of IBD increased from 4.7 (95% CI 4.4 – 4.9) in 1994 to 5.7 (95% CI 5.5 – 6.0) per 100,000 children in 2008; lower than the incidence of the BCCH cohort which increased from 4.3 to 9.6 per 100,000. Children aged 10-17 had the highest and greatest rise in incidence. Overall, the hospital days-of-stay rate for IBD-related stays was 5.2 times greater than for non-IBD-related stays (95%CI 3.7 – 7.0), higher in older children. Older children also had 35% more IBD-related outpatient physician visits PPY (95%CI 2% – 79%) than younger children. However, there was a decrease in the rate of IBD-related physician visits from 1996-98 to 2006-08 of almost 1 visit per person year (0.94; 95%CI: 0.5 – 1.4). Finally, we explored the efficacy of using prescription records to better identify IBD cases. The most stringent definition identified a net potential increase of 313 cases, a 28% gain.
Conclusions: Though pediatric IBD and associated health care utilization are increasing in BC, we identify limitations of applying province-specific case definitions and propose further investigation.

A216
HEALTH CARE UTILIZATION PATTERNS BASED ON HEALTH ADMINISTRATIVE DATA ARE MODERATELY EFFECTIVE AT PREDICTING DISEASE BEHAVIOUR AT DIAGNOSIS IN ULCERATIVE COLITIS PATIENTS
T. Shukla[2], S. Murthy[3], M. Belair[2], T. Ramsay[2], G.C. Nguyen[1], E. Benchimol[2]

1. Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; 2. Internal Medicine, University of Ottawa, Ottawa, ON, Canada; 3. University of Ottawa, Ottawa, ON, Canada

Aims: Population-based health administrative data (HAD) is becoming increasingly popular to conduct observational studies in patients with inflammatory bowel disease (IBD). The inability to ascertain IBD phenotypes using HAD is a major limitation of using this data for research. We evaluated whether combinations of health care utilization patterns ascertained from HAD in Ontario, Canada could be used to predict disease activity and extent at diagnosis in ulcerative colitis (UC) patients. This would significantly improve the quality of future HAD-based research in UC patients.
Methods: Consecutive patients who were diagnosed with UC at The Ottawa Hospital (TOH) between October 1, 2001 and March 31, 2012 were identified from a large hospital database and characterized through chart review on endoscopic disease extent and activity at initial diagnosis. Colitis extent was classified as proctitis, left-sided colitis or extensive colitis, based on the Montreal classification, and colitis activity was classified as normal, mild, moderate or severe, using the Mayo endoscopic classification. These patients were linked to Ontario HAD using unique identifiers. Health care utilization patterns and outcomes that were suspected to be associated with disease extent and/or activity were ascertained from Ontario HAD for each patient. Variables were individually tested for their association with disease phenotypes over 1, 2 and 3 years following UC diagnosis to determine the optimal exposure timeframe. Multivariable logistic regression was used to model 6 unique phenotypic classification schemes. Backwards elimination was used to produce parsimonious models and bootstrap validation was performed to produce accurate estimates of model performance statistics.
Results: 587 UC patients characterized on disease extent and activity at diagnosis were linked to Ontario HAD to validate the predictive models. Health care utilization and outcome parameters performed best when ascertained over 1 year following diagnosis. Multicollinearity was not observed for any of the 20 independent variables tested in the regression models. Following variable selection and bootstrapping, the final models modestly predicted disease phenotypes, with c-statistic values ranging between 0.663 and

EPIDEMIOLOGY

EPIDEMIOLOGY

0.729. Interaction terms and transformations of variables did not impact model fit or predictive power.
Conclusions: Health care utilization patterns based on Ontario HAD are moderately effective at predicting disease behaviour at diagnosis in ulcerative colitis patients. External validation of the models will be conducted in future work. Similar strategies to improve the quality of studies in IBD should be adopted in other jurisdictions that use HAD.

A217
HOSPITAL RE-ADMISSION IS ASSOCIATED WITH DE-CREASED SURIVIVAL IN PATIENTS WITH CIRRHOSIS: A POPULATION-BASED STUDY
J.A. Flemming, Y. DeWit, P. Groome, C.M. Booth

Queen's University, Kingston, ON, Canada

Background: Patients with cirrhosis have high rates of hospital re-admission. The association between short-term re-admission and long-term survival at the population level is unknown.
Aims: Our study aimed to examine the relationship between 30 and 90 day hospital re-admission and overall survival in patients with cirrhosis in Ontario, Canada.
Methods: Population-based cohort study using the data holdings from the Institute of Comparative Evaluative Sciences from 1992-2015. Individuals with cirrhosis were identified using validated administrative coding algorithms. Those with at least one hospital admission after cirrhosis diagnosis from 1992-2012 resulting in discharge were included with follow-up to 2015. Data on demographics, hospitalizations, and survival were defined using linked administrative datasets. Overall survival (OS) after index hospital discharge was described using Kaplan-Meier curves and the log-rank test. The association between 30 and 90 day hospital re-admission and OS post-discharge were evaluated using multivariate Cox proportional hazards regression.
Results: Out of 178,152 patients with cirrhosis, a total of 116,047 had a least one hospital admission resulting in 443,706 unique hospitalization events and formed the cohort; 61% male, median age 58 yrs (IQR 47-68 yrs) and 60% died during a median follow-up of 7.6 yrs (IQR 3.0-14.5 yrs). A single hospital admission was identified in 30% while 5 or more admissions occurred in 27%, median length of stay was 5 days (IQR 2-10 days). The 30 and 90 day re-admission rates were 19.9% and 33.4% respectively. The median OS post-discharge was considerably shorter in patients re-admitted by 30 days (2.6 yrs, 95% CI 0.5-9.7 yrs) or 90 days (3.0 yrs, 95% CI 0.7-10 yrs) compared to those > 90 days/never re-admitted (6.0 yrs years, 95% CI 1.6-16.7 yrs, P < .001). After adjusting for potential confounders, those re-admitted within 30 or 90 days had a higher hazard of death post-discharge then those who were not (HR 1.51, 95% CI 1.48-1.53, P < .001; HR 1.42, 95% CI 1.40-1.44, P < .001 respectively). Other factors associated with decreased OS were a liver-related admission (HR 1.32, 95% CI 1.29-1.34, P <.001), receipt of paracentesis (HR 1.55, 95% CI 1.50-1.59, P <.001), male gender (HR 1.19, 95% CI 1.17-1.22, P < .001), older age (HR 1.20 per 5-yr, 95% CI 1.19-1.20, P < .001) and Charlson score ≥ 4 (HR 2.31 95% CI 2.23-2.39, P < .001).
Conclusions: Re-admission at 30 or 90 days in patients with cirrhosis is a strong predictor of a decreased OS. These results can be used when counselling patients and families regarding prognosis and identifying high-risk patients where interventions to prevent re-admission may improve outcomes.

A218
VALIDATION OF A CIRRHOSIS CASE DEFINITION IN CANADIAN ADMINISTRATIVE DATA
J.A. Flemming[1], D. Carlone[1], Y. DeWit[3], L. Lapointe-Shaw[4], J. Kwong[4], J. Feld[2]

1. Queen's University, Kingston, ON, Canada; 2. Medicine, University Health Network University of Toronto, Toronto, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Kingston, ON, Canada; 4. University of Toronto, Toronto, ON, Canada

Background: Administrative and population-based databases can be utilized for health services research related to cirrhosis. The performance of coding algorithms for the identification of patients with cirrhosis in Canadian administrative data has not been previously defined.
Aims: To validate the use of International Classification of Disease (ICD) algorithms to identify patients with cirrhosis using administrative data from Ontario, Canada.
Methods: We performed primary chart abstraction of 458 consecutive patients seen in the tertiary care Liver Clinic at Hotel Dieu Hospital in Kingston, Ontario from May – August 2013. In order to define the presence or absence of cirrhosis and related decompensations, details regarding the etiology and severity of liver disease were abstracted. The gold-standard definition of cirrhosis was based on the presence of cirrhosis after chart review by two hepatologists. This data was then linked to the administrative databases of the Institute for Clinical Evaluative Sciences. We used ICD-9, ICD-10 and Ontario Health Insurance Plan billing codes for cirrhosis, cirrhotic decompensations, and chronic liver diseases to develop multiple coding algorithms for the identification of cirrhosis. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each based on the gold standard cirrhosis definition.
Results: A total of 10 different algorithms were evaluated. Overall, the use of one inpatient or one outpatient code for cirrhosis resulted in the highest

sensitivity (79%; CI 74% - 84%) with a specificity of 79% (CI: 73% - 85%), PPV 81% (CI: 75%-86%), and NPV 78% (CI: 71%-83%). Using 2 outpatient or 1 inpatient codes for cirrhosis plus a decompensation code plus a chronic liver disease code resulted in the highest specificity (99%; CI: 96% - 100%) and PPV 95% (CI: 86% - 99%), however this was associated with a large drop-off in sensitivity (24%; CI: 19% - 31%) and NPV 54% (CI: 49% - 59%).
Conclusions: The use of ICD coding algorithms can effectively identify patients with cirrhosis using administrative data from Canada and can be used in future health services research studies.

Funding Agencies: Southeastern Ontario Academic Medical Association New Clinician Scientist Award

A219
HEPATITIS C IN NOVA SCOTIA PATIENTD WITH HEREDITARY BLEEDING DISORDERS: AUDIT FOR IDENTIFICATION OF PATIENTS FOR POTENTIAL TREATMENT WITH DIRECT ACTING ANTIVIRAL AGENTS
A. Alahmadi[1], S. Mishra[1], G. Hirsch[3], B. carla[2], K. Robinson[2], K.M. Peltekian[2]

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

Background: Individuals with hereditary bleeding disorders (HBD) represent a unique population who were exposed to hepatitis C virus (HCV) through blood products prior to 1990. The Krever Commission in 1997 described the flawed organization of blood product delivery in Canada and recommended the federal/provincial governments identify and treat these patients.
Aims: Our primary goal was identifying all HBD patients with ongoing HCV viremia who would be candidates for treatment with direct acting antiviral agents. Secondary goal was to describe the burden of HCV in our cohort of HBD patients.
Methods: We retrospectively audited the charts of all patients seen at the Adult Hereditary Bleeding Disorder Clinic at the Queen Elizabeth II Health Sciences Centre (QEII-HSC) in Halifax, Nova Scotia, Canada from 1997-1999 who were infected with Hepatitis C. We recorded current survival status, sustained virologic response (SVR), hepatic decompensation, and need for transplantation. Thereafter the pre-existing hepatology medical records was used to determine how many patients were referred for transplantation their status up to the summer of 2015.
Results: A total of 40 HCV(+) patients, 29 males (72.5%) and 11 females (27.5%) were identified with 1 lost for follow up (2.5%). HCV-PCR was positive in 29 (80.6%). Only 15 (51.7%) were treated previously for HCV with sustained viral response in 10 (66.67%) – the

majority with interferon-based therapies. Hepatic decompensation occurred in 7 patients (18%), HCC in 2 (5%), 2 underwent transplantation (5%) and 8 patients were deceased (20.5%).
Conclusions: Our chart audit resulted in identification of 11 HCV infected patients who are still alive from the original cohort of 40 patients who may be candidates for therapy with interferon-free direct acting antiviral agents.

Funding Agencies: None

A220
THE EFFECT OF HOMELESSNESS ON HCV TREATMENT OUTCOMES AMONG PEOPLE WHO INJECT DRUGS
A. Singh, G. Kiani, R. Shahi, A. Alimohammadi, T. Raycraft, B. Conway

Vancouver Infectious Diseases Centre, Vancouver, BC, Canada

Background: Recent European guidelines have identified people who inject drugs (PWID) as a priority population to receive HCV treatment. Achievement and maintenance of a sustained virologic response (SVR) may be influenced by a number of factors, including the social determinants of health in such vulnerable populations. One such variable may be unstable housing.
Aims: We sought to evaluate the impact of homelessness on the achievement and maintenance of SVR in both HCV mono-infected and hepatitis C/human immunodeficiency virus (HCV/HIV) co-infected PWID receiving HCV therapy at a tertiary clinic located in downtown Vancouver.
Methods: The target population consisted of HCV-infected PWID receiving HCV therapy according to contemporary clinical guidelines within the multidisciplinary program at the Vancouver Infectious Diseases Center (VIDC), providing care to address medical, psychological, social and addiction-related needs. Demographic information was collected including patters of recreational drug use. Self-declared homelessness was ascertained by a self-administered questionnaire. The initial endpoint of the study was achievement and maintenance of SVR, with patients followed every 6 months after SVR, more frequently in the setting of suspected HCV re-infection, with such re-infection post-SVR considered a failure of treatment.
Results: The study population included 38 individuals of whom 7 (12.5%) women, 20 (53%) HIV co-infected, 24 (63%) genotype 1, 20 (53%), on opiate substitution therapy, with mixed patterns of recreational drug use (39% opiates, 17% cocaine, 47% amphetamines). Homelessness was present in 38 (100%). The crude SVR rate was 79% (30/38), higher in HCV mono-infected individuals (89% vs. 70%). In addition, 2 cases of HCV re-infection were documented, all among HIV co-infected individuals, leading to an effective SVR rate of 60% in this sub-group. Overall, homelessness was

associated with a 30% increase in risk of not achieving and maintaining SVR. Type of recreational drug use (opiates vs. stimulants) was not associated with the likelihood of HCV treatment success.

Conclusions: High rates of response to HCV treatment can be achieved and maintained among active PWID. However, in this vulnerable population, attention must be paid to non-traditional factors that may influence outcomes, including homelessness, especially among those who are co-infected with HIV. As more PWID are offered HCV therapy, programs must be developed to address short and long-term housing to maximize the impact of these interventions.

Funding Agencies: None

A221

A RETROSPECTIVE ANALYSIS OF PATIENTS WITH BIOPSY PROVEN NASH IN AN URBAN CENTRE.

K. Boctor[1], M. Elkhashab[3], M. Magnes[2]

1. Gasteroenterology & Hepatology, Toronto Liver Center, Toronto, ON, Canada; 2. Toronto Liver Centre, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada

Background: Fatty Liver Disease (FLD) has become the most common liver disease in Canada with at least 25% of the population afflicted. With that number on the rise, the need for non-invasive tools for diagnosis and management has become vital.

Aims: We sought to gain a better understanding of the population of patients affected with FLD in order to better understanding of the burden of disease on the community. We also compared liver fibrosis diagnosed via liver biopsy to those diagnosed with fibroscan (liver stiffness).

Methods: 67 patients who had undergone a Liver Biopsy for confirmative diagnosis of NASH (non-alco-holic steatohepatitis) and staging of liver fibrosis. All Liver biopsies with were conducted at one facility and interpreted by a liver pathologist. Fibroscan tests were conducted at a separate facility and liver stiffness was measured in kilopascals. Data was collected and retrospectively analysed for: patient demographics, fibroscan values, and Liver Biopsy report. Only patients with NAS≥2 (NASH Activity Score) were included in the study.

Results: The primary reason for referral for all 67 patients was an elevated ALT discovered by family physicians. Of the 67, 41 males, and 26 females. Mean age for males was 48.39, and females 52.46.

Of the 67 patients studied, 65 underwent both a fibroscan and biopsy with a mean time of 161.46 days in between the two tests.

Fibroscan: Mean LS was 11.60kPa, with 11.60kPa, and 11.30kPa for males and females, respectively. (Table 2 for gender breakdown). 39 of the 67 patients

underwent serial fibroscans.

Liver Biopsy: 6 of 7 patients with NAS=2 had significant fibrosis by Brunt. NAS score correlated to LS with P-value of 0.021. Only 2 patients underwent serial liver biopsies. (Refer to Table 1 for fibrosis stages by Brunt.)

Conclusions: Based on our study cohort, more males at a younger age were effected by NASH. A discrepancy was found between fibrosis staging by fibroscan vs. biopsy. Meanwhile, NAS score strongly correlated to LS suggesting that LS proves to be a useful non-invasive tool to diagnose and monitor patients with NASH.

Fibrosis Staging by Liver Stiffness (kPa) vs Fibrosis (Brunt/4).

No. of Patients Diagnosed By:	Liver Stiffness (kPa)	Liver Biopsy (Brunt)
Firbosis Stage		
0	0	7
0 to 1	3	2
1	4	19
1 to 2	7	0
2	15	6
2 to 3	8	7
3	12	15
3 to 4	7	3
4	5	7
Cirrhosis	4	1
Total No. of Patients	65	67
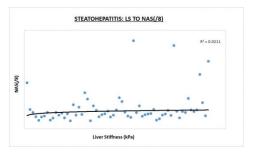
Figure 1: Assessment of Fibrosis by Liver Stiffness (kPa) vs. NASH Activity Score (NAS).

Funding Agencies: None

A222

INCREASING PREVALENCE OF CIRRHOSIS IN ONTARIO OVER THE LAST 20 YEARS: A POPULATION-BASED STUDY

J. Saperia, Y. DeWit, C.M. Booth, P. Groome, J.A. Flemming

Queen's University, Kingston, ON, Canada
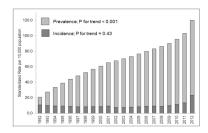
Background: It is estimated that 1 in 4 Canadians have chronic liver disease and are at risk of developing cirrhosis. There is a paucity of population-based studies examining the temporal trends in the burden of cirrhosis in North America.

Aims: To describe secular trends in the epidemiology of cirrhosis in Ontario, Canada over the past two decades.

Methods: This is a retrospective population-based cohort study of patients with cirrhosis in Ontario from 1992-2012 using data from the Institute of Comparative Evaluative Sciences. Follow-up was until December 31, 2015. Individuals with cirrhosis were identified using validated administrative coding algorithms. Data on demographics and survival were defined using linked administrative datasets. Annual adjusted incidence and prevalence rates were calculated standardizing to the 1991 Canadian population stratifying on age and sex. Comparison between rates was done using Poisson regression.

Results: A total of 178,152 patients with cirrhosis were included. Median age at diagnosis was 56 years (IQR 45-67 years), 61.6% male with 53% dying over a median follow-up of 5.2 years (IQR 1.5-11.4 years). The adjusted incidence rate did not change over the study period with an average rate of 10.4/10,000 (P = 0.43, figure). However, there was a significant rise in the adjusted prevalence with the rate increasing from 20.7/10,000 in 1992 vs. 120/10,000 in 2012 (P <.001, figure) representing an almost 6-fold increase. The growth in disease burden was higher in men than in women (P <.001) with the majority occurring in males over the age of 55 years and the most dramatic increase in men over the age of 80 years (prevalence rate 56.2/10,000 in 1992 vs. 419.4/10,000 in 2012, P <.001).

Conclusions: The burden of cirrhosis in Ontario has increased at a rapid rate over the last two decades likely due to the aging hepatitis C population and the epidemic of fatty liver disease while at the same time is becoming a disease of the elderly men. These results support the urgent need for both a national hepatitis C and liver strategy in attempt to reverse these trends.

A223
MOSAIC: AN INTERNATIONAL MULTICENTRE PROSPECTIVE OBSERVATIONAL STUDY TO EVALUATE THE EPIDEMIOLOGY, HUMANISTIC AND ECONOMIC OUTCOMES OF TREATMENT FOR CHRONIC HEPATITIS C VIRUS (HCV)

M. Elkhashab[3], W. Ghesquiere[6], S. Lee[5], S. Shafran[4], D. Webster[7], E. Tam[8], C. Pinsonnault[1], N. Ackad[2]

1. Medical, Abbvie Corporation, Saint-Laurent, QC, Canada; 2. Medical Affairs, Abbvie Corporation, Montreal, QC, Canada; 3. Toronto Liver Centre, Toronto, ON, Canada; 4. University of Alberta, Edmonton, AB, Canada; 5. University of Calgary, Calgary, AB, Canada; 6. Medicine, Vancouver Island Health Authority, Victoria, BC, Canada; 7. Dalhousie University, Halifax, NS, Canada; 8. LAIR centre, Vancouver, BC, Canada

Aims: The advent of direct acting antivirals is expected to improve the management of Chronic Hepatitis – C (c-HCV).

Methods: MOSAIC an observational study conducted in 30 countries describes the profile of c-HCV patients and the impact of Interferon (IFN) treatment on Patient Reported Outcomes and outpatient consultations (Table). Consecutive c-HCV patients initiated on IFN-based treatment were followed for 48 weeks.

Results: Of 346 invited patients 279 participated; (189 treatment-naïve and 90 treatment-experienced). IFN-treatment was initiated for 55 (20%): DAA+peg-IFN+RBV: 5, peg-IFN+RBV: 19, IFN+RBV: 1, other: 30. Main reasons for not initiating IFN for physicians were: waiting for new options (32%, 13%); tolerability (15%, 7%); contraindications (9%, NA); costs (7%, 1%) and for patients inconvenience (2%); impact on social/family life and work (9%).

Demographic characteristics {Mean (SD) [Range]} of the 55 treated patients: Age: 52.1 (10.39) [31-74] yrs; Duration since HCV diagnosis: 10.8 (10.1) [0 – 46] yrs; and 69.1% male. Baseline cirrhosis status was: minimal/no fibrosis: 20(36.4%), bridging fibrosis: 16(29.1%), cirrhosis: 11(20.0%), portal fibrosis: 4(7.3%) and NA: 4(7.3%).

Genotype was G1: 34(61.8%), G3: 11(20.0%), G2: 6(10.9%), G6: 2(3.6%) and n = 1 (1.9%) each for G4, G5. Baseline HCV-RNA level was <800,000 IU/ml: 20(36%), > 800,000 IU/ml: 26(47%) x IU/mL, positive by qualitative assay: 5 (9%), NA: 4(7%).
Employment decreased from 46% to 33%. Outpatient consultation during treatment was none: 64%; 1: 11%. >=4: 20%.

Conclusions: IFN use in c-HCV patients in MOSAIC is low. Patients treated with IFN-containing regimens experience a substantial negative impact on QoL and productivity. Anticipated availability of new IFN-free

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

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regimens is the main reason for not initiating treatment with IFN.

Change from baseline

Measure Mean (SD) [n]	Baseline	4 weeks	12 weeks	EOT
EQ-5D-5L	0.8(0.20) [54]	-0.03(0.13) [48]	-0.05(0.15) [48]	-0.04(0.14) [45]
HCV-PRO	64(20.6) [54]	-7.3(16.0) [51]	-11.4 (20.4) [48]	-10. (21.8) [46]
WPAI−Absenteeism (%)	13(22) [20	12.5(30.1) [12]	23.7 (40.5) [9]	-13.5 (30.5) [8]
WPAI−Presentism (%)	18(25) [21]	15.7(19.9) [14]	24.2 (29.7) [12]	29.2 (33.7) [12]
WPAI−WPI	27(32) [20]	24.7(27.0) [12]	32.4 (37.0) [9]	29.4 (36.6) [8]
WPAI−AI	20.3(25) [29]	23.3(21.2) [24]	27.7 (35.3) [26]	31.3 (37.0) [24]

EOT: End of Treatment; EQ-5D-5L: EuroQol 5; HCV-PRO: Hepatitis C Patient Reported Outcome Instrument; WPAI: Work Productivity and Activity Impairment Questionnaire; WPI: Work Productivity Impairment; AI: Activity Impairment.

ESOPHAGUS, GASTRIC AND DUODENAL ULCER DISORDERS

A224
RISK OFGASTRIC CANCER IN PATIENTS WITH GASTRIC INTESTINAL METAPLASIA AT 5-YEAR FOLLOW-UP

R. Pittayanon[1], R. Rerknimitr[2], N. Klaikaew[2], A. Sanpavat[2], P. Kullavanijaya[2], A.N. Barkun[1]

1. McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 2. King Chulalongkorn Memorial Hospital AND Chulalongkorn University, Bangkok, Thailand

Background: Gastric intestinal metaplasia (GIM) is a premalignant condition of intestinal-type gastric cancer. However, its management is not well-established.
Aims: The objective of this study was to determine the risk factors for gastric cancer in a population of patients with GIM in order to propose appropriate clinical recommendations in a setting of low prevalence area of gastric cancer.
Methods: Ninety-one patients with previously diagnosed GIM between 2004 and 2014 were recruited for surveillance EGD every 6 to 12 months until a diagnosis of gastric cancer or completion of the planned 5-year follow-up duration. Possible risk factors for gastric cancer that were assessed included sex, age, smoking,

alcohol, salty and preservative food ingestion, *H. pylori* infection, family history of gastric cancer, staging of Operative Link on Gastritis Assessment (OLGA) and Operative Link on Gastric Intestinal Metaplasia Assessment (OLGIM), type of GIM, serum pepsinogen I, pepsinogen II, IL-1RN and IL-1B, as well as histological appearance (mature versus immature GIM and the presence of dysplasia).
Results: The mean follow-up period was 4.05±2.5 years. At initial presentation, 81 of the 91 patients (89%) had mature GIM (mGIM), whereas the remaining 11% had a study entry diagnosis of immature GIM (iGIM). No cancer developed amongst patients with mGIM. In contrast, 5 of the 10 patients exhibiting iGIM (50%) progressed to HGD (n=2) or cancer (n=3). Male gender (p=0.027), iGIM (p=0.001) were associated with high risk histology (dysplasia or cancer, diagnosed in 6 patients) by study end. A trend suggested a possible association with smoking as well (P=0.08)
Conclusions: Male patients and those with iGIM are at greatest risk of developing dysplasia or early gastric cancer. Six- monthly interval surveillance with EGD in elderly male patient with iGIM is justified for early detection of possible progression, so that curative treatment may be offered.

A225
THE UTILITY OF SEPARATE DISTAL AND MID-ESOPHAGEAL BIOPSIES IN THE DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS (EOE).
ALKHATTABI M[1,3], KUBICA M[2], DRIMAN D[2], GREGOR J[1]
1 DEPARTMENT OF MEDICINE, WESTERN UNIVERSITY.
2 DEPARTMENT OF PATHOLOGY, WESTERN UNIVERSITY.
3 DEPARTMENT OF MEDICINE, KING ABDULAZIZ UNIVERSITY, RABIGH CAMPUS, SAUDI ARABIA.

M. Alkhattabi[1], M. Kubica[2], D. Driman[2], J.C. Gregor[1]

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

Background: EoE is an increasingly recognized cause of upper gastrointestinal symptomatology particularly dysphagia. The gold standard for diagnosis is the presence of increased eosinophils on esophageal biopsies. To distinguish EoE from esophageal eosinophilia due to gastroesophageal reflux disease (GERD), many physicians routinely separate biopsies from the mid and distal esophagus, theorizing that eosinophils will be more numerous in the distal esophagus in GERD and more diffusely distributed in EoE. The aim of our study was to determine if this approach was truly helpful in clinical practice.
Aims: To determine the utility of comparing distal and mid-esophageal counts in differentiating EoE from GERD.

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

Methods: All endoscopically obtained biopsies of the esophagus taken at London Health Sciences Centre between July 1, 2011 and June 30, 2014 were eligible for review. Patients were only included if they were 18 year old or older and biopsies were taken from the mid and distal esophagus for non-neoplastic findings and separated for review. The pathology was then reviewed by a pathologist blinded to diagnosis and a mean eosinophil count per high-power field (hpf) was calculated for each area. A delta eosinophil count (DEC) was calculated by subtracting the mean count in the distal esophagus from the mean count in the mid-esophagus. If multiple endoscopies were performed, only the first biopsy after the study initiation date was used.
Results: 603 patients were included in the analysis. Of these 138 (22.9 %) had a final diagnosis of GERD, 124 (20.6 %) EoE and 341 (56.5 %) normal. The most common predominant symptoms in GERD were heartburn 99 (71.7 %) and dysphagia to solids 70 (50.7 %). The most common predominant symptoms in EoE were dysphagia to solids 90 (72.6 %), atopic symptoms 41 (33.1 %), heartburn 40 (32.3 %) and food impaction 38 (30.6 %). The most common endoscopic findings in EoE were furrows 81 (65.3 %), trachealization 70 (56.4 %) and stricture 29 (32.4 %). The mean eosinophil count in the distal and mid-esophagus respectively was 6.6 and 2.8 in GERD, 80.4 and 76.9 in EoE and 0 and 0 in normal patients. The DEC was positive in 20.3 % of GERD patients and 41.1 % of EoE patients. The mean DEC was -3.8 in GERD patients and -3.5 in patients with EoE.
Conclusions: Mucosal eosinophilia is significantly more pronounced in patients with EoE although the difference between eosinophil counts in the mid and distal appears to be of only marginal value in distinguishing between the two diagnoses. Separating specimens for analysis does not appear to be necessary.

Funding Agencies: None

A226
PEDIATRIC COLLAGENOUS GASTRITIS: ENDOSCOPIC & HISTOLOGIC EVOLUTION
B. Chen[1], O. Popescu[3], C. Barker[2]

1. British Columbia Children's Hospital, Vancouver , BC, Canada; 2. British Columbia Children's Hospital, Vancouver, BC, Canada; 3. British Columbia Children's Hospital, Vancouver, BC, Canada

Background: Collagenous gastritis (CG) is a rare condition, characterized by gastric subepithelial collagen bands greater than 10 μm with an inflammatory cell infiltrate within the lamina propria. There is limited understanding of its pathogenesis. Pediatric patients present with anemia and abdominal pain, while adults present with diarrhea associated with collagenous colitis or celiac disease. The natural history of this condition is unknown.
Aims: Case series was performed to describe the clinical, endoscopic and histologic features and evolution of children with collagenous gastritis.
Methods: Chart reviews were conducted on 6 children diagnosed with collagenous gastritis at BC Children's Hospital between 2007 and 2016. Demographic, clinical, endoscopic, and histologic details were collected.
Results: Case details are summarized in Table 1. The series included 4 females and 2 males. All patients underwent at least one upper endoscopy and 2 underwent multiple upper endoscopies. Two patients had colonoscopy performed and another underwent capsule endoscopy, all of which were normal.

Anemia was the primary presentation in 5 of 6 patients. Other symptoms included abdominal pain (2/6), vomiting (2/6) and hematemesis (1/6). All patients tested negative for H. pylori via CLO test on biopsy. Five out of 6 patients underwent serologic testing for celiac disease, which was negative.

Macroscopic findings most commonly included gastric mucosal nodularity followed by erythema, erosions and ulcers. Histology confirmed collagenous gastritis. Two patients also had collagenous duodenitis. Patient 3 was initially diagnosed with eosinophilic gastritis. Subsequent endoscopy demonstrated collagenous gastritis on biopsy. Patient 6 had gastric and antral eosinophilia in addition to gastroduodenitis. Duration of follow-up ranged from 3 months to 3 years.

Treatments for these patients included iron (5/6), budesonide (3/6), and proton pump inhibitor (1/6). All patients either had borderline normal or low ferritin on follow-up, and 2 patients continued to have iron deficiency anemia. Of the 2 patients who had follow-up biopsies, neither had endoscopic or histologic improvement.
Conclusions: Collagenous gastritis is a chronic condition in children. A precursor lesion may be chronic active gastritis with gastric eosinophilia, followed by formation of a subepithelial band of collagen. The endoscopic and histologic evolution warrants further characterization. Anemia and chronic active gastritis may suggest the possibility of developing collagenous gastritis, after common causes are excluded. Current treatments for collagenous gastritis do not appear to alter its course.

TABLE 1

Case	Age	Gender	Location	Presentation	Upper endoscopy (#)	Treatment and follow-up

ESOPHAGUS/GASTRIC

#	Age/Sex	Location	Symptoms	Endoscopic findings	Outcome
1	6 Yr Male	Gastric Duodenal	Iron deficiency anemia, vomiting	(1) Gastric, proximal duodenum: edematous, cobbled (2) Gastric: thickened rugae, antral nodularity Duodenal: nodularity (3) Gastric: edematous, thickened rugae	Budesonide, iron No improvement in symptoms, iron deficiency persistent
2	7 Yr Female	Gastric	Iron deficiency anemia, abdominal pain	(1) Gastric: nodularity in body, fundus	Iron Resolution of abdominal pain, persistent iron deficiency anemia
3	10 Yr Male	Gastric	Iron deficiency anemia	(1) Gastric: hypertrophic rugae, erythema, friability (2) Gastric: erythema, small ulcers, nodularity in fundus (3) Gastric: nodularity, decreased vascularity in body	Budesonide, iron Persistent iron deficiency
4	13 Yr Female	Gastric Duodenal	Iron deficiency anemia, fatigue	(1) Gastric: antral nodularity	Iron Asymptomatic, improvement of iron deficiency anemia
5	14 Yr Female	Gastric	Iron deficiency anemia, hematemesis	(1) Gastric: multiple erosions in body, 2 Mallory-Weiss tears at gastroesophageal junction	Iron, omeprazole Asymptomatic, persistent iron deficiency anemia
6	15 Yr Female	Gastric	Early satiety, abdominal pain, vomiting	(1) Gastric: polyps, body and antral nodularity Duodenal: nodularity	Budesonide Asymptomatic

A227
ASSESSING THE BIOEQUIVALENCE OF NON-PRE-SCRIPTION ESOMEPRAZOLE 20 MG BANDED CAP-SULES AND MULTIPLE-UNIT PELLET SYSTEM TABLETS UNDER FASTED AND FED CONDITION

V. Kumaran[1], J. Li[1], C. Pollack[1], S. Moreira[2]

1. Pfizer Consumer Healthcare, Madison, NJ; 2. GSK Consumer Healthcare, Warren, NJ

Background: Esomeprazole (ESO) 20 mg will soon be available in Canada without a prescription for treating frequent heartburn.
Aims: This study assessed bioequivalence between ESO 20 mg multiunit pellet system (MUPS) tablets and banded capsules.
Methods: This open-label, randomized, 6-period cross-over, partial-replicate study administered single doses of each study drug to healthy males and females under fasted and fed conditions. Reference product (banded capsules) administration was replicated in both the fasted and fed states to establish intrasubject variability for determining the bioequivalence method that will be used. For endpoints with high variability (based on intrasubject standard deviation [SD]) with the reference product ($S_{wr} \geq 0.294$) a reference-scaled average bioequivalence (RSAB) approach was used; an unscaled approach was used for endpoints with low intrasubject variability ($S_{wr} < 0.294$). The primary endpoints were ESO area under the concentration-time curve from zero to infinity (AUC_{inf}) and peak plasma concentrations (C_{max}) while fasted and fed. Bioequivalence was based on the geometric mean ratios (GMRs) being within 0.80, 1.25 and 95% criteria bound (CB) being ≤ 0 for the RSAB approach, and the 90% confidence intervals (CIs) of the GMR being within 80%, 125% for the unscaled approach.
Results: Of the 60 randomized subjects, 46 (76.7%) completed all study periods. While fasted, the mean (SD) ESO AUC_{inf} was 1035.5 (925.7) ng*h/mL for the banded capsules and 985.5 (802.1) ng*h/mL for the MUPS tablets. The GMR (90% CI) was 0.948 (0.890, 1.010), indicating bioequivalence (unscaled). The fasted mean (SD) ESO C_{max} was 511.3 (287.5) ng/mL for the banded capsule and 528.3 (292.1) ng/mL for the MUPS tablet. The GMR (95% CB) was 1.009 (-0.050), indicating bioequivalence (RSAB). Consistent with historical data, ESO AUC_{inf} and C_{max} were noticeably lower in the fed state for the ESO 20 mg banded capsule (537.9 [538.2] ng*h/mL; 154.5 [109.7] ng/mL) and MUPS tablet (637.1 [586.8] ng*h/mL; 217.9 [162.0] ng/mL) versus the fasted state. The GMR (95% CB) for AUC_{inf} met bioequivalence criteria (0.994 [-0.061]), but C_{max} (1.341 [-0.156]) did not (both RSAB).
Conclusions: The ESO 20 mg MUPS tablets and banded capsules were found to be bioequivalent based on ESO AUC_{inf} and C_{max} under fasted conditions, suggesting these products can be used interchangeably.

ClinicalTrials.gov Registration: Per the FDAAA 801 definition of an applicable clinical trial, this phase 1 trial was not registered.

A229
CLINICAL AND ENDOSCOPIC CHARACTERISTICS OF LYMPHOCYTIC ESOPHAGITIS

T. JEYALINGAM, A. Almazroui, C. Streutker, M.A. Scaffidi, D.J. Low, S.C. Grover

Medicine, St. Michael's Hospital, Toronto, ON, Canada

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Background: Lymphocytic esophagitis (LE) is a pathologic diagnosis characterized by intraepithelial lymphocytic (IEL) infiltration of the esophageal epithelium. It is a recently acknowledged disease entity, and remains underexplored in the literature. Moreover, the pathophysiology, clinical presentation and endoscopic associations of LE are still unclear.
Aims: To characterize the demographic, clinical, pathologic and endoscopic findings of LE.
Methods: This is a case series conducted at a single academic centre. Patients with histologic findings suggestive of LE from esophageal biopsies done from 2010 to 2016 were identified from a clinical database. Patient demographics, comorbidities, clinical presentations, treatments, imaging findings and endoscopic features were extracted from electronic medical records and descriptive statistics were performed.
Results: Twenty-four patients with LE were identified. The average age was 58.5 and 71% were male. Common comorbidities included HIV (20.8%), asthma (16.7%), and diabetes mellitus (12.5%). The most prevalent clinical presentations were dysphagia (75%), reflux (66.7%), and food bolus obstruction (16.7%). Endoscopy and imaging most frequently demonstrated esophageal rings or webs (50%), esophagitis (20.8%), strictures (20.8%), and furrows (16.7%). In 20.8% of patients, the treating gastroenterologist did not make a definitive clinical diagnosis. Treatments employed included proton pump inhibitors (62.5%), esophageal dilatation (37.5%) and topical steroids (16.7%).
Conclusions: LE occurs predominately in males and a sizeable proportion demonstrate HIV positivity, dysphagia or reflux; frequent endoscopic abnormalities include esophageal rings, webs, and strictures. Treatment approaches were variable, although the most common modalities used were proton pump inhibitors, endoscopic dilatation and topical steroids. Further studies are needed to confirm these findings as well as characterize the natural history and efficacy of treatment modalities for this rare condition.

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A230
DRESS: AN UNUSUAL CASE OF UPPER GASTROINTESTINAL BLEED
B.P. Chan[2], K. Khan[1]

1. McMaster University, Hamilton, ON, Canada; 2. Gastroenterology, McMaster University, Hamilton, ON, Canada

Background: A 77-year-old male was admitted to hospital after a four week course of Piperacillin Tazobactam for a liver abscess, with a diffuse morbiliform rash. He was found to have drug reaction with eosinophilia and systemic symptoms (DRESS). During his in-hospital course, he had a severe upper gastrointestinal bleed (UGIB) and endoscopy revealed a large, circumferential ulcer at the incisura.

Aims: We present a case of upper gastrointestinal bleed secondary to DRESS and review the literature of DRESS and upper gastrointestinal bleed.
Methods: A literature search of DRESS and gastrointestinal bleeds was performed on the OVID Medline(R) and PubMed databases. Search terms for DRESS were "DRESS syndrome," "drug reaction with eosinophilia and systemic symptoms," "drug rash with eosinophilia and systemic symptoms," "drug hypersensitivity and eosinophilia," and "drug-induced hypersensitivity syndrome." Search terms for gastrointestinal bleed were "upper gastrointestinal bleed," "gastrointestinal bleed," "gastrointestinal hemorrhage," and "peptic ulcer." There were no limits placed on publication year or language.
Results: DRESS is an adverse systemic reaction to a variety of medications, with a high mortality rate. Antiepileptics and allopurinol are the most commonly described causative agents. Gastrointestinal bleed has previously been reported in association with DRESS, although this has only been in the setting of cytomegalovirus (CMV) reactivation.
Conclusions: We report the first known case of severe upper gastrointestinal bleed in the setting of DRESS with negative CMV status. We propose the pathogenesis underlying gastrointestinal bleed and DRESS is similar to other inflammatory conditions predisposing patients to upper gastrointestinal bleeds.

Funding Agencies: None

A231
A RANDOMIZED CLINICAL TRIAL TO DETERMINE THE EFFICACY OF THE BIOVAC DIRECT SUCTION DEVICE DURING UPPER GASTROINTESTINAL BLEEDING: A FEASIBILITY ANALYSIS
H. Gregor[1], D. Segal[6], a. rammal[2], B.S. Thomas[4], J.C. Gregor[3], B. Yan[5], M. Sey[3]

1. Gastroenterology, London Health Sciences Centre, London, ON, Canada; 2. London health science centre , London , ON, Canada; 3. Western University, London, ON, Canada; 4. Medicine, Western University, London, ON, Canada; 5. Medicine, Gastroenterology, Western University, London, ON, Canada; 6. department of medicine, western university, London, ON, Canada

Background: Inadequate visualization during upper gastrointestinal bleeding (UGIB) is a common problem. The BioVac direct suction device is designed to enhance endoscopic suction to improve visualization. We initiated a randomized clinical trial to determine the efficacy of this device (NCT02150941).
Aims: In this report, we present the results of a feasibility analysis.
Methods: Between July 2014 and June 2016, patients admitted to two academic hospitals undergoing endoscopy for UGIB with suspicion of active bleeding (ie. fresh blood hematemesis, hemodynamic instability, acute drop in hemoglobin) were invited to participate. EGD was performed and patients where the source of

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bleeding was not found due to poor visualization after 5 minutes were randomized to BioVac or standard endoscopy suction. Due to the difference in suctioning power, a placebo was not possible. Instead, the procedure was recorded and assessed by a blinded outcome assessor. The procedure was otherwise performed at the discretion of the endoscopist without input from the study staff. The primary outcome was whether the bleeding source was found. Secondary outcomes included the mucosa visualization score, endoscopic therapy, need for repeat endoscopy within 7 days, rebleeding, and 30-day mortality.

Results: Over 24 months, a total of 70 subjects were recruited. 60 subjects were excluded due to the source of bleeding being found within the first 5 minutes or there being no blood in the upper GI tract. Of the 10 subjects randomized, 7 were assigned to standard endoscopy suction and 3 to BioVac. The mean (SD) age was 68.3 (13.4) and 30% were females. 60% presented with fresh blood hematemesis, 30% had a history of cirrhosis, 50% bled as an inpatient, and 60% had an ASA score of ≥4. The source of bleeding was found in 66% in the BioVac group and 71% among the controls. The mean (SD) mucosal visualization score was 15.3 (2.6) for BioVac and 7.7 (3.3) for controls although there was no difference in the application of endoscopy therapy (33% in both groups). 33% in the BioVac group and 83% in the control group required a repeat endoscopy within 7 days. No patients rebleed or died in the BioVac group compared to 3 who rebleed and 4 who died in the control.

Conclusions: Study feasibility is hampered by low recruitment and high exclusion rates. A multi-centre approach to increase recruitment and the development of a better clinical prediction tool for active bleeding are required.

Funding Agencies: Vantage Endoscopy

A232
COMBINATION OF EVAC AND BARIATRIC STENTS IN THE MANAGEMENT OF ESOPHAGEAL PERFORATION
N. Clermont Dejean, J. Phaneuf, C. Ménard

Medecine, CHUS, Sherbrooke, QC, Canada

Background: Treatment of oesophageal perforation relies on endoscopic procedures.
Aims: We present a case of iatrogenic oesophageal perforation treated with a novel endoscopic treatment
Methods: Review of litterature with PubMed, Ovid Medline. Key words EVAC, stent, esophageal perforations, vaccum system
Results: An 84-year-old lady was refered for an oesophageal perforation following a para-esophageal hiatal hernia repair. The perforation was complicated by a intra-thoracic collection. A previous percutaneous drainage had failed. A first gastroscopy (EGD) performed demonstrated a 1x2cm distal oesophageal perforation leading to a 13.7x22.1cm cavity. A

22mmx120mm stent (Hanarostent Esophaus Bening BS (CCC), M.I. Tech, South Korea) was put in place. A barium swallow 2 days later revealed a persistent leak and partial migration of the stent. A second EGD was performed, an EVAC system was constructed with a sponge (V.A.C. Therapy GranuFoam, Kinetic Concepts, USA) fixed to a nasogastric tube. The material was positioned at the perforation site and sealed in place with a 28x240mm bariatric stent (Hanarostent Esophagus Bariatric Surgery (CCC)). Oral nutrition was resumed and tolerated. Fourteen days later, an EGD showed a 50% reduction in the size of the cavity. The EVAC was reinstalled and a regular 22x120mm stent was placed (Hanarostent Esophagus Benign BS (CCC)). In order to prevent its migration its proximal portion was anchored to the nasogastric tube with a clip (Resolution Clip, Boston Scientific, USA). Unfortunately a leak occurred and a fouth EGD was required 6 days later. The stent was replaced by a 28x240mm bariatric stent. Twenty-one days later the last EGD confirmed complete regression of the cavity and healing of the oesophageal defect. The endoscopic material was removed and oral nutrition continued. To our knowledge this is the first case in which an iatrogenic oesophageal perforation is managed using the combination of EVAC and bariatric stents. Gubler et al described the use of EVAC with regular endoscopic stents but in their cases oral nutrition could not be resumed between the endoscopic interventions and the use of stents was required after removal of the EVAC system. We believe that the use of bariatric stents was the corner stone of our management. With their larger diameter they provide complete apposition of the material to the mucosal wall providing excellent sealing, allowing oral nutrition between the interventions. This technic enabled us to us to manage and treat the cavity without percutaneous drainage or surgery

Conclusions: The combination of EVAC with bariatric stents should be considered as a first line management option for the treatment of oesophageal perforation when using minimally invasive interventions. These results need to be validated in prospective studies

Funding Agencies: None

A233
ENDOSCOPIC ASSISTED ENUCLEATION OF SMALL GASTRIC SUBEPITHELIAL TUMORS: AN EARLY SINGLE CENTER EXPERIENCE
M.A. Alsahafi, F. Donnellan

Vancouver General Hospital, Division of Gastroenterology, University of British Columbia, Vancouver, BC, Canada

Background: Gastric subepithelial tumors (SETs) are not uncommonly discovered on routine endoscopy. They are often associated with a diagnostic challenge and require follow up to ensure no interval growth suggestive of malignant potential. Endoscopic assisted

enucleation is a technique to facilitate a tissue diagnosis and removal.

Aims: To report an early single center experience with endoscopic assisted enucleation of small gastric SETs.

Methods: A retrospective case series of prospectively collected data for patients who underwent endoscopic assisted enucleation of small gastric SETs at Vancouver General Hospital. All patient underwent prior endoscopic ultrasound (EUS) for lesion characterization. Endoscopic interventions include: suction-ligation-unroofing-biopsy (SLUB) or retraction-ligation-unroofing-biopsy (RLUB). The technical success of the procedures, diagnostic yield and complication were described.

Results: A total of 7 patients underwent endoscopic assisted enucleation between October 2015 and October 2016. The mean age was 59 years and 71% were female. Gastric SETs were incidentally discovered on gastroscopy in 5 patients and on CT scan in 1 patient. 1 patient presented with anemia with ulcerated SET. On EUS, the median size was 2 cm (range 1.1 to 3), 3 arise from the fourth layer, 2 from the third and 2 from the second layer. 2 patients underwent EUS guided biopsies and both were non diagnostic. The initial endoscopic procedure was successful in 6 patients but failed in 1 patient. This patient had a 3 cm SET and is awaiting surgery. Biopsies after unroofing provided specific diagnosis in 4 (gastrointestinal stromal tumor, neuroma, lipoma, heterotrophic pancreas) and non-specific diagnosis in 2. There were no complications. Follow up endoscopy data was available in 4 patients: 3 had no visible lesion, 1 had the endoloop remains in place.

Conclusions: Endoscopic assisted enucleation of gastric subepithelial tumors is technically feasible and safe. It facilitates diagnosis and potential cure limiting the need for surveillance.

Funding Agencies: None

A234
A CASE OF OBSCURE GASTROINTESTINAL BLEEDING CAUSED BY BENIGN GASTRIC HYPERPLASTIC POYLPS
S. Shaffer[1], D.C. Moffatt[2]

1. University of Manitoba, Winnipeg, MB, Canada;
2. Department of Medicine, University of Manitoba, Winnipeg, MB, Canada

Background: An 81 year-old female on Apixaban for atrial fibrillation was referred to gastroenterology for a persistently dropping hemoglobin, requiring blood transfusions. She symptomatically felt weak but was otherwise hemodynamically stable. She denied any history of hematemesis, melena, or blood per rectum. She underwent a push enteroscopy and colonoscopy which did not find a source of bleeding. A capsule endoscopy was then performed which did not find a source of bleeding, but showed 2 red polyps in the stomach. An upper endoscopy was then repeated and 10 gastric polyps were seen, ranging from 0.5 to 1.5cm. Pathology showed them to be non-dysplastic hyperplastic polyps. After the removal of these polyps, her hemoglobin stabilized, and she was able to re-start her Apixaban with no further bleeding and no further transfusions over the next 6 months.

Aims: To describe a rare cause of obscure GI bleeding from a commonly benign GI pathology.

Methods: Retrospective case study and literature review.

Results: Gastric polyps are abnormal growths of tissue projecting from the gastric mucosa. They are found in 5-7% of patients undergoing gastroscopy. Hyperplastic polyps account for 17% of all discovered gastric polyps. They are classically associated with atrophic gastritis; secondary to either *H. pylori* infection, or autoimmune gastritis. In recent years though, these polyps have been found in normal or reactive mucosa, with no evidence at all of current or prior *H.pylori* infection. Endoscopically, they are often smooth, dome-shaped, and between 0.5-1.5cm. If they are large enough, they can become lobulated, pedunculated, and their surface epithelium can become eroded, which has been described to lead to chronic blood loss and iron-deficiency anemia. Up to 20% of hyperplastic polyps can have some level of dysplasia. While the prevalence of carcinoma is less than 2%, this risk increases in polyps greater than 2cm. Hence, polyps larger than 1cm are often removed completely. Biopsies of unaffected mucosa should also be obtained to determine if there is *H.pylori* associated gastritis. If present, and *H.pylori* is eradicated, any small remaining hyperplastic polyps will likely regress or disappear.

Hyperplastic polyps have been rarely described to be the source of gastrointestinal blood loss. Cases have been described whereby patients' anemia did not correct with treatment of other potential bleeding sources, but their anemia did resolve after removal of hyperplastic gastric polyps.

Conclusions: Hyperplastic gastric polyps, although relatively common in older populations, are present in only a small percentage of patients undergoing investigation for gastrointestinal blood loss. While often overlooked, they should be recognized as a potential treatable cause of anemia and obscure GI bleeding especially in patients on anticoagulant and antiplatelet medications.

Capsule endoscopy picture of red hyperplastic polyp

FIBROGENESIS, PORTAL HYPERTENSION, COMPLICATIONS OF CIRRHOSIS

Poster of Distinction

A235
SYSTEMATIC REVIEW AND META-ANALYSIS: COMPARING OF ESTIMATED ENERGY REQUIREMENTS IN CIRRHOTIC PATIENTS USING INDIRECT CALORIMETRY VERSUS PREDICTION EQUATIONS

T. Eslamparast[1], B. Vandermeer[2], M. Raman[3], V. Mathiesen[4], D. Belland[4], M. Ma[2], 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. Alberta Health Services, Edmonton, AB, Canada

Background: Malnutrition is common in cirrhosis and an independent predictor of mortality. Dietary recommendation is the mainstay of therapy. Most dietitians utilize predictive equations to estimate resting energy expenditure (REE) and target energy need as these are more time-efficient than gold-standard indirect calorimetry. However, predictive equations are associated with over- and under-estimation of energy requirements.
Aims: As accurate nutrition prescriptions are important in cirrhosis patient care, our aim was to compare the estimated energy requirements using indirect calorimetry measurements (measured REE, mREE) versus prediction equations (predicted REE, pREE).
Methods: We included full-text English language studies on adults with cirrhosis comparing pREE versus mREE. Excluded studies had >20% of patients with hepatocellular carcinoma. A DerSimonian-Laird random-effects meta-analysis was used to pool the mean differences across studies.
Results: A total of 20 studies (2 separately reporting data in men and women) comprising 1883 patients (1991 to 2016) fulfilled selection criteria and were analyzed. The Harris-Benedict equation was used to estimate the pREE in 15 studies (75%). A total of 14 studies underestimated caloric requirements using the predictive equations. The percentage difference between the mREE and the pREE, ranged from -12.0% (overestimation) to +22.2% (underestimation) kilocalories per day (kcal/d). When pooled, the mean difference across studies was an underestimate of 75.9 (95% CI: 12.83-138.96) kcal/d. The pooled analysis was associated with significant heterogeneity (I^2=93%, Fig 1).
Conclusions: It is important to recognize that predictive equations have a wide margin of error and are more likely to underestimate rather than overestimate caloric requirements of cirrhotic patients. Our results highlight the need to accurately define the subgroup of patients at risk for underestimation of caloric requirements and have them complete indirect calorimetry assessment. Future work will analyze individual patient data evaluating the impact of liver disease severity (e.g., ascites, obesity, and hospitalization) to identify this at-risk subgroup.

Fig 1. Forest plot of comparison: measured Resting Energy Expenditure (mREE) *vs.* predicted REE (pREE). Abbreviations in parenthesis show the predictive equations employed by each study (HB: Harris-Benedict, FFM & FFM in reg.: using the individual fat free mass in the linear regression equation derived from cirrhotic or control group, sex reg.: using gender specific regression equations derived from healthy population)

A236
METRONIDAZOLE IN THE TREATMENT OF RECURRENT HEPATIC ENCEPHALOPATHY: A CASE SERIES.

A. Amin[1], D. Shah[4], L. Cabrera-García[1], M. Carbonneau[3], K. Newnham[3], P. Tandon[4], J. Abraldes[2]

1. (Core) Internal Medicine Program, University of Alberta, Edmonton, AB, Canada; 2. Liver Unit, University of Alberta, Edmonton, AB, Canada; 3. Cirrhosis Care Clinic, University of Alberta Hospital, Edmonton, AB, Canada; 4. University of Alberta, EDMONTON, AB, Canada

Background: Hepatic encephalopathy (HE) affects 50-70% of cirrhotic patients. Lactulose is first-line

therapy in HE prevention and in preventing recurrent HE. Rifaximin (RIF) is the next therapeutic choice for HE prevention after two recurrent HE episodes despite lactulose treatment. RIF has been suggested to have the additional benefit of improving circulatory dysfunction in cirrhosis. A special access program (SAP) for RIF was discontinued in January 2014. Due to its high cost, only a few patients could remain on RIF through private insurance. AASLD/EASL guidelines suggest either neomycin or metronidazole (MET) as potential alternatives, but only MET is available in Canada. However, the evidence on MET's efficacy and safety in the treatment of HE is very limited.

Aims: The aims of the present study were to describe our experience with MET in patients with recurrent HE, and to assess if treatment with MET was associated with changes in readouts of circulatory and liver function in patients with advanced cirrhosis.

Methods: This was a retrospective case-series study including: 1) patients receiving RIF for the prevention of recurrent HE and then switched to MET (250mg PO BID) at the end of the special access program (SAP) (n=5); 2) patients started *de novo* on MET after the end of the SAP (n=14); and 3) patients who received RIF as a part of the SAP and continued on it (n=12). Treatment was initially limited to 6 months due to the risk of toxicity. Demographics, clinical and laboratory parameters were collected from 3 months before the index date to 6 months after.

Results: Table 1 summarizes the characteristics of the patients. During the 6 months of MET treatment, 2 of the 19 patients treated with MET developed a total of 3 episodes of HE. Among the 12 patients continued on RIF, 3 of them developed a total of 3 episodes of HE. During the study follow-up there were no significant changes in the mean creatinine, sodium, bilirubin or albumin in any of the three study groups, or toxicity directly associated with the use of MET.

Conclusions: Despite the limited evidence that a case-series can provide, MET appears to be a safe and effective interim alternative for the prevention of recurrent HE in settings with limited access to RIF.

Table 1: Summary of Patient Characteristics (At Antibiotic Index Date)

	MET after RIF (n=5)	De Novo MET (n=14)	Continued RIF (n=12)
Median Age (yrs) [IQR]	48.0 [47.0 – 58.0]	58.5 [53.0 – 61.3]	57.5 [50.0 – 64.8]
Male	3/5 (60.0%)	6/14 (42.9%)	9/12 (75%)
Etiology of Cirrhosis			
Alcohol	0/5 (0.0%)	3/14 (21.4%)	7/12 (58.3%)
HCV	0/5 (0.0%)	5/14 (35.7%)	2/12 (16.7%)
Alcohol + HCV	3/5 (60.0%)	0/14 (0.0%)	1/12 (8.3%)
Others	2/5 (40.0%)	6/14 (42.9%)	2/12 (16.7%)
Types of Decompensation			
Encephalopathy	5/5 (100.0%)	14/14 (100.0%)	12/12 (100.0%)
Ascites	4/5 (80.0%)	10/14 (71.4%)	11/12 (91.7%)
Edema	3/5 (60.0%)	8/14 (57.1%)	6/12 (50.0%)
Previous Variceal Bleeding	2/5 (40.0%)	3/14 (21.4%)	4/12 (33.3%)
Other Complications			
HCC	1/5 (20.0%)	1/14 (7.1%)	3/12 (25.0%)
PVT	1/5 (20.0%)	2/14 (14.3%)	3/12 (25.0%)
TIPS	3/5 (60.0%)	3/14 (21.4%)	1/12 (8.3%)
Median Child Pugh Score [IQR]	6.5 [5.0 – 8.5]	7.0 [6.0 – 8.0]	7.0 [6.0 – 8.8]
Median MELD-Na Score [IQR]	14.0 [10.0 – 17.3]	13.0 [10.0 – 16.8]	13.0 [10.0 – 15.5]

A237
DEVELOPMENT AND EVALUATION OF A WEB-BASED EDUCATIONAL TOOL FOR THE HEPATOPULMONARY SYNDROME

J. Marianayagam, K. Griffin, J. Sykes, S. Gupta

St. Michael's Hospital, Toronto, ON, Canada

Background: Hepatopulmonary syndrome (HPS) is a rare shunting lung disease that is caused by liver disease. This complex disease entails high informational needs for patients and their caregivers.

Aims: We sought to analyze existing web resources for HPS patients, to assess patients' and caregivers' informational needs, and to develop and evaluate a tailored web-based educational resource for this population.

Methods: We performed a Google™ search for existing web-based resources for HPS. We then administered an electronic needs assessment survey to patients with HPS [liver disease, intrapulmonary vascular dilatation (IPVD) and hypoxemia)/pre-HPS (liver disease, IPVD and normal oxygenation) in the Toronto HPS Clinic Database, and their caregivers. In response to these needs, we developed an HPS website, applying best practices in health website design. We administered electronic questionnaires to assess changes in self-efficacy (Likert-scale questions) and knowledge (standardized knowledge test) after website use, website quality (DISCERN score) and usability [System Usability Score (SUS)].

Results: We identified 21 unique HPS websites, with a mean DISCERN score of 19.9 ± 5.2 (out of 45) and Flesch-Kincaid reading grade of 16.8 ± 4.2. We recruited 35 (15 HPS, 5 pre-HPS, 15 caregivers) of 59

FIBROGENESIS

(59.3%) eligible participants for the needs assessment. Of these, 27 (77.1%) had searched online for HPS information; 5/27 (18.5%) had found the information they sought and 8/27 (29.6%) had found the information easy to understand. Participant-reported self-efficacy (see Figure) improved after interaction with the website, as did knowledge scores [64.9% ± 16.8 to 72.7% ± 18.5 (n=30; p=0.015)]. A higher SUS score (p=0.048) and lower level of comfort browsing the Internet (p=0.020) predicted improvement in knowledge score in both univariate and multivariable models. The mean DISCERN score for our website was 38.5 ± 4.3 (out of 45); SUS score was 76.6±16.2 (out of 100); and reading grade was 8.3.

Conclusions: HPS patients often seek information on the internet, yet existing web resources were few, scored poorly on a validated test of health information quality, and had a reading level far above the 8th grade recommended threshold. A website designed through evidence-based criteria for health educational website design was able to improve self-efficacy and knowledge among patients and caregivers with HPS. The importance of user-centered design is demonstrated by the fact that users with a lower comfort level browsing the Internet were even more likely to experience knowledge gains. All patients/caregivers affected by HPS should be made aware of the availability of this beneficial resource.
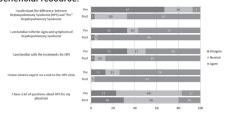
Figure. Participant Self-Efficacy Pre- and Post-Website Interaction.
Responses were entered on a 5-point Likert scale labeled 1 (disagree); 3 (neutral); and 5 (agree). For the purposes of this figure, scores of 1 and 2 were considered "disagree," and 4 and 5 were considered "agree." Each bar demonstrates the proportion of participants with each response, for each statement. This includes 30 participants for the pre- and post- assessment (19 patients with hepatopulmonary syndrome and 11 caregivers).

Funding Agencies: None

A238
A COMPARATIVE ANALSYS OF FIBROSIS BY TRANSIENT ELASTOGRAPHY AND LIVER BIOPSY IN PATIENTS WITH BIOPSY PROVEN NASH.
K. Boctor[1], M. Magnes[2], M. Elkashab[3]

1. Gasteroenterology & Hepatology, Toronto Liver Center, Toronto, ON, Canada; 2. Toronto Liver Centre, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada

Background: According to the Canadian Liver Foundation, the death rate from liver disease has risen to nearly 30 percent. Fatty liver disease (FLD) more specifically has been highlighted to affect nearly 30 percent of the Canadian population, with Non-alcoholic steatohepatitis (NASH); a sub-type of FLD, causing a 50 percent increase in mortality secondary to cirrhosis & its complications. This value equates to greater number of hospitalizations, emergency room admissions, & more frequent visits to general practitioners and specialists.

Aims: As liver biopsy remains the gold-standard for the diagnosis of NASH, & transient elastography a non-invasive tool in the assessment & monitoring of liver disease. Our aim was to study how the NASH activity Score (NAS), & its components (Steatosis, Ballooning, & Fibrosis) correlated to Liver Stiffness (LS) by fibroscan.

Methods: 67 patients who had undergone a Liver Biopsy for confirmative diagnosis of NASH and staging of fibrosis. All Liver biopsies with were conducted at one facility and interpreted by a liver pathologist. Fibroscan tests were conducted at a separate facility and liver stiffness was measured in kilopascals. Data was collected and retrospectively analysed for: Liver stiffness (LS), and various aspects of the Pathology report. Only patients with NAS≥2 (NASH Activity Score) were included in the study.

Results: Of the 67 included in our cohort, 41 were males, & 26 females. Mean age for males was 48.39, and females 52.46. 65 patients underwent both a fibroscan and biopsy with a mean time of 161.46 days in between the two tests.

Fibroscan:
LS to NAS showed a strong correlation with a P-value of 0.021. (Figure1)
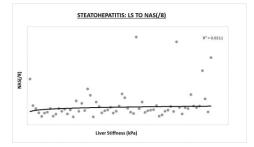
Mean LS was 11.60kPa, with 11.60kPa, and 11.30kPa for males and females, respectively. 58.2% of our cohort underwent serial fibroscans.

Liver stiffness (kPa) values varied significantly when compared to Brunt fibrosis on Liver biopsy. No particular range of stiffness was identifiable to a specific stage of brunt fibrosis. (Table 1)

When comparing LS to Ballooning, there was no significant correlation, with a linear regression model resulting in R^2 value of 0.0007. While LS to Lobular Inflammation resulted in a R^2 value of 0.0142.

Conclusions: Although Liver stiffness by transient elastography shows a strong correlation to NAS; however, it does not prove to be correlated to any one individual component of the NAS score. We plan to further assess these findings in a larger cohort in the future.

Table 1: Liver Fibrosis (Liver stifffness Vs. Brunt Fibrosis)

Fibrosis By Brunt (/4)	LS (kPa) High	LS (kPa) Low	LS (kPa) Mean	LS (kPa) SD	No. of Subjects
0	21.80	9.40	13.89	4.22	7
0-1	13.80	48.00	30.90	24.18	2
1	59.20	5.80	15.48	12.85	18
1-2	-	-	-	-	0
2	13.20	5.80	10.20	2.16	7
2-3	22.20	6.20	11.06	5.00	5
3	32.80	8.20	13.96	6.76	14
3-4	13.90	7.30	10.60	3.30	2
4	19.50	6.40	11.97	4.26	7
4-Chirrhosis	62.70	62.70	62.70	0.00	1

STEATOHEPATITIS: LS TO NAS(/8)

$R^2 = 0.0211$

NAS(/8)

Liver Stiffness (kPa)

Funding Agencies: None

A239
QUALITATIVE EVALUATION OF THE DECISIONS AND EXPERIENCES OF PEOPLE WHO INJECT DRUGS WHO RECEIVED A LIVER DISEASE ASSESSMENT AS PART OF A LIVER HEALTH PROMOTION CAMPAIGN: THE LIVERLIFE STUDY
A.D. Marshall[1], C. Treloar[2], G.J. Dore[1], J. Grebely[1]

1. The Kirby Institute, UNSW, Sydney, New South Wales, Australia; 2. Centre for Social Research in Health, UNSW, Sydney, New South Wales, Australia

Background: A liver health promotional campaign took place in New South Wales, Australia (May to October 2014), with 235 people who inject drugs (PWID) receiving FibroScan®-based disease assessment. Participant follow-up occurred 2-16 weeks post-enrolment.
Aims: The aim of this qualitative sub-study was to evaluate the decisions and experiences of participants who received a liver disease assessment, including interpretation of FibroScan® score and subsequent health behaviours.
Methods: Participants were recruited from two opioid substitution treatment clinics and one medically supervised injecting centre between November 2015 and February 2016. The four recruitment categories were: a) high FibroScan® score (≥9.5 kPa)/ attended LiveRLife follow-up; b) high score/did not attend follow-up; c) low score (≤9.4 kPa)/attended follow-up; and d) low score/did not attend follow-up. Participants were not reminded of their category during recruitment. Inclusion criteria were: participation in the LiveRLife campaign, received a FibroScan® score, and informed written consent. Interviews were audio-taped and transcribed verbatim. Data was analysed using thematic analysis.
Results: Of 33 semi-structured interviews [category a (12 participants); category b (2); category c (11); category d (8); 21% female], reasons for wanting to receive a FibroScan® were varied. Most participants interpreted their level of liver disease correctly based on their recalled FibroScan® score. Persons with higher scores frequently recalled feeling shocked by their score (e.g. 'wake-up call') whereas participants with lower scores were typically pleasantly surprised (e.g. incentive to keep liver healthy). Some positive health changes were stated with several relating their score to hepatitis C treatment. Additionally, some confusion regarding causes of increased liver disease persisted despite this information being provided in the campaign. Further analyses will explore health-seeking behaviours (or lack thereof) by category.
Conclusions: Results provide greater insight into strategies to enhance knowledge and 'linkage to care' for PWID with, and at-risk of, advanced liver disease.

Funding Agencies: The study was funded from MSD, Australia.

A240
AN UNUSUAL PRESENTATION OF HEPATIC ENCEPHA-LOPATHY: RECURRENT GLOBAL APHASIA
E. Wishart, H. Block, A. Bedi

University of Saskatchewan, Saskatoon, SK, Canada

Background: Hepatic encephalopathy (HE) is impairment in a brain function caused by liver dysfunction and portosystemic shunting. It is a frequent and debilitating complication of cirrhosis, the pathophysiology of which is complex and not fully elucidated. HE is associated with poor survival and has a high risk of recurrence. Hepatic encephalopathy can present as a wide spectrum of neurological and psychiatric abnormalities ranging from subclinical alterations to coma and death. Despite the wide range of presentations there have been no published cases of hepatic encephalopathy presenting as global aphasia.
Aims: We describe a case of a patient with alcoholic

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cirrhosis with recurrent presentations of HE presenting as global aphasia.

Methods: A case of HE with global aphasia is reviewed and literature review on HE with focal findings is explored and summarized.

Results: A 57 y/o F with decompensated alcoholic cirrhosis presents to hospital with acute onset global aphasia. Her past medical history is significant for two previous left parieto-occipital lobe hemorrhagic strokes and medically controlled seizures after these strokes. CT/CTA showed no acute changes consistent with stroke and EEG demonstrate triphasic waves consistent with metabolic derangement. Serum ammonia was elevated at 136 µmol/L. On collateral history the patient was reported to be non-compliant with lactulose. The patient was restarted on lactulose in hospital and quickly improved to baseline.

6 months later the patient presented again with global aphasia. A CT ruled out stroke and HE was found to be responsible for her aphasia with an ammonia of 106 µmol/L. Her HE was precipitated by an upper gastrointestinal bleed and ongoing alcohol use. EGD revealed portal hypertensive gastropathy, gastric ulcers, and small varices not amenable to banding. Paracentesis was completed to rule out spontaneous bacterial peritonitis and ultrasound ruled out hepatocellular carcinoma. Rifaxamin was added to the patients' medication regime and her symptoms resolved.

Conclusions: In this case, we present a review on the literature of HE presenting with focal deficits. Despite the wide range of presentations of HE with focal neurologic signs - including hemiplegia, hemiparasia, hemiagnosia, abnormal extraocular movements, and apraxias - there have been no published cases of hepatic encephalopathy presenting as global aphasia. This is the first documented case of global aphasia being the focal neurological sign in HE. Alternatively, we postulate that the encephalopathy brought out the patient's deficits from her prior left parieto-occipital strokes.

Funding Agencies: None

GASTRO INTESTINAL ONCOLOGY

Poster of Distinction

A241
TIME FROM DIAGNOSTIC ENDOSCOPY TO CURATIVE RESECTION IN PATIENTS WITH COLON CANCER: A POPULATION-BASED STUDY
J.A. Flemming, S. Nanji, X. Wei, C. Webber, P. Groome, C.M. Booth

Queen's University, Kingston, ON, Canada

Background: Factors associated with time-to-surgery (TTS) and survival in patients with colon cancer has not been well studied. Cancer Care Ontario recommends surgery within 42 days of diagnosis and that 90% of patients meet this benchmark.

Aims: We describe factors associated with TTS and survival in routine clinical practice.

Methods: Retrospective population-based cohort study of patients receiving elective colonic resection after diagnosis of colon cancer in Ontario, Canada from 2002-2008. Factors associated with TTS were identified using multivariate log-binomial and Quantile regression at 42 days and 90th percentiles. The association between TTS and cancer-specific (CSS) and overall survival (OS) were examined using multivariate Cox regression.

Results: 4,326 patients; median age 71 years and 52% male. Median TTS was 24 days (IQR 14-37); at the 90th percentile 56 days. Factors associated with TTS ≥ 42 days and > 90th percentile included older age, co-morbid illness, surgeon volume, and stage I disease (P < 0.05 for all). In patients whose TTS was either at 42 days or 90th percentile, those ≥ 80 years old waited two weeks longer than those < 60 years, individuals with co-morbid illness waited 10 days longer than those without co-morbidity, and patients with stage I disease waited 10 days longer than those with stage IV disease (P < 0.05 for all). Delay in TTS > 42 days or > 90th percentile was not associated with OS or CSS.

Conclusions: Age, co-morbidity, and stage of cancer are associated with TTS. There was no association between TTS and CSS or OS.

A242
THE P2 ISOFORM CLASS OF THE TRANSCRIPTION FACTOR HNF4A PLAYS DNA REPAIR ROLE IN COLORECTAL CANCER
S. Wilson, J. Babeu, F. Boisvert, F. Boudreau

Université de Sherbrooke, Sherbrooke, QC, Canada

Background: In Canada, cancers of the colon and rectum are among the deadliest forms of the disease. Colorectal carcinomas typically feature an abnormal regulation of the transcription factor HNF4α. The *HNF4A* encoding gene gives rise to two isoform classes, P1- and P2-HNF4α, that have opposing roles in colorectal cancer. The latter, P2-HNF4α, promotes cell proliferation and is upregulated in many instances of colorectal cancer when compared to P1-HNF4α. Despite this, the functional role that P2-HNF4α plays in the phenotype of colorectal cancer is unknown.

Aims: The goal of this research was to elucidate the functional role of P2-HNF4α in colorectal cancer by the identification of its protein cofactors in colorectal cancer cell lines.

Methods: We chose a representative member of the P2-HNF4α class, HNF4α8, to overexpress in 293T and HCT116 cells. The cofactors of P2-HNF4α were

identified by two separate co-immunoprecipitation techniques, GFP-Trap and BioID, coupled to quantitative mass spectrometry. Following induced genotoxic stress, P2-HNF4α's cofactors were identified anew by GFP-Trap and HNF4α's nuclear localization was visualized by immunofluorescence.
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. The two co-immunoprecipitation assays had 31 mutual cofactors, and several of these cofactors shared 'DNA repair' as common gene ontology. Many common targets are known to be involved in DNA repair and are also known to be involved in cancer, including TP53, NPM1, RAD50, and MCM3/4.

Following genotoxic stress, induced by micro-irradiation or etoposide, the relationship between DNA repair and P2-HNF4α was further tested. Immunofluorescence revealed that HNF4α colocalizes to DNA damage loci (p-H2A.X) in the nucleus of HT-29 and Caco-2/15 colorectal cancerous cell lines.
Conclusions: The functional role of P2-HNF4α in colorectal cancer could be clarified by the isoforms class' association with DNA repair proteins. These cofactors suggest a DNA repair activity for P2-HN-F4α. Furthermore, HNF4α's involvement in DNA repair represents the prospect of a previously undescribed non-transcriptional role for the transcription factor. This link between the transcription factor and DNA repair proteins could become exploitable for therapeutic remedy of colorectal cancer thanks to the manipulability of P2-HNF4α as a ligand-binding nuclear factor.

Funding Agencies: CAG, CIHR

A243
FUNCTIONAL ROLES OF NCOR1 AND CHD8 PROTEIN INTERACTION IN HUMAN COLORECTAL CANCER CELLS.
A. Loiselle, S. St-Jean, F. Boisvert, F. Boudreau

Université de Sherbrooke, Sherbrooke, QC, Canada

Background: The nuclear receptor co-repressor 1 (NCOR1) is a protein with transcriptional repression activity interacting with nuclear receptors. NCOR1 is involved in targeting gene transcription related to intestinal inflammatory response and colorectal cancer. We have previously identified the chromatin helicase DNA binding 8 (CHD8) protein as a potential interactor of NCOR1. CHD8 is a DNA helicase that functions as a transcription repressor by remodeling chromatin structure.
Aims: To investigate the functional and biological roles of CHD8 interaction with NCOR1 in colorectal cancer.
Methods: HT-29 and Caco-2/15 cell lines were depleted in NCOR1 or CHD8 by RNAi. Cell proliferation of the generated cell lines was measured by cell counts. Overall changes in transcriptome was determined by high-throughput RNA sequencing. Chromatin immunoprecipitation (ChIP) was performed with the use of a specific CHD8 antibody. Multiple HA and V5 epitope-tagged domain fragments of NCOR1 and CHD8 were generated for interaction assays.
Results: Depletion of NCOR1 in HT-29 and Caco-2/15 cells led to a strong reduction of cell proliferation, while depletion of CHD8 led to a less robust effect. High-throughput RNA sequencing identified more than 60 common genes for which the expression was modulated in both NCOR1 and CHD8 depleted HT-29 and Caco-2/15 cell populations. Among these modulated genes, the Brain Derived Neutrophic Factor (BDNF), known to be involved in cancer cell motility, was identified as a common gene target for both NCOR1 and CHD8. ChIP with the use of a CHD8 specific antibody was optimized in colorectal cancer cell lines to monitor the level of CHD8 chromatin occupancy among the identified genes. Finally, various tagged constructs representative of specific domains of NCOR1 and CHD8 have been generated and validated by Western blot. Interactions strategies are currently undergoing to functionally validate NCOR1 and CHD8 biological link.
Conclusions: NCOR1 and CHD8 interact together, affect common genes and negatively influence colorectal cancer cell proliferation. Identification of the specific nature of this interaction will highlight novel strategies to disrupt NCOR1-CHD8 interaction in order to regulate colorectal cancer cell proliferation.

Funding Agencies: CIHR

A244
THE FECAL IMMUNOCHEMICAL TEST (FIT): SELECTED ASPECTS REGARDING ITS EFFECTIVENESS FOR COLORECTAL CANCER SCREENING IN QUEBEC CITY.
M. Caron[1], G. Lamarre[1], P. Grégoire[2], D. Simonyan[3], N. Laflamme[3]

1. Faculty of Medicine, Universite Laval, Quebec, QC, Canada; 2. CHU de Québec, Quebec, QC, Canada; 3. Centre de recherche du CHU de Québec, Quebec, QC, Canada

Background: The FIT has been used in Quebec since September 2013 in replacement for guaiac fecal occult blood test (gFOBT) as part of the province's colorectal cancer (CRC) screening program (PQDCCR). Its value has already been ascertained elsewhere in Canada and worldwide. For instance, one Canadian study including the data from five provinces obtained a positive predictive value (PPV) of 4.3% for the detection of CRC in average-risk patients. The performance of the FIT needs to be assessed in our province, especially as we use a higher positivity threshold value than in most screening programs. Moreover, there seems to remain a gap between formal indications for a FIT and its actual use in clinical practice. Thus, this research aims to evaluate

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some aspects related to the effectiveness of the FIT in our setting and its application by prescribers.

Aims: The primary aim of the study was to determine the PPV for the detection of CRC, advanced adenomas (AA), and significant colorectal lesions (SCL, i.e. CRC and AA combined).

The secondary aims of the study were to (i) examine the influence of specific variables on the test's PPV, such as age, sex, presence of alarm features, and adequacy of the prescription of a FIT, and (ii) identify the FITs that were unjustified, i.e. that were requested for other than asymptomatic, average CRC risk patients.

Methods: Using the software Endoworks® (Olympus®), in which all colonoscopy reports are saved, we identified retrospectively all colonoscopies conducted for a positive FIT in 2014 at two reference centers of the PQDCCR in Quebec City. We then reviewed manually every corresponding medical record to complete data collection.

Results: 559 colonoscopies were reviewed. We obtained PPVs of 6.8% and 46.9% for the detection of CRC and AA, respectively. The PPV for the detection of SCL was 56.1% among men and 45.0% among women (OR 1.56, 95% CI 1.11 – 2.20), whereas it was 59.5% among justified FITs and 43.9% among unwarranted ones (OR 1.88, 95% CI 1.34 – 2.63). Results for AA detection were similar to those of SCL. The PPV for the detection of CRC was 25.0% in the presence of an unexplained iron deficiency anemia and 6.5% when anemia was absent (p=0.0058). In 49.9% of cases, the prescription of a FIT was inappropriate, most often due to macroscopic rectal bleeding.

Conclusions: The PPV of the FIT for detecting CRC is higher in our setting than in the rest of Canada, but the clinical significance of this difference is unclear. The test holds a better PPV for detecting SCL and AA among men, and when it is indicated according to PQDCCR recommendations. Unexplained iron deficiency anemia is associated with a higher rate of CRC detection. Half of the positive FITs were not indicated initially. Therefore, physicians should be made more aware of the appropriate use of the FIT.

Funding Agencies: None

A245
THE ROLE OF P53 ON P2Y6R EXPRESSION IN COLORECTAL CANCER.

C.M. Molle, G. Arguin, M. Placet, F. Gendron

Anatomy and Cellular Biology, University of Sherbrooke, Sherbrooke, QC, Canada

Background: The G protein-coupled P2Y$_6$ receptor (P2Y$_6$R) is activated by extracellular UDP. In the colonic epithelium, it participates in the maintenance of the hydric balance by regulating NaCl secretion. More recently, P2Y$_6$R activity was reported to worsen inflammatory symptoms in a mouse model of inflammatory bowel diseases (IBD). Long-term IBD-suffering patients are at higher risk of developing colorectal cancer (CRC). In response to chronic exposure to inflammatory stressors, p53 is one of the first mutated oncogene, which leads to colitis-associated CRC. We focused on the potential role of p53 in the regulation of P2Y$_6$R expression in CRC.

Aims: The **hypothesis** is that the presence of a mutant form of p53 will differentially regulate P2Y$_6$R expression as compared to the wild-type protein. The **general aim** of our work is to characterize the molecular mechanisms associated with p53-dependent regulation of P2Y$_6$R in CRC. More specifically, we will **1)** determine and characterize the *P2RY6* promoter in cancerous intestinal epithelial cells (cIEC) and **2)** study the role of wild-type or mutant p53 on P2Y$_6$R expression.

Methods: The *P2RY6* gene encodes for 8 messenger RNA (mRNA) variants. Most of them are encoding for the P2Y$_6$R isoform 1 which is well characterized. However, mRNA variant 9 codes for an uncharacterized form of the receptor: isoform 2. We used 5'RACE experiments to identify the different transcription start sites (TSS) corresponding to the several mRNA variants and determined the amount of each variant in cIECs. We then cloned four consensus regions (R1, R2, R3 and R4) of the *P2RY6* promoter encompassing the four previously identified TSS upstream of the luciferase reporter gene in the pGL4.10 vector. The pGL4.10-*P2RY6* promoter constructs were cotransfected with wild-type p53 and mutant forms and transcription activity measured by luciferase assays. Chromatin immunoprecipitation (ChIP) assays were used to confirm the luciferase results.

Results: We identified four TSS in the *P2RY6* promoter region and showed that Caco-2 cells expressed predominantly mRNA variant 9. Using luciferase assays, we showed that wild-type p53 can activate the promoter R1 and R4 regions, whereas p53 R273H mutant (p53[R273H]) has no effect on the transcriptional activity of the R1 region but significantly stimulated the R4 promoter region. The ChIP experiments showed that p53[R273H] could occupy the R4 but not the R1 region; whereas wild-type p53 could bind both R1 and R4 regions. Finally, AlphaScreen Surefire assays suggest that UDP also activates P2Y$_6$R isoform 2.

Conclusions: We showed that wild-type p53 and p53[R273H] mutant differently regulate P2Y$_6$R expression in cIEC. Hence, p53[R273H] mutant seems to favor the expression of P2Y$_6$R isoform 2 for which the function is not yet identified but are likely linked to stimulation of cell proliferation and resistance to apoptosis.

Funding Agencies: CIHR

A246
DUAL DELETION OF EPITHELIAL *BMPR1A/PTEN* IN MICE IMPAIRS COLONIC MUCOSA IDENTITY.

V. Pomerleau, J. Babeu, F. Boudreau, N. Perreault

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

NOT PUBLISHED AT AUTHOR'S REQUEST

A247
RECOGNITION OF LYNCH SYNDROME AMONGST NEWLY DIAGNOSED COLORECTAL CANCER AT ST. PAUL'S HOSPITAL
S. Pi[1], E. Nap-Hill[2], J.J. Telford[2], R.A. Enns[2]

1. Internal Medicine, University of British Columbia, Vancouver, BC, Canada; 2. St. Paul's Hospital, Vancouver, BC, Canada

Background: Lynch syndrome (LS) is the most common cause of inherited colorectal cancer (CRC). Numerous strategies exist for identifying patients with LS. In British Columbia, clinical criteria (Amsterdam II criteria, Revised Bethesda guidelines, or the BC Cancer Agency's Hereditary Cancer Program (BCCA HCP) criteria) are first used to determine who should undergo further first-line testing in the form of microsatellite instability (MSI) testing or immunohistochemistry (IHC) staining. Limitations exist with this strategy, including ease of access and, consequently, LS is thought to be under-recognized.
Aims: The purpose of this study is to investigate whether LS is truly under-recognized when compared to the reported prevalence and, if so, identify what factors are contributing to this.
Methods: A retrospective chart review of all CRC diagnosed at St. Paul's Hospital from 2010-2013 was conducted. The list of all CRC was obtained through St. Paul's Hospital Department of Pathology after ethics approval.
Results: Of 246 patients who met inclusion criteria, 96% (235 of 246) had a family history available in their chart. 76% (83 of 109) with a family history of malignancy were unable to recall the specific malignancy or age of diagnosis. 18% (45 of 235) were apparently only asked about a history of gastrointestinal related malignancy and 26% (65 of 246) met at least one of the three clinical criteria but only 21% (13 of 63) received further investigation in the form of MSI testing, IHC staining, or BCCA HCP referral. When compared to the entire study population, patients who received further testing had a statistically significant younger age (66 vs. 49, p<0.01), past medical history of malignancy (0.16 vs. 0.38, p=0.03) and family history of malignancy (0.46 vs. 0.92, p<0.01). Only 1.6% (4 of 246) were found to have LS compared to the reported prevalence of 2-5% of all CRC.
Conclusions: This data supports our hypothesis that LS is under-recognized. Contributing factors include poor recollection of family histories by patients, incomplete family histories by physicians, and under-investigation for those at risk of LS which we speculate is, in part, due to difficulty accessing MSI-testing and IHC staining. The present system of reliance on histories and patients to report their family histories appear to be inadequate and need modification. A system such as that suggested by the latest AGA Guidelines where all cancers are universally tested needs implementation to minimize the risk of missing LS patients.

A248
INDICATIONS FOR COLONOSCOPY PRE- AND POST-COLON SCREENING PROGRAM AT ST. PAUL'S HOSPITAL
S. Pi[2], E. Nap-Hill[1], R.A. Enns[1], J.J. Telford[1]

1. Medicine, Gastroenterology , St Paul's Hospital, Richmond, BC, Canada; 2. Internal Medicine, University of British Columbia, Vancouver, BC, Canada

Background: Colorectal cancer (CRC) is a commonly diagnosed cancer with a lifetime prevalence of 4.5%. The removal of adenomas as well as the detection and resection of early CRC have been shown to reduce the incidence and mortality of CRC. The Canadian Task Force on Preventative Health Care recommends utilizing fecal occult blood testing (FOBT) or fecal immunochemical testing (FIT) every 2 years in men and women between the ages of 50-74. In addition, the routine use of colonoscopy for CRC screening is not recommended. In November 2013, the Colon Screening Program (CSP) was implemented with the goal of standardizing British Columbia's CRC screening strategy. Prior to this, no provincial strategy existed and significant variation existed with regards to the indication for colonoscopy.
Aims: The purpose of this study is to investigate how the implementation of the CSP in BC has changed the indications for colonoscopy amongst newly diagnosed patients with colorectal cancer.
Methods: A retrospective chart review of all CRC diagnosed at St. Paul's Hospital from 2010-2015 was conducted. The list of all CRC was obtained through the St. Paul's Hospital Department of Pathology after ethics approval.
Results: After the implementation of the CSP, a lesser proportion of patients were diagnosed with CRC via symptoms (42% vs 57%, p=0.002) or primary colonoscopy (0.6% vs 4%, p=0.038). A greater proportion of patients were diagnosed via positive FIT + FOBT (48% vs 34%, p<0.001) and surveillance colonoscopy (6% vs 3%, p=0.03). In addition, a greater proportion were diagnosed by FIT (47% vs. 22%, p<0.001) and a lesser proportion diagnosed by FOBT (1% vs 11%, p<0.001) when compared to pre-CSP era.
Conclusions: Implementation of the CSP has led to a

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greater proportion of colorectal cancers being diagnosed by FIT screening and surveillance colonoscopy as well as an overall reduction in colorectal cancer being diagnosed via symptoms or primary colonoscopy. The data also suggests that family physicians in BC are almost universally favouring FIT testing over the guaiac based FOBT. These results support that the CSP has been successful in aligning the indications for colonoscopy with the recommendations made by the Canadian Task Force on Preventative Health Care.

INDICATIONS FOR COLONOSCOPY PRE- AND POST-CSP

Pre-CSP	n (%)	Post-CSP	n (%)	p-value
Indication for colonoscopy: Symptomatic	139 (57)	Indication for colonoscopy: Symptomatic	62 (42)	0.002
- IDA	27 (11)	- IDA	13 (9)	0.37
- Bleeding	73 (30)	- Bleeding	41 (28)	0.51
- Bowel Habits	39 (16)	- Bowel Habits	8 (5)	<0.001
Positive FIT + FOBT	83 (34)	Positive FIT + FOBT	72 (48)	<0.001
- Positive FIT	55 (22)	- Positive FIT total	70 (47)	<0.001
- xx	N/A	- Positive FIT In CSP criteria	42 (28)	N/A
- xx	N/A	- Positive FIT Out of CSP criteria	28 (19)	N/A
- Positive FOBT – guaiac	28 (11)	- Positive FOBT – guaiac	2 (1)	<0.001
Primary colonoscopy	9 (4)	Primary colonoscopy	1 (0.6)	0.038
Family History	7 (3)	Family History	5 (3)	0.8
Surveillance	8 (3)	Surveillance	9 (6)	0.03
Total	246	Total	149	

A249
NEW POTENTIAL ROLE FOR TRANSCRIPTION FACTOR EB IN DNA REPAIR
M. Groleau[1], B. Marchand[2], M. Boucher[1]

1. Université de Sherbrooke, Sherbrooke, QC, Canada;
2. médecine/Gastroentérologie, Université de Sherbrooke, Sherbrooke, QC, Canada

Background: We previously demonstrated that prolonged GSK3 inhibition triggers an apoptotic response specifically in pancreatic cancer cells leaving intact pancreatic normal cells. However, we recently observed that the apoptotic response is counterbalanced by pro-survival autophagic signals dependent on the transcription factor EB (TFEB). In order to identify potential mechanisms by which TFEB limits cell death, mass spectrometry analysis was performed to identify new TFEB interacting partners. Many proteins involved in DNA repair were found associated with TFEB upon GSK3 inhibition including PARP1.
Aims: The aim of this study was to assess whether TFEB participates in DNA damage detection/repair in human pancreatic cancer cells.
Methods: The experiments were performed using stable population of the pancreatic cancer cells MIA PaCa-2 and PANC1 (PDAC-shCTL) with reduced expression levels of TFEB (PDAC-shTFEB). The specific GSK3 inhibitor CHIR99021 (5uM) was used. Cells were challenged with DNA damaging agents doxorubicin (1uM) or etoposide (10uM). The phosphorylation of H2AX on S139 was evaluated as an indication of DNA damage.
Results: 1- GSK3 inhibition induced DNA damage. 2- DNA damaging agents induced DNA damage that were exacerbated in PDAC-shTFEB populations as compared to control PDAC-shCTL populations. 3- TFEB depletion impaired DNA repair upon treatment with DNA damaging agents. 4- PDAC-shTFEB cells were more sensitive to cell death upon GSK3 inhibition or treatment with DNA damaging agents.
Conclusions: For the first time, our results provide evidence that TFEB-depleted pancreatic cancer cells are less efficient at repairing DNA damage and are more prone to apoptosis upon treatment with DNA damaging agents. These results suggest that interfering with TFEB function may synergize with GSK3 inhibition and/or DNA damaging agents to promote death of pancreatic cancer cells.

A250
UNRESEQUABLE AND METASTATIC PANCREATIC ADENOCARCINOMA IN THE ELDERLY: A 10-YEAR SINGLE-CENTER EXPERIENCE
M. Langlois, F. Lemay, A. Beaudoin

Université de Sherbrooke, Sherbrooke, QC, Canada

Background: Pancreatic adenocarcinoma is the fourth leading cause of cancer deaths in Canada and mainly affects individuals older than 60 years of age. Because of its retroperitoneal location, pancreatic cancer follows a relatively silent clinical course and is more often diagnosed at an advanced stage. When faced with a diagnosis of unresectable pancreatic adenocarcinoma, patients may be offered palliative chemotherapy. Unfortunately, a paucity of data exists regarding the use of chemotherapeutic agents in the elderly population with pancreatic cancer.
Aims: The objective of this study is to obtain adequate profiling of the elderly patients with pancreatic cancer to better assess factors influencing outcomes and decision-making.
Methods: This is a retrospective observational study of all patients aged older than 75 years old with a diagnosis of unresectable or metastatic pancreatic cancer at the CHUS between June 2005 and June 2015. Data was retrieved using the local patient

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database program Ariane.

Results: During the study period, 225 patients were included according to the entry criteria. Median age at diagnosis was 82 years old with a slight female gender predominance (52% vs 48%). Location of the primary tumor was in the head of the pancreas in 46% of cases, and evenly distributed between the pancreatic body and tail. Diagnosis was made by the general practitioners or gastroenterologists in 73.4% of cases. High blood pressure, diabetes mellitus and coronary atherosclerosis were the most frequently encountered comorbidities. Other biochemistry parameters at diagnosis suggested a more fragile population; median albumin level of 32 g/L, median creatinine value of 155 µmol/L and minor anemia (median = 11.7 g/dL). Among all patients, only 10 opted for palliative chemotherapy. ECOG status was unfortunately far from uniformly documented, although among the 10 patients treated, all had either ECOG 0 or 1 scores. Nine received Gemcitabine as first line whereas one patient was treated with Folfirinox. Seven completed the treatment with the standard regimen dosage for each cycle. Patients received a median of 5 cycles and end of treatment was dictated by severe asthenia complicating treatment. Only 2 patients, non-responders, received second-line agents (5FU/LV) that were subsequently stopped, again for non-response.

Conclusions: Results of this unicentric observational retrospective study suggest an overall diminished clinical performance status in elderly patients diagnosed with unresectable or metastatic pancreatic cancer when compared to their younger counterparts. Due to our small sample size, it remains difficult to draw conclusions on ideal patient selection criterion and palliative treatment for advanced pancreatic cancer in the elderly. The present study does, however, underline the dire need for further studies on the matter.

Funding Agencies: None

A251
TC-325 USE IN MALIGNANT UPPER GASTROINTESTINAL BLEEDS: A MULTICENTRE RETROSPECTIVE STUDY
K.J. Marr[2], Z. Meng[1], R. Mohamed[2], P.D. James[1]

1. The University of Ottawa, Ottawa, ON, Canada; 2. The University of Calgary, Calgary, AB, Canada

Background: TC-325 has recently been proposed as a potential therapeutic agent for use in traditionally difficult to treat malignant upper gastrointestinal bleeds (UGIB).
Aims: The aim of this study is to assess the proportion of patients with malignant UGIB treated with either TC-325 alone or in combination with conventional therapy that achieve long-term hemostasis.
Methods: This is a multicentre retrospective study at the University of Calgary and University of Ottawa assessing the efficacy of TC-325 in achieving hemostasis in malignant UGIB between January 1, 2010 and July 30, 2016. TC-325 use was identified via staff polling, product order forms, and endoscopic records review. Once identified, patient charts and online records (Sunrise Clinical Manager, Calgary; vOACIS, Ottawa) were reviewed to identify those with malignant UGIB and to assess our primary and secondary endpoints. The primary outcome was hemostasis at 7 days. Secondary outcomes include immediate hemostasis, the need for repeat endoscopy, surgical intervention, transarterial embolization, and 30-day mortality.
Results: TC-325 was utilized for malignant UGIB in 19 patients. The median age was 68 (IQR 57-78), 11 were males (58%). Fifteen patients (79%) were Forrest Classification 1B with a median Blatchford score of 11 (IQR 7-12). TC-325 was utilized as the primary modality for hemostasis in 15 patients (79%). Eighteen patients (95%) achieved immediate hemostasis post-TC-325 and 8 patients (42%) eventually rebled after this. Three patients (16%) had recurrent bleeding within 24 hours. Only 13 patients had sufficient data to examine our primary endpoint of 7 days and 4 (31%) rebled by that time (all in Calgary). Three patients died before 7 days and 3 changed their goals of care. At 14 days, 3 patients (25%) rebled. A repeat endoscopy was required in 7 patients (37%). Two patients (11%) required surgical intervention. Transarterial embolization was not required. Ten patients died by 30 days (53%); one due to perforation of their malignant ulcer and another from an uncontrollable malignant UGIB. There were no complications directly associated with TC-325.
Conclusions: This is the first multicenter study evaluating 7-day hemostasis when TC-325 is used in malignant UGIB. TC-325 is effective at immediate and early hemostasis. However, rebleeding risk is increased by day 7 post-treatment. TC-325 may be utilized to immediately achieve hemostasis. Up to a third of patients may require another definitive intervention to achieve long-term hemostasis.

Funding Agencies: None

A252
IMPROVED QUALITY OF LIFE AFTER ENDOSCOPIC THERAPY FOR BARRETT'S ESOPHAGUS: A CANADIAN EXPERIENCE (2010-2016).
J. David[2], P.J. Belletrutti[1], M. Gupta[1]

1. Dept. of Medicine, Univ. of Calgary, Calgary, AB, Canada; 2. Alberta Health Services, Calgary, AB, Canada

Background: Radiofrequency ablation (RFA) and endoscopic mucosal resection (EMR) are safe and effective modalities to eradicate Barrett's esophagus (BE). There is limited Canadian data as to the value of these endoscopic therapies particularly the impact on patient quality life (QoL).
Aims: To determine the efficacy of RFA +/- EMR therapy

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for BE in the Calgary Zone including QoL impact.
Methods: A retrospective review was completed of a prospectively maintained database of patients who underwent endoscopic therapy of BE in the Calgary Zone from June 2010-August 2016. Treatment response was evaluated primarily as complete remission of dysplasia (CRD =absence of dysplasia on 2nd surveillance endoscopy post-treatment) and complete remission of intestinal metaplasia (CRIM =absence of BE on 2nd surveillance endoscopy post-treatment). Since 2014, all patients who received endoscopic therapy were invited to complete QoL questionnaires at each visit. QoL responses from baseline and 9-15 months later were analysed.
Results: Forty-two patients (95% male, mean age=67) with a mean BE length of 6.4cm completed endoscopic therapy. In those with high-grade dysplasia or intramucosal cancer (n=20), 18 had CRD (90%) and 15 achieved CRIM (75%) after a mean 3.2 RFA sessions (range 1-6). For low-grade dysplasia (n=15), 14 patients (93%) had CRD and 11 (73%) achieved CRIM after a mean 3.4 RFA sessions (range 1-8). In non-dysplastic BE (n=7), 6 (86%) achieved CRIM after a mean 4.7 RFA sessions (range 3-7). Overall, 15 (36%) patients had EMR during the course of treatment. Four patients (9%) developed a symptomatic stricture as a result of treatment. In the QoL survey (Table 1), after endoscopic treatment of BE, patients had significantly reduced worry about esophagectomy (p=0.01) and less stress due to their esophageal condition (p=0.03). There was also a trend toward decreased disease worry (p=0.14).
Conclusions: In Calgary, endoscopic therapy was safe and highly effective in achieving CRD and CRIM. Impact of these treatments on QoL is also significant, as patients progressively had less worry about esophagectomy and associated stress. Further prospective data is needed to confirm this response is sustained.

QoL responses in patients who completed Barrett's endotherapy (n=18).

QoL QUESTION VISUAL ANALOG SCALE 0-10 (0=none, 10=extreme)	RESPONSE AT BASELINE	RESPONSE AT FOLLOW-UP	p VALUE
Esophagectomy, worry - yes/no	27%	16%	0.01
Adenocarcinoma, worry - yes/no	61%	61%	1.0
Disease, worry -yes	2.2 (0-5.7)	1.9 (0.6-4.5)	0.14
Depression - median	0.4 (0-2.4)	0.4 (0-1.9)	0.79
Daily QoL - median	1.3 (0.2-2.1)	0.6 (0-1.5)	0.24
Stress, amount	1.0 (0-4.1)	0.7(0.1-1.5)	0.03
Satisfaction, amount	4 (1.9-7.8)	2.2 (1.7-5.6)	0.15
Sleep, difficulty	0.9 (0-2.1)	0.5 (0-1.7)	0.30
Work or family life, negative impact	0.6 (0-2.9)	0.7 (0-1.6)	0.55
Fear of death due to esophageal condition	1.4 (0-4.5)	1.2 (0.1-2.2)	0.24

QoL responses are expressed as median (interquartile range).

A253
MEASUREMENT OF NATURAL KILLER CELL ACTIVITY (NKA) IN SUBJECTS UNDERGOING COLONOSCO-PY:TEST PERFORMANCE OF A NEW BLOOD TEST AT DIFFERENT CUT-OFFS FOR THE DETECTION OF COLORECTAL CANCER (CRC)

M. Provençal[2], L. Rioux[1], G. Jobin[3], B. Katia[1], R. Rodriguez-Suarez[1]

1. gastroenterology, Hôpital Maisonneuve-Rosemont, Montréal, QC, Canada; 2. Maisonneuve-Rosemont Hospital, Montréal, QC, Canada; 3. Hôpital Maisonneuve-Rosemont, Montréal, QC, Canada

Background: Low NKA has been linked to a higher risk of cancer and has been reported in CRC patients.A novel simple blood test *in vitro* diagnostic device (IVDD) which measures NKA in a small volume of whole blood is now available.
Aims: Tha aim of the study is to evaluate the test performance metrics of the IVDD at different cut-offs in subjects with CRC and adenomatous polyps (AP).
Methods: This study measured NKA in 1081 subjects presenting for screening or prescribed colonoscopies using a biological assay performed as per the manufacturer's directions.
Results: In the 872 evaluable subjects,statistically significant differences were found between the NKA of subjects positive for CRC (n=23), and that of subjects negative for CRC (n=849) [CRC mean 317.1 pg/ml (DS:845.5),CRC-negative mean 745.7 pg/ml (SD:1028.5),p=0.001; CRC median 86.0 pg/ml (IQR:43.3-151.0),CRC-negative median 298.1 pg/ml (IQR:100.4-920.2),p<0.001]. The prevalence of CRC was 2.6% and of AP >10 mm was 14.6%. Receiver Operator Characterisitcs (ROC) analysis show an optimum cut-off for detection of CRC at 181 pg/ml,with an area under the curve of 73% (p<0.0001). At cut-offs of 200 pg/ml, high sensitivity and negative predictive values for detection of CRC were seen.
At cut-offs of 300 and 500 pg/ml, a slight improvement in the test performance was seen in the sensitivity for AP>10 mm. The odds ratio for the NKA IVDD for the detection of cancer at a cut-off of 200 pg/ml was 10.3 (95% CI 3.03-34.9).
Conclusions: The clinical results in the present study using new simple blood test for measurement of NKA confirm that there are limited benefits of using different cut-offs other than the optimal cut-off (220 pg/ml) for this new IVDD as determined by ROC analysis for detection of CRC

A254
SYNCHRONOUS GASTRIC ADENOCARCINOMA, MUCO-SA-ASSOCIATED LYMPHOID TISSUE LYMPHOMA AND GASTROINTESTINAL STROMAL TUMOR.

B. Adamowicz[1], E. Desilets[3], M. Bensoussan[3], L. Lamarre[2], T. Maniere[3]

1. Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Université de Sherbrooke, Charles-Lemoyne Hospital, Pathology Department, Longueuil, QC, Canada; 3. Université de Sherbrooke, Charles-Lemoyne Hospital, Medicine and Gastroenterology Department, Longueuil, QC, Canada

Background: Presently, there is very little literature on the simultaneous existence of different types of gastric cancers.
Aims: We present a case of rare concomitant cancers (adenocarcinoma, mucosa-associated lymphoid tissue lymphoma and gastrointestinal stromal tumor) in the stomach. It is important for clinicians to be aware of the various presentations of gastric cancers, as it may alter the treatment and prognosis.
Methods: This is a case report.
Results: We present the case and histology of a *H. pylori* negative 70-year-old man with concomitant adenocarcinoma, mucosa-associated lymphoid tissue lymphoma (MALT) and gastrointestinal stromal tumor of the stomach who was successfully treated with total gastrectomy and oesophago-jejunostomy Roux-en-Y anastomosis.
Conclusions: Although *H. pylori* seems to play an important role in the pathogenesis of gastric adeno-carcinoma and mucosa-associated lymphoid tissue lymphoma (MALT), its role in the carcinogenesis of gastrointestinal stromal tumors is still unknown. In addition, the link between these tumours becomes more complex in *H. pylori* negative patients. Many authors have argued that the discovery of synchronous neoplasms in a single tissue is coincidence. It is for this reason that some physicians may underreport the incidence of concomitant tumours. It is important for clinicians to be aware of the various presentations of gastric cancers, as it may alter the treatment and prognosis.

Post surgical stomach pathology demonstrated concomitant GIST (A), MALT (B) and adenocarcinoma (C).

A255
FULL-THICKNESS ENDOSCOPIC COLONIC RESECTION USING AN OVER-THE-SCOPE CLIP: A CASE REPORT

N.C. Shahidi[1], S. Moosavi[1], W. Xiong[2], E. Lam[1]

1. St. Paul's Hospital, Division of Gastroenterology, Department of Medicine, University of British Columbia, Vancouver, BC, Canada; 2. St. Paul's Hospital, Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada

Background: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are established methods for removing colonic polyps. However, both have their limitations, specifically in the setting of recurrence with scarring and fibrosis increasing the technical difficulty and the potential for procedure-related adverse events.
Aims: To describe the first Canadian experience of endoscopic full-thickness resection performed with an over-the-scope clip.
Methods: Case Report.
Results: A previously healthy average-risk 80-year-old female underwent colonoscopy (CSPY) for a positive fecal immunochemical test (871 ng/ml) which identified a 20mm sessile ascending colon polyp. On staged CSPY, the polyp was removed by EMR and the resection site tattooed. Pathology showed tubular adenoma with focal high-grade dysplasia. After 6 months, interval CSPY was performed which identified recurrence of a 10mm sessile polyp at the previous resection site. During EMR a "non-lifting" sign was identified with methylene blue injection. Therefore, biopsies of the resection site were taken. Pathology of the EMR specimen showed tubular adenoma however biopsies of the resection site showed fragments of tubular adenoma with high-grade dysplasia. In follow-up, the risks and benefits of surgery versus endoscopic resection were discussed and the patient consented for endoscopic full-thickness resection. The patient was positioned in left lateral decubitus and received conscious sedation (total: midazolam 3mg intravenous; fentanyl 50 mcg intravenous). Using a pediatric colonoscope, equipped with an over-the-scope clip device, the previous resection scar was identified. Cautiously, the scar and surrounding bowel were brought into the cap with gentle suction; After which the over-the-scope clip was deployed. Using a hexagonal snare, the bowel entrapped by the over-the-scope clip was then resected in a single specimen. No subsequent endoscopic intervention was required and the endoscope was withdrawn with no immediate peri-procedural complications. On pathology, a single polypoid fragment showed residual tubular adenoma with no high-grade dysplasia and clear margins. Deep aspects of the biopsy contained muscularis propia highlighting full-thickness resection.
Conclusions: This is the first Canadian experience of

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endoscopic full-thickness resection. It highlights not only the safety of the procedure, but also the feasibility with conscious sedation.

Funding Agencies: None

A256
DETERMINATION OF PROTEOMIC SIGNATURE OF RESPONSE TO NEOADJUVANT RADIO-CHEMOTHERAPY IN COLORECTAL CANCER PATIENTS
A. Chauvin[1], A. Mathieu[1], V. Lacasse[1], C. Wang[1], S. Geha[1], P. Garde-Granger[3], F. Boisvert[2]

1. Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada; 3. Université de Sherbrooke, Sherbrooke, QC, Canada

Background: Neoadjuvant radio-chemotherapy (NRCT) is current standard care for patients with colorectal cancer (CRC). Patients are often diagnosed late with locally advanced tumor completely invading wall of rectum (T3) or peripheral tissues or organs (T4), or if regional lymph node metastases are founded (N1/N2). In these cases, standard treatment is preoperative radiotherapy with concomitant chemotherapy. It reduces tumor infiltration and decreases tumor stage (down-staging), which is important because it increases a complete resection rate during surgery and improves loco-regional tumor control, patient survival and quality of life by preserving sphincter function, urinary and sexual organs. The Centre Hospitalier de l'Université de Sherbrooke (CHUS) processes approximately 50-80 new cases of CRC and undergoes this standard treatment protocol.
Aims: While 60% of patients show positive response, including up to 17% with complete remission, a subset of patients with same tumor stage and having been treated with same technique do not respond favourably. Considering the severe secondary effects observed, there is a strong incentive to be able to predict outcome of the treatment. Clinical markers currently used are not able to predict individual response of patient that would allow personalization of treatment. Relevant biological factors to guide patient to customized adjuvant chemotherapy are missing to guide clinician in clinical decisions. Our aim is to investigate protein profile to identify prognostic biomarkers of response before and after NRCT by mass spectrometry.
Methods: Tumor tissues obtained from biopsy and from surgery, before and after NRCT respectively, are used to identify an expression profile predictive of response. Paraffin-embedded samples are heated in detergents and xylene to remove paraffin and reverse formaldehyde crosslinking. Proteins are separated by SDS-PAGE and gel lane is subjected to in-gel trypsin digestion. Desalted peptides are analysed by mass spectrometry to determine expression of thousands of proteins.
Results: Experiments allowed us to determine proteomic signature representative of different clinical outcomes. We have validated method of extraction and protein identification and completed 37 human CRC samples, resulting in identification and quantification of over 3000 proteins, and we are currently processing a second batch of 115 samples received from pathology department. We identified several pathways and potential biomarkers that could be predictive of the outcome of treatment.
Conclusions: Informations from this study generated large amount of data on proteins involved in processes of resistance to treatment. Using a novel proteomic approach, this multidisciplinary project will establish a personalized approach to optimize treatment of CRC.

Funding Agencies: Merck

A257
PANCREATOBILIARY CANCER WITH UNUSUAL SITE OF METASTASIS
M.H. Alageeli[1], K. Qumosani[2]

1. Gastroenterology , UWO, London , ON, Canada; 2. UWO, London, ON, Canada

Background: Pancreatobiliary cancer can present as a locally advanced tumor or with distal metastasis. The common sites for metastases are the liver, lungs, lymph nodes and peritoneal cavity. Metastasis to colon and anal canal are extremely rare.
Aims: To descripe a rare presentation of Pancreatobiliary cancer which need a high index of suspicion to diagnose and treat early.
Methods: A 65-year-old with multiple co-morbidities, who was initially referred to Gastroenterology team for evaluation for GI bleed associated with significant weight loss. He underwent an upper and lower scope, which revealed only mild radiation proctitis .He had abdominal CT, which showed portal vein thrombosis and to further evaluate this clot he underwent endoscopic ultrasound (EUS) which did not reveal any evidence of cancer. However. It only showed that the main pancreatic duct in the body was slightly dilated. His Alkaline Phosphatase and glutamytransferase were elevated . For further evaluation of his abnormal liver profile and weight loss, MRCP was ordered but it returned back normal.
Few months latter, he presented to the emergency department with weakness and bright red bleeding per rectum. He was diagnosed with left MCA stroke and admitted to ICU. Interestingly, his LFTs results showed significant increase ,specifically ALP and GGT levels, from his baseline.
Flexible Sigmoidoscopy was done to further evaluate his lower GI bleed and it showed again an evidence of radiation proctitis but this time multiple biopsies were taken from the rectum. His rectal biopsy showed: Atypical glandular structures straddling the muscularis mucosa highly suggestive for malignancy from pancreatcobiliary tree. He had full work up for his elevated ALP including AMA, which was negative. CA 199 was

ordered and the result was extremely high >10000 units/ml(rest of the tumor markers including CEA and AFP were unremarkable). Looking at the full picture including his presentation with weight loss, finding on his rectal biopsy and elevated CA19-9 fulfill the diagnosis of metastatic pancreatobiliary cancer, most likely infiltrative cholangiocarcinoma.

Results: Diagnosis of pancreatobiliary cancer based on extremely elevated CA19-9 and rectal metastasis .

Conclusions: Based on the literature, a small number of colon metastases have been reported to occur in relation to cholangiocarcinomas(only 4 cases)and pancreatic adenocarcinomas(only 3 cases).In fact, the rectal metastasis wasn't described in the literature before and this was the first case to show a rectal metastasis from a pancreatobiliray cancer. Finally, as we know to increase specificity and PPV of CA199 to diagnosis pancreatobiliary cancer we need a higher level (100 or even >1000 Units/ml), in our case the level was very high which makes other causes to be unlikely.

IMMUNOBIOLOGY AND LIVER TRANSPLANTATION

A258
HISTOLOGICAL FINDINGS IN PROTOCOL BIOPSIES FOLLOWING PAEDIATRIC LIVER TRANSPLANTATION: LOW INCIDENCE OF ABNORMALITIES WITH TACROLIMUS MONOTHERAPY AT FIVE YEARS
A. Sheikh[1], H.M. Evans[2]

1. Gastroenterology, Hepatology & Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 2. Starship Children's Health, Auckland, New Zealand

Background: Histological abnormalities (chronic hepatitis, fibrosis & steatosis) are increasingly reported in liver biopsies of children after liver transplantation (LT). These changes may be progressive & represent a form of rejection. Liver biochemistry is often initially normal. The LT programme in New Zealand began in 2002, utilising tacrolimus and low-dose steroids for the first year. Patients undergo a protocol biopsy at one year post LT prior to stopping steroids, then at 5 yrs and every 5 yrs thereafter. Target tacrolimus levels are 5-8 g/L and 3-5 g/L after 3 and 12 months respectively.

Aims: The evaluate the incidence and characteristics of histological abnormalities in protocol biopsies at 1 and 5 yrs post paedritric LT in a cohort of patients on predominantly tacrolimus monotherapy

Methods: Between 2002-2009, 51 children underwent LT; 50 (98%) and 49 (96%) patients survived for 1 and 5 yrs respectively. 41 patients (median age at LT 2.3 yrs) underwent a protocol biopsy at 1yr (16 male; median time post LT 12.5 months), and 43 (20 male; median time post LT 5.1 yrs) at 5 yrs. By 5 yrs, 3 had transferred to adult services; 1 was re-transplanted for

graft failure & 1 moved overseas. Most patients (30/43) were on tacrolimus monotherapy at 5 yrs**.**

Results: At 1 & 5 yrs 29/41 (71%) & 29/43 (67.5%) biopsies were normal respectively. 2/43 had chronic immune hepatitis at 5 yrs. 1/41 & 3/43 had fibrosis, 3/41 & 3/43 steatosis, and 2/41 and 3/43 acute rejection at 1 & 5 years respectively. Other findings included predominantly biliary changes (6/41 & 2/43 at 1 & 5 yrs respectively). Tacrolimus levels at 5 yrs were slightly higher than anticipated (median trough level 5.1 g/L).

Conclusions: With an immunosuppressive regimen of tacrolimus and low dose steroids for 1 year followed by tacrolimus monotherapy thereafter, the majority of protocol liver biopsies were normal and no progressive changes were observed at 5 yrs. Compared to other LT programmes, we have reduced rates of chronic allograft hepatitis, steatosis and fibrosis at 5 yrs. However, the tacrolimus levels at 5 yrs were higher than planned & this may have played a role. Further evaluation is also required to determine the potential long-term adverse effects of corticosteroid use on linear growth and bone mineral density

RESULTS

	HISTOLOGY	NUMBER (%)	Median ALT iu/L (range)	Median trough tacrolimus g/L (range)
1 YR BIOPSIES	Normal	29 (72.5)	26 (9-580)	6.9 (4-10.5)
	Immune hepatitis	0	0	0
	Rejection	2 (5)	456.5 (149-764)	7.6 (6.3-7.2)
	Steatosis	3 (7.5)	23 (15-83)	7.4 (6.8-7.2)
	Fibrosis	1 (2.5)	30	3.9
	Other	6 (12.5)	132 (42-764)	6.1 (4.2-11.1)
5 YR BIOPSIES	Normal	29 (67.5)	16 (10-119)	5.1 (1.5-10.7)
	Immune hepatitis	2. (4.5)	23.5 (8-39)	6.6 (4-9.2)
	Rejection	4 (9.5)	32.5 (12-115)	7.3 (5.2-9.4)
	Steatosis	3 (7)	28 (21-35)	4.2 (4.2-11.6)
	Fibrosis	3 (7)	64 (18-110)	5.7 (4.1-7.2)
	Other	2 (4.5)	97.5 (74-121)	10.2 (4.2-16.4)

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ELEVATED BIOCHEMICAL LIVER TESTS WITHIN 1-YEAR TRANSPLANT PREDICTS RECURRENT PSC

S. Wasilenko[1], E. Lytvyak[4], A.J. Montano-Loza[2], A.L. Mason[3]

1. University of Alberta, Edmonton, AB, Canada; 2. Division of Gastroenterology & Liver Unit , University of Alberta , Edmonton, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. University of Alberta, Edmonton, AB, Canada

Background: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease affecting bile ducts leading to cirrhosis and end-stage liver disease. Liver transplant is the only effective treatment however 6-59% of those transplanted develop recurrent PSC (rPSC). Many risk factors for recurrence have been proposed yet only the presence of ulcerative colitis has been validated in multiple studies. We hypothesized patients who develop rPSC have elevated liver tests within the first year following transplant, as previously observed with recurrent hepatitis C and recurrent autoimmune hepatitis.

Aims: To determine if elevated liver tests within 1 year of transplant predicts rPSC.

Methods: PSC patients who underwent liver transplant at the University of Alberta Hospital from 1991 to 2015 were included. Recurrent PSC was defined by cholangiography and/or histological findings. Recurrence free survival and graft loss was compared between patients with and without rPSC. Liver tests including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin were assessed at 3, 6, 9, and 12 months after liver transplant. Abnormal liver tests were defined as values above the ULN for ALT, AST and bilirubin or 1.5XULN for ALP.

Results: One hundred and thirty-one patients were included. Mean transplant age was 43 years with 98 (75%) males and rPSC occurred in 40/131 (30%) patients. Mean recurrence time was 70 months (4 to 172 months) with rPSC rates of 4% and 20%, at 1 and 5 years, respectively. Median survival time was similar between rPSC and non-rPSC (132±11 *vs* 175±13 months, P=0.28). Mean time to graft loss was lower in those with rPSC (109±12 *vs* 180±13 months, P=0.003). Recurrent PSC patients with AST and ALT≥ULN at 12 months had disease recurrence occur earlier than those with normal AST and ALT (19±17 *vs* 78±50 months, P=0.001) and rPSC developed sooner in patients with ALP≥1.5XULN and ALT≥ULN at 6, 9, and 12 months inclusive (13±4 *vs* 66±51months, P=0.001). Multiple liver test abnormalities were identified that predict the development of rPSC (see table).

Conclusions: Post-transplant abnormal hepatocellular and cholestatic biochemical liver tests within the 1st year or transplant predicts rPSC.

Hazard Ratios (HR) for Developing rPSC:

Liver Tests	Months	HR	95% Confidence Interval	P-value
ALT≥ULN	3	3.3	1.4-7.7	0.005
ALT≥ULN	9	2.7	1.1-6.4	0.023
ALT≥ULN	12	4.1	1.9-9.2	0.001
ALP≥1.5XULN	3	2.1	1.0-4.3	0.049
ALP≥1.5XULN	9	2.3	1.2-4.7	0.017
ALP≥1.5XULN	12	2.4	1.2-4.8	0.015
ALT≥ULN and AST≥ULN	12	5.1	2.3-11.4	0.001
ALP≥1.5XULN and ALT≥ULN	6	2.7	1.2-6.3	0.022
ALP≥1.5XULN and ALT≥ULN	9	4.3	1.7-10.7	0.002
ALP≥1.5XULN and ALT≥ULN	12	10.7	4.4-26.3	0.001
ALP≥1.5XULN and ALT≥ULN	6, 9, 12	17.1	4.4-67.0	0.001

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OUTCOMES OF LIVER TRANSPLANTATION FOR ACUTE LIVER FAILURE AMONG RECIPIENTS WITH ABO-IDENTICAL VS. ABO-COMPATIBLE VS ABO-INCOMPATIBLE GRAFTS

Z. Bahreini

Gastroenterology, Western University, London, ON, Canada

Background: Acute liver failure is associated with a high mortality rate due to multi-organ failure, sepsis and cerebral edema. Liver transplantation remains the only life saving treatment available for these critically ill patients. Urgent liver transplantation within 48 to 72 hours has shown to be crucial for reducing the waiting list mortality of these patients. However, liver grafts are a scarce resource, leading to a significant rate of mortality for patients in need of urgent liver transplant. ABO-incompatible (ABO-in) liver transplantation is occasionally used as a rescue alternative when an ABO-identical (ABO-id) or compatible (ABO-c) graft is not available. The outcomes of ABO-in liver transplantation using deceased donors have been variable but mostly reported to be associated with poor graft function, early graft loss and an increased rate of complications. There are however limited studies examining long term outcomes of liver transplantation with ABO-in grafts.

Aims: The aim of the study was to compare long term mortality and graft survival of patients undergoing liver transplantation with ABO-id vs. ABO-c and ABO-in donor grafts. A secondary objective was to determine other predictors of poor outcome in patients requiring urgent liver transplantation for acute liver failure.

Methods: A retrospective cohort study was done to examine adult patients who underwent urgent liver

transplantation between 1985 and 2016 in London, Ontario. Patients were divided into three cohorts depending on their grafts' ABO compatibility: ABO-id, ABO-c and ABO-in. Transplant outcomes in the peri and post transplant period were collected for all three cohorts. Multivariate logistic regression was used to assess ABO-compatibility as a predictor of graft failure and patients' death.

Results: 73 patients with emergency liver transplantation were studied. Of those, 9.6% received an ABO-in graft. Rate of retransplantation in ABO-id, ABO-c and ABO-in groups was 2.5%, 11.5% and 57%, respectively. The OR of graft failure in the ABO-in group was 13 times greater when compared to ABO-id (OR 13.3, p 0.02). There was no statistically significant difference in graft survival between ABO-c and ABO-id groups (OR 3.5, p 0.12). OR of death was not significantly different between the three groups. Age (OR 1.06, p0.04), need for inotropic support (OR 6.2, p0.02) and stroke (OR 15.2, p0.03) were more important predictors of death than ABO compatibility itself.

Conclusions: ABO-in liver transplantation was associated with higher rates of graft failure and retransplantation however there was no significant difference in long term mortality in these patients. In select adult patients with acute liver failure in need of an emergency liver transplantation, ABO-in transplants should be viewed as an important lifesaving therapeutic option with comparable results in long term survival.

A261
DIRECT ACTING ANTIVIRAL THERAPY IS EFFECTIVE IN RECURRENT HEPATITIS C IN BOTH TREATMENT NAIVE AND EXPERIENCED LIVER TRANSPLANT RECIPIENTS: CLINICAL AUDIT OF THE ATLANTIC MULTI-ORGAN TRANSPLANT PROGRAM

G. Hirsch[4], M. Miles[2], S.E. Peltekian[4], J. Kiberd[1], B.I. Brown[8], M. O'Brien[9], J. Leonard[3], L.C. McKnight[7], M. McLeod[8], M. Laryea[5], K.M. Peltekian[6]

1. Division of Gastroenterology, Dalhousie University, Halifax, NS, Canada; 2. Internal Medicine, Dalhousie University, Halifax, NS, Canada; 3. Health Sciences Centre, St. John's, , Canada; 4. Hepatology Services, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; 5. Queen Elizabeth II Health Sciences Center, Halifax, NS, Canada; 6. Atlantic Multi-Organ Transplantation Pogram, Queen Elizabeth II Health Sciences Centre, Halifax, NS, Canada; 7. Saint John Regional Hospital, Saint John, NB, Canada; 8. Atlantic Multi-Organ Transplant Program, Halifax, NS, Canada; 9. Upper River Valley Hospital, Waterville, NB, Canada

Background: Hepatitis C virus (HCV) has been the main indication for liver transplantation (LT) with universal recurrence after transplantation and significant morbidity and mortality post LT. The newer interferon-free direct acting antiviral agents have been effective in achieving sustained viral response (SVR).

Aims: To document the efficacy, safety and tolerability of interferon-free direct acting antiviral agents in the treatment of HCV recurrence in all genotypes in liver transplant patients from Atlantic Canada.

Methods: As part of quality improvement audit, we searched the AMOTP liver transplant database for all patients with HCV who had undergone LT. We then specifically extracted data on the LT patients who had direct acting antiviral agents initiated to assess efficacy of therapy. Post treatment SVR was determined by HCV RNA levels at week 12.

Results: Between July 1985 and June 2016, 583 liver transplants were done within the Atlantic Multi-Organ Transplant Program (AMOTP). Of those 119 (20%) recipients were HCV-Antibody positive at time of liver transplant. By end of study period, 62 with HCV-Antibody were still alive. Between July 2014 and August 2016, 24 liver transplantation recipients from across Atlantic Canada with HCV recurrence [defined as positive HCV-RNA by PCR and liver biopsy proven disease showing at least grade 2 (inflammation) and/or stage 2 (fibrosis)] were started on interferon-free orally direct acting antiviral. Most patients (88%) received sofosbuvir (SOF) based regimes (sovaldi + ribavirin (RBV), n=5; SOF + RBV, n=5; SOF + ledipasvir + RBV, n=13; SOF + sovaldi, n=1). The mean age of these patients was 62.8 ± 4.9 years with the majority being genotype 1 (75%) and male (79%). Eighteen of twenty-two (82%) patients have undetectable HCV RNA viral loads at the end of treatment, with two patients still undergoing evaluation. Thirteen of seventeen (76.5%) patients have achieved SVR with 2 non-responders, 1 relapse and 1 early discontinuation due to non-compliance. The remaining 5 patients are still undergoing evaluation.

Conclusions: Treatment of HCV infected patients with interferon-free regimens after liver transplantation appears efficacious and well tolerated.

A262
QUALITY OF LIFE IN PRE-ADOLESCENT CHILDREN AFTER PEDIATRIC LIVER TRANSPLANT FOR BILIARY ATRESIA IS SIMILAR IN EUROPE AND CANADA

m. miserachs[2], A. Bakula[4], J. pawlowska[4], L. Hierro[5], l. D'antiga[6], I. Goldschmidt[7], U. baumann[7], V. mclin[8], D. Debray[9], P. Mckiernan[10], S. beath[10], A. Otley[1], V. Ng[3]

1. Pediatrics, Dalhousie University, Halifax, NS, Canada; 2. Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 3. Division of Pediatric GI/Hepatology/Nutrition, The Hospital for Sick Children, Toronto, ON, Canada; 4. Instytut Pomnik-Centrum Zdrowia Dziecka, Warsaw, Poland; 5. Hospital La Paz, Madrid, Spain; 6. Hospital Papa Giovanni XXIII, Bergamo, Italy; 7. Medizinischen Hochschule Hannover, Hannover, Germany; 8. Hôpitaux Universitaires de Genève, Geneve, Switzerland; 9. Hôpital Necker-Enfants Malades, Paris, France; 10.

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Birmingham Children's Hospital, Birmingham, United Kingdom

Background: Biliary atresia (BA) is the commonest indication for pediatric LT performed in infants, with excellent long-term patient and graft survival world-wide. Optimizing durable outcomes for this patient population can be enhanced by understanding health-related quality of life (HRQoL) concerns.

Aims: This pilot study aimed to evaluate and compare HRQoL of middle-school aged BA subjects who underwent LT in Europe and Canada, and to explore the relationship between HRQoL with demographic and medical variables.

Methods: Following available guidelines, the English-version of a pediatric liver transplant-specific HRQoL questionnaire (PeLTQL) available for children 8 to 18 years, was translated and cross-culturally adapted into five different languages.

Inclusion criteria included BA subjects with current age between 8 to 12 years who underwent LT before the age of two years followed in one of 8 different pediatric LT centers in Canada or in a ChilSFree/EPLTN network program. Patients completed validated disease-specific (PeLTQL) and generic (PedsQL™) HRQoL tools. Their parents completed the corresponding, validated parent-proxy tools. Total PeLTQL and PedsQL™ scores range between 0 and 100, with higher scores indicating better HRQoL. Patient demographics and medical variables were also reviewed.

Results: A total of 64 [female 54%, white 83.4%, median age 9.77 (range 8.05-12) years] BA subjects 6 or more years after LT were evaluated. Polish, Spanish, Italian, English, German and French questionnaires were completed by 19, 18, 10, 10, 5 and 2 BA subjects respectively. High correlation was seen between patient-reported and parent-reported PeLTQL scores (r=.71, p <0.0001) and between PeLTQL and PedsQL™ scores (r=.61, p<0.0001). Total PedsQL and PeLTQL scores were not statistically different between different language-speaking populations. Higher total PeLTQL scores were seen in subjects on immunosuppression monotherapy (60.9%, 100% on Tacrolimus) compared to patients on dual or multiple therapy (n = 39 vs 23; PeLTQL Total Score 78.4±12.9 vs 68.5 ±18.5, p= 0.03).

Conclusions: Total PedsQL and PeLTQL scores were not different in pediatric LT recipients with BA across six different language-speaking populations in this pilot study, suggesting similarity of broader determinants of health issues. Ongoing work is targeting better understanding of the impact of immunosuppression requirements on HRQoL.

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Poster of Distinction

A263
IBS-D MICROBIOTA INDUCES GUT-BRAIN DYSFUNCTION BY DISRUPTING INTESTINAL NEURAL AND IMMUNE PATHWAYS

V. Serkis, G. De Palma, S. Cocciolillo, M. Pigrau, J. Lu, E. Verdu, P. Bercik, S.M. Collins

McMaster University, Hamilton, ON, Canada

Background: Irritable Bowel Syndrome (IBS) is a disorder of the gut-brain axis, with altered gut function and frequent psychiatric co-morbidity. We have previously shown in gnotobiotic mice that fecal microbiota from patients with IBS with diarrhea (IBS-D) and co-morbid anxiety induces faster gastrointestinal transit, gut barrier dysfunction, immune activation and anxiety-like behavior. However, the exact mechanisms underlying these abnormalities are not understood.

Aims: To investigate and characterize the role of neural and immune factors in the microbiota-mediated alteration of gut physiology and behaviour.

Methods: The expression of 72 murine genes related to neural, immune, and epithelial function was measured with NanoString nCounter® gene assay on total RNA extracted from colonic sections of mice colonized with microbiota from IBS-D patients or healthy volunteers. Colonic histology sections were stained for F4/80+ cells and multi-parameter flow cytometry was used to survey population of conventional and innate-like lymphocytes from various lymphoid compartments including the spleen, mesenteric lymph nodes, lamina propria, and intra-epithelial lymphocytes.

Results: Mice colonized with IBS-D microbiota had a strong upregulation of neural genes involved in secretomotor function (VIP, ChAT, CALB), visceral sensitivity (NR2D and GABA-B), innate immunity (CD11c, CCR2, GATA-3, and GPR44) and regulation of epithelial integrity and control of commensal microbiota (Trefoil factor 3 and Lysozyme) compared to mice colonized with healthy microbiota. Lamina propria macrophages levels were higher in IBS-D colonized mice compared to healthy controls. Multi-parameter flow cytometry revealed similar frequencies of conventional T cells (CD3+CD4+ and CD3+CD8+) or B cells (CD19+B220+) in the spleen, MLN, and intestinal compartments between mice with IBS-D microbiota vs. healthy controls. However, there was a higher relative frequency of TCRαβ-TCRγδ -RORγt+ cells in the colonic lamina propria of mice with IBS-D microbiota compared to healthy controls.

Conclusions: Our results demonstrate that the intestinal microbiota from patients with IBS-D and co-morbid anxiety alters multiple immune and neural system pathways involved in the regulation of gut function. IBS-D microbiota appears to affect the innate but not the adaptive immune system, with macrophages and innate lymphoid cells playing a key role.

A264
AUTOPHAGY IS CRITICAL FOR GOBLET CELLS TO MAINTAIN HOMEOSTASIS UNDER HIGH METABOLIC STRESS
S. Tiwari[1], F. Moreau[3], K. Chadee[2]

1. Microbiology, Immunology and Infectious Diseases, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada; 2. Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, AB, Canada; 3. Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

Background: Cellular stress induced by external or internal agents lead to the activation of several processes to maintain homeostasis. These processes involve the unfolded protein response (UPR), apoptosis and autophagy. Autophagy is a catabolic pathway that mediates the degradation of cellular components into double-membrane vesicle fused with lysosomes forming autolysosomes that lead to the removal of non-functional proteins and organelles. Goblet cells in the gut secrete MUC2 mucin to form the mucus layers which serves as a protective barrier against invading microbes and noxious substances. Autophagy has been suggested to play a role in the regulation of mucin secretion and cell survival by an unknown mechanism. AMPK has been shown to be an essential mediator to activate autophagy through mTOR inhibition to maintain metabolic homeostasis and cell survival. As goblet cells undergo increased ER stress to produce MUC2 mucin under inflammatory and disease conditions we hypothesize that autophagy plays a role in MUC2 degradation and/or cell survival.
Aims: To quantify the autophagy response and AMPK signaling in high and low MUC2 producing HT29 cells.
Methods: High MUC2-producing human HT29-H cells and a clone of HT29-H silenced for MUC2 (HT29-L) by lentivirus shRNA was used in the study. Autophagy proteins were evaluated in HT29H/L cells by Western blot using monoclonal antibodies for ULK1 and their phospho-antibodies. AMPK signaling was quantified by anti-AMPKα antibody. Autophagy and AMPK genes were quantified transcriptionally by RT-PCR. Acadesine (AICAR) and Torin1 was used to activate AMPK signaling and autophagy respectively.
Results: High MUC2 producing HT29-H cells under metabolic stress accumulated misfolded MUC2 proteins and impaired basal autophagy protein expression (LC3-II and ULK1) as compared to HT29-L cells. Basal phosphorylation of pULK1(S555) was upregulated through an AMPK-mediated mechanism in HT29-H cells whereas pAMPKα (T172) was downregulated in HT29-L cells. Cells stimulated with the AMPK agonist, acadesine (AICAR), enhanced pAMPKα (T172) and ULKI phosphorylation in HT29-H but not HT29-L cells. Similarly, stimulation with Torin1 (an autophagy inducer) increased the expression of AMPKα and ULK1 in HT29-H but not HT29-L cells. These results suggest that the impaired phosphorylation events in autophagy and AMPK signaling in HT29-H may lead to perturbed homeostasis.
Conclusions: The interplay between autophagy with AMPK signaling helps to maintain homeostasis in intestinal epithelial cells. This study demonstrates that impaired autophagy in high MUC2 mucin-producing cells might be a cellular defense to enhance cell survival.

A265
INVOLVEMENT OF LRP6 IN INTESTINAL HOMEOSTASIS AND INFLAMMATION
j. raisch, M. Langlois, E. Lemieux, N. Rivard

Université de Sherbrooke, Sherbrooke, QC, Canada

Background: Self-renewal of the intestinal epithelium is tightly regulated by interacting intracellular signaling pathways, which control stem cell proliferation and differentiation. In particular, Wnt/b-catenin signalling controls crypt cell proliferation and survival and is required for maintenance of intestinal stem cells. Additionally, maturation of Paneth cells in the intestine also depends on this pathway. Wnt signals are transduced through Frizzled receptor and LRP5/LRP6 coreceptor to downregulate GSK3β activity, resulting in increased nuclear β-catenin. Recently, LRP6 was identified as a new candidate gene in ileal Crohn's Disease (Koslowski, PLoS Genet 2012).
Aims: In the present study we would like to explored whether LRP6 is required for the maintenance of intestinal homeostasis and barrier function.
Methods: Using the Cre/loxP system, mice with an intestinal epithelial cell-specific deletion of LRP6 (LRP6[IEC-KO] mice) were generated. Tissue architecture was visualized with hematoxylin-eosin staining and Paneth cells by lysozyme staining. Intestinal permeability was evaluated by dextran-FITC method. Crypts were isolated from control and mutant mice and organoid cultures were established as an *ex vivo* model of epithelial regeneration. The sensitivity of mice to inflammation was evaluated by giving 2% DSS to mice for 7 days. Mice were scored based on a scale of 0 to 4 for stool consistency, rectal bleeding, colon hardness and blood loss, and a cumulative disease activity index (DAI) was calculated.
Results: Loss of LRP6 expression was validated in LRP6[IEC-KO] mice compared to control mice. At 4 weeks of age, no difference in body weight of LRP6[IEC-KO] mice was noticed in comparison to control mice. Histological analyses indicate that the architecture of the small and large intestine was apparently not altered. Surprisingly, the number of proliferative cells remained unchanged in LRP6[IEC-KO] mice and no difference in Paneth cell number was seen. However, intestinal permeability was markedly increased in 3-month-old LRP6[IEC-KO] mice compared to control littermates. Furthermore, deletion

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of LRP6 clearly impaired organoid development as determined by measurement of both organoid growth and budding. Finally, LRP6[IECKO] mice were much more sensitive to DSS treatment in comparison to control littermates.

Conclusions: These results suggest that LRP6 regulates IEC-mediated mucosal homeostatic and inflammatory responses.

A266
AMYLASE TRYPSIN INHIBITORS FROM WHEAT EXACERBATE GLUTEN-INDUCED PATHOLOGY AND ALTER GUT MICROBIOTA IN MICE

J. McCarville[2], M. Pigrau[1], V. Zevallos[3], A. CAMINERO FERNANDEZ[2], J. Jury[2], P. Bercik[2], D. schuppan[3], E. Verdu[2]

1. Institut de Recerca Hospital Vall d, Hamilton, ON, Canada; 2. McMaster University, Hamilton, ON, Canada; 3. University Medical Center of the Johannes Gutenberg University, Mainz, Germany

Background: Celiac disease (CeD) is an autoimmune enteropathy triggered by gluten in genetically susceptible individuals expressing HLA DQ2 or DQ8. The adaptive immune response is characterized by a gluten-specific T-cells, anti-gluten and anti-tissue transglutaminase-2 antibodies. Proliferation and activation of intraepithelial lymphocytes (IELs) is central to the innate immune response, although the triggers and receptors remain unclear. Amylase trypsin inhibitors (ATIs) are pest-resistant molecules in modern wheat with TLR4-activating capacities in mononuclear phagocytic cells.
Aims: Our aim was to determine whether ATIs act as innate activators, enhancing gluten immunopathology in mice.
Methods: NOD/DQ8 mice sensitized with cholera toxin and gliadin received a diet containing: 1) ATIs with no gluten (ATIs), 2) gluten de-enriched of ATIs (G-deATIs), or 3) G supplemented with ATIs (G+ATIs), for 2 weeks. Non-sensitized NOD/DQ8 (controls) received a wheat-free diet (WFD) for 2 weeks. To determine if ATIs could induce symptoms of wheat-sensitivity in non-genetically susceptible mice, C57BL/6 were placed on WFD or ATI diet for 1 week. CD3^{+} IELs were measured by immunohistochemistry, paracellular permeability by Ussing chambers and 16s profiles of cecal contents via Illumia MiSeq.
Results: NOD/DQ8 mice receiving G+ATIs developed increased paracellular permeability, higher CD3^{+} IEL counts and decreased villous-to-crypt (V/C) ratios compared with controls fed a WFD. Mice receiving ATIs and G+ATIs had lower *Lactobacillus* abundance in comparison with mice on a WFD and G-deATIs, respectively. An *in vitro* screen of ATI metabolism by bacteria, suggested that commensals are capable of degrading ATIs, including some *Lactobacillus* strains. C57BL/6

mice on an ATI diet developed increased paracellular permeability and CD3^{+} IELs in comparison to mice on a WFD, but no decreases in V/C ratios.
Conclusions: Our results indicate that ATIs induce IELs and exacerbate gluten-induced pathology in susceptible mice, while only leading to innate immune activation in WT mice. Thus, ATIs in wheat may initiate innate immunity in celiac disease or promote symptom generation in people with Non-Celiac Wheat Sensitivity. Supplementation with *Lactobacillus* strains involved in ATI metabolism may help attenuate gluten-related disorders.

A267
EPIGENETIC ERASERS HDAC1 AND HDAC2 DRIVE INTESTINAL EPITHELIAL CELL BEHAVIOR

A. Gonneaud[1], N. Turgeon[4], F. Boisvert[3], F. Boudreau[2], C. Asselin[2]

1. Department of Anatomy and Cell Biology, Faculty of Medicine and Health Sciences, 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. Université de Sherbrooke, Sherbrooke, QC, Canada

Background: Histone deacetylase Hdac1 and Hdac2 regulate gene expression and protein function by removing acetyl groups on lysines. Hdac1 and Hdac2 influence many biological processes, from chromatin organization and cell differentiation, to cell cycle and inflammation. As we reported before, intestinal epithelial cell (IEC) Hdac1 and Hdac2 are essential regulators of intestinal homeostasis related to differentiation and inflammatory responses, among others. However, the specific Hdac1 and Hdac2 downstream targets still remain to be determined.
Aims: To better understand the molecular mechanisms driven by Hdac1 and Hdac2 in IEC, we need a full picture of the proteomic IEC-specific changes occurring upon *Hdac1* and/or *Hdac2* deletion or HDAC pharmacological inhibition.
Methods: Floxed mice for both *Hdac1* and *Hdac2* alleles were crossed with *villin*-Cre mice, to insure IEC-specific deletion. 3-month-old mutated mice were used for the experiments. For pharmacological inhibition, the HDAC class I inhibitor CI994 was injected intraperitoneally in 2-month-old Balb/c mice, once a day for 5 days. Jejunal epithelial cells were isolated by the EDTA method. Cell lysates from control IEC, from *Hdac1*, *Hdac2* and *Hdac1/2* deleted IEC and from CI994 treated IEC were labeled with different isobaric chemical tags (Tandem Mass Tag reagents). Labeled cell lysates were mixed, digested with trypsin and used for liquid chromatography-tandem mass spectrometry and data analysis. Bioinformatic pathway analysis was achieved with the DAVID 2.0 software for gene ontology

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biological processes, for proteins showing two-fold increases or decreases.

Results: More than 3000 proteins were detected by mass spectrometry analysis for each sample. Differential protein expression was observed in *Hdac1/2-* (800), *Hdac1-* (150) or *Hdac2-*depleted (200), and CI994-treated IEC (150). Translation and chromatin assembly were among the top biological processes respectively up- and down-regulated in *Hdac1/2-*depleted IEC, with decreased expression of goblet and Paneth cell proteins (Zg16, Muc2, Lyz1) and increased enterocyte proteins (Sis, Alpi). Interestingly, while the top negative biological process for both *Hdac1-* and *Hdac2-*depleted IEC was "antigen processing and presentation of peptide antigen", the immune response pathway and the protein kinase/intracellular signaling cascade pathway were increased respectively in *Hdac1* and *Hdac2* knockout IEC. Surprisingly, CI994-treated IEC displayed "homeostatic process", as the top increased biological process, and chromatin assembly, as the top decreased biological process.

Conclusions: Targeting HDAC, genetically or pharmacologically, changes IEC behavior. Hdac1 and Hdac2 regulate similar as well as distinct protein expression programs, thereby indicating specific molecular functions in IEC.

A268
TESTING AND TREATMENT OF CLOSTRIDIUM DIFFICILE INFECTION IN HOSPITALIZED INFLAMMATORY BOWEL DISEASE PATIENTS

J. Reinglas[1], S. Murthy[2]

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

Background: Inflammatory bowel disease (IBD) is associated with an increased risk of contracting clostridium difficile infection (CDI) as well as an increased mortality risk in the setting of CDI. As such, early testing and treatment of CDI in IBD patients hospitalized for a disease flare is of paramount importance.

Aims: To assess rates of C. difficile testing and treatment patterns among IBD patients admitted to The Ottawa Hospital for a disease flare.

To characterize factors associated with appropriate testing of Clostridium Difficile infection (CDI) in this setting.

Methods: A cross-sectional study was conducted in 200 consecutive patients admitted to our tertiary-care center for an IBD flare between January 1, 2011 and December 31, 2013. Outcomes assessed include the frequency and timing of CDI testing, type of CDI treatment and colectomy. Multivariable logistic regression was conducted to assess factors associated with CDI testing within 48 hours of admission.

Results: Of 193 patients without known CDI at presen-

tation, 162 patients (84%) were tested for CDI during admission and 153 patients (79%) were tested within 48 hours of presentation. Patients were more likely to be tested for CDI within 48 hours if they had ulcerative (UC) (vs. Crohn's disease (CD)) (88.7% vs 75.4%, p =0.048), if they were not on immunosuppressive (IS) therapy (vs. on IS therapy) at presentation (95.2% vs 76.5%, p=0.0075) and if they were admitted under a gastroenterologist (vs. non-gastroenterologist) (90.1% vs 74.1%, p < 0.0001). In multivariable analysis, UC diagnosis (aOR 2.4, 95% CI 1.1-5.1), admission under a gastroenterologist (aOR 3.1, 95% CI 1.4-6.8) and absence of corticosteroid therapy at presentation to hospital (aOR 3.2, 95% CI 1.5-6.8) were associated with higher rates of CDI testing within 48 hours of presentation. Of 20 patients who were positive for CDI, 16 patients (80%) received vancomycin +/- metronidazole as first line therapy. Fifteen patients (83%) with CDI diagnosed within 48 hours of admission received supplemental IS therapy for treatment of IBD. In-hospital colectomy was performed in 15% vs 6% of patients with and without CDI, respectively.

Conclusions: A substantial proportion of IBD patients admitted to a tertiary-care center for a disease flare are not tested for CDI in a timely fashion. Patients who have UC, who are not on corticosteroids at presentation and who are admitted under a gastroenterologist are more likely to undergo CDI testing. Treatment of CDI in this setting is inconsistent and does not follow recommendations for first-line use of vancomycin in many patients. Better education of physicians who care for IBD patients is required to reduce these gaps in quality of care.

A269
IRRITABLE BOWEL SYNDROME PATIENT EXPERIENCE IN CANADA

G.P. Attara[1], J. Gray[3], G. Aumais[2]

1. Gastrointestinal Society, Vancouver, BC, Canada; 2. Université de Montréal, Montreal, QC, Canada; 3. University of British Columbia, Vancouver, BC, Canada

Background: Irritable bowel syndrome (IBS) is a chronic, often debilitating, functional gastrointestinal disorder with symptoms that include abdominal pain and altered bowel behaviours of constipation and/or diarrhea, affecting approximately 13-20% of Canadians. The real world experience of patients is still poorly understood.

Aims: To learn the how the symptoms of irritable bowel syndrome affect these patients in Canada.

Methods: The Gastrointestinal Society hosted a survey on its English (www.badgut.org) and French (www.mauxdeventre.org) websites during spring 2016. Links to this survey were posted on social media and via invitation using a market research company. To qualify, survey participants had to be living in Canada and

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have IBS or be the parent/guardian of a child with IBS. Questions were on a broad range of topics, including symptom severity, medication use, diet, experience with the health care system, comorbidities, and quality of life.

Results: Respondents from every province and territory totalled 2,961. 90% were between 30-69 years of age, 86% female, 97% were adults with IBS. 53% had IBS for more than 10 years. 35% had IBS-D, 18% IBS-C, 41% IBS-M, and 6% unsure. In IBS-C patients, abdominal pain was identified as a distinct predominant symptom. Those with IBS-D experienced many symptoms, with abdominal pain, bloating, urgency, and diarrhea identified as highly concerning. 24% experienced severe abdominal pain in the last 3 months, with severe pain being constant in a high proportion. 62% of patients indicated they experienced pain continuing after bowel movement. The top factors driving patients to see their physician were pain/discomfort and impact of IBS on their personal/professional/daily life. Approximately 93% and 49% of patients consulted with a family doctor and gastroenterologist, respectively, for their IBS. 60% had a colonoscopy. 12% have been hospitalized for IBS. 76% indicated that their symptoms interfere with everyday life and 46% missed work or school due to IBS. Most IBS patients use ≥2 medications on a regular basis to control their symptoms yet only 21% are confident their symptoms are under control. Compounding the issue, 16% are unable to afford any of their prescribed medications, and 26% can only afford some of them.

Conclusions: Canadian IBS patients suffer from multiple symptoms, with the pain experienced by patients being the prime motivating factor to seek care. 79% have symptoms not under control. The conventional standard of care for IBS requires many different treatments to manage the multiple symptoms, with the majority of IBS patients requiring 2 or more treatments on a regular basis. IBS patients experience a wide range of symptoms and comorbidities. It can be a struggle for them to find treatments that are effective and affordable.

A270
EFFECTS OF KETOPROFEN AND ITS HYDROGEN SULFIDE-RELEASING DERIVATIVE ON THE IMMATURE HUMAN INTESTINE
M. Thibault[1], É. Tremblay[1], J.L. Wallace[2], J. Beaulieu[1]

1. Laboratoire de pathophysiologie intestinale, Dép. anatomie & biologie cellulaire, Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Dept of Physiology and Pharmacology, University of Calgary, Calgary, AB, Canada

Background: The use of nonsteroidal anti-inflammatory drugs (NSAIDs) among neonates is associated with a broad spectrum of life-threatening adverse effects on the gastrointestinal tract. Indeed, we have previously demonstrated that NSAIDs, such as indomethacin (INDO), induce damaging effects on the immature intestine (Perron et al. Genomics, 2013). Hydrogen sulfide (H_2S) has been reported to exert a number of cytoprotective and anti-inflammatory effects in many organ systems. Thus, in order to minimize the deleterious effects caused by NSAIDs, several H_2S-releasing derivatives have been developed, including ATB-352, an H_2S-releasing derivative of ketoprofen.

Aims: In the present study, we determined the effects of ketoprofen (KETO) and its H_2S-releasing derivative on the human mid-gestational intestine using serum-free organ culture, and compared them with those previously described for INDO.

Methods: The representative genes involved with the deleterious effect of INDO were used as reference to compare the effect of KETO and/or its derivative ATB-352 on the mid-gestation human small intestine after a treatment of 48 hours. Gene expression levels were measured by qRT-PCR.

Results: By determining the gene expression of COX2 in cultured human small intestinal explants, we observed two distinct patterns of response that allowed to divide the specimens into two groups: 1) those with an increased expression of COX2 mRNA (KETO-responder group), and 2) those where COX2 remained unchanged (non-responder group). For the non-responder group, no significant change was observed compared to control. Although the inflammatory response observed between INDO and the KETO-responder group was similar (CXCL14 and TFF1), the negative effects on oxidoreductase activity (DUOX2, NOS2, SOD2) and intestinal permeability (OCLN, CLDN1) induced by INDO were not found with KETO, suggesting a beneficial effect of KETO on the small intestinal mucosa. In addition, the use of the H_2S-releasing derivative of KETO did not induce significant changes compared to KETO on these metabolic pathways.

Conclusions: Our results show that KETO (responder group) has beneficial effects on oxidoreductase activity and epithelial permeability in the immature human small intestine compared to INDO. However, the lack of beneficial effects of H_2S on the small intestinal mucosa in organ culture suggests a systemic type mechanism rather than a local one.

A271
UNCOVERING GENDER-BASED DIFFERENCES IN UNDIAGNOSED CELIAC DISEASE
C.L. Jansson-Knodell, K. King, J. Larson, J.a. Murray, A. Rubio-Tapia

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

Internal Medicine, Mayo Clinic, Rochester, MN

Background: Celiac disease affects numerous aspects of women's health. There is a gap in research focused on gender-based differences in undiagnosed populations with celiac disease.
Aims: The aim of this study was to estimate gender-based differences in a unique population-based cohort of patients seropositive for celiac disease with respect to 1) age, 2) anthropomorphic measurements, and 3) associated diseases.
Methods: Stored serum from a population-based sample of 30,610 people in a Minnesota county was tested for celiac disease based on tissue transglutaminase (TTG) and endomysial antibody (EMA) positivity. Study subjects lived in Olmsted county, provided consent for waste blood testing and were aged 18-49 years old. Laboratory testing occurred between 6/2006 and 10/2009. Clinical data were systematically abstracted from the electronic medical record of a population-based undiagnosed cohort of patients who were seropositive for celiac disease defined as TTG and EMA positive testing. Categorical data were analyzed with Chi-square and Fisher's exact test. Age was explored with the equal variance T-test.
Results: In this population-based cohort 281 (0.94%) subjects were identified with undiagnosed celiac disease. That group was comprised of 179 females and 102 males; the female to male ratio was 1.75:1. Seropositive women were younger with an average age of 33.8 years compared to 37.4 years in their male counterparts (p=0.002). Women in the seropositive group had a lower body mass index (BMI), averaging 26.2 versus 28.1 in men (p=0.028). Concurrent autoimmune diseases were documented in 36 of the females and 25 of the males (females 20.6%; males 24.8%; p=0.42). Depression was recorded at a high rate in seropositive males and females with a female predominance (females 27.7%; males 9.8%, p=0.0004). Decreased bone mineral density (osteopenia or osteoporosis) rates were low in this group aged 49 years or less (females 0.6%; males 2%, p=0.36). Median follow up time was 6.73 years (95% CI 6.44, 6.93).
Conclusions: Celiac disease is common. The finding of high seropositivity emphasizes the importance of testing patients when there is clinical suspicion for disease. These results indicate the potential of gender-based differences in terms of age at diagnosis, anthropometric measurements, and associated diseases that can co-occur with celiac disease. These findings may be clinically relevant for uncovering cases of celiac disease in the community and once identified, managing them comprehensively.

Funding Agencies: None

A272
PERFORMANCE OF TISSUE TRANSGLUTAMINASE ANTIBODIES FOR A DIAGNOSIS OF CELIAC DISEASE IS DECREASED IN ADULTS WITH OTHER COMORBIDITIES

A. Therrien[1], G. Bernard[2], N. Presse[3], P. Hetu[4], C. Vincent[5], M. Bouin[1]

1. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Département de Médecine, Service de Gastroentérologie, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; 2. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; 3. Département de Nutrition, Université de Montréal, Montreal, QC, Canada; 4. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Département de Biochimie, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; 5. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Département de Médecine Service d'Hépatologie, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada

Background: Tissue transglutaminase antibodies(tTG) is a first step for detection of celiac disease(CeD). However, in a pediatric population, an increase of <3 times UNL was poorly predictive of CeD. In adults, discrepancies between tTG and histology were reported with liver disorders and how these and other comorbidities influence the performance of tTG remains unknown.
Aims: To determine the positive predictive value(PPV) of the degree of increase of tTG for newly diagnosed biopsy-proven CeD(BxCeD) in adults with and without other comorbidities.
Methods: Retrospective study based on chart review from August 2003 to June 2016. Inclusion criteria: all patients with a dosage of tTG at the Centre Hospitalier de l'Université de Montréal and duodenal biopsies done three months before to six months after tTG. Exclusion criteria: inadequate histologic specimen, CeD already known or being on a gluten free diet. Patients were identified as BxCeD if histology corresponded to Marsh type 1 up to 3c. Medical records were reviewed for comorbidities at the time of the dosage of tTG, namely liver disorders, auto-immune, infectious diseases and inflammatory states. Patients with and without these comorbidities were classified as Dis+ or Dis- groups. ROC curve analysis was performed to determine the UNL threshold where sensitivity(Sn) and specificity(Sp) are optimized for diagnosis of BxCeD in both groups. PPVs below and above these thresholds were calculated and compared with Fisher's exact tests.
Results: 206 patients were included; 63% of women; mean age(±SD) 48(±16)years. BxCeD was identified in 80% of patients(n=164). Overall, 73 patients were found with ≥1 relevant comorbidities(Dis+ group), mainly liver diseases(n=32), connective tissue diseases(n=11), and inflammatory bowel diseases(n=7). BxCeD was found in 60% of them while this proportion was of 90% in the Dis- group. ROC curve in the Dis- group revealed that Sp/Sn were optimized at 2.74 times UNL. When PPV were calculated according to this threshold (Table), PPVs were significantly lower in the Dis+ group vs. the Dis- group. In the Dis+ group,

the threshold optimizing the Sp/Sn of the tTg test was 3.83 times UNL, which increased the PPV to 88% among these patients.

Conclusions: The performance of the tTG test for detecting biopsy-proven CeD is decreased significantly by the presence of comorbidities such as liver disorders, other auto-immune diseases, infections, and inflammatory states.

PPV of the tTG for BxCeD according to the presence of other comorbidities

	PPV			
tTG (times UNL)	All %	Dis - %	Dis + %	p-value
1-2.74	49.0	60.7	31.6	0.075
≥2.74	88.7	98.1	70.4	<0.001
≥3.83	95.7	99.0	87.5	0.008

Dis +: either liver, auto-immune, infectious or inflammatory disease at the time of tTG

Funding Agencies: None

A273
HISTOLOGICAL FINDINGS IN GASTRIC BIOPSIES AT DIAGNOSIS IN AN ADULT CELIAC DISEASE POPULA-TION
A. Therrien[1], G. Bernard[2], P. Hetu[3], M. Bouin[1]

1. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Département de Médecine, Service de Gastroentérologie, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; 2. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; 3. Centre de recherche du Centre Hospitalier de l'Université de Montréal, Département de Biochimie, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada

Background: Chronic gastritis (CG) and lymphocytic gastritis (LG) have been described in pediatric populations with celiac disease (CeD). A US national review of gastric and duodenal biopsies showed an association between duodenal histology compatible with CeD and the presence of CG or LG. However, this transversal study did not include clinical or serological data.
Aims: To evaluate, in an adult CeD cohort, the gastric histological findings at diagnosis of CeD.
Methods: Longitudinal chart review study at Centre Hospitalier de l'Université de Montréal from August 2003 to June 2016. Were included every new cases of CeD (presence of tissue transglutaminase antibodies (tTG) and duodenal biopsies corresponding to Marsh 1 to 3c classification, without any notion of previous gluten-free diet). Medical record, endoscopic and pathology reports were reviewed. Mann-Whitney U test was used to compare continuous data and Fisher's

exact test to compare categorical data.
Results: 186 cases of CeD were diagnosed (mean age(SD) 47.3±15.9 years; 64% female). Concomitant gastric biopsies were done in 43% of them (n=80). Gastroscopy findings were abnormal in 33.8% (n=27), the main finding being mucosal erythema (n=18). Gastric histology was abnormal in 63,75% (n=51). Findings included inactive CG(n=27), active CG without helicobacter pylori (*Hp*) (n=7), *Hp* infection (n=5), reactional gastropathy (n=4), gastric polyps (n=2), LG (n=3), parietal cells pseudohypertrophy (n=2) and intestinal metaplasia(n=1). No difference was found between the level of increase of tTG in the subgroup with abnormal gastric histologic findings (his+) and the subgroup with normal findings (his-). The two groups were also similar for the proportion of patients with moderate to severe duodenal villous atrophy. Among patients with his+, 58,8% had a normal endoscopic appearance of the stomach, compared to 79,3% in the group with his-(p=0,09). No difference was found between the proportion of patients with GI symptom-atology or anemia in his+ and his- groups.
Conclusions: Gastric histologic findings at diagnosis in an adult population with celiac disease are variable and do not seem associated with severity of celiac disease.

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A274
THE EFFECT OF PRUCALOPRIDE ON SMALL BOWEL TRANSIT TIME FOR INPATIENTS UNDERGOING SMALL BOWEL CAPSULE ENDOSCOPY
M.A. Alsahafi, P. Cramer, N. Chatur, F. Donnellan

Vancouver General Hospital, Division of Gastroenterol-ogy, University of British Columbia, Vancouver, BC, Canada

Background: Inpatient small bowel capsule endoscopy (SBCE) has been associated with a decrease in the completion rate compared to outpatient SBCE. However delaying the performance of SBCE until hospital discharge may result in a decrease in the diagnostic yield. Therefore, interventions to shorten small bowel transit time are needed to increase the completion rates. Prucalopride is 5-HT4 receptor agonist that has been shown to decrease the whole gut transit time.
Aims: To investigate the effect of prucalopride on small bowel transit time for hospitalized patients undergoing SBCE.
Methods: This was a retrospective study that included all hospitalized patients who underwent SBCE between November 2011 and September 2016 at Vancouver General Hospital. In the period between March 2014 and December 2015, all patients received prucalopride at the time of capsule ingestion. Prucalopride was not given outside of this period. SBCE studies were excluded if the capsule was retained, other prokinetic agents were given, technical failure, endoscopic placement or if patients had prior small bowel

resection.

Results: A total of 66 SBCE were performed. 12 SBCE were excluded. For the 54 included studies, the mean age for patients was 64 years. 64% of SBCE were done in male patients. The indications were obscure gastrointestinal bleeding in 51 and abnormal radiology in 3 patients. 29 patients received prucalopride. The overall completion rate was 85% and the mean small bowel transit time was 186 minutes. The prucalopride group had a significantly shorter small bowel transit time (132 vs. 277, p<0.001), and higher diagnostic yield (75% vs. 44%, p= 0.03) compared to the non prucalopride group. There was a trend for higher completion rate in the prucalopride group (93% vs. 76%, p= 0.16).

Conclusions: Our results suggest that prucalopride is an effective intervention to shorten small bowel transit time, increase the diagnostic yield and potentially increases the completion rate.

A275
DONOR BODY MASS INDEX (BMI) DOES NOT IMPACT RECIPIENT BMI FOLLOWING FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION

J.D. Smith[3], B. Roach[3], A. Hassanzadeh Keshteli[2], D.H. Kao[1]
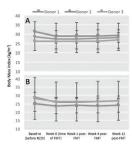
1. University of Alberta, Edmonton, AB, Canada; 2. Centre of Excellence for Gastrointestinal Inflammation and Immunity Research, University of Alberta, Edmonton, AB, Canada; 3. Gastroenterology, University of Alberta, Edmonton, AB, Canada

Background: Fecal microbiota transplantation (FMT), which restores gut dysbiosis, is an effective treatment option for recurrent *Clostridium difficile* infection (RCDI). Although there are guidelines for stool donor screening to minimize risk of disease transmitted by stool, there are no recommendations on donor BMI. Obesity, a condition associated with intestinal dysbiosis, can be transferred by FMT in the mouse model. Further, there is a case report of a woman who developed new-onset obesity after receiving stool from a healthy but overweight donor. However, it remains unknown whether stool donor BMI has any significant impact on recipient BMI after FMT in RCDI.

Aims: The aim of this study was to determine the impact of stool donor BMI on recipient BMI in RCDI.

Methods: Forty-six patients with RCDI were randomized to receiving FMT by colonoscopy or by capsules (1:1) from one of three different volunteer donors registered with the Edmonton FMT Program. The donors are healthy and between the ages of 32-45, with BMIs of 18.3 kg/m^2, 24.9 kg/m^2, and 30 kg/m^2. Pre-FMT weight and height were measured at screening visit, and weight was measured 1 week, 4 weeks and 12 weeks post-FMT. Weight lost during RCDI was recorded to calculate baseline BMI. Statistical measures were used to determine trends in weight loss from RCDI, changes in BMI over time, and effects of donor and method of FMT delivery on recipient BMI.

Results: There were no significant differences between participant baseline characteristics. The mean reported weight loss from RCDI was 5.44 ± 4.34 kg in the capsules arm and 3.72 ± 4.73 kg in the colonoscopy arm (p = 0.89). Participant BMI was significantly lower at time of FMT delivery when compared to reported baseline BMI (p < 0.05). Compared to BMI at baseline, BMI at week 12 was not significantly different, irrespective of donor or treatment method (Fig. 1). Fourteen patients (30%) gained weight 12 weeks post-FMT compared to baseline, but the difference was not statistically significant; furthermore, this observation was not donor or FMT method dependent.

Conclusions: Our study highlighted the trends in weight recovery in RCDI patients after receiving FMT. Most patients regained weight lost during RCDI by week 12, irrespective of donor BMI or method of FMT delivery. For those patients who gained weight after FMT, the difference was not significant, and was not dependent of stool donor or FMT treatment modality.

Trends of weight loss from RCDI.

	Capsules (N=20)	Colonoscopy (N=26)	P-value
Weight following RCDI (mean in kg ± S.D.)	66.88 ± 19.72	75.83 ± 14.36	0.07
Mean reported weight loss (mean in kg ± S.D.)	5.44 ± 4.34	3.72 ± 4.73	0.89
Percentage of participants with no weight loss	19%	46.2%	0.06
Percentage of participants with <5% loss of baseline body weight (≠0)	9.5%	15.4%	0.55
Percentage of participants with 5-10% loss of baseline body weight	52.5%	19.2%	0.02
Percentage of participants with >10% loss of baseline body weight	19%	19.2%	0.99

INTESTINAL DISORDERS

Figure 1. A) Changes in patient BMI over 12 weeks for patients receiving FMI by colonoscopy. BMI is significantly lower at week 0 when compared to baseline (p<0.05). Compared to baseline, patients receiving FMT from donor 1 were back to baseline at week 4, patients receiving FMT from donor 2 were back to baseline at week 12, and patients receiving FMT from donor 3 were back to baseline at week 1. Overall, BMI at week 12 in all patients receiving colonoscopy was not significantly different from baseline, irrespective of stool donor. B) Changes in patient BMI over 12 weeks for patients receiving FMI by capsules. BMI is significantly lower at week 0 when compared to baseline (p<0.05). Compared to baseline, patients receiving FMT from donor 1 were back to baseline at week 4, patients receiving FMT from donor 2 were back to baseline at week 2, and patients receiving FMT from donor 3 were back to baseline at week 1. Overall, BMI at week 12 in all patients receiving capsules was not significantly different from baseline, irrespective of stool donor.

A276
INVESTIGATING THE ROLE OF TTC7A THROUGH ITS IN-TERACTION WITH UBR5 TO MAINTAIN CELL SURVIVAL
N. Dhingani, C. Guo, N. Warner, R. Murchie, A. Muise

Hospital for Sick Children , Toronto, ON, Canada

Background: Patients with mutations in Tetratricopep-tide Repeat Domain 7A (TTC7A) results in a severe and untreatable form of inflammatory bowel disease with the majority dying before 2 years of age. Pathological features of these patients include intestinal apoptosis and disrupted apicobasal polarity. Since the molecular function of TTC7A is still poorly understood, we recently carried out a screen identifying potential TTC7A binding partners in an attempt to reveal its pathway of action. TTC7A is part of an evolutionarily conserved pathway and acts as a scaffolding protein recruiting phosphatidylinositol 4-kinase, PI4KIIIα, to the plasma membrane where it also binds to EFR3B. This conserved pathway helps PI4KIIIα phosphorylate phosphatidylinositol (PI) to PI-4-phosphate (PI4P) which has been implicated in cell survival and the maintenance of cell polarity. In addition, the E3 ubiquitin ligase, UBR5, was identified as a potential TTC7A binding protein and may play a role in stabilizing TTC7A protein levels. Furthermore, UBR5 is suggested to be a colorectal oncogene because it interacts with β-catenin to upregulate canonical Wnt signaling. UBR5 has also been implicated as a tumour suppressor gene and in regulating apoptosis.
Aims: To understand the role of TTC7A and UBR5 in cell survival. We hypothesize that UBR5 is involved and required in the PI4KIIIα-TTC7A-EFR3B pathway to maintain cell survival.
Methods: Vector constructs were created harbouring patient derived TTC7A mutations (E71K, Q526X, A832T) and expressed in HEK 293T cells. TTC7A immunoprecipitates (IP) were analyzed by tandem mass spectrometry identifying various binding proteins. To validate these potential TTC7A interacting proteins, co-IP was performed by co-transfecting cells with appropriate expression plasmids and then lysing the cells after 24hrs. Protein of interest was IP using the target antibody. Whole cell lysate and co-IP samples were subject to Western blot analysis.
Results: Preliminary results show an interaction between the UBR5 and TTC7A along with the patient derived TTC7A variants. They also show the presence of PI4KIIIα in the UBR5/TTC7A complex. Furthermore, they suggest that β-catenin only interacts with UBR5 in the presence of TTC7A.
Conclusions: The presence of PI4KIIIα in the UBR5/TTC7A complex implies that UBR5 is part of the conserved pathway to maintain cell survival through the downstream PI4P levels. Western blot analysis shows that UBR5 interacts most strongly with the TTC7A Q526X. A possible explanation is that the truncated TTC7A Q526X is ubiquitinated by UBR5 for proteasomal degradation, resulting in decreased PI4P levels. Also, the study suggests that TTC7A recruits β-catenin for ubiquitination by UBR5. Together, the research supports the notion that TTC7A is involved in multiple pathways with UBR5 to maintain cell survival or in causing colorectal cancer.

A277
CHARACTERISTICS OF PEDIATRIC IBD AT DIAGNOSIS ASSOCIATED WITH SUBSEQUENT USE OF BIOLOGIC THERAPY: A RETROSPECTIVE STUDY
D.J. Mulder, M. Zachos, M. Sherlock

McMaster Children's Hospital, Hamilton, ON, Canada

Background: Inflammatory bowel disease (IBD) is a heterogeneous group of idiopathic conditions commonly treated with increasingly potent anti-inflammatory and immunomodulator medications. The most efficacious medications currently available are biologic agents (TNF-α antagonists). Limited evidence exists to guide the decision to start biologic therapy. Identification of risk factors at presentation that are associated with the eventual use of biologics could be useful for facilitating earlier treatment decisions.
Aims: To identify the clinical, biochemical, and radiographic characteristics of IBD at diagnosis associated with subsequent use of biologic therapy.
Methods: Charts of all IBD patients actively followed at our centre were reviewed. Data pertaining to clinical, biochemical, and radiologic characteristics at diagnosis were extracted. Disease activity was described using the Pediatric Crohn's Disease Activity Index (PCDAI) and the Pediatric Ulcerative Colitis Activity Index (PU-CAI). Therapeutic course was also reviewed, including the timing of immunomodulator and/or biologic therapy initiation. Analyses were performed using SPSS version 21.
Results: 218 patients with IBD were identified, 124 (57%) with Crohn's disease, 61 (28%) with ulcerative colitis and 33 (15%) with IBD-type unclassified. 122 (56%) patients received biologic treatment. Time to

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biologic use was negatively associated with disease activity index at diagnosis for both Crohn's disease (R^2=0.06, P=0.024) and ulcerative colitis (R^2=0.33, P<0.002). For all patient groups, binary logistic regression demonstrated that lower height percentile, decreased albumin, and increased CRP at diagnosis (Nagelkerke R^2=0.29) were associated with biologic use. Receiving biologics within nine months of diagnosis was associated by multivariate logistic regression with lower height percentile, decreased albumin and increased age at time of diagnosis. (Nagelkerke R^2=0.22). **Conclusions:** In our cohort, we identified patient characteristics at the time of IBD diagnosis, which were associated with early use of biologic therapy. Further prospective evaluation will help to determine if initiation of biologics based on patient characteristics at the time of IBD diagnosis leads to improved outcomes.

A278
PLASMA CITRULLINE HAS LIMITED UTILITY TO PREDICT INTESTINAL ADAPTATION IN NEONATAL SHORT BOWEL SYNDROME

M. Lansing[1], J. Turner[1], C. Lavallee[1], D.W. Lim[2], M. Muto[6], P. Wizzard[1], P.N. Nation[4], P.B. Pencharz[5], R. Ball[3], P. Wales[5]

1. Department of Pediatrics, University of Alberta, Edmonton, AB, Canada; 2. Department of Surgery, University of Alberta, Edmonton, AB, Canada; 3. Department of Agricultural, Life & Environmental Sciences, University of Alberta, Edmonton, AB, Canada; 4. Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada; 5. The Hospital for Sick Children, University of Toronto, Toronto, ON, Canada; 6. Department of Pediatric Surgery, Kagoshima University, Sakuragaoka Kagoshima, Japan

Background: In the absence of intestinal adaptation, neonates with short bowel syndrome (SBS) depend on long-term parenteral nutrition (PN). This can lead to recurrent sepsis, liver disease, loss of vascular access and poor quality of life. Early referral for transplantation or consideration of novel trophic therapies may be advantageous in this setting. However, current methods to assess the progress of adaptation in neonates are limited. Citrulline has been proposed to have utility as a non-invasive biomarker of intestinal adaptation.
Aims: Our goal was to evaluate plasma citrulline in two experimental models of SBS that vary in potential for adaptation.
Methods: Neonatal piglets (2 to 4 days old) were randomly allocated to either a 75% distal gut resection (jejunucolic/ JC, n=9), mid- intestinal resection (jejun-oileal/JI, n= 5) or sham control (n=8). A jugular catheter was inserted for PN feeds and a gastric tube for trophic enteral nutrition. On day 7 (D7) small intestinal length and weight were measured and jejunum collected for

evaluation of villus height and crypt depth. Plasma citrulline levels were measured day 0 (D0) and D7 using DC/LC-MS. Statistical analysis included independent t tests, one-way ANOVA and linear regression.
Results: In all cases average citrulline level declined D0 to D7. Including sham with the SBS piglets, citrulline level correlated with final (D7) length (p< 0.01) and with mucosal mass (p< 0.01). However, considering only SBS piglets, citrulline level did not correlate with length (p=0.68), mucosal mass (p=0.8) or jejunal villus height (p= 0.9). JI, compared to JC, demonstrated more adaptation with increased length post-resection (p <0.01) and mucosal mass (p< 0.01). However, D7 citrulline levels did not differ between the two groups (p=0.63).
Conclusions: Plasma citrulline levels do not discriminate between anatomical subtypes of short gut that vary in potential for adaptation, nor correlate with their actual adaptive changes.

	JC	JI	SHAM	P VALUE
Intestine length, day 0, post resection	140	155	583	<0.01
Intestine length, day 7	124	173	636	<0.01
Mucosal mass, day 7	7.1	13.2	27.3	<0.01
Plasma citrulline, day 0	2101	2218	1829	0.22
Plasma citrulline, day 7	786	729	1088	0.04
Jejunum villus height	6.6	8.7	7.0	0.11
Jejunum crypt depth	1.8	1.7	1.6	0.30

Mean values shown, P value is shown using one-way ANOVA significance was set at p < 0.05. Intestinal length values in cm, Jejunum measurements each unit is 0.1 mm, citrulline levels in Pico-moles.

A279
THE EFFECT OF SHAM FEEDING ON SMALL BOWEL TRANSIT TIME IN PATIENTS UNDERGOING CAPSULE ENDOSCOPY

G. Ou[2], D. Prichard[4], C. Galorport[3], R.A. Enns[1]

1. Medicine, St Paul, Vancouver, BC, Canada; 2. St. Paul, Vancouver, BC, Canada; 3. Medicine, Div. of Gastroenterology, St. Paul's Hospital , Vancouver, BC, Canada; 4. Mayo Clinic, Rochester, MN

Background: Small bowel capsule endoscopy (CE) has limited recording time and does not visualize the entire length of the small intestine in approximately 16.5% of the cases. We hypothesize that bacon-chewing is potent stimulus of cephalic response, which may reduce capsule transit times and improve complete examination rate (CER).
Aims: To determine if sham feeding with bacon-chewing improves small bowel transit time and completion rate in patients undergoing capsule endoscopy.

Methods: A prospective, single-blinded, randomized controlled trial at St. Paul's Hospital in Vancouver, BC has been recruiting since 01/2015. Inclusion: outpatient CE, age ≥ 19. Exclusion criteria: ongoing use of motility-enhancing or slowing drugs, active bowel obstruction, bowel resection, swallowing disorder, diabetes with end-organ damage, untreated thyroid disorder, and endoscopic placement of capsule camera. Given Imaging PillCam SB3™ (Yoqneam, Israel) were used.

Participants were assigned to either bacon or control group via concealed allocation based on unrestricted randomization sequence generated prior to study initiation.

All subjects underwent bowel preparation with 2L PEG3350 with electrolytes the day before, and fasted ≥ 2h prior to the procedure. They were allowed to drink clear fluids and resume normal diet 2h and 4h post-capsule ingestion, respectively. Immediately after swallowing the capsule, subjects in the bacon group were asked to chew and spit 10 pieces of bacon, each over 30 seconds at one-minute intervals. This process was repeated an hour after ingesting the capsule.

Gastric transit time (GTT), small bowel transit time (SBTT), and CER were compared between the groups.

This study was approved by institutional research ethics board and registered on clinicaltrials.gov (NCT02353208).

Results: Between 01/2015 to 09/2016, 109 CE's were included in the study, 89 of which were for GI bleeding. CE did not pass the pylorus in four patients in the bacon group during the recording, and were excluded from further transit time analyses. One and two additional CE's in the control and bacon group, respectively, did not reach cecum during recording and were excluded from SBTT analysis. There was no statistically significant difference in GTT, SBTT, or CER.

Conclusions: Sham feeding by chewing and spitting bacon does not alter transit times or CER, and therefore should not be used in an attempt to improve CE yield.

Results

	Control (n=54)	Bacon (n=55)	P value
Age (mean ± SD)	57.2 ± 15.6	57.9 ± 17.5	0.83
Female (%)	30 (55.6%)	30 (54.5%)	0.92
Charlson Comorbidity Index	3.4 ± 2.4	3.3 ± 2.8	0.99
GTT (minutes) mean ± SD median (IQR)	41.4 ± 47.2 24.7 (13.9, 55.7)	56.7 ± 126.5 17.2 (10.3, 68.6)	0.20
SBTT (minutes) mean ± SD median (IQR)	230.0 ± 106.2 217.6 (157.4, 282.3)	223.1 ± 128.5 198.5 (119.6, 294.8)	0.38
CER (%)	53 (98.1%)	49 (89.1%)	0.054

A280
SPECIALIZED FORMULA USE FOR THE TREATMENT OF COW MILK PROTEIN ALLERGY
V. Avinashi, K. Sadiq, S. Nicol

BC Children's Hospital, Vancouver, BC, Canada

Aims: Cow milk protein allergy (CMPA) is a common condition of infancy, with an incidence of between 2-5% amongst formula fed infants. Despite the regularity with which this condition is encountered, there is a paucity of data, in part due to the diverse clinical presentation and lack of definitive diagnostic tests. Current management beyond dietary exclusion of cow's milk protein involves the use of a semi-elemental or elemental formula.

Methods: A retrospective chart review of applications made to the Home Enteral Nutrition (HEN) program for CMPA was undertaken. The HEN program is a provincial service co-ordinating the allocation of formula to children requiring specialised formula.

Results: From 2004 - 2014, 210 patients were provided semi-elemental or elemental formula on the basis of suspected CMPA. Overall, an increasing trend in referrals was seen. In 2004 only 3 patients were provided specialized specialised formula vs 41 in 2013. The median age at application was 3.5 months (IQR: 2.0; 6.3) with 51.4% being male.
Symptoms at presentation indicated that bloody diarrhoea with or without emesis was present in 53.4% of patients, with other presentations including isolated emesis in 16.2%, non-bloody diarrhoea in 13.3%, and a combination of vomiting and diarrhoea in 8.6%. Miscellaneous symptoms including failure to thrive, irritability, and others make up the remaining 8.6%.
The median weight-age Z score at baseline was -0.81 (IQR: -1.85; 0.02), indicative of an underweight for age population. The referral pathway most commonly utilised included pediatric gastroenterologist in 49.6% and paediatricians in 45.2% of referrals. Family doctor referrals accounted for only 5.2% of the cases.
Elemental formula was used in 66.7% of cases. Feed administration was achieved orally in 96% of patients, with only 4% of children requiring ng tube feeds.
The median duration for utilisation of specialised formula was 10.5 months (IQR: 6; 12), with a median age at termination of HEN support at 13 months (IQR: 12; 18), indicative of successful transition to milk protein containing diet at one year of age in the majority of patients. The duration of formula use did not differ depending on the formula type or presentation (bloody diarrhea or not) (p=0.577). 100% of patients had discontinued the use of the specialized formula by three years of age.
Conclusions: An increased trend was seen for the

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number of children utilizing specialized formula for CMPA, however the duration of formula supplementation is in keeping with other international centres. Our group did have a higher use of elemental formula (vs. semi-elemental) however this may be on account of the incremental cost of elemental formula. Presenting symptoms did not highlight a differential duration of formula use and all patients improved with time.

A281
EFFECT OF A GLUTEN FREE DIET ON SYMPTOMS IN IBS PATIENTS STRATIFIED BY ANTIGLIADIN ANTIBODIES

E. Ignatova, Y. Ge, A.i. Nardelli, N. Causada Calo, R. Borojevic, S.M. Collins, M.I. Pinto Sanchez, E. Verdu, P. Bercik

McMaster University, Hamilton, ON, Canada

Background: Specific food components, such as gluten and FODMAPs, may trigger symptoms in patients with irritable bowel syndrome (IBS). Previous studies suggested that IBS patients with positive anti-gliadin antibodies (AGA) may preferentially respond to a gluten-free diet (GFD). However, GFD removes, apart from gluten, many potential dietary triggers, such as inulin that is part of FODMAPs.
Aims: To evaluate the dietary patterns and nutrient intake in healthy controls and IBS patients before and after one month of GFD.
Methods: IBS patients were diagnosed using Rome III criteria and stratified by the presence of AGA (INOVA Inc, San Diego, US). A group of healthy subjects (HV) served as controls. All participants underwent a gluten-free diet (GFD) for one month. Gastrointestinal symptoms were assessed by the IBS Birmingham score. A food frequency questionnaire (FDQ VES2- Victoria, Australia) was used to assess: 1) dietary patterns, 2) nutrient intake, and 3) FODMAP consumption before and after GFD.
Results: 41 IBS patients (22 AGA+; 19 AGA-) and 24 HV were recruited. GFD improved symptoms in IBS AGA+, but not in IBS AGA- patients. IBS AGA+ patients had lower baseline intake of specific nutrients including protein, calcium, iron, magnesium, niacin, phosphorus, potassium, and sodium (p<0.05 vs AGA- and HV). IBS AGA+ patients had lower baseline intake of eggs, nuts, yoghurt, fish, fruit, vegetables, and red wine (p<0.05 vs AGA- and HV). The GFD led to increased intake of eggs, bananas, peppers, and lettuce, as well as decreased intake of cakes, meat pies, hamburgers, and beer in IBS AGA+ patients (p<0.05). AGA- patients increased their consumption of bananas and zucchini, and decreased their intake of bread, cakes, meat pies, hamburgers, sausages and pizza (p<0.05). Importantly, there was no overall change on FODMAP intake after the GFD, except for some particular wheat-containing foods.
Conclusions: Intake and quality of food differ between subsets of IBS patients, suggesting that patients may already select the food based on the association with their symptoms. IBS AGA+ patients had lower nutritional value intake compared to IBS AGA- patients. The GFD improves gastrointestinal symptoms in AGA+ patients, and this seems to be independent of overall FODMAPs consumption.

A282
DOES SERUM ADALIMUMAB LEVEL CORRELATE WITH DISEASE SEVERITY IN PATIENTS WITH CROHN'S DISEASE?

M. Gandhi[1], L. Stitt[2], J.C. Gregor[1]

1. Medicine, Western University, London, ON, Canada; 2. 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's 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's disease patients that had a measured adalimumab level. Sixty-five patients were identified between January 2015 and January 2016. Disease severity was determined using the Harvey-Bradshaw Index. Patients were stratified based on their dosing intervals.
Results: For patients with weekly dosing (n=16), 8 were in remission. Mean trough adalimumab levels for remission and active disease groups were 8.8 and 7.3 respectively. There was no statistically significant relationship between trough adalimumab level and disease severity, weight, CRP or albumin. For patients with biweekly dosing (n=49), 32 were in remission. Mean trough adalimumab levels for remission and active disease groups were 8.5 and 6.1 respectively. The correlation between trough adalimumab level and weight was -0.44 (p=0.002). Similarly, the correlation between trough adalimumab level and CRP was -0.39 (p=0.031). Trough adalimumab level did not have a statistically significant relationship with albumin or disease severity.
Conclusions: In both groups, patients in remission tended to have higher trough adalimumab levels. In patients with biweekly dosing, higher drug levels correlated with lower patient weight and lower CRP values. This likely stems from higher consumption of adalimumab with active inflammation present in active disease. The absence of statistically significant relationships for patients with weekly adalimumab dosing is likely a factor of the smaller sample size. Ultimately, larger study with prospective data may yield more helpful information.

A283
THE IMPACT INFLAMMATORY BOWEL DISEASE HAS ON BREASTFEEDING PATTERNS

SARAH ANDRISHAK, ALISHA MANOCHA,KARREN KROEKER, LECINUS DIELEMAN,BRENDA HALLO-RAN,RICHARD FEDORAK, VIVIAN HUANG
S.R. Andrishak[5], V. Huang[3], K.I. Kroeker[3], L.A. Dieleman[4], B.P. Halloran[2], R. Fedorak[1], A. Manocha[2]

1. Los Alamos National Laboratory, 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; 5. medicine and dentistry , University of Albetra, Rocky Mountain House, AB, Canada

Background:

Background:
Inflammatory Bowel Disease (IBD) is a group of diseases characterized by inflammation of the digestive tract.Crohn's disease(CD) can affect any part from the esophagus to the anus, whiled ulcerative colitis (UC) only affects the large intestine. Factors that can contribute to the development of IBD include genetics, environment and microbiome. Breastmilk influences development of the neonatal microbiome and immune system. It is recommended that infants breastfeed until 12 months,to ensure nutritional and immunological development. Women with IBD have been reported to breastfeed less than healthy women.
Aims:
Purpose:
To investigate the impact IBD has on breastfeeding patterns
Methods:
Methods:
Adult women with IBD attending the Pregnancy in IBD clinic were invited to fill out questionnaires regarding breastfeeding 2 or 3, 6, 9 and 12 months post partum (PP). They were asked if they were breastfeeding or not, and why not at each time points. They were also asked about their clinical disease activity using Harvey Bradshaw Index (HBI) for CD and Partial Mayo (pMayo) for UC. For subjects who are still in follow up (within the 12 months), we included any of their completed surveys up until July 2016. Incomplete or missing surveys were excluded from the analyses. SPSS 23.0 was used to analyze the data.
Results:
Results:
Fifty women completed surveys; 46% of patients had stopped breastfeeding by 12 months, while 36% of the patients (who completed all time points) breastfed through to 12 months. There was no significant pattern when breastfeeding stopped. The top three reasons

reported for cessation of breastfeeding were insufficient milk, medications and sickness. Cessation of breastfeeding was not correlated to disease activity.
Conclusions:
Conclusion:
Almost half of patients with IBD stopped breastfeeding by 12 months postpartum. Having IBD itself was not found to be associated with cessation of breastfeed-ing. Insufficient milk, medications, and fatigue were the top 3 reported reasons for cessation of breastfeed-ing. Additional studies are being conducted to investigate if IBD affects milk production, and to address patient concerns about medications in breastfeeding.

A284
ARGON PLASMA COAGULATION ALONE OR IN COMBINATION WITH HEMOSPRAY FOR RADIATION PROCTITIS

A. Kayal, A. Weiss

Gastroenterology, University of British Columbia, Vancouver, BC, Canada

Background: Radiation proctitis is a common complication of radiation therapy. Although, argon Plasma Coagulation (APC) is the standard therapy for this condition, not all patients respond well. Hemospray (HS) is a relatively new endoscopic method for hemostasis. It is unclear if the addition of HS to APC would result in symptomatic improvement.
Aims: To compare the effect of the combination therapy (APC and HS) to APC alone on recurrent rectal bleeding.
Methods:
This was a randomized controlled trial. All patients who were referred for rectal bleeding and had a history of pelvic radiation were invited to participate. Patients were randomly assigned to either APC alone or APC+HS if radiation proctitis was endoscopically diagnosed. The primary outcome was the subjective improvement of rectal bleeding as reported by patients. The outcome was considered positive for 50% or more improvement in bleeding as reported by patients. Assessment of response was done through follow up clinic visits or follow up phone calls for patients who had no clinic follow up.
Results: A total of 18 patients were included in the study between April 2014 to July 2016. The mean age was 78 years. 16 (89%) were male patients treated for radiation for prostate cancer. 2 (11%) were female patients with endometrial cancer. 10 (55.5%) patients were randomly assigned to the combination therapy (APC+HS) and 8 (44.5%) to APC only. Mean follow up was 9.3 months after therapy. 7 out of 10 patients (70%) in the combination group reported positive response compared to 6 out of 8 (75%) in patients treated with APC only. There was no significant difference in response between the two groups (P

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value=1)

Conclusions: In this pilot study, the addition of hemospray to argon plasma coagulation did not result in an improvement of rectal bleeding.

A285

PREDICTORS FOR LOCAL RECURRENCE POST-ENDO-SCOPIC MUCOSAL RESECTION(EMR) OF COLONIC LESION WITH 3CM IN SIZE OR MORE

a. rammal[1], M. Sey[3], N. Khanna[4], J.C. Gregor[2], N. Hussain[5]

1. London health science centre , London , ON, Canada; 2. Medicine, Los Alamos National Laboratory, London, ON, Canada; 3. Western University, London, ON, Canada; 4. Western University , London, ON, Canada; 5. Western University, London, ON, Canada

Background: Colorectal cancer (CRC) is the second most common cause of death in Canada amongst all cancer deaths. Colonoscopy and polypectomy are effective in reducing the incidence of colorectal cancer and CRC-related mortality. Large lesions are challeng-ing to remove endoscopically, and surgery is the primary management technique in most centers especially if the lesion is 3 cm or more. Endoscopic mucosal resection EMR is a minimally invasive procedure for removal of large polyps.It has high success rates and minimal morbidity and mortality, but outcome studies have not shown enough evidence of that because only a few studies are available for the large lesion >3cm

Aims: To evaluate the predictors that'll increase the recurrence rate post EMR of colonic lesion of 3 cm in size or more and to define the best time to repeat the colonoscopy post resection to detect the recurrence as early as possible to decrease the likely hood of surgical intervention which will reduce the mortality and morbidity

Methods: A retrospective study, chart review, we recruit 100 patients who had a colonoscopy with EMR of colonic lesion of 3 cm in size or more between January 2010 and January 2016. Clinical data will be collected (age, size of the polyp, location, shape(flat or sessile), Histology, Follow-up colonoscopy in 3-6 month and presence of recurrence at that time, Follow-up colonoscopy in 6-18 month and presence of recurrence ta that time, using APC or clipping)will be determined from a retrospective chart review

Results: Overall recurrence was 16 cases (16%) (Recurrence detected between 3-6 months was 9%, Recurrence detected between 6-18 months was 8%), out of this 16 recurrent cases : 9 polyps were flat vs 7 were sessile, 8 polyps were in Right colon, 2 in Left,2 in Transverse,4 in Rectum, APC was used in 9 of the recurrent polyps, clips were used in 9 cases, 3 polyps were Tubular Adenoma with LGD, 7 were Tubulovillous (TV)Adenoma with LGD, 2 were TV Adenoma HGD, 8

were SSA ,1 was TSA and 1 was Adenocarcinoma

Conclusions: Based on our result, having a Flat polyp, polyps in Rt colon, Tubulovillous Adenoma with LGD or SSA will increase the risk of the recurrence rate and we recommend repeating the colonoscopy within 3 to 6 month if any of this predictor was found.Using APC or clips will not affect the recurrence rate, although the sample size was low as well as the recurrence rate the but this kind of procedure is not that common especially with a large polyp size

A286

MULTIFACTORIAL ETIOLOGY OF PROTEIN LOSING GASTROENTEROPATHY FOLLOWING FONTAN'S PROCEDURE

H. Odeh[1], M. Ropeleski[2]

1. Gastroenterology, Queens University, Kingston, ON, Canada; 2. Queens University, Kingston, ON, Canada

Background: Protein-Losing Enteropathy (PLE) post Fontan operation is thought to be due to multiple aetiologies including venous congestion, abnormal mesenteric vascular resistance, primary and\or secondary intestinal lymphangiectasia, & inflammation. An incidence of 3.7% has been reported in multicentre series of >3000 Fontan patients.

Aims: We report a case where take down of the Fontan did not improve PLE. This highlights the importance of non-vascular mechanisms or irreversible vascular changes in these patients.

Methods: A detailed review of the case and the literature was undertaken.

Results: A 20-year-old Caucasian female was referred to the adult GI clinic with a history of PLE since 2004. She has a complex history of congenital heart disease including dextrocardia, transposition of the great arteries, pulmonary atresia and VSD. In 2000, she underwent a non-fenestrated Fontan procedure. In 2004, she developed progressive PLE presenting with diarrhea, ascites & edema. The albumin was 11g/L, IgG <1.09 g/L, IgA < 0.4 g/L, IgM <0.25 g/L along with iron deficiency anemia, hypocalcaemia, hypomagnesemia and secondary hyperparathyroidism. Other complica-tions include osteoporosis with multiple vertebral fractures, recurrent respiratory infections, and problematic soft tissue infections requiring multiple admissions for IV antibiotics and IVIG. In 2007, she underwent takedown of her Fontan in an attempt to control her PLE. Diarrhea and hypoalbuminemia persisted and she was given 5 years to live. She eventually had a partial response to medical treatment which consisted of budesonide, enoxaparin, and a diet of high protein and high medium chain triglyceride intake. There was partial improvement of symptoms and the hypoalbuminemia 18-20g/L. The budesonide was weaned down from 9mg daily to 3mg every other day. Any attempts at further weaning or stopping of the

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enoxaparin have resulted in worsening of her symptoms and biochemistry. A CT scan in 2008 showed mild dilatation of small bowel, extensive collateralisation, high attenuation in the distal small bowel extending to the rectum, and relative mucosal enhancement within segments of small bowel. A Doppler US showed patent hepatic and portal veins. **Conclusions:** This case highlights the importance of the multifactorial nature of PLE post Fontan procedure. Reversing the hemodynamics of the heart is not enough to reverse the PLE in some cases. Permanent secondary intestinal lymphangiectasia, inflammation with enterocyte dysfunction as well as tissue matrix remodelling may be other possible aetiologies that contribute to the pathogenesis of this condition. We speculate that the gut undergoes irreversible vascular and lymphatics changes due to the congenital abnormalities in hemodynamics.We also wonder if the high intraluminal protein and Ig levels have a detrimental effect on the microbiome hence leading to secondary autoimmune disease.

MICROBIOLOGY AND PARASITE-HOST INTERACTIONS

Poster of Distinction

A287
PHYSICAL ACTIVITY AS A MODULATOR OF INTESTINAL MICROBIOTA, IMMUNE RESPONSES, AND SHORT-CHAIN FATTY ACIDS PRODUCTION
M. Estaki, J. Pither, P. Baumeister, J.P. Little, S.K. Gill, S. Ghosh, K. Marsden, Z. Ahmadi-Vand, D.L. Gibson

Biology, UBC - Okanagan, KELOWNA, BC, Canada

Background: The trillions of bacteria residing along the mammalian intestine, referred to as the gut's microbiome, are integral in various physiological function of their host. Disruptions in these communities, or dysbiosis, are implicated in various illnesses such as inflammatory bowel disease and colorectal cancer. Many factors such as diet, method of birth, and environmental exposures are known to influence the intestinal microbiota, however the role of physical activity (PA) remains unclear.
Aims: A) To explore the relationship between cardiorespiratory fitness (CRF) and gut microbiota in humans and; B) confirm causation between PA and the microbiota using a mouse model of PA
Methods: A) Using high-throughput DNA sequencing, we compared fecal microbiota of 39 individuals with varying CRF level as determined by peak oxygen uptake test (VO_2peak). Fecal short-chain fatty acids (SCFA) were analysed using GC. B) Female C57BL/6 mice were randomly categorized into voluntary wheel running (VWR), or sedentary (SED) group (n=8). Intestinal

bacterial community, morphology, and gene expression of various cytokines was analyzed after 7 weeks.
Results: A) VO_2peak in humans was significantly correlated with increased microbial biodiversity and distinct metagenomic functions. The microbial profiles of fit individuals were associated with increased production of buryate, a SCFA known for its anti-inflammatory properties, through increased abundances of key butyrate-producing taxa: *Clostridiales*, *Roseburia*, *Lachnospiraceae*, and *Erysipelotrichaceae*. B) VWR mice gained weight at a significantly higher rate than SED group, absent changes in their food intake. *Firmicutes* phyla was significantly higher (29.0%, p<0.05) in VWR mice while *Bacteroidetes* was higher (260%, p<0.05) among SED mice. VWR had a higher *Firmicutes* to *Bacteroidetes* ratio, previously associated with increased energy harvest and weight gain. Histological analysis revealed no group differences in the number of goblet cells, crypt lengths, or total muscularis externa. A significance 2.1 and 1.9 fold increases in gene expression of the cytokines TGFβ and TNFα, respectively, was observed among the SED mice suggesting immunogenic differences induced by PA.
Conclusions: VO_2peak in humans was correlated with increased microbial diversity and production of butyrate through increases in several key butyrate-producing taxa. Further, wheel running in mice increased the *Firmicutes* to *Bacteroidetes* phyla ratio, likely leading to increased energy harvest and weight gain without changes in food intake. Wheel running was also associated with suppressed gene expression of the pro-inflammatory cytokine TNFα, and TGFβ, a marker of cell proliferation, suggesting an overall healthier gut among physically active mice.

Poster of Distinction

A288
DISTINCT ROLES IN INNATE HOST DEFENSE AND SUSCEPTIBILITY TO COLONIC INJURY IN MUC2 MUCIN DEFICIENT AND SUFFICIENT MICROBIOTA
A. Leon-Coria[2], F. Moreau[2], M. Workentine[2], M. Surette[1], K. Chadee[3]

1. McMaster University, Hamilton, ON, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, AB, Canada

Background: The intestinal epithelium is covered with a thick viscous MUC2 mucin bilayer that acts as a protective barrier and is the habitat for 10^{14} microorganisms that form the microbiota. Even though disruption of colonic mucus and alterations in microbial composition are intimately linked to gastrointestinal health and disease, their distinct contribution in the pathogenesis of colitis is not well understood.
Aims: To interrogate the impact of alterations in the

microbial composition in animals with/without Muc2 mucus in colonic epithelial barrier dysfunction and inflammation.

Methods: To quantify the role of the microbiota in disease pathogenesis Muc2+/+ and Muc2-/- littermates were treated with a cocktail of antibiotics that reduced indigenous bacteria (up to 80%) as revealed by 16s rRNA sequencing analysis, and then fecal transplanted (FMT) with littermate stool and susceptibility to chemical (dextran sulphate sodium (DSS)) and pathogen-induced *(Citrobacter rodentium)* quantified.

Results: Sequencing analysis revealed that even though Muc2+/+ and Muc2-/- mice share similar phyla distribution, their distinct gastrointestinal phenotypes remained intact. Muc2-/- animals basally show low-grade ongoing inflammation, increased gastrointestinal permeability and alterations in tight junction proteins that were significantly restored following antibiotic treatment. In FMT studies, Muc2+/+ mice that received Muc2-/- microbiota were highly susceptible to DSS-induced colitis/mortality as compared to Muc2+/+ receiving their own microbiota. Sequencing analysis revealed that this impact could be explained through OTUs from distinctive families (Bacteroidaceae, Enterobacteriaceae, Verrucomicrobiaceae) that are transplantable to Muc2 +/+ littermates. Similarly, following antibiotic treatment, Muc2+/+ but not Muc2-/- were more susceptible to C. rodentium pathology and DSS-induced colitis with rapid weight lost and mortality.

Conclusions: These studies highlight that Muc2+/+microbiota with an intact mucus barrier play a protective innate role against DSS-induced colitis, while microbiota from Muc2 deficient animals does not. Importantly, Muc2 deficiency alters the colonic microbiota that enhanced susceptibility to pathogen and DSS-induced colitis in Muc2+/+ littermates demonstrating a critical role for Muc2 mucus in shaping a healthy microbiota in intestinal homeostasis.

A289
THE CROHN'S DISEASE-ASSOCIATED ADHERENT-INVASIVE E. COLI INDUCES MITOCHONDRIAL FRAGMENTATION IN ENTERIC EPITHELIUM THAT IS NOT DEPENDENT ON BACTERIAL SOLUBLE PRODUCTS OR MITOCHONDRIAL REACTIVE OXYGEN SPECIES

N. Mancini[2], A. Wang[2], J. Shearer[2], D.M. McKay[1]

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

Background: Introduction: Despite the popular depiction, mitochondria are not distinct organelles; they exist as a dynamic network that is constantly remodelling via the balanced processes of fission and fusion to meet the energy demands of the cell and allow recycling of damaged mitochondria. Mitochondrial dysfunction has been described in IBD and pharmacologically-induced mitochondrial dysfunction leads to increased epithelial permeability. The Crohn's disease-associated pathobiont, adherent-invasive E. coli (AIEC) can stimulate reactive oxygen species (ROS) production from epithelial cells and be apoptotic. Little is known of microbial regulation of enterocytic mitochondrial dynamics and nothing of the potential of AIEC to perturb the critical metabolic function that mitochondria fulfill for the cell.

Hypothesis: AIEC induce mitochondrial fission in intestinal epithelial cells in an invasion-dependent manner that requires ROS.

Aims: 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 AIEC or a non-invasive E. coli and the following readouts assessed: (a) visualization of mitochondria morphology and membrane potential with confocal microscopy; (b) immunoblotting of whole cell protein extracts for the mitochondrial fusion protein Optic Atrophy Factor 1 (OPA1); (c) ROS neutralized by the antioxidants; and, (e) measurement of mitochondrial fragmentation and OPA1 protein expression following treatment with spent medium from bacterial cultures.

Results: AIEC infection resulted in reduced ATP levels, reduced mitochondrial membrane potential and dramatic mitochondrial fission (fragmented mitochondria and OPA1 cleavage) in gut epithelia in a time- and dose-dependent manner. The mitochondrial fragmentation was not reproduced by exposure to AIEC conditioned medium and was not abrogated by treatment with a general (vitamin C) or a mitochondrial-specific (mitoTEMPO) anti-oxidant co-treatment. Invasion of epithelial cells by AIEC was unaffected by use of pharmacological inhibitor of mitochondria fission, P110.

Conclusions: As a putative cause or contributor to the pathophysiology of Crohn's disease, AIEC are shown to drive massive mitochondrial fission in epithelial cells independent of ROS generation or AIEC soluble factors. We speculate this perturbation of mitochondrial dynamics would disrupt the epithelial barrier function and lead to apoptosis which could perpetuate inflammation.

A290
THE ATF6 ARM OF ER STRESS ANTAGONIZES METABOLIC STRESS-INDUCED DECREASES IN EPITHELIAL BARRIER FUNCTION TO COMMENSAL BACTERIA BY PROMOTING XENOPHAGY

F. Lopes[4], A. Keita[8], J.L. Reyes[5], N. Mancini[4], A. Al Rajabi[4], A. Saxena[6], A. Wang[4], r. van dalen[7], W. MacNaughton[3], H. Jijon[4], J.D. Soderholm[1], D. Philpott[7], D.M. McKay[2]

1. Clinical and Experimental Medicine, Linköping University, Linköping, Sweden; 2. Physiology & Pharmacol-

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ogy, Uni. Calgary, Calgary, AB, Canada; 3. Univ Calgary, Calgary, AB, Canada; 4. University of Calgary, Calgary, AB, Canada; 5. Physyology, University of Calgary, Calgary, AB, Canada; 6. Physiology & Pharmacology, Gastrointestinal Research Group, University of Calgary,- Calgary, AB, Canada., Calgary, AB, Canada; 7. University of Toronto, Toronto, ON, Canada; 8. Linkoping Universi- ty, Linkoping, Sweden

Background: The barrier function of the intestinal epithelium is a first-line of defense that is compro- mised in IBD. We have shown that epithelia treated with dinitrophenol (DNP: uncouples oxidative phosphor- ylation) have a dramatic impairment in their barrier function, and internalize non-invasive commensal *E. coli*. Mitochondria do not function in isolation; they are closely aligned with the endoplasmic reticulum (ER).
Aims: To investigate the interaction of mitochondrial dysfunction, ER stress and autophagic processes as a key determinant of epithelial-bacterial interaction, transcellular permeability and the fate of commensal bacteria that gain access to the intracellular compart- ment as a consequence of metabolic stress.
Methods: Methods: Human colonic biopsies were mounted in Ussing chambers, murine epithelial colonic organoids were re-suspended and grown as a monolay- er, and human colon-derived epithelial cell lines were cultured on transwell filters or on plastic. Bacteria were added to the luminal buffer and the tissue treated with DNP ± the ER stressor, tunicamycin (TM), and bacterial internalization and translocation assessed. Mechanistic studies involved measuring ATP production, immuno- blotting, assessment of LC3 activation for autophagy and gene knock-down (KD) by siRNA and CRISPR/cas9.
Results: Results: DNP promoted the translocation and internalization of *E. coli* and, remarkably, TM reduced this barrier defect. TM did not prevent the DNP-evoked drop in ATP or the rate of epithelial update of inert beads, but *E. coli*, DNP and TM-treated cells had increased autophagy. The effect of TM was lost in cells lacking the autophagy protein, ATG16L1, suggesting that the ER-stress promoted killing of the internalized bacteria. Of the 3 major arms of the ER stress response, only KD of ATF6 ablated the TM antagonism of the DNP-evoked barrier effect; the increase in autophagy evoked by TM was absent in ATF6 KD epithelia. Phar- macological studies indicate that the kinase, DAPK1 is required from the ER stress-ATF6 signal to drive autophagy to kill the internalized *E. coli*.
Conclusions: Conclusion: The ATF6 arm of ER stress antagonizes metabolic stress-induced decreases in epithelial barrier function to commensal bacteria by promoting xenophagy via upregulation of DAPK1.

A291
INVESTIGATING THE ROLE OF ANTIBIOTICS AND ADHERENT-INVASIVE *E. COLI* IN THE PATHOGENESIS OF CROHN'S DISEASE

A. Oberc[2], A. Fiebig-Comyn[2], B.K. Coombes[1]

1. McMaster University, Hamilton, ON, Canada; 2. Biochemistry and Biomedical Sciences, McMaster University, Hamilton, ON, Canada

Background: Crohn's disease (CD) is an immune-me- diated intestinal illness that is a significant health concern in many developed countries. CD is believed to have a complex etiology consisting of both host susceptibility factors and environmental insults. Multiple epidemiological studies have linked antibiotics with subsequent CD diagnosis. CD is also associated with increased abundance of an unusual phenotypic group of *Escherichia coli* known as adherent-invasive *E. coli* (AIEC) in many patients. AIEC are characterized by their ability to adhere and invade various cell types, to stimulate the production of inflammatory cytokines, and also tend to be resistant to multiple classes of antibiotics. Our lab has found that chronic colonisa- tion of conventional mice with AIEC leads to intestinal inflammation and fibrosis.
Aims: Our objective was to use this mouse model to investigate the impact of antibiotics on AIEC colonisa- tion, pathology, and immune responses.
Methods: Mice were treated with various antibiotics in drinking water or by oral gavage. These mice were infected with various doses of AIEC either before or after antibiotic treatment.
Results: We found that certain antibiotics administered prior to infection greatly reduced the infectious dose of bacteria required and led to greater bacterial burden. Mice administered antibiotics after infection similarly showed an expansion of AIEC in the feces and tissues. We are continuing to investigate how antibiotics alter AIEC colonisation by studying the metabolic and immune consequences of antibiotic treatment.
Conclusions: These results show that antibiotics may create a favourable environment for AIEC colonisation in CD patients. Future work will continue investing how antibiotics impact the gut environment in the context of CD.

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NLRP$_3$-DEPENDENT PRODUCTION OF ANTIMICROBIAL PEPTIDES DURING CO-INFECTION WITH *GIARDIA INTESTINALIS* AND *E. COLI*

A. Manko[4], J. Motta[3], J. Cotton[3], A. Oyeyemi[5], B. Val- lance[2], J.L. Wallace[1], A. Buret[5]

1. Antibe Therapeutics Inc., Toronto, ON, Canada; 2. BC Children's Hospital, Vancouver, BC, Canada; 3. Biological Sciences, University of Calgary, Calgary, AB, Canada; 4. Biological sciences, University of Calgary, Calgary, AB, Canada; 5. University of Calgary, Calgary, AB, Canada

Background: Infectious diarrheal disease represents a

critical concern for child health in developing countries. Recent findings indicate that in such environments, infection with *Giardia intestinalis* may protect against bacterial driven diarrhea via mechanisms that remain unknown.

Aims: We hypothesized that cysteine protease(s) released by *Giardia* in co-infection with enteropathogenic *Escherichia coli* (EPEC) activate the NLPR3 inflammasome pathway, increasing antimicrobial peptides (AMPs) production and secretion.

Methods: Mice (wild type or NLRP3 -/-) were infected with *G. muris* and/or *Citrobacter rodentium* to model co-infections with *Giardia* and EPEC in humans. AMP production, bacterial pathogen burdens, and colonic disease activity were assessed. Human enterocytes (Caco-2) were pretreated or not for 30 min with glyburide (NLRP3 inhibitor; 100 mm), and infected with *Giardia duodenalis* trophozoites (with or without pre-treatment with cathepsin B inhibitors) and EPEC separately or in combination. Human β-defensin-2 (HBD-2) and trefoil-factor 3 (TFF3) protein and mRNA expression were assessed by immunofluorescent (IF) staining and by RT-qPCR, respectively.

Results: Infection with *G. muris* increased colonic levels of murine β-defensin and TFF3, inhibited bacterial colonization, and reduced disease activity in co-infected animals. The effects were lost in NLRP3 $^{-/-}$ mice. IF staining intensity of HBD-2 and TFF3 was the highest in co-infected epithelial cells, compared to EPEC-infected only. The effects were reversed by the administration of the NLRP3 inhibitor. HBD-2 and TFF3 mRNA levels were increased in the co-infected caco-2 cells, as compared to cells infected only with EPEC, also in a NLRP3-dependent manner. Pre-treatment of *Giardia* trophozoites with a selective cathepsin B inhibitor abolished the effects of *G. intestinalis*. Co-infection *in vitro* also reduced bacterial numbers retrieved after the experiment compared with bacterial numbers retrieved from the cells infected only with EPEC. Moreover, *G. intestinalis* directly inhibited EPEC growth *in vitro*, in a cathepsin B-dependent manner.

Conclusions: Our data suggest novel mechanisms involved in the production of antimicrobial peptides. *Giardia* co-infection with EPEC activates expression and secretion of AMPs in human intestinal epithelial cells through activation of the NLRP$_3$ pathway. *Giardia* cathepsin B-like proteases participate in this effect, which protects an infected host during co-infections with bacterial enteropathogens like EPEC.

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INFLAMMASOME ACTIVATION INCREASES MACRO-PHAGE MIGRATION THROUGH EPITHELIAL BARRIER DURING *CITROBACTER RODENTIUM* INFECTION

M. Bording-Jorgensen[2], H. Armstrong[1], E. Wine[1]

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

Background: The proinflammatory cytokine interleukin (IL)-1β is released from macrophages and mono-cytes through a class of protein complexes called inflammasomes. 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 IL-1β with the exception of IBD, where its dysregulation leads to an IL-1β reduction. The mouse pathogen *Citrobacter rodentium,* a common mouse model pathogen for enteropathogenic *E. coli,* is used to understand the dynamic relationship between pathogens, the inflammasome, and the epithelial barrier. We have previously shown that ATP-activated macrophages increase clearance of *C. rodentium in vitro.* Our hypothesis was that inflammasome activation will increase macrophage recruitment and facilitate migration through the epithelial barrier.

Aims: To determine the role of the inflammasome in bacterial-epithelial-macrophage interplay

Methods: Mouse colonic epithelial cells (CMT-93) were seeded on collagen coated transwells until tight junctions were formed [documented using transepithelial electrical resistance (TEER)]. CMT-93 cells were then infected with *C. rodentium* on the apical membrane. ATP (2.5mM) and LPS (10ng/ml) were used to activate the inflammasome in macrophages and then added to the basolateral membrane for 24hrs. Tight junction permeability was measured every 2 hrs using TEER. Macrophage migration was observed using confocal microcopy with F4/80 as the macrophage stain along with GFP *C. rodentium* and epithelial ZO-1 staining. The tight junction proteins Claudin-1, Occludin, and ZO-1 were assessed in macrophages.

Results: ATP-activated macrophages were recruited to the apical membrane during *C. rodentium* infection of epithelial cells. *C. rodentium* adherence to epithelial cells after 24 hours was found to be significantly reduced and there was an increase in epithelial barrier recovery, measured by TEER; these effects were inhibited when YVAD was present. We also documented an increase in macrophage tight junction proteins during *C. rodentium* infection, suggesting a potential for active interaction with epithelial cells.

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, due to impairments in the ability to clear pathogens. Our multi-cell type models highlights the important relationship between epithelial cells and macrophage inflammasomes in maintaining the epithelial barrier in IBD patients, which could allow development of new treatments.

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

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ROLE OF MACROPHAGE IN GUT MICROBIOTA-BRAIN SIGNALING

S. Cocciolillo, G. De Palma, M. Pigrau, J. Lu, P. Bercik, S.M. Collins

Farncombe Family Digestive Health Research Institute, Department of Medicine, McMaster University, Hamilton, ON, Canada

Background: Gut microbiota shapes host's immune system, which plays an important role in host's behavior and brain development. Peripheral macrophages have been implicated in sickness-like behavior induced by endotoxin and recent studies have highlighted the existence of a novel axis between the immune system and the brain involving monocytes trafficking to the brain, regulating mood and behaviour. However, the role of macrophages in microbiota-gut-brain signaling has not yet been investigated.
Aims: To investigate the role of macrophages in altered behaviour in a murine model of antibiotic-induced dysbiosis.
Methods: Specific pathogen−free (SPF) BALB/c mice (6−8 weeks old) received i.p. injection of clodronate encapsulated liposomes to deplete macrophages or phosphate buffered saline (PBS). Two days later the mice received a mixture of non-absorbable antimicrobials (ATM) in drinking water or placebo for 7 days. Behavioural profiles (the light preference and the step-down test) were assessed, and the mice were sacrificed thereafter. F4/80 positive cells were evaluated in colonic tissues and gut microbiota composition was analyzed by 16S rRNA gene sequencing with Illumina technique. Statistical analyses were performed using un-paired t test (Mann-Whitney U test) or Kruskal−Wallis test followed by Dunn post-test as appropriate.
Results: ATM administration induced anxiolytic behavior and increased exploratory behavior during the light preference test in all mice regardless of clodronate liposomes injections. Interestingly, only antibiotic treated mice that did not receive clodronate's injections showed a reduced latency to step down in comparison to age matched controls. As expected, clodronate liposomes's injections induced a depletion significantly the number of F4/80 positive cells in colonic lamina propria. Antibiotic treatment alone did not alter the number of F4/80 positive cells in colonic lamina propria.
Conclusions: Our preliminary data suggest that macrophages might be involved in the modulation of mouse behaviour induced by intestinal dysbiosis and that antibiotic treatment alone did not alter the number of macrophages in colonic lamina propria . Further studies are needed to understand the exact role of macrophages in microbiota-gut-brain signaling.

A295
FUCOSE AVAILABILITY AND ITS UTILIZATION IMPACT

***IN VIVO* ENTERIC PATHOGEN VIRULENCE.**

J.M. Allaire[1], K. Bhullar[1], S.M. Crowley[1], M. Stahl[1], H. Yang[1], E. Verdu[2], H. YU[1], B. Vallance[1]

1. BC Children's Hospital Research Institute, Vancouver, BC, Canada; 2. McMaster University, Hamilton, ON, Canada

Background: Attaching and effacing (A/E) pathogens such as Enterohemorrhagic *E. coli* (EHEC) are important causes of diarrheal disease worldwide. Interestingly, little is known about how these bacteria obtain key nutrients, and whether these nutrients modulate pathogen colonization and gut infection. For example, fucose is an important sugar and bacterial food source cleaved from host glycans found on the intestinal mucosal surface via the actions of commensal microbes expressing fucosidase enzymes. Interestingly, although the mouse A/E pathogen *Citrobacter rodentium* does not itself express a fucosidase, recent studies have found that it and EHEC use a fucose sensing system to modulate their pathogenicity *in vitro*. At present, it is unclear what role fucose metabolism may play in A/E pathogen virulence and metabolism *in vivo*. To address this, we focused on *C. rodentium* enzyme L-fuculose kinase (encoded by the *fucK* gene), which plays a key role in the L-fucose metabolic pathway and fucose utilization as a food source.
Aims: We investigated the roles of fucose and the enzyme L-fuculose kinase in controlling *C. rodentium* pathogenesis.
Methods: Wildtype (WT) and Δ*fucK C. rodentium* were used for *in vitro* assays (type three secretion, growth and adhesion assays) and for *in vivo* infection. C57Bl/6 mice were infected either separately, or with both *C. rodentium* strains at a dose of 10^8 colony forming units. In some infections, mice were pretreated with streptomycin (20mg 24h pre-infection) or were fed fucose (200ul of 25mM L-fucose 2x/day). Bacterial burdens, pathology score and competitive assay were assessed on day 6 post-infection.
Results: *In vitro* virulence assays identified no significant differences between Δ*fucK* and WT *C. rodentium* regarding type three secretion, growth or adherence to cultured epithelial cells. Moreover, both WT and Δ*fucK C. rodentium* readily colonized the intestines of mice either pretreated (or not), with streptomycin, with pathogen burdens, localisation and histological pathology scores similar between the two strains. In contrast, simultaneous infection by both strains (competitive assay) within the same mice revealed the $\Delta fucK$ strain was significantly impaired when competing with WT *C. rodentium* (no streptomycin). In contrast, $\Delta fucK$ was able to equally compete with WT *C. rodentium* when streptomycin pretreatment was given to deplete commensal bacteria. Feeding fucose to these streptomycin treated mice again reduced the ability of the $\Delta fucK$ strain to compete with WT *C. rodentium*.
Conclusions: These results indicate that the fucK-dependent fucose metabolic pathway promotes but is

not essential to *C. rodentium* pathogenesis. Moreover these findings suggest that commensal microbes play a key role in controlling fucose availability in the gut, and thereby impact A/E pathogen metabolism and virulence.

A296
THE ANTI-COLITIC EFFECT OF INFECTION WITH
***HYMENOLEPIS DIMINUTA* IS NOT OBSERVED IN**
ANTIBIOTIC TREATED MICE.
A.J. Shute, A. Wang, M. Strous , A. G. Buret, D.M. McKay

University of Calgary , Calgary, AB, Canada

Background: Infection with helminth parasites can ameliorate concomitant inflammatory disease: we showed that mice infected with *H. diminuta* display significantly less sever di-nitrobenzene sulphonic acid (DNBS)- induced colitis. The commensal bacteria make a significant contribution to gut homeostasis and perturbation of this complex microbiota is often observed in colitis. Thus, the hypothesis arises that *H. diminuta* evoked protection against colitis is mediated, in least in part, via changes in the colonic microbiota.
Aims: To determine if infection with the helminth parasite, *H. diminuta*, evokes distinct changes in the colonic microbiota that are required for the anti-inflammatory effect in the DNBS model of colitis.
Methods:
Bacterial DNA was isolated from colon tissue samples from control and *H. diminuta*-infected (5 cysticercoids) Balb/c ± DNBS treatment (3 mg, ir, 72h) and amplified using 16s rRNA primers prior to sequencing (Illumina miSeq). Sequence results were demultiplexed and OTU's were generated on the University of Calgary's MetaAmp pipeline and mice. Colitis was assessed by colon length, weight loss, a cumulative disease activity score and histopathology. The anti-colitic effect of infection with *H. diminuta* was assessed in mice given a broad spectrum antibiotic (Abx) regimen.
Results: Sequence analysis of the microbiota of *H. diminuta*-infected and control mice revealed no statistical differences. Abx-treated mice produced a natural Th2 and anti-helminth immune response towards infection with *H. diminuta*. *H. diminuta*-infected mice were protected from colitis. DNBS-treated mice ± *H. diminuta* had a similar colonic microbiota with a major shift from firmicutes to bacteroidetes/proteobacteria. However, *H. diminuta*-evoked protection against DNBS-induced colitis was significantly reduced in mice with a colonic microbiota that had been significantly reduced by antibiotic treatment (n=4).
Conclusions: Infection with *H. diminuta* may have subtle effects on the colonic microbiota of mice, but the bacteria appear not to be a requirement for either the induction of a helminth-directed TH2 response or successful expulsion of *H. diminuta*. While there were

no striking differences in the microbiota of DNBS versus DNBS+*H. diminuta* treated mice, the anti-colitic effect of infection with *H. diminuta* was negated in antibiotic-treated mice. Suggesting that bacteria are involved in this beneficial effect of infection with a cestode parasite in a non-permissive system.

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GOBLET CELLS AND INTESTINAL TREFOIL FACTOR
PLAY CRITICAL ROLES IN INNATE PROTECTION
AGAINST CLOSTRIDIUM DIFFICILT COLITIS AND
MEDIATE RECOVERY FOLLOWING CDIF COLITIS.
H. Tang[1], J. Nguyen[1], Y. Li[3], J.A. MacDonald[2], P. Beck[2]

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

Background: Cdif colitis is a leading cause of morbidity and mortality in many populations including elderly hospitalized, those with inflammatory bowel disease, and the immunosuppressed. Although depletion of the density and diversity of the intestinal microbiome is clearly the main underlying mechanistic risk factor, little is known of the innate mechanisms involved in protection against Cdif and those involved in recovery following Cdif colitis. One of the hallmarks of Cdif colitis are pseudomembranes (composed of mucus, fibrin and debris). Altered mucus secretion (MUC2) has been described in pts with Cdif colitis.
Aims: The hypothesis of the present study was to assess the role of goblet cells, mucins and associated growth factors (ITF, secreted by goblets cells) in mediating protection against Cdif induced injury/inflammation and recovery following Cdif colitis.
Methods: Colitis was induced in C57Bl6 mice either via intrarectal administration of Cdif toxin (A&B) or in the Cdif oral gavage infection model. Human tissue models included; in vitro (CaCO2, IECs) & ex vivo studies (fresh human colonic biopsies exposed to toxin A/B). Cdif injury/inflammation was assessed via histology, MPO, cytokine release, permeability, LDH release, apoptosis markers. ITF, MUC2, KGF and goblet cells were assessed via WB, PCR, AB/PAS + immunostaining.
Results: Cdif toxin and infection significantly depleted goblet cells, the protective growth factor ITF and MUC2 in mouse and human tissues. Recovery from Cdif colitis was associated with increased ITF expression, MUC2 and goblet cell number. MUC2 -/- mice were more susceptible to Cdif colitis vs wt mice (increased MPO, histological scores). ITF -/- mice had similar levels of acute Cdif colitis but had marked impairment in recovery from colitis at 24 and 48h post toxin exposure. We then assessed the role of keratinocyte growth factor (KGF) which is upstream of ITF and induces ITF expression. KGF -/- mice had decreased

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ITF and increased toxin induced goblet cell depletion and markedly impaired recovery from Cdif colitis. Exogenous KGF (i.p.) enhanced recovery from Cdif colitis in wt and KGF-/- mice but not in ITF-/- mice. In our human tissue models ITF or KGF exposure reduced Cdif toxin induced injury (barrier function, LDH release, apoptosis and cytokine release).

Conclusions: Goblet cells, MUC2 and growth factors ITF and KGF are important in the innate protection against Cdif colitis and are critical in the recovery from Cdif colitis. These findings mat lead to new approached in the management of patients with Cdif coltis.

A298
A SWITCH FROM MUC2 TRANSCRIPTION TO MUC5AC IS A COMPENSATORY MECHANISM AGAINST THE MUCOLYTIC ACTIVITY OF *GIARDIA DUODENALIS*

C.B. Amat[2], J. Motta[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

Aims: *Giardia duodenalis* is a diarrheagenic parasite of the small intestine characterized by acute and chronic illnesses including irritable bowel syndrome. MUC5AC mucin in the stomach and MUC2 in the intestine are normally protective against pathogens. We hypothe-sized that *Giardia* is able to disrupt this barrier by several mechanisms that may contribute to both acute and chronic disease.

Methods: Muc2$^{-/-}$ (KO-inf) and C57BL/6 (WT-inf) mice were gavaged with *Giardia* trophozoites and euthanized on day 7. Tissues were collected for histological staining, qPCR, and analysis of bacterial translocation. Human colonic biopsies were exposed to *Giardia* trophozoites to quantify intracellular mucins. *In vitro*, *Giardia* trophozoites were incubated with or without a cysteine protease inhibitor, E64, then with a human mucus-producing cell line, LS174T, to assess intracellular mucin content and MUC2 transcription. *Giardia*'s secreted products were incubated with purified human MUC2 to assess proteolysis via western blot.

Results: KO-inf mice had a higher parasitic load compared to WT-inf mice and failed to gain weight over the period of infection. Compared to non-infected mice, WT-inf mice exhibited novel transcription of Muc5ac and decreased transcription of Muc2 in the jejunum. Both Muc2 and Muc5ac mRNA were increased in the colon. Of note, Muc5ac transcription was not induced in KO mice. WT-inf mice had larger colonic mucus granules but a thinner mucus layer, demonstrated by staining with periodic-acid Schiff/Alcian blue, wheat germ agglutinin, and with the use of microbiota markers using fluorescent *in situ* hybridization. Infected mice had increased aerobic and anaerobic bacterial

translocation into the liver and spleen. *In vitro, Giardia*'s secreted products degraded human MUC2. This was attenuated by E64. Human biopsies exposed to *Giardia* had less intracellular mucus granule content. *Giardia* reduced intracellular mucin content in LS174T cells after 20, 40, and 60 minutes post-infection (also inhibited by E64), whereas it increased mucin content by 3 hours post-infection. *In vitro*, *Giardia* infection increased Muc2 transcription after 1 hour.

Conclusions: In mice, Muc2 was protective against parasite accumulation and induced weight loss, but *Giardia* disrupted the mucosal barrier function by reducing the mucus layer and causing an alteration of mucin gene transcription, specifically an increase of Muc5ac and a decrease of Muc2 in the jejunum. Proteolysis of MUC2 could be a potential mechanism by which *Giardia* alters barrier function *in vivo*. Resultant loss of the mucus barrier was associated with increased bacterial translocation and may contribute to both acute and chronic disease. Mucin degradation and depletion were attenuated by a cysteine protease inhibitor, indicating a potential target to reduce *Giardia*-induced pathology.

A299
IDENTIFICATION OF PATHOGENIC BACTERIAL STRAINS IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASES USING IMMUNOGLOBULIN G AS A MARKER OF VIRULENCE

M. Alipour[1], H. Armstrong[1], R.S. Valcheva[2], D. Zaidi[1], J. Jovel[1], Y. Lou[5], A. Mason[1], G. Wong[1], K. Madsen[2], L.A. Dieleman[2], M.W. Carroll[6], H.Q. Huynh[4], E. Wine[3]

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

Background: Inflammatory bowel diseases (IBD), including Crohn disease (CD) and ulcerative colitis (UC), are a group of chronic and severely debilitating gastrointestinal disorders, with an exacerbated immune response to the gut microbiota.

Aims: We hypothesized that pathogenic bacteria are more likely to be bound by immunoglobulin (Ig) G antibodies and identification of these strains could help identify mechanisms of immune activation.

Methods: Aspirate washes were obtained from the terminal ileum of pediatric IBD and non-IBD patients during endoscopy. Samples were fixed in paraformalde-hyde and stringently washed to separate bacteria. Prior to fluorescence-activated cell sorting (FACS), samples were stained with propidium iodide (PI) and an anti-IgG fluorescent antibody with proper controls to differenti-ate bacteria bound by IgG (IgG+) from all others (IgG-).

Validation in a select set of samples involved image cytometry. DNA was extracted from sorted bacteria using bead beating extraction and phenol/chloroform purification. Analysis of bacterial DNA samples was completed using the Ilumina MiSeq platform for 16S rRNA gene sequencing.

Results: Quality of patient bacterial DNA samples was used to identify those suitable to be sequenced resulting in 36 total washes from children without IBD (n=10), and with CD (n=17) or UC (n=9). Firmicutes and Bacteroidetes phyla were most commonly identified; however, no significant differences were found between IBD and non-IBD controls upon examining the composition of the ileal mucosa-associated microbiome. There was a 2 and 1.5 fold increase in the overall ratio of IgG+/IgG- bacteria in CD and UC, respectively. In CD, there was an increase in IgG+/IgG- ratio of both Bacteroidetes and Proteobacteria phyla. In UC this ratio was increased for Actinobacteria. IgG binding favored specific family level strains including Porphyromonadaceae (Bacteroidetes) and Enterobacteriaceae (Proteobacteria) in CD; Barnesiellaceae (Bacteroidetes) and Bifidobacteriaceae (Actinobacteria) in UC; and Clostridiaceae and Veillonellaceae (Firmicutes) in non-IBD, although considerable variation was noted between patients.

Conclusions: This study demonstrated selective increase of mucosa associated bacteria bound by IgG in the ileum of pediatric IBD patients compared to non-IBD. Further use of this method in larger cohort studies can identify individual microbes as therapeutic targets facilitating the development of targeted diagnostic and improved therapeutic approaches for IBD.

MOTILITY AND NERVE GUT INTERACTIONS

Poster of Distinction

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DIET-MICROBIOTA INTERACTIONS UNDERLIE SYMPTOMS IN IBS

G. De Palma[1], D.E. Reed[2], M. Pigrau[1], J. Lu[1], S. Sidani[1], Y. Zhang[2], Y. YU[2], N.N. Jiménez-Vargas[2], J. Sessenwein[2], C.D. Lopez Lopez[2], J.O. Jaramillo Polanco[2], E. Verdu[1], S.M. Collins[1], 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

Background: The mechanisms underlying IBS are poorly understood but growing evidence suggests that immune activation and the microbiota may be involved. We recently demonstrated that a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols (FODMAP) improves symptoms in IBS patients and this is correlated with decreased mast cell activation and changes in the microbiota composition. Thus, FODMAPs may be a useful tool to evaluate IBS mechanisms.

Aims: To investigate the interplay of host's gut function, intestinal microbiota and immune factors 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 (P1) or low (P2) urinary histamine level (n=20 mice /patient), suggesting differing levels of immune activation. Mice were assigned to a custom-made low or high FODMAP diet (LF and HF, respectively). Three weeks later, GI transit (beads study), cecal volume (CT scan) and intestinal permeability (FITC-Dextran) were assessed. Animals were then euthanized and neuronal excitability assessed 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 from mice receiving LF or HF diets.

Results: P1 mice receiving a HF diet had slower GI transit (p=0.02), increased cecal volume (p=0.004), indicative of increased gas content, increased permeability (FITC-Dextran: p=0.04), and lower weight gain (p=0.04) compared to P1 mice on a LF diet. In electrophysiological studies, the rheobase was decreased (24%; p=0.003) and mechanosensitivy increased (p=0.06) in the HF compared to the LF mice. The decreased rheobase was blocked by a H1 or a PAR2 antagonist. In contrast, P2 mice receiving the HF diet displayed modest increase in cecal volume (p=0.02) but no differences in GI transit, permeability or weight compared to those on the LF diet. The rheobase was modestly decreased (17%, p<0.05) but no changes were found in mechanosensitivity.

Conclusions: Fermentable carbohydrates cause changes in GI function that likely underlie symptoms of IBS, and the magnitude of these functional changes is determined by gut microbiota. Our data suggests the microbiota-diet interactions play a key role in IBS pathogenesis and symptom generation.

First two authors contributed equally to this work. Funded by grants from CIHR and CAG.

Poster of Distinction

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GUT MICROBIOTA FROM A PATIENT WITH GENERALIZED ANXIETY DISORDER INDUCES ANXIETY-LIKE BEHAVIOUR AND ALTERED BRAIN CHEMISTRY IN GNOTOBIOTIC MICE

E. Perez Guzman[2], R. Anglin[3], G. De Palma[1], J. Lu[4], R. Potts[1], M. Amber[1], R. McCabe[1], E. Verdu[1], S.M. Collins[1], M. Surette[1], P. Bercik[2]
1. McMaster University, Hamilton, ON, Canada; 2. Med-

icine, McMaster University, Hamilton, ON, Canada; 3. Psychiatry and Medicine (Gastroenterology), McMaster University, Hamilton, ON, Canada; 4. McMaster University, Hamilton, ON, Canada

Background: Depression and anxiety have overlapping etiologies and their pathophysiology remains largely unknown. Accumulating data suggest that gut microbiota modulates brain function and behaviour and may play a role in the pathophysiology of depression and anxiety

Aims: To investigate whether gut microbiota from patients with Generalized Anxiety Disorder (GAD) induces anxiety-like behaviour in gnotobiotic mice and whether this is accompanied by changes in brain chemistry and immune markers.

Methods: Germ-free NIH Swiss mice (n=15) were colonized with microbiota from either a patient with GAD and history of depression (n=7) or from an age and sex-matched healthy control (HC) (n=8). Both the GAD patient (female, 19 years) and healthy control (female, 20 years) were well characterized and selected based on their Depression, Anxiety, and Stress Scale (DASS) scores from a pool of participants of an ongoing clinical study. Three weeks post-colonization, the mice underwent behavioural assessment using standard psychometric tests. Stool β-defensin levels were measured by ELISA. Microbiota profiles were assessed by 16S rRNA based Illumina analysis. Lastly, BDNF expression in brain samples was measured by immunofluorescence and neural gene expression by Nanostring gene assay.

Results: GAD-colonized mice had a distinct microbiota profile from that of HC-colonized mice and each group clustered around their respective human donor. Fecal β-defensin levels were higher in the GAD patient than the HC (109.5ng/ml vs 18.01ng/ml). Similarly, mouse fecal β-defensin levels were significantly higher in GAD-colonized mice than in HC-colonized mice (M= 62.26 vs M= 29.10, p < 0.005). Mice colonized with GAD microbiota exhibited significantly greater anxiety and depressive-like behaviour than HC-colonized mice, as they spent less time in the center of the open field arena, buried a greater number of marbles, spent a greater time digging and remained more time immobile. GAD-colonized mice had increased BDNF expression in the amygdala but decreased expression in the hippocampus. GAD-colonized mice also exhibited differential expression of neural genes in both the amygdala and hippocampus.

Conclusions: Our results suggest that GAD microbiota can induce anxiety and depressive-like behaviour, accompanied by elevated immune markers. This is associated with altered neural gene and BDNF expression in brain regions involved in emotional processing. Altogether, our data suggest that gut microbiota may contribute to the pathophysiology of anxiety and depression, at least in a subset of patients with signs of gut immune activation. These findings may lead to the development of novel biomarkers and treatments for mood disorders.

A302
LUMINAL SHORT-CHAIN FATTY ACIDS RESTORE MOTILITY IN GERM-FREE MICE
A.D. Vincent[2], X. Wang[1], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. Physiology and Pharmacology, McMaster University, Hamilton, ON, Canada

Background: The bidirectional relationship between colon motility and microbiota needs further study. Germ free (GF) mice are unable to ferment resistant starch into short-chain fatty acids (SCFA). Previous studies have shown that these mice have a significantly longer transit time than controls.

Aims: We investigated motility patterns in isolated GF mouse colons in an attempt to elucidate the role microbiota-derived metabolites play in governing motility.

Methods: The mouse colon was luminally-perfused inside an organ bath. After equilibration of 30min, a phosphate buffer (PBS) was perfused into the lumen, followed by a cocktail of SCFA (1mM butyrate & propionate, 5mM acetate) dissolved in PBS. Motility was video recorded and spatiotemporal maps were produced by plotting diameter changes along the colon over time. The outflow from the colon was connected to a pressure transducer that recorded the volume of outflow produced by each contraction. ICC were identified by immunohistochemistry using cKit antibodies.

Results: GF mice had abnormal motility patterns. GF baseline conditions were either dominated by slowly propagating contractions that did not produce outflow (Figure1B) and long distance contractions (LDCs) that were interrupted by relaxation in the mid colon. The 20 cpm ICC slow wave driven background contractions appeared normal. The GF baseline condition had a significantly higher number of contractions than the control baseline condition (P<0.001). Under the same conditions, control activity was dominated by normal propulsive LDCs. The average volume of output per contraction was significantly higher in the control baseline than the GF baseline condition (P<0.05). After adding SCFA, motor patterns from the GF mouse closely resembled that of the control, characterised by rhythmic LDCs that were not interrupted (Figure1B). The percentage of contractions that were LDCs increased significantly following SCFA administration to the GF colon (P<0.001). c-Kit staining of the ICC networks in both strains of mice showed no difference in the structural integrity of these networks.

Conclusions: The results indicate that in the absence of SCFA, the GF colon had normal myogenic ICC directed motility but the stimulus dependent motor activity was abnormal. Our hypothesis is that distention-induced motor patterns do not develop in a typical manner when the inner mucus layer does not contain microbiota-derived metabolites, in particular SCFA. Administering SCFA provided the correct mucosal stimulation envi-

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

ronment required to generate normal rhythmic propulsive contractions. We hypothesize that SCFA indirectly activate 5-HT release from enterochromaffin cells thereby lowering the threshold for distention-induced LDCs. The reduced transit time observed in GF mice is due to reduced ability to generate distension-induced propulsive LDCs although the neural machinery to produce LDCs is fully present.
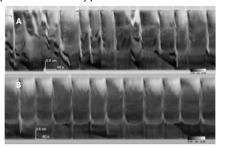
Figure1: Spatiotemporal maps of the germ free mouse colon. Above, Image A shows the germ free baseline condition and below, Image B shows the same mouse with intraluminal perfusion of SCFA. Both images are 20 minutes in length.

Funding Agencies: CIHR

A303
SIMULTANEOUS PRESSURE WAVES ARE A KEY COMPONENT OF HUMAN COLON MOTOR FUNCTION ASSESSMENT, USING HIGH-RESOLUTION COLONIC MANOMETRY (HRCM)
J. Chen[1], E. Ratcliffe[2], D. Armstrong[1], P. Bercik[1], J.D. Huizinga[1]

1. McMaster University, Hamilton, ON, Canada; 2. McMaster Children's Hospital, Hamilton, ON, Canada

Background: Colonic dysmotility is common, yet its nature is not fully understood through low-resolution manometry. High-Resolution Colonic Manometry (HRCM) is capable of revealing detailed motor patterns and their functions can be tested in the clinical setting.
Aims: Our objective was to identify clinically relevant propulsive motor patterns in healthy volunteers and to improve interpretation of motor pattern functions through an *in vitro* study of equivalent patterns in the proximal rabbit colon.
Methods: Healthy adult volunteers (n=13) received 84-sensor HRCM with different stimuli: balloon distention in proximal and transverse colon, a meal, and bisacodyl in the proximal colon and rectum. In rabbits (n=7) pressure patterns (by HRCM) and motor patterns (by video-recorded diameter changes expressed as spatio-temporal maps) were recorded simultaneously, in vitro, to characterize propulsive pressure patterns.
Results: In adult volunteers, High Amplitude Propagating Pressure Waves (HAPCs) were only observed after stimulation (balloon distention or bisacodyl administration). In contrast, Simultaneous Pressure Waves (SPWs) were observed at baseline. SPWs ranged in amplitude from 5 mmHg to >100 mmHg. SPWs were associated with gas and/or content expulsion and internal sphincter relaxation, consistent with a propulsive and neurogenic nature. Gas expulsion never occurred without SPWs. SPWs spanned between 80% and 100% of the colon. Proximal HAPCs sometimes developed into SPWs. SPWs increased in response to a meal and became prominent in amplitude during balloon distention and after bisacodyl administration. In response to bisacodyl, higher amplitude SPWs were associated with an urge to defecate. SPWs were found to occur in isolation or forming a rhythmic pattern with a dominant frequency of ~ 1 wave/min. When forming a rhythmic pattern, SPWs could inhibit non-propulsive motor patterns suggesting that the absence of a motor pattern can be due to competition from propulsive activity. Studies in the rabbit model identified SPWs similar to those found in humans, with SPWs caused by fast propagating contractions with velocities greater than 5 cm/s and associated with expulsion of colonic contents.
Conclusions: The literature suggests that SPWs are artifacts or inhibit transit. Here we report that SPWs are the most common propulsive motor activity of the human colon, associated with internal anal sphincter relaxation and gas or content expulsion. SPWs should be considered, together with HAPCs, as an important propulsive motility pattern to characterize when evaluating motor patterns in patients with colonic dysmotility.

Funding Agencies: CIHRHamilton Academic Health Sciences Organization (Ratcliffe)

A304
FOOD ANTIGEN-STRESS INTERACTION INCREASES PERIPHERAL PAIN SIGNALING IN A MOUSE MODEL OF IBS
C.D. Lopez Lopez, J.O. Jaramillo Polanco, S. Vanner, D.E. Reed

Gastrointestinal Diseases Research Unit, Queen's University, Kingston, ON, Canada

Background: Food and stress are common triggers of symptoms in irritable bowel syndrome (IBS). However, it is unknown whether a specific food antigen alone can induce symptoms such as abdominal pain or if a second trigger, such as stress, is required for a food antigen to increase pain signaling.
Aims: To determine if a food antigen (ovalbumin) can induce hyperexcitabiity in nociceptive neurons alone and/or in combination with stress.
Methods: Mice were exposed to water avoidance stress (WAS; 1 hr for 6 days). On day 2, mice were gavaged ovalbumin (20mg) daily after completing WAS (WAS/OVA). These were compared to 3 groups: no WAS and

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no ovalbumin (control); WAS but no ovalbumin (WAS); and ovalbumin (OVA) alone. On day 8, WAS, OVA and WAS/OVA mice were given ovalbumin (50 µg) subcutaneously; 3 hours later euthanized. Colons were removed and incubated with ovalbumin (100 µg/ml) for 4 hrs. Supernatants were collected and DRG neurons from control mice were incubated overnight with supernatants from each of the four groups. Changes in neuronal excitability were examined by measuring the rheobase (minimal current to evoke an action potential) using perforated patch clamp recording techniques. Stress effects on intestinal permeability in the ileum and colon were assessed in Ussing chambers. One way ANOVA and Bonferroni post hoc test or unpaired t test were used to analyze the data.

Results: Incubation with supernatants obtained from WAS/OVA mice evoked hyperexcitability in DRG neurons compared to incubation with control supernatant (rheobase: control = 82±10 pA vs WAS/OVA = 56±4 pA, p < 0.05). Similarly, WAS/OVA supernatant decreased the rheobase compared to both OVA mice (OVA = 80±8 pA, p<0.05) and WAS mice (WAS = 81±9 pA, p<0.05). The effect of supernatants from OVA mice and WAS mice did not differ from controls. In a separate series of experiments, the PAR2 antagonist GB83 inhibited the effect of WAS/OVA supernatant (p < 0.01). There was no effect of GB83 on WAS or OVA supernatants. Stress decreased tissue resistance in ileum (p<0.05) but not in colon.

Conclusions: The food antigen ovalbumin induced hyperexcitability in DRG nociceptive neurons only when combined with stress. This action was PAR2 dependent suggesting a role of tissue proteases. Stress may cause a loss of oral tolerance to ovalbumin by increasing mucosal permeability in the small intestine. The interaction of food antigens and stress may be a mechanism of meal induced increase in abdominal pain in IBS.

A305
THE PRONOCICEPTIVE EFFECT OF HIGH DOSE OPIOIDS ON MOUSE DRG NEURONS IS MEDIATED BY DELTA OPIOID RECEPTORS
J.O. Jaramillo Polanco, C.D. Lopez Lopez, Y. Zhang, D.E. Reed, A.E. Lomax, S. Vanner

Gastrointestinal Diseases Research Unit, Queen's University, Kingston, ON, Canada

Background: Opioid drugs can be efficacious in the treatment of abdominal pain, but escalating doses of these drugs can also induce pronociceptive signalling in patients and paradoxically worsen pain. The analgesic actions of opioid drugs on dorsal root ganglia (DRG) neurons innervating the intestine are largely mediated by mu opioid receptors (MOR) but there is growing evidence that delta opioid receptors (DOR) could be important targets for pain signaling and to

prevent opioid tolerance. However, it is unknown whether MOR and DOR are co-expressed on colonic DRG neurons and whether DOR play a role in pain signaling in the gut.

Aims: The present study examined whether exposure to low and high concentrations of the opioid receptor agonist DAMGO had differing effects on the excitability of nociceptive DRG neurons, and if so, whether these actions involved MOR and/or DOR signaling.

Methods: Single unit afferent recordings were obtained in situ from mouse colons to determine the effects of the MOR agonist DAMGO (100nM) and the DOR agonist DADLE (100nM) on mechanosensitive responses. To examine the effects of high and low dose opioids, nociceptive mouse DRG neurons were dissociated from control mice and incubated overnight with 10 nM or 10 µM DAMGO or media alone. Changes in neuronal excitability were recorded by measuring the rheobase using patch clamp recordings. To determine whether changes in cell excitability were mediated by MOR or DOR, neurons were incubated with the MOR antagonist CTOP (100 nM) or DOR antagonist SDM25N (1 µM) 30 min prior to the incubation with DAMGO.

Results: Single unit recordings from mouse colon were inhibited by both MOR and DOR agonists in 38% of afferents (3/8). Overnight incubation with 10 nM DAMGO inhibited neurons (rheobase increased by 43%, p <0.001) whereas 10 µM DAMGO had an excitatory effect (rheobase decreased by 31%, p <0.01). The inhibitory effect of low dose DAMGO was blocked by the MOR antagonist but the DOR antagonist had no effect. In contrast, the excitatory effect of the high dose DAMGO was completely blocked by the DOR antagonist.

Conclusions: Many colonic DRG neurons co-express MOR and DOR. High concentrations of opioids paradoxically increase excitability of nociceptive DRG neurons, potentially by signaling to MOR-DOR heterodimers. This could lead to increased pain signaling and targeting DOR may be a potential target to mitigate this action.

A306
***LACTOBACILLUS RHAMNOSUS* JB-1 AMELIORATES COLONIC AGE-RELATED DYSMOTILITY**
C. West, Y.K. Mao, A. Stanisz, J. Bienenstock, W.A. Kunze
McMaster University Brain-Body Institute, Hamilton, ON, Canada

Background: Aging induces a range of physiological effects on the body, which includes gastrointestinal function and its microbiota. Studies of aged individuals and animals frequently reveal decreased transit and motility, which may contribute to the increased incidence of constipation in old age.

Aims: The purpose of this study was to test whether the neuroactive microbe *Lactobacillus rhamnosus* (JB-1™)

might reverse age-related hypomotility when added to the colon lumen. Our previous research with JB-1 has shown therapeutic effects in the treatment of stress-related dysmotility in adult mice (West et al. 2016), and we hypothesized that JB-1 might also have beneficial effects on motility in the aged colon.
Methods: Ex-vivo colonic motility experiments were performed in an organ bath perfusion chamber using 4-cm colon segments from 18-month old CD1 male mice. The colon was cannulated at both the oral and anal ends and perfused luminally with a 34°C oxygenated Krebs buffer control, followed by intraluminal addition of 10E8 cfu/mL JB-1 in Krebs buffer applied for 30 min followed by Krebs only washout. Video recordings were converted to spatiotemporal maps (Dmaps), for which propagating contractile cluster (PCC) velocity, frequency, and amplitudes were measured and analyzed using paired t-tests for control and treatment groups.
Results: Previous research in our lab showed that for 1-year old mice PPC velocity, frequency, and amplitude were reduced by 47%, 54%, and 46% respectively in comparison to 2-month old mice (Kunze et al. 2014). JB-1 treatment of old-age mice increased PCC colonic velocity by 69% (N = 12, P = 0.002). PCC colonic frequency was increased by 22% (N= 12, P = 0.244) all within 15 min of application. PCC amplitude was increased by 16% (N= 12, P = 0.493) from controls.
Conclusions: The results suggest that luminal *Lactobacillus rhamnosus* JB-1 application may help to reverse colon hypomotility dysfunction in old mice. Oral administration of JB-1 bacteria may have translational potential to improve constipation or hypomotility in old age.

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A307
EFFECT OF SLOW SYNAPTIC EXCITATION ON MY-ENTERIC INTRINSIC PRIMARY AFFERENT NEURON BKCA CHANNEL ACTIVITY
C. Brown[1], K. Neufelk[3], Y.K. Mao[3], J. Bienenstock[1], W.A. Kunze[2]

1. McMaster University, Hamilton, ON, Canada; 2. Psychiatry, McMaster University, Hamilton, ON, Canada; 3. Brain-Body Institute , Hamilton, ON, Canada

Background: The large conductance calcium dependent potassium (BK$_{Ca}$) channels are expressed in a large variety of cell types including neurons where they modulate excitability and action potential shape. Within the enteric nervous system, stretch-sensitive BK$_{Ca}$ channels are expressed on intrinsic primary afferent neurons (IPANs) where they decrease the neurons' excitability during intestinal contractions[1]. A major determinant of peristalsis is slow excitatory neurotransmission (sEPSPs) within the IPAN to IPAN sensory network, and we wondered whether such transmission might also alter BK$_{Ca}$ channel opening.
Aims: To determine if slow synaptic excitatory input alters BKCa channel activity.
Methods: All experiments were performed on longitudinal-muscle myenteric preparations prepared from jejunal segment taken from freshly euthanized adult male Swiss Webster mice. Segments were placed into a 95% carbogen bubbled Krebs solution containing 2 μM nicardipine and 1 μM scopolamine, and the myenteric plexus exposed by microdissection. BK$_{Ca}$ channel activity was recorded *in situ* patch clamping in cell-attached mode. BK$_{Ca}$ channel activity was recorded at trans-patch potentials that were varied by 20 mV steps to determine voltage-sensitivity. Such recordings were performed before during and after presynaptic electrical stimulation designed to evoke postsynaptic sEPSPs. After recording the morphotype was verified by intracellular injection of a marker dye (neurobiotin).
Results: Analysis of unitary channel recordings revealed increased BK$_{Ca}$ open probability (NPo) at fixed trans-patch potentials following sEPSPs. An increased NPo which lasted 30 s to 1 min was also observed. All BK$_{Ca}$channels were independently voltage sensitive with increased NPo during patch depolarisation.
Conclusions: This study demonstrates that sEPSPs within the enteric nervous system modulate the function of BK$_{Ca}$ channels in IPANs adding to the mechanistic understanding of enteric synaptic transmission and providing a potential target for therapeutic modulation of enteric nervous system excitability.

A308
A PRACTICE AUDIT ON THE EFFECTIVENESS OF BIO-FEEDBACK THERAPY IN A TERTIARY CARE CENTRE
C.H. Parker[2], L.W. Liu[1]

1. Medicine, University Health Network, Toronto, ON, Canada; 2. Medicine, University of Toronto, Toronto, ON, Canada

Background: Chronic constipation (CC) and fecal incontinence (FI) are common disorders that can often be related to pelvic floor neuromuscular sensory

and motor dysfunction. These disorders have been shown to impair patients' quality of life. Conventional therapies for both conditions include dietary changes, behavioural modification and pharmacologic therapies. However, these are frequently insufficient to achieve satisfactory outcomes in a subset of patients. Biofeedback therapy (BFT) involves training patients to improve the ano-rectal sensory, motor and coordination via verbal and visual feedback. BFT has been shown to be an effective treatment strategy in those patients who have failed conventional therapy with response rates often exceeding 50% of participants.

Aims: To review the effectiveness of BFT as performed at a tertiary centre in Canada. A secondary aim was to determine the subset of patients who benefit most from BFT in our cohort.

Methods: A retrospective chart review was performed on all patients who underwent BFT at our institution between January 1, 2008 and August 15, 2016. Demographic information, reason for referral, baseline and post-biofeedback ano-rectal manometry (ARM) data, and patient subjective report of changes in symptoms were collected. A positive response to BFT was defined as an improvement in the patient's ARM profile (i.e. improvement in sphincter function, normalization of the balloon expulsion time, etc) and/or patient reported improvement of pre-BFT symptoms. Patients who completed a course of BFT were included. Descriptive statistics were used to analyze the data.

Results: 130 patients had a complete data set for the analysis. The average age of the patients was 56.1±16.3 yr and 76.8% were female. The average number of completed biofeedback session was 2.9. 43.1% of patients were referred for CC, 37.7% for FI, 16.9% for both CC and FI, and 2.3% for rectal pain. 76.2% of the patients had a positive response to BFT. Amongst those, 27.3% had an improvement in their ARM profile alone, 7.1% reported symptomatic improvement alone, 65.6% demonstrated both manometric and symptomatic improvement. Patients, who responded to both symptom and ARM profile, were more likely to present with FI (65.3%) or both CC and FI (54.5%), as compared to those presenting with CC alone (37.5%). Examining the CC group (n=56), those with dyssynergic defecation (DD, n=53) were more likely to have ARM profile and symptom response than those without (39.6% vs. 0%).

Conclusions: This practice audit illustrates that our BFT program achieves a similar overall response rate as compared with previously published reports. Our cohort demonstrates that patients presented with both FI and CC, FI, or CC with DD are more likely to respond. This data will be used to further examine our BFT program and to develop quality improvement initiatives within the program to improve patient outcomes.

A309
ANTIBIOTIC DRIVEN CHANGES IN GUT MOTILITY

HIGHLIGHT DIRECT MODULATION OF ENTERIC NERVOUS SYSTEM

T.N. Delungahawatta, J.Y. Amin, A. Stanisz, J. Bienenstock, P. Forsythe, W.A. Kunze

McMaster University Brain-Body Institute, Hamilton, ON, Canada

Background: The microbiome-gut-brain axis is a bidirectional network that influences brain chemistry and behaviour. Antibiotics are known to alter several aspects of gut-brain signaling but the underlying mechanisms remain equivocal. As prior assessments of these mechanisms have been limited to changes in gut microbiota, we hypothesized that antibiotics may directly modulate neurons and neural reflexes.

Aims: To identify whether transient exposure of the gastrointestinal tract to antibiotics can acutely modulate peristaltic reflexes that depend on the enteric nervous system (ENS).

Methods: 4 cm colon segments excised from adult male Swiss Webster mice were submerged in an organ bath chamber (34°C oxygenated Krebs buffer solution) and cannulated at both the oral and anal ends. Gut lumens were perfused with Krebs saline control followed by either Krebs diluted Bacitracin (1, 3 or 10 mM) or Penicillin V (3, 10, 30 or 100 mM). Gut motility was recorded by video which was subsequently converted to spatiotemporal diameter maps for quantitative analysis. Paired t-tests were performed for before and after measurements.

Results: Alterations in ENS-dependent propagating contractile cluster (PCC) velocity and frequency were evoked by Bacitracin at concentrations of 1, 3 and 10 mM and Penicillin V above 10 mM. For Bacitracin, PCC velocity (mm/s) increased from 0.23±0.06 to 0.35±0.13 (n=20, P<0.001) at 1 mM, from 0.28±0.11 to 0.33±0.13 (n=20, P= 0.034) at 3 mM and increased from 0.26±0.11 to 0.28±0.11 (n=20, P=0.8) at 10 mM. Similarly, PCC frequency (Hz) increased from 0.009±0.002 to 0.011±0.003 (n=20, P=0.037) at 1 mM, from 0.012±0.003 to 0.013±0.003 (n=20, P=0.05) at 3 mM and remained at 0.01±0.004 Hz (n=20, P=0.9) at 10 mM. Similar results were produced in experiments using >10 mM Penicillin V. PCC velocity (mm/s) increased from 0.21±0.05 to 0.22±0.04 (n=20, P=0.15) at 10 mM, 0.17±0.04 to 0.54±0.2 (n=16, P<0.001) at 30 mM and from 0.17±0.04 to 0.65±0.2 (n=16, P<0.001) at 100 mM. PCC frequency (Hz) increased from 0.01±0.001 to 0.012±0.002 (n=20, P=0.013) at 10 mM, from 0.01±0.002 to 0.04±0.03 (n=16, P=0.008) at 30 mM and from 0.01±0.002 to 0.05±0.03 (n=16, P=0.001) at 100 mM.

Conclusions: These experiments suggest that luminal antibiotics acutely alter ENS dependent reflexes. Therefore, studies attributing the effects of antibiotics solely to disruption of the gut microbiota should be interpreted with caution.

A310
THE INHIBITION OF PTP1B REVERSES IMPAIRED VAGAL AFFERENT SENSITIVITY CAUSED BY DIET-INDUCED OBESITY, REDUCING NITRIC OXIDE AND 2 PORE DOMAIN K⁺ CONDUCTANCE

S. Park, M.J. Beyak

Queen's University, Kingston, ON, Canada

Background: We have demonstrated that diet-induced obesity impairs vagal afferents and that the effects of high concentrations of leptin on vagal afferents in vitro, mimic the effects of obesity. One of downstream molecules in leptin signaling is protein tyrosine phosphatase 1B (PTP1B), which plays a role in negative regulation.
Aims: We hypothesized that inhibition of PTP1B would prevent an impairment of vagal afferents caused by diet-induced obesity/hyperleptinemia
Methods: Diet-induced obese (DIO) mice were fed diets composed of 60% or 10% kCal fat for 12-16 weeks. Nodose neurons from DIO mice or standard diet fed mice were incubated overnight with leptin (100nM) and PTP1B inhibitor (10mM). Current and voltage clamp were performed to assess membrane excitability and two-pore domain K⁺ (K2P) conductance, respectively. NO was measured in culture media using Nitrate/Nitrite fluorometric Assay kit. Media was collected after cell incubation for 24 hrs.
Results: Leptin (100nM) incubation reduced the excitability of vagal afferents. PTP1B inhibitor reversed this inhibitory effect of leptin. PTP1B inhibitor significantly decreased rheobase (100.8 ± 18.6 pA, n=12, leptin) vs. 64.7 ± 5.2 pA (n=15, Leptin + PTP1B inhibitor), ∗p=0.0497) and significantly increased input resistance (353.8 ± 36.2 MΩ (n=12, leptin) vs. 508.2 ± 52.7 MΩ (n=15, Leptin + PTP1B inhibitor), ∗p=0.0305). Leptin significantly increased K2P conductance (0.280 ± 0.022 nS (n=17, control) vs. 0.377 ± 0.035 nS (n=16, leptin), ∗p=0.0108). Inhibition of PTP1B significantly decreased the conductance (0.249 ± 0.013 pA (n=14, Leptin + PTP1B inhibitor), ∗∗p=0.0028) in leptin-incubated neuron. In mice fed a HFF diet, there is reduction in vagal excitability, which was reversed by the inhibition of PTP1B. PTP1B inhibitor significantly decreased rheobase (112.1 ± 14.6 pA (n=14, leptin) vs. 70.8 ± 8.1 pA (n=12, HFF + PTP1B inhibitor), ∗p=0.0268). Rheobase was not significantly different in LFF. Inhibition of PTP1B significantly decreased K2P conductance both in LFF and HFF neurons (LFF; ∗∗p=0.0050; HFF; ∗∗p=0.0041). PTP1B inhibitor significantly reduced NO fluorescence in leptin-incubated media (33.1 ± 2.2 (Leptin) vs. 12.2 ± 1.0 (Leptin+PTP1B inhibitor), ∗∗∗<0.0001, n=6) and in neurons from HFF mice (43.4 ± 0.7 (HFF) vs. 29.9 ± 0.6 (HFF+PTP1B inhibitor), ∗∗∗<0.0001 n=6), but not in LFF (27.8 ± 1.3 (LFF) vs. 25.8 ± 0.8 (LFF+PTP1B inhibitor), NS n=6).
Conclusions: Iinhibition of PTP1B reverses the effects

of HFF and elevated leptin on NO production and K2P conductance in nodose ganglion neurons. Consistent with this, the inhibitory effects of leptin and diet-induced obesity on the excitability of vagal afferent neuron were also reversed by PTP1B blockade. We suggest PTP1B may be a pivotal regulator and potential drug target in obesity.

A311
INTERACTION BETWEEN SOCS3 AND NITRIC OXIDE SIGNALLING IN THE EFFECTS OF DIET-INDUCED OBESITY AND LEPTIN ON VAGAL AFFERENT EXCITABILITY

S. Park, M.J. Beyak

Queen's University, Kingston, ON, Canada

Background: We have recently shown that suppressor of cytokine signaling-3 (SOCS3), a negative regulator in leptin signalling, plays a role in vagal hyposensitivity associated with diet-induced obesity and high concentrations of leptin. Diet-induced obesity also enhances nitric oxide (NO) production, which also has a negative effect on vagal afferent sensitivity.
Aims: The present study aimed to examine the potential interaction between SOCS3 and NO signalling pathways in diet-induced obesity and in vitro effect of leptin.
Methods: C57Bl6J mice were rendered obese by feeding a diet of 60% calories from fat (HFF) for 12-16 weeks; mice fed 10% calories from fat (LFF) were used as controls. To mimic the hyperleptinemia that is seen in obesity, in vitro , nodose neurons from standard diet fed mice were incubated overnight with leptin (100nM). Zoledronic acid (ZA) used as an inhibitor of SOCS3. Current clamp recordings were performed 18-24 h post-dissociation. NO was measured in culture media using a Nitrate/Nitrite fluorometric Assay kit. Media was collected after cell incubation for 24 hrs.
Results: ZA prevented the inhibitory effect of high concentration of leptin and diet-induced obesity on vagal afferent excitability. ZA (10 mM) significantly decreased rheobase in leptin incubated neuron (86.4 ± 8.2 pA (n=14, Leptin) vs. 57.1 ± 5.5 pA (n=17, ZA+Leptin, ∗∗p=0.0045)). ZA significantly decreased rheobase in neurons from HFF mice (111.9 ± 9.1 pA (n=16, HFF) vs. 45.3 ± 4.7 pA (n=15, HFF + ZA) ∗∗∗p<0.0001), but not in LFF mice (66.9 ± 5.1 pA (n=16, LFF) vs. 59.3 ± 7.6 pA (n=15, LFF + ZA) NS). The NOS inhibitor L-NNA (0.1 mM, 30 min) significantly decreased rheobase in leptin-incubated neurons (99.3 ± 14.9 pA (n=15, leptin) vs. 42.1 ± 3.7 pA (n=14, leptin + L-NNA) ∗∗p=0.0013). L-NNA (0.1 mM, 30 min incubation) also significantly decreased rheobase in HFF neurons (112.1 ± 14.6 pA (n=14, HFF) vs. 57.8 ± 10.9 pA (n=9, HFF + L-NNA) ∗∗p=0.041), not in LFF. The effect of ZA on endogenous NO production was tested. ZA significantly reduced NO fluorescence in HFF (43.4 ± 0.7 (HFF) vs. 31.8 ± 2.1 (HFF+ZA), ∗∗∗0.0003 n=6), but not in LFF (27.8 ± 1.3 (LFF) vs. 31.4 ± 1.9 (LFF+ZA), NS n=6). Leptin signifi-

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cantly increased NO fluorescence (23.6 ± 1.0 (control) vs. 33.1 ± 2.1 (Leptin), **0.0027, n=6). ZA reduced NO fluorescence in leptin-incubated media (27.5 ± 2.5 (Leptin+ZA), n=6).

Conclusions: Inhibition of SOCS3 reversed the inhibitory effects of obesity and high leptin concentrations and reduced NO levels. We suggest there is a link between SOCS3 and NO signaling in vagal afferents. SOCS3/NO pathway may be an important therapeutic target in obesity/hyperleptinemia.

A312
INVOLVEMENT OF INOS-DERIVED NO IN THE IMPAIRMENT OF MOUSE VAGAL AFFERENT SENSITIVITY IN DIET-INDUCED OBESITY
S. Park, M.J. Beyak

Queen's University, Kingston, ON, Canada

Background: Our previous studies have demonstrated impaired vagal afferent sensitivity to satiety mediators and distention of the gut in high fat fed (HFF) obese mouse iNOS (inducible nitric oxide synthase) knockout mice are protected against high fat diet-induced metabolic dysfunction. In addition, NO has an inhibitory effect on the sensitivity of a select population of vagal afferents.

Aims: The aim of this study was to examine the involvement of iNOS-derived NO in obesity-induced impairment of vagal nerve sensitivity.

Methods: All experiments were performed in accordance with the guideline of Canadian Council for Animal Care. Nodose ganglion and jejunum were obtained from high (60% calories from fat) and low (10%) fat fed male C57/BL6 mice. NO was measured using a Nitrate/Nitrite fluorometric assay kit. Membrane excitability of nodose neurons was assessed by whole cell patch clamp. Afferent discharge was recorded from jejunal mesenteric nerves.

Results: In comparison with low fat fed (LFF) mice, NO concentration in the jejunum from high fat fed (HFF) mice was significantly increased (P<0.05, N≥7, unpaired t-test) and pre-treatment with L-NIL (10 mg/kg, IP injection) reversed this change (P<0.001, N≥7, unpaired t-test). Excitability of nodose neurons was significantly increased by pre-incubation with L-NIL (10 mM), as evidenced by decreased rheobase (P<0.05, N≥10, unpaired t-test) and increased action potentials at twice rheobase (P<0.05, N≥10, unpaired t-test). In addition, IP injection of L-NIL in HFF mice significantly augmented afferent response to 5-HT (10 mM, P<0.001, N=10, unpaired t-test) and ramp distention (P<0.05, N≥12, two-way ANOVA), while cholecystokinin (CCK, 100 nM) response was partially increased (P=0.09, N≥8, unpaired t-test). In line with this observation, NO donor, sodium nitroprusside (10

mM) inhibited afferent response to 5-HT (P<0.05, N=7, paired t-test) and distention (P<0.001, N=13, two-way ANOVA) instead of CCK in LFF mice. Single unit analysis revealed that NO had diverse effects on the sensitivity of different afferent units.

Conclusions: These data suggest that iNOS may be a key molecule in obesity-induced impairment of vagal nerve sensitivity and thus a potential therapeutic target for obesity-related dysfunction.

A313
MUCOSAL PROTEASES FROM IBS PATIENTS PRODUCE LONG TERM HYPEREXCITABILITY IN NOCICEPTIVE DRG NEURONS BY ACTIVATING NOVEL INTRACELLULAR SIGNALING PATHWAYS
N.N. Jiménez-Vargas[3], D.E. Reed[2], N. Bunnett[1], S. Vanner[4]

1. Columbia University, New York City, NY; 2. GIDRU Wing, Kingston General Hospital, Kingston, ON, Canada; 3. Medicine, Quuen's University, Kingston, ON, Canada; 4. queen's , Kignston, ON, Canada

Background: BACKGROUND: Patients suffering from the irritable bowel syndrome report exaggerated and sustained abdominal pain. We have shown that activation of protease activated receptor 2 (PAR2) on nociceptive (pain sensing) dorsal root ganglia (DRG) neurons evoke long term hyperexcitability but the mechanisms of this sustained pain signaling are unclear. Recent studies show that trypsin activates canonical PAR2 signaling causing endocytosis and this leads to sustained PAR2-endosomal signaling. Proteases such as elastase and cathepsin S, however, act at non-canonical sites and do not cause receptor endocytosis. We have shown that protease activity is increased in IBS tissues but it is unclear whether this leads to sustained neuronal excitation.

Aims: AIMS: To examine whether proteases in tissues from IBS patients lead to sustained nociceptive signaling and, if so, what intracellular mechanisms are involved.

Methods: METHODS: DRG neurons (T9-T13) from C57BL/6 mice were pre-incubated (10 min) with Trypsin (50nM) or supernatants (30 min) from colonic biopsies obtained from diarrhea predominant IBS patients or controls then washed with F12 media. We measured neuronal excitability by perforated patch-clamp, recording changes in rheobase (minimum current to fire action potential) and action potential discharged at twice rheobase immediately after washing with F12 media (time 0) or ~ 30 min later (time 30). PAR2 (10 μM I-343) and ERK1/2 (50 μM PD8059) inhibitors were applied 30 min before IBS supernatant or trypsin. Two way ANOVA and post hoc Tuckey's tests were used to analyze the data.

Results: RESULTS: IBS supernatants increased DRG

neuronal excitability acutely (time 0) as well as sustained hyperexcitability (time 30) (Table 1). This was blocked by the PAR2 antagonist I-343. This sustained excitability was also blocked by antagonist of ERK1/2. Sustained excitability evoked by trypsin was also inhibited by the ERK1/2 antagonist.

Conclusions: CONCLUSIONS: Proteases in IBS tissues, acting through PAR2, evoke long term hyperexcitability of nociceptive signaling in DRG neurons that is ERK1/2 dependent. In addition, the sustained excitability evoked by the serine protease trypsin, which we previously have shown is mediated by PAR2-endosomal signaling, was also ERK1/2 dependent. Thus, serine proteases in IBS tissues may be signaling through similar pathways and these could provide a novel therapeutic target to treat pain in patients with IBS.

	Control Supernatant	IBS-D Supernatant	IBS-D Supernatant + I-343	IBS-D Supernatant + PD8059	Control	Trypsin	Trypsin + I-343	Trypsin + PD8059
Rheobase (pA) T=0				-	83	59**	80↑	59*
Rheobase (pA) T=30	79	54*	78↑	83↑	83	60.6*	80↑	87↑

NUTRITION, OBESITY AND AGING

A314
INTESTINAL EPITHELIAL SPECIFIC DELETION OF HNF4α PREVENTS OBESITY IN HIGH-FAT DIET FED MICE WITHOUT AFFECTING INTESTINAL UPTAKE OF FATTY ACIDS

R. Girard[1], M. Darsigny[1], C. Jones[1], F. Maloum[1], S. St-Jean[1], J. Coulombe[2], N. Perreault[1], M. Plourde[2], F. Boudreau[1]

1. Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada; 2. Medicine/Geriatric Division, Université de Sherbrooke, Sherbrooke, QC, Canada

Background: HNF4α, also referred as maturity onset diabetes of the young (MODY-1), is a transcription factor that regulates differentiation, inflammation and metabolism. HNF4α regulatory function of carbohydrate-lipid metabolism has been mostly studied in relation to liver and pancreatic functions. Since the gut can actively participate in regulating metabolism, we have investigated HNF4α potential regulatory role in this context.

Aims: To evaluate the effect of intestinal epithelial conditional deletion of HNF4α on lipid metabolism.

Methods: Control and HNF4α mutant mice were fed with a high-fat diet (HFD) composed of 21.3% protein, 23.6% fat and 41.2% carbohydrate. Physiological parameters were measured using metabolic cages. Fatty acids (fecal, tissular and plasmatic) were assayed by gas chromatographic analysis. Circulating hormones were assessed by ELISA. The intestinal transcriptome was analyzed by qPCR and Affymetrix microarrays.

Results: HNF4α mutant mice maintained on HFD were resistant to weight gain as opposed to control mice.

This observation was correlated with a significant reduction of visceral adiposity and hepatic lipid storage in mutant mice when compared to controls. Food consumption was not significantly altered among both groups. To investigate whether this phenotype was dependent on altered intestinal epithelial lipid absorption, we assessed lipid transport by measuring residual fecal as well as circulating fatty acids. HNF4α mutant mice exposed to HFD displayed similar levels of fatty acids both in the feces and in circulation when compared to controls. To explore how intestinal epithelial cells could interfere on the resistance to obesity phenotype, transcriptome profiles were compared between mutant and control mice. No specific expression change was observed among gene transcripts linked to lipid transport and metabolism. However, the gastric inhibitory peptide (GIP) gene transcript was found to be significantly reduced in mutant mice. ELISA confirmed a drastic 90% reduction of GIP circulating levels in mutant mice.

Conclusions: Conditional deletion of HNF4α from the intestinal epithelium led to a resistance to HFD-induced obesity. This phenomenon was not dependent on gut lipid malabsorption. Since GIP expression is functionally linked to adipose tissue and control obesity state, investigation are currently undergoing to explore a relationship between intestinal epithelial HNF4α regulatory action on GIP hormone expression and obesity outcome.

A315
FREQUENCY AND PREDICTORS OF FASTING ORDERS IN INPATIENTS WITH ULCERATIVE COLITIS: THE AUDIT OF DIET ORDERS - ULCERATIVE COLITIS (ADORE-UC) STUDY

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

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

Background: Current clinical practice guidelines suggest that ulcerative colitis (UC) patients admitted due to a disease flare should be offered a normal diet or enteral nutrition unless such a diet is not tolerated. Despite this recommendation, concerns about iatrogenic malnutrition from unjustified NPO or clear liquid diet (CLD) orders exist.

Aims: We aim to describe the frequency and audit the appropriateness of NPO and CLD orders among hospitalized UC patients and identify predictors of unjustified fasting.

Methods: We conducted a retrospective cohort study of all UC patients who were admitted to the gastroenterology (GI) service or the general internal medicine (GIM) service at an academic hospital between January 2009 and December 2014. The frequency and duration

of bowel rest orders and the number of meals missed because of these orders were assessed. Bowel rest orders were considered justified if the patient had intractable nausea or vomiting, pancreatitis, bowel obstruction, toxic megacolon or were awaiting endoscopy, or if alternative enteral or parenteral nutrition was provided. Patients with unjustified fasting orders were identified and the number of missed meal opportunities was measured. A logistic regression model was used to assess predictors of unjustified fasting in admitted UC patients.

Results: A total of 187 admissions in 158 UC patients were identified during the study period and included in the final analysis. The majority of the admissions were under the GI service (148/187, 79.1%). The mean age at admission was 35.0 years (standard deviation [SD] = 15) and 83/158 (52.5%) were female. The median length of stay was 8 days (interquartile range [IQR] = 4 − 12). Registered dietician consultation was obtained in only 32 admissions (17.1%), and admission weight was recorded in only 68 (36.4%) admissions. A total of 252 NPO or CF dietary orders were encountered in 142 admissions (75.9%). Of those, 112 orders were unjustified (44%). On average, patients with unjustified NPO or CF orders spent 3 days on an NPO or CF diet, which corresponded to a mean of 10 missed meals. Significant predictors of unjustified NPO or CF dietary orders were: NPO or CF diet ordered on admission [odds ratio, OR = 12.9, 95% confidence interval, 4.78−34.9]; admission to non-GI service [11.7, 95% CI 2.63−52.2], and lack of inpatient prednisone or biologics [3.4, 95% CI 1.4−11.6].

Conclusions: There is a high burden of prolonged bowel rest among hospitalized UC patients. Further studies are needed to assess the nutritional impact of prolonged bowel rest on UC patients. Our findings also suggest that targeted interventions are needed to decrease the frequency of inappropriate bowel rest among hospitalized UC patients.

A316
ANTIMICROBIAL LOCKS FOR THE PREVENTION OF CATHETER-RELATED BLOOD STREAM INFECTIONS (CRBSI) IN PATIENTS ON PARENTERAL NUTRITION (PN)− A SYSTEMATIC REVIEW

Y. Lu, C. Saroli Palumbo, M. Martel, A.N. Barkun

McGill University Health Center, Montreal, QC, Canada

Background: CRBSI are serious complications for patients on PN. Antimicrobial lock solutions have been used as a prophylaxis against CRBSI, however their efficacy in the PN population is unclear.
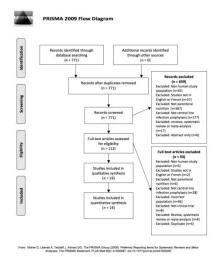
Aims: To conduct a systematic review on the efficacy of antimicrobial lock solutions to prevent CRBSI in patients on PN.

Methods: We performed a systematic search of EMBASE, MEDLINE, CENTRAL, ISI Web of Knowledge (from earliest date to December 2015) for randomized controlled trials (RCT) and observational studies evaluating the efficacy of antimicrobial locks compared to control solutions (heparin or saline) to prevent CRBSI in adult and pediatric PN patients. Two independent reviewers performed study selection and data extraction. Critical appraisal of possible bias was performed using the Cochrane Risk of bias tool (RCT) and ROBINS-I (observational studies).

Results: The literature search identified 771 citations, 112 were reviewed in full, and 19 studies were selected, totaling 536 patients, including 9 pediatric (122 patients) and 10 adult (414 patients) studies. Nine studies assessed an ethanol lock solution, 9 taurolidine, and 1 gentamycin. Two open-labeled RCT were included, both using taurolidine (Klek and Bisseling). The remaining studies were observational, and employed a pre- and post-design at moderate to high risk of bias. Methodological and clinical heterogeneity precluded pooling of the data by meta-analysis. All studies, except one by Klek who used taurolidine in low-risk patients, report lower CRBSI rate in the treatment group (ethanol, taurolidine ± citrate, and gentamycin lock) compared to controls (heparin or saline). The negative trial by Klek et al. documented 1 CRBSI (0.273/1000 catheter-days) in the taurolidine plus citrate arm, and none in the taurolidine or control arms (p=1.000). This finding is in contrast to Bisseling et al. who reported lower CRBSI rates (0.19 versus 2.02 CRBSI/1000 catheter-days, p=0.008), and longer mean infection-free survival in the taurolidine arm (641 (95% CI 556-727) vs 175 (95% CI 85-266) days, log-rank p<0.0001 in the control group (heparin)).

Amongst the observational studies, catheter infection rates ranged from 0 to 14.3 CRBSI/1000 catheter-days for antimicrobial locks vs 3.53 to 26.5 CRBSI/1000 catheter-days in the controls. The calculated CRBSI rate ratios of intervention vs control groups are all <1 (range 0-0.54), suggesting a protective effect attributable to antimicrobial lock solutions as prevention of CRBSI, most pronounced in taurolidine studies.

Conclusions: Pooled results would appear to support the use of antimicrobial lock solution as prophylaxis for CRBSI in PN patients, yet are limited by low study quality and modest sample sizes. High quality studies are needed to confirm these findings, and define optimal parameters for their use.

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

PRISMA 2009 Flow Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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A317
THE EFFECT OF OMEGA-3 PUFA ON THE DEVELOPING MICROBIOTA AND IMMUNITY OF INFANTS
C.S. Quin, D.M. Pasquale, J.A. Barnett, S. Ghosh, D.L. Gibson

University of British Columbia Okanagan, Kelowna, BC, Canada

Background: It is currently unknown how maternal supplementation with fish oils during gestation or lactation affects the microbiome-immune nexus in their infants. Our lab has previously shown that feeding in pregnant mice alters the gut microbiome, blocks inflammation, and increases mortality in the offspring during gut infection. In a recently published meta-analysis, we report that fish oil supplements in humans may adversely affect immune development in infants. Taken together, these evidences indicate that maternal exposure to fish oil supplements impairs gut immunity in growing infants. We then furthered these findings with a prospective clinical study.
Aims: The aim of this study is to determine how maternal exposure to fish oil supplements affect offspring's gut microbiome and immunity.
Methods: 109 pregnant or lactating women who either had or had not supplemented their diets with fish oil, rich in omega-3 polyunsaturated fatty acids (PUFA), were recruited. To participate in our trial, the infants of these women had to be healthy, full term infants born in the Okanagan valley. The women in the supplemented group were directed to consume fish oil supplements until their infants were 6 month of age, whereas the

women in the control group did not take any fish oil supplements during this time. We collected the meconium and stool from the infants at 1 week of age, and then again every month for 6 months. Concurrently, we collected breastmilk samples from the mothers for fatty acid analysis to ensure compliance with our instructions. To determine how maternal fish oil supplements altered the offspring's gut microbiome, we compared the fecal bacteria composition of the infants over time using Illumina MiSeq.
Results: We analyzed the breastmilk samples for lipid contents and immune markers and found that women supplementing with fish oil had significantly greater EPA, but not DHA, in their breastmilk. We also found that the supplementing women had less IgA in their breastmilk compared to their non-fish oil counterparts as well as a trend towards higher anti-inflammatory and less pro-inflammatory cytokines suggesting fish oil decreased immune responsiveness.
Conclusions: Our results suggest that maternal fish oil supplements change the composition of the mother's breastmilk, which in turn, alters their infant's microbiome. This has implications on the current recommendations for infant health.

A318
OUTCOMES OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY IN CHILDREN: A 15 YEAR REVIEW
J. Breton, J. Lemale, V. Marchand

Pediatric Gastroenterology, University of Montreal, Montreal, QC, Canada

Background: Percutaneous gastrostomy (PEG) has become a key element in managing children with nutrition or feeding issues. Reversal of malnutrition shortly after gastrostomy has been shown in many pediatric studies, however literature on maintenance of nutritional status following initial catch-up growth is limited.
Aims: To analyze the long-term follow-up of children with PEG in terms of nutritional outcomes as defined by improvement in weight-for-height z scores.
To review the procedure-related complication rates specific to our center.
Methods: This is a retrospective review of all PEG procedures performed at our tertiary Children's Hospital from 1999 to 2015. All PEGs were placed by the same team of pediatric gastroenterologists using the standard pull technique. Prophylactic antibiotics were given for 24h. Nutritional outcomes were evaluated by comparing the weight-for-height z scores (CDC growth charts) at the time of tube placement and either at the time of last follow-up for children receiving gastrostomy feeding, or at the time of tube removal, fundoplication or death. PEG-related complications were recorded.
Results: In the 256 patients who underwent successful PEG placement, diagnoses were as follow: neuromus-

cular disease (n=136, 53%), cystic fibrosis (n=30, 12%), metabolic disease (n=18, 7%), chromosomal abnormalities/genetic syndromes (n=18, 7%), nonorganic failure to thrive (n=39, 15%) and other (n=15, 6%). Median age at the time of PEG placement was 3.9 years (0.4-19.9 years) and median follow-up duration was 3.2 years (0-16 years). Significant improvement in weight-for-heigth z score was reported for all subgroups except for the "metabolic disease" and "other" subgroups: neuromuscular disease (Δ=0.62, P=0.0008), cystic fibrosis (Δ=0.8, P=0.004), metabolic disease Δ=0.37, P=0.4), chromosomal abnormalities/genetic syndromes (Δ=1.01, P=0.01), nonorganic failure to thrive (Δ=0.7, P=0.005). A total of 61 complications were reported: 35 cellulitis including 17 requiring intravenous antibiotics, 16 accidental dislodgements, 7 buried bumper syndromes, and 2 perforations. A total of 123 patients had known reflux prior to PEG placement, while 39 (32%) had resolution of symptoms, 84 (68%) had persistent reflux with 18 requiring fundoplicature.

Conclusions: Our study illustrates that improvement in nutritional status following PEG is maintained during the long term, reinforcing the benefits of gastrostomy feeding when enteral nutrition is required. PEG is a safe method to provide enteral feeding in children. Future studies defining preoperative clinical factors to help clinicians to predict which patient populations are at higher risk of poor nutritional rehabilitation, complications or need for anti-reflux surgery are needed.

A319
A NOVEL METHOD FOR PEG-J TUBE INSERTION USING SINGLE BALLOON ENTEROSCOPY AND THE WEDGE TECHNIQUE
H. Gregor[1], B. Yan[4], J.C. Gregor[2], M. Sey[3]

1. Gastroenterology, London Health Sciences Centre, London, ON, Canada; 2. Medicine, Los Alamos National Laboratory, London, ON, Canada; 3. Western University, London, ON, Canada; 4. Medicine, Gastroenterology, Western University, London, ON, Canada
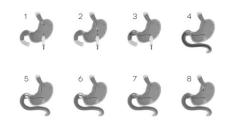
Background: Percutaneous endoscopic gastrostomy tubes with jejunal extensions (PEG-J) are used to deliver nutrition and medications directly into the proximal jejunum. Insertion can be difficult due to a tendency for the J-extension to fall back into the stomach during the procedure.
Aims: To describe a new technique using a single balloon enterscope to wedge the J-extension in place to prevent backwards migration during the procedure.
Methods: A case series over an 18 month period was performed using this novel technique. In brief, a J-extension was fed through a pre-existing PEG tube, grasped with a biopsy forcep, and brought into the proximal jejunum using the single balloon enteroscope with the overtube deflated in the duodenal bulb. Once the desired depth was reached, the overtube balloon

was inflated and the enteroscope withdrawn while holding the tip of the J-extension in place with the biopsy forcep. Next, the biopsy forcep was opened and pulled back into the enteroscope while the overtube balloon remained inflated to wedge the J-extension in place. Finally, the overtube balloon was deflated and withdrawn with the enteroscope. The primary outcome was successful insertion into the proximal jejunum confirmed on a post-procedure abdominal xray (AXR). Secondary outcomes included the number of pyloric intubations required to insert the J-extension and the duration of the J-extension portion of the procedure.
Results: 17 patients underwent PEG-J tube insertion during the study. The mean age (SD) was 61.8 (16.9) and 64.7% were females. 58.8% of procedures were performed with a combination of benzodiazpene and narcotic and 41.2% with propofol. The wedge technique successfully inserted the J-extension into the proximal jejunum confirmed on AXR in all patients. Only one pyloric intubation was required in 15 patients (88%) and 2 patients required a second intubation (12%). The mean (SD) time for the J-extension insertion was 16.9 minutes (8.6). There were no adverse events related to the J-extension insertion.
Conclusions: The wedge technique is a quick and effective method for inserting a J-extension and prevents proximal migration back into the stomach during the procedure.

A320
A CURIOUS CASE OF FOUL SMELLING FLATUS
C. Lim, T.L. Krishnamoorthy

Singapore General Hospital, Singapore, Singapore

Aims: Describing a case of Trimethylaminuria.
Methods: A 40 year old woman presented with a complaint of increased flatulence production. She had no significant family history of note. Physical examination and blood investigations were normal. Endoscopic examination was unremarkable. A presumptive diagnosis of bacterial overgrowth syndrome was made and a course of Ciprofloxacin followed by a course of probiotics was given with little effect. Concurrently she was diagnosed with bacterial vaginosis by a Gynaecologist and was treated with no benefit. On subsequent clinic

visits, she reported less flatulence but also described a profoundly bad odor, which she suspected was a result of "leaking" flatus and resulted in social isolation from her associates. Around 6 months from her initial presentation, she developed symptoms of hyposmia and consulted an Otolaryngologist. A CT brain and post nasal space evaluation was performed and were normal. The patient continued to have significant anxiety about the odor and with no apparent cause found, she was offered psychiatric evaluation to exclude possible olfactory reference syndrome. She did not attend the appointment. She decided to do her own research and came across the possible diagnosis of Trimethylaminuria (TMAU). She attended the paediatric hospital and after much effort, convinced them to do urine testing. **Results:** Patient's urine trimethylamine (TMA) was 150.0 (2.5-10.8) umol/mmol creat, TMA-n-Oxide (TMAO) was 173.1 (17.0-147.0) umol/mmol creat and TMA/TMAO ratio 0.87 (0.05-0.21). The findings showed markedly increased TMA excretion and were in keeping with a diagnosis of TMAU. A sample of her serum was sent for Flavin containing Monooxygenase 3 (FMO3) gene testing but no pathogenic mutation was detected. A diagnosis of Secondary TMAU was made. She was referred to a dietitian for advice on low choline diet and started on regular charcoal. She had difficulties adhering to the prescribed diet and experienced iron deficiency due to reduced meat intake. Her episodes of offensive odour however improved markedly as did her mood.
Conclusions: TMAU is a condition where TMA accumulates and is excreted in urine, sweat and breath of affected patients. TMA is a volatile amine which smells of rotting fish. Bacterial degradation of choline and carnitine produces TMA and is oxidized by FMO3 into TMAO, which is non-odorous. The worldwide incidence of TMAU is not known. Secondary TMAU has been described in viral hepatitis, transiently during menstruation and gut flora disease. There are no consensus guidelines in treating this condition. Treatment focuses on dietary management but careful monitoring is required to avoid significant nutritional deficiencies that may arise from it.

A321
USING BEDSIDE ULTRASOUND AS A TOOL TO DETECT SARCOPENIA FOR CIRRHOTIC PATIENTS ON TRANSPLANT LIST
M. Alfawaz[2], I. sinclair[2], M. Hilwah[2], B.M. Aljudaibi[3], P. Marotta[1], K. Qumosani[2]

1. London heatlh sciences Center, University of Western Ontario, London, ON, Canada; 2. University of Western, London, ON, Canada; 3. Gastroenterology, london health science centre, London, ON, Canada

Background: Muscle atrophy is present in as many as 40% of cirrhotic patients and associated with increased morbidity and mortality in those awaiting liver transplantation. A two-fold increase in mortality when compared to non-sarcopenic patients occurs independent of liver dysfunction evaluated using Model for End-Stage Liver Disease (MELD) score which does not incorporate markers of nutritional status, or muscle loss. Ultrasound offers the possibility of a non-invasive and affordable method to evaluate skeletal muscle at the bedside. It has been validated and is emerging as a valuable prognostic indicator of muscle atrophy, thereby improving detection of malnutrition at the individual level.
Aims: We aim to evaluate quadriceps muscle layer thickness (QMLT) using ultrasound in cirrhotic patients waiting for liver transplantation across a range of nutritional risk scores based on Royal Free Hospital Nutrition Prioritizing Tool (RFNS). QMLT will also be compared to functional measures such as hand-grip and blood tests.
Methods: A prospective study started in July 2016 using QMLT measures in a cohort of adult patients waiting for liver transplantation. Written informed consent is obtained on an individual bases. Measures of QMLT are obtained using the ultrasound probe at frequency 9 htz for each thigh at the middle and two-third point from superior iliac spine (SIS). Two residents who received expert training conduct measures. These measures will be compared to a nutrition score as well as synthetic markers of malnutrition, and functional measures of strength and endurance.
Results: Ten patients have been recruited so far. The average QMLT measured at two-thirds from SIS is 3 cm on both legs. The average thickness at the mid-point is 4.2 cm for both legs. Those patients considered at severe risk of malnutrition based on RFNS had either lower, or close to average QMLT when compared to the entire group. Two of the severely malnourished patients had a higher than average measurement which may reflect significant lower-leg edema. Serum vitamin A, and D levels were low in 6 patients and none of those had a higher than average QMLT. Average NaMELD score was 21 in 4 patients with low QMLT. Interestingly, the high RFNS patients had lower NaMELD scores. Hand grip measures on two patients were considered low for both of those who also had low QMLT. Results were consistent between both residents.
Conclusions: Based on this prospective study, QMLT may offer and valuable and objective prognostic tool for detection of sarcopenia and high nutritional risk with consistent results. Significant lower leg edema may present a limitation of this tool. Future work is needed to optimize the ability of QMLT and to determine its importance in assessing the role of lean body mass in cirrhotic populations.

A322
ALBUMIN MODIFIED BODY MASS INDEX FOR THE ASSESSMENT OF CIRRHOTIC PATIENTS UNDERGOING

PANCREATICO-BILIARY DISEASE

ORTHOTOPIC LIVER TRANSPLANT
C.F. Rueda-Clausen, F.S. Cardoso, N. Kneteman, C.D. Karvellas, S. Veldhuyzen van Zanten

University of Alberta, Edmonton, AB, Canada

Background: Body Mass Index [BMI: weight(kg)/height(m)2] has been previously identified a key predictor of mortality in orthotopic liver transplant (OLT) recipients. However, the interpretation of BMI in subjects with cirrhosis is rather controversial due to ascites/anasarca-induced errors. Albumin modified BMI (amBMI= BMI*albumin/40) is an alternative parameter that corrects BMI for potential third spacing in patients with significant hypoalbuminemia.
Aims: To compare the 5yrs-mortality prediction and discriminatory value of amBMI vs. traditional BMI in cirrhotic subjects undergoing OLT.
Methods: This single center retrospective cohort study included subjects undergoing OLT at the University of Alberta between 2002-2012. Clinical information was extracted from a dedicated computerized database (OTTR) and audited. The primary outcome was all-cause mortality and/or graft failure at 5 years. Bland-Altman plots and linear correlation between methods were estimated. Prediction models were constructed using Cox proportional hazard regression techniques. Change in models performance using BMI and amBMI was evaluated. Models assumptions and discrimination capacity were tested. Ethics approval was obtained from the local ethics board.
Results: A cohort of 524 patients (mean follow-up time 3.1y and 130 (24.9%) events) was assembled. Baseline characteristics include (median[IQR]): age 54[48-59]y, male sex 68%, MELD-score 15[11-23], BMI 25 [23-28], serum albumin 34[30-39]g/L and amBMI 21[18-25]. Cirrhosis aetiologies included HCV(24%), HCC(21%), cholestasis(18%), alcohol(13%) and NASH(8%).
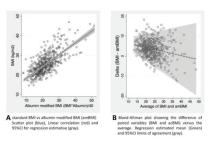
Correlation between BMI and amBMI was 71%, (p<0.0001) linear regression and Bland-Altman plots are presented in **figures A and B**.

BMI categories classification concordance between methods was 34%. in 47% of cases amBMI corresponds to a lower BMI category compared to conventional BMI. Compared to conventional BMI, amBMI classified more patients as Underweight ([BMI<18.5] 31 vs 5%, p<0.01) or Severely Underweight ([BMI<16], 14 vs. 0.6%, p<0.001). Despite the significant change in BMI assessment with the two methods, substitution of BMI by amBMI in current survival prediction models did not improve the accuracy nor discrimination capacity of the models. (C^2= 21.5, p=0.0007, C-index 0.61 with amBMI vs. C^2= 26.2, p=0.0001, C-index 0.63 with BMI).
Conclusions: Anthropometric nutritional assessment of patients with cirrhosis can be challenging due to third spacing induced error. amBMI can differ significantly from BMI in this population and may provide an alternative parameter to assess health status and nutrition

in this patients. In our OLT cohort, using amBMI instead of conventional BMI did not improve the discriminatory capacity of current models to predict mortality.

A standard BMI vs albumin modified BMI (amBMI) Scatter plot (blue), Linear correlation (red) and 95%CI for regression estimative (gray).

B Bland-Altman plot showing the difference of paired variables (BMI and acBMI) versus the average. Regression estimated mean (Green) and 95%CI limits of agreement (gray).

PANCREATICO-BILIARY DISEASE

Poster of Distinction

A323
A PERSONALIZED MEDICINE APPROACH TO THE ROLE OF RECTAL INDOMETHACIN IN PREVENTING POST -ERCP PANCREATITIS: A META- ANALYSIS OF AGGREGATE SUBGROUP DATA
M. YAGHOOBI [4], M.A. Alzahrani[5], J. McNabb-Baltar[1], M. Martel[2], F. Tse[4], A.N. Barkun[3]

1. Brigham and Women's Hospital, Harvard Medical School, Montreal, QC, Canada; 2. McGill University Health Center, Montreal, QC, Canada; 3. Gastroenterology, McGill University, The Montreal General Hospital, GI Division, Montreal, QC, Canada; 4. McMaster University, Hamilton, ON, Canada; 5. gastroenterology, McMaster university , Hamilton, ON, Canada

Background: Despite initial evidence in the literature favoring rectal indomethacin in preventing post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP), recent studies have been controversial in supporting its universal use, in part due to varying patient selection.
Aims: To identify optimal patient subgroups who might benefit the most from rectal indomethacin.
Methods: Data source: A comprehensive electronic literature search was done.
Study selection: Randomized controlled trials (RCTs) comparing rectal indomethacin and placebo in preventing PEP.
Data extraction and Synthesis: Methodological quality was assessed by the Cochrane risk of bias tool as well as Jadad scale. Statistical heterogeneity was assessed. Several subgroup, sensitivity and individual participant data were completed based on specific risk factors or patient characteristics to characterize patient populations who benefit most from the intervention.

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Main outcomes and Measures: The rate of PEP.
Results: A total of seven out of 336 trials published between 2007 and 2016 (n=3096) were included. The pooled proportion estimate of PEP rate was 5.6% with indomethacin and 8.7% with placebo. Random model meta-analysis showed the overall rate of pancreatitis was significantly lower with rectal indomethacin [OR=0.54(0.36-0.82), number needed to treat =19]. In subgroup analysis, the difference was not significantly different in an unselected population, but was when restricting the analysis to high-risk patients [OR: 0.42 (0.27-0.66)]. Subgroup analysis showed that administering rectal indomethacin before rather than during or after procedure significantly reduced the rate of PEP [OR:0.53(0.37-076)]. Individual participant data showed rectal indomethacin significantly prevented PEP in patients with sphincter of Oddi dysfunction (SOD) [0.47(0.28-0.77)] and those undergoing biliary sphincterotomy [OR:0.72 (0.52-0.99)], but not in those undergoing pre-cut or pancreatic sphincterotomy, or prophylactic pancreatic stent placement. Rectal indomethacin also significantly decreased the rate of moderate to severe PEP in all patients [OR: 0.47 (0.28-0.79)]. Sensitivity analysis showed that the lower quality of studies favored indomethacin.
Conclusions: Rectal indomethacin significantly reduces the risk of PEP in high-risk, and more specifically SOD patients; it decreases the occurrence of moderate to severe PEP in all patients, only if given pre-procedure. Additional data are needed to assess the additional contribution of prophylactic pancreatic stent placement.

Funding Agencies: None

A324
FOUR OR MORE EUS-FNA PASSES FOR PANCREATIC SOLID LESIONS IS ASSOCIATED WITH INCREASED RISK WITHOUT IMPROVING DIAGNOSTIC YIELD: RESULTS FROM THE OTTAWA HOSPITAL EUS RYSE QA INITIATIVE
M.J. Abunassar[1], A. Chatterjee[1], C. Marginean[2], G. Martel[3], S. Murthy[1], C. Dube[1], A. Rostom[1], P.D. James[1]

1. The University of Ottawa, The Ottawa Hospital, Department of Medicine, Division of Gastroenterology, Ottawa, ON, Canada; 2. The University of Ottawa, The Ottawa Hospital, Department of Pathology , Ottawa, ON, Canada; 3. The University of Ottawa, The Ottawa Hospital, Department of Surgery, Division of Hepatobiliary Surgery, Ottawa, ON, Canada

Background: Endoscopic ultrasound (EUS) is an established procedure for the investigation of the gastrointestinal and hepatobiliary systems. Due to study limitations such as small sampling and data quality, adverse events (AEs) related to EUS procedures may be underreported. Further the relationship between EUS-FNA diagnostic yield and adverse event risk has not previously been described.

Aims: To examine risk factors associated with AEs from EUS procedures performed at The Ottawa Hospital (TOH).
Methods: A retrospective chart-review of all EUS cases was performed from September 2009 until August 2015. AEs considered a priori included perforation, bleeding, infection, aspiration and pneumonia. All patient encounters to the emergency department and/or hospitalizations within 30 days of the EUS procedure were reviewed. Each possible AE case was reviewed by three of the authors (MA, PJ, AC) to determine the likelihood that the event was related to the EUS procedure. The TOH AE Database was then merged with the TOH EUS Procedure Database to examine patient and procedure factors associated with AE risk.
Results: 1,389 procedures were included. 663 (48%) EUS procedures were performed on women. 44 possible or definite adverse events related to EUS procedures were identified (3.2%) and 28 (2%) resulted in hospitalization. Infection (n=7), abdominal pain (n=6), pancreatitis (n=5), bleeding (n=5) were identified AEs. The risk of EUS alone was 0.9% which increased to 1.8% when an FNA was performed. Cases involving anesthesia support were more likely to result in AEs (5.4%) vs 2.7% for non-anesthesia cases. The presence of an advanced endoscopy fellow was associated with an increased risk of AEs 23 (3.8%) vs 2.3% when a fellow was not present). For EUS-FNA of solid pancreatic tumours, AE risk increased with the number of passes performed: 0% AEs with 2 or less passes, 2% with 3 passes and 5% when 4 or more passes were performed. We have previously shown that performing more than 4 passes is not associated with increased diagnostic yield.
Conclusions: This is the largest EUS-related adverse event study performed in Canada to date. Anesthesia assistance, the presence of a fellow in training and performing an FNA increase the overall risk of AEs. Performing four or more FNA passes may subject the patient to increased risk without increasing diagnostic yield.

Funding Agencies: None

A325
RISK EVALUATION OF ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)-RELATED CONTRAST MEDIA (CM) ALLERGIC REACTION AMONG PATIENTS KNOWN FOR ADVERSE REACTION TO IODINE CONTAINING PRODUCT
F. Trottier-Tellier, L. Harvey, H. Bernard, J. Baillargeon

CHUS, Sherbrooke, QC, Canada

Background: Few cases of ERCP-related CM adverse reactions have been reported in the current literature. Patients known for any allergy or a prior allergy-like reaction to CM are considered at higher risk of CM adverse reaction. There is a lack of standardisation in practice regarding premedication prophylaxis for at risk patients undergoing ERCP and few data to guide the

practitioners.

Aims: Our goal is to evaluate the risk of CM allergic like reaction in a group of patients with a past-history of reaction to iodine product undergoing ERCP.

Methods: A retrospective chart review study was performed of all adult patients who underwent ERCP at our single centre from January 2010 to December 2015. Data regarding demographics, history of allergy (especially iodine), ERCP indication and post-ERCP anaphylactoid reaction were collected for all patients. Additional data were collected for patients with a past-history of reaction to iodine product: hospitalisation status, premedication prophylaxis (corticosteroid and antihistaminic), type of contrast used, post-ERCP time of observation and any ERCP related CM reaction. Severe reaction was defined as an anaphylactic shock or an allergic-like reaction with hypotension or respiratory distress.

Results: Among 1766 patients, 2295 ERCP were performed from 2010 to 2015. 828 (36.1%) ERCP were performed on patients with a past history of any allergy and 127 (5.5%) on patients with prior iodine adverse reaction. Among 2295 ERCP, no anaphylactoid or severe adverse reaction occurred. 1 (0.04%) ERCP-related CM benign reaction was reported in a patient known for penicillin allergy but no prior CM reaction; he had a delayed diffuse pruritic rash with a favorable response to medical treatment. Among 1766 patients, 75 were known for prior reaction to iodine product. Previous iodine reactions were rash (n=22), oedema (n=16), severe CM reaction (n=10) or other-not specified (n=27). Among 127 ERCP performed on these patients, 121 procedures were done without and 6 with a premedication prophylaxis. In both groups, no ERCP-related CM reaction occurred.

Conclusions: To our knowledge, we report the largest cohort of iodine allergic patients undergoing ERCP ever published. Among a group of patients known for prior iodine reaction, 121 ERCP were performed without premedication and no CM adverse reaction were reported. Moreover, among 2295 procedures performed, no severe ERCP-related CM adverse reaction occurred and only 1 (0.04%) benign reaction was reported. These results suggest that ERCP-related CM adverse reactions are very rare even among patients at risk for CM reaction. Therefore, we suggest CM premedication prophylaxis for ERCP should not be given routinely among patients with a past-history of CM reaction.

A326
HOSPITALIZATIONS FOR ACUTE AND CHRONIC PANCREATITIS IN A FRENCH-CANADIAN FOUNDER POPULATION

K. Tremblay, D. Gaudet

Université de Montréal Community Genomic Medicine Center and ECOGENE-21 Clinical and Translational Research Centre, Saguenay, QC, Canada

Background: Acute pancreatitis (AP) is one of the most frequent gastrointestinal causes of hospitalization. Although less frequent, chronic pancreatitis (CP) also contributes to this burden. The severity, recurrence and risk trajectory (cancer, pancreas insufficiency) of pancreatitis vary among individuals. Heavy alcohol consumption or gallstones contribute to ~80% of all cases. Less frequent causes such as hereditary, idiopathic, autoimmune, metabolic or drug-induced, contribute less to the burden of hospitalizations but involve an important genetic component. The French Canadian founder population of the Saguenay-Lac-Saint-Jean (SLSJ) region (QC, Canada) is genetically less heterogeneous, which facilitates the identification of the genetic backbone of several diseases.

Aims: This study is a component of a broader research program on the genetic dissection of the natural history of common and rare causes of pancreatitis, and aims to document the causes and relative burden of hospitalizations for AP and CP in the SLSJ population.

Methods: This is a retrospective, population-based study of all hospitalizations for AP or CP in the SLSJ population between 2006 and 2014. Data were collected from the Quebec Ministry of Health hospitalizations registry (MED-ECHO). All pancreatitis events were reported according to the *International Classification of Diseases-10* codes (CIM-10-CA). The analyzed data included diagnosis at discharge, age, sex and duration of stay. The yearly incidence of hospitalizations for AP and CP has been calculated and the Quebec registry on causes of deaths was used to estimate the pancreatitis-related mortality in the SLSJ region between 2000 and 2011.

Results: Overall, 93% of pancreatitis-related hospitalizations were for AP (n=1610) (mean age of 57±19 years; men/women ratio of 1.08) and 7% for CP (n=118) (mean age of 53±17 years; men/women ratio of 1.31). Inhospital length of stay (mean±SD) was 7±10 days for AP and 7±7 days for CP. During the studied period, 13% of hospitalizations for AP were related to alcohol, 21% to gallstones, 6% were idiopathic, 2% drug-induced and 58% were categorized as "undefined". For CP, 31% were related to alcohol and 69% were undefined. The mean incidence of hospitalizations for AP or CP in the SLSJ was 148 cases yearly during the studied period. Also, there was a mean of four pancreatitis-related deaths yearly between 2000 and 2011 in this region.

Conclusions: The burden of hospitalizations for AP was 13-fold that of CP. Altogether, alcohol and gallstones were associated with less than one third of hospitalizations for AP or CP during the studied period, suggesting that genetic factors may play a role in pancreatitis expression in this population. This is the case for severe hypertriglyceridemia due to lipoprotein lipase deficiency, a cause of recurrent AP which is 200-fold more prevalent in SLSJ than in the rest of the world.

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A327
OPTIMAL TIMING OF BILIARY DRAINAGE IN SEVERE ASCENDING CHOLANGITIS

J.G. Coneys[2], L. Shafer[2], D.C. Moffatt[1]

1. Department of Medicine, University of Manitoba, Winnipeg, MB, Canada; 2. Universtiy of Manitoba, Winnipeg, MB, Canada

Background: Optimal timing of biliary drainage in ascending cholangitis (AC) is unclear. Early drainage is recommended in moderate and severe AC cases. However, demonstrable benefit in mortality and morbidity outcomes based on timing of biliary drainage is lacking.
Aims: To investigate if the time to biliary drainage provides benefit in mortality and morbidity outcomes in severe AC.
Methods: We completed an updated retrospective database analysis and chart review of ICU admitted AC cases between 2000 and 2014. This was completed using the University of Manitoba Adult ICU Database and manual chart review of flagged ICU admitted cholangitis cases in order to verify the diagnosis and assess clinical outcomes. Statistical analysis has included creation of linear and logistic regression models and survival analysis for mortality and length of stay.
Results: In total, 198 cases were flagged in the database. After chart review, 114 cases of AC were identified in 113 patients. The population mean age was 72 (SD 13.5), gender was 44% female, and mean APACHE II score was 22.3 (SD 8.0). The majority of cases (79%) were managed predominantly in tertiary care hospitals compared with community ICUs (21%). The mean time to biliary drainage was 49 hours (SD 56.0) and 16 cases did not undergo biliary drainage (14 of whom died). Mean length of hospital stay was 32.7 days (SD 76.7). In unadjusted logistic regression, biliary drainage was associated with significantly reduced odds of mortality (OR 0.11, p = 0.007, 95% CI 0.02 – 0.55). Logistic regression of time to biliary drainage, when controlling for APACHE score, did not appear to be associated with death (OR 1.0, p = 0.82). Survival analysis predicting length of stay in hospital by time to biliary drainage, though not statistically significant, suggested a possibly reduced hazard rate for those groups that were drained between 15-69 hours (HR .56, p = 0.24) and 70+ hours (.49, p = .24) compared with those drained in less than 15 hours.
Conclusions: In severe AC, biliary drainage may be associated with reduced mortality; however, time to biliary drainage in this analysis has not demonstrated to be associated with altered mortality. Early biliary drainage showed a non-significant trend toward shorter hospital length of stay. Rigorous competing risks analysis is ongoing to assess for confounders and to investigate the associations between these and other health related outcomes.

A328
FACTORS PREDICTIVE OF MALIGNANCY IN PATIENTS WITH BILIARY BRUSHINGS OBTAINED BY ERCP

T. Kulai, T. Arnason, E. Filter, S.E. Gruchy

Dalhousie University, Halifax, NS, Canada

Aims: Biliary brushings for cytology obtained during endoscopic retrograde cholangiopancreatography (ERCP) are the most commonly used method of evaluating patients with biliary strictures for potential underlying malignancy. Patients generally proceed to a pancreatoduodenectomy if there is concern for pancreatic or peripancreatic neoplasm and the patient is an operable candidate. Some patients undergo pancreatoduodenectomy for what is eventually determined to be benign disease. We sought to analyze ERCP brushings to determine predictive factors for malignancy at our centre and whether brushing results influenced decision for pancreatoduodenectomy.
Methods: Retrospective review was conducted on adult patients who underwent ERCP with biliary duct brushings for cytology at the QEII Health Sciences Centre in Halifax, NS, from 2013-2014. Bile duct brushing cytology reports were identified by electronic search of hospital pathology archives (Cerner Millenium, Cerner, Kansas City, MO). Information on gender, age, symptoms, biliary stricture location and endoscopic impression, presence of pancreatic mass, cytologic impression of brushings, CA 19-9 level, CEA level, surgical intervention and clinical outcome was collected. Abnormal cytology was defined as samples reported as suggestive of malignancy or positive for malignant cells. Basic descriptive statistics and qualitative analysis were performed.
Results: A total of 185 ERCP patients had biliary brushings for cytology during the study time period. Patients who received biliary brushings were more likely to be between ages 60 to 79 (56%) with a mean age of 66. Presenting symptoms included elevated liver enzymes (82%), jaundice (75%) and pain (48%). Location of biliary stricture, age and gender were not associated with abnormal cytology results. Endoscopic impression of the biliary stricture was malignant in 53% of cases and associated with increased likelihood of abnormal cytology (39/92; p < 0.001). Pancreatic mass on imaging, seen in 38%, was associated with abnormal cytology (25/69, p = 0.001). Elevated CEA, but not CA 19-9, was associated with abnormal cytology (13/23; p = 0.008). Patients who received a pancreatoduodenectomy were not more likely to have abnormal cytology (5/18, p = 0.051). Patients eventually diagnosed with malignancy were more likely to have abnormal cytology on biliary brushing (49/120, p < 0.001).
Conclusions: Age, gender, location of stricture and elevated CA 19-9 were not associated with abnormal

cytology suggestive of malignancy. The presence of a pancreatic mass, elevated CEA and eventual diagnosis of cancer were associated with abnormal cytology. Patients who received a pancreatoduodenectomy were not more likely to have abnormal cytology, which may reflect the scarcity of surgical candidates due to advanced disease at diagnosis.

Funding Agencies: None

A329
ROLE OF AMPULLARY BIOPSY IN AUTOIMMUNE PANCREATITIS

M.H. Laghari[1], K. Chiu[1], D.F. Schaeffer[2], F. Donnellan[1]

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

Background: Autoimmune pancreatitis (AIP) is a rare disorder of the pancreas with a prevalence and incidence of 4.6/100,000 & 1.4/100,000 population in Japan. Clinical presentation includes abdominal pain (65%), jaundice (62%), weight loss (42%), with approximately 85% of patients having abnormalities of the pancreas on imaging. The Mayo Clinic HISORt criteria is most commonly used for diagnosis. However, often the diagnosis is ambiguous and can lead to significantly morbid surgical resections for a disease that is responsive to immunosuppression. Therefore, endoscopic ampullary biopsies have been proposed as an adjunct to the diagnosis. There have relatively been a few studies looking at the diagnostic yield of amp-ullary biopsies in AIP, most reporting a high specificity and a sensitivity of 50-60%
Aims: (i) To correlate ampullary biopsy specimens on patients diagnosed with AIP via HISORt criteria. We aim to determine the diagnostic yield for ampullary biopsies in AIP in our cohort of patients. We believe ampullary biopsies provide valuable diagnostic information in AIP and should be used as an adjunct in the diagnostic work up for AIP. (ii) We also aim to correlate positive ampullary biopsies with abnormalities in serum IgG-4 levels (normal range 0.05 – 1.25 g/L)
Methods: We conducted a retrospective chart review of patients with autoimmune pancreatitis fulfilling the HI-SORt criteria, seen at the Vancouver General Hospital, Vancouver BC, from January 1, 2011 till July 31, 2016, who also had ampullary biopsies taken endoscopically. A positive biopsy, as defined in the literature, was more than 10 IgG-4 Immunohistochemically (IHC) positive plasma cells per 1 high power field (HPF) at a magnifi-cation of x400. We also collected serum IgG-4 values for this cohort of patients
Results: To date, there have been 20 patients, mean age of 62 with 80% males, with AIP as per HISORt crite-ria, that have also had ampullary biopsies taken. Out of these, only 6 met the definition for a positive ampullary biopsy, giving a diagnostic yield of 30%, whereas the rest did not meet a histological diagnosis of AIP on am-pullary biopsies. Out of the 20 patients, 50% (10) had elevated serum IgG-4 levels. All patients with a positive ampullary biopsy had an elevated serum IgG-4 level
Conclusions: Ampullary biopsies, if positive, provide a specific diagnostic adjunct in patients with presumed Autoimmune Pancreatitis as per the HISORt criteria. However, this is true only in approximately one third of such patients, as per this retrospective chart review. This is similar to prior studies. Additionally, we found serum IgG-4 levels only elevated in half of our cohort of patients with AIP. Serum IgG-4 levels however, cor-relate strongly with positive ampullary biopsies. More prospective studies will be needed to further confirm these findings

Funding Agencies: None

A330
MANAGEMENT OF COMPLEX PANCREATIC FLUID COL-LECTIONS USING THE NAGI™ COVERED EXPANDABLE METAL STENT

S.A. Taylor[3], M. Byrne[1], A. Weiss[2], F. Donnellan[1]

1. Gastroenterology, Vancouver General Hospital, Vancouver, BC, Canada; 2. Vancouver General Hospital, Vancouver, BC, Canada; 3. University of British Colum-bia, Vancouver, BC, Canada

Background: Covered self-expandable metallic stents (CSEMS) are a novel device designed for transmural drainage of symptomatic pancreatic fluid collections (PFC's). Theoretical advantages over conventional double plastic pigtail stents are due to a larger luminal diameter optimizing drainage particularly in cases of walled of necrosis (WON).
Aims: The aim of our study was to evaluate the efficacy and safety of a NAGI™ stent in the management of PFC'S.
Methods: This was a retrospective single center study. Between February 2015 and July of 2016, 17 patients underwent EUS guided PFC drainage using the NAGI™ CSEMS. Primary endpoints included technical success (stent deployment), clinical success identified by radiographic resolution (PFC<2cm) and symptomatic resolution, stent related complications and rates of re-intervention.
Results: There were 17 patients (mean age: 53.5) with symptomatic PFC's: 12 patients (71%) with WON and 5 (29%) with a simple pancreatic psuedocyst. The NAGI™ stent was successfully placed via the transgastric approach in all 17 patients and left in situ for a median of 46 days (range 12-146). Endoscopic trans mucosal drainage was clinically successful in 100% of patients with pancreatic pseudocysts and 43% for WON. In the patients with WON, 58% (7/12) required additional necrosectomy and/or irrigation: 4 required one intervention and 3 required more than one intervention to achieve resolution. Major complications were identified in 2 of 17 patients secondary to PFC infection due to stent obstruction. Minor complications

identified included self-limited bleeding secondary to tract puncture (n=1), transient fever (n=1) and possible reflux esophagitis secondary to stent malposition.
Conclusions: Our study supports the literature that the CSEMS are an effective, and safe modality for the treatment of PFC's. Future studies are needed to assess for superiority over conventional plastic stents and other existing FSCEMS particularly in the drainage of WON.

Funding Agencies: None

A331
BOUVERET'S SYNDROME: A RARE CAUSE OF GASTRIC OUTLET OBSTRUCTION
M. Fine[1], T. Xenodemetropoulos[2]

1. Gastroenterology, McMaster University, Oakville, ON, Canada; 2. Medicine, McMaster University, Hamilton, ON, Canada

Background: Bouveret's syndrome (BS) is a rare variant of a gallstone ileus (itself a rare condition) accounting for less than 5% of all mechanical bowel obstructions. In BS, a gastric outlet obstruction (GOO) is caused by the migration and impaction of a gallstone through a cholecystoduodenal or cholecystogastric fistula and into the duodenum or pylorus of the stomach.
Aims: The aim of this case report is to bring to light a rare but significant cause of GOO. In addition, we hope to illustrate the need for safe, minimally invasive endoscopic techniques for the treatment of this condition.
Methods: This was a real case encountered on the gastroenterology ward at a tertiary care hospital in Hamilton, Ontario.
Results: We present a case of BS in an 83-year-old woman with multiple comorbidities who presented to the gastrointestinal (GI) service with a week-long history of nausea, vomiting, and epigastric pain. She was found to be severely hypovolemic and with an acute kidney injury. Investigations revealed a cholecystogastric fistula and a gallstone impacted in the patient's gastric outlet. Endoscopic retrieval of the stone was attempted, although ultimately unsuccessfully. The patient declined surgical intervention and died during this hospitalization.
Conclusions: This case illustrates a rare cause for a common presentation, and emphasizes the importance of including BS in the differential diagnosis for nausea and vomiting. It also illustrates the need for minimally invasive treatment techniques as many patients with BS are poor surgical candidates.

Endoscopic image of gall stone impacted in patient's gastric outlet.

Funding Agencies: None

A332
ERCP COMPETENCY ASSESSMENT TOOL: DEVELOPMENT OF A PROCEDURE-SPECIFIC ASSESSMENT TOOL FOR ERCP.
C.M. Walsh[1], S.C. Grover[2], I. Plener[3]

1. Gastroenterology, Hepatology and Nutrition, Hospital for Sick Children and The Wilson Centre, Toronto, ON, Canada; 2. University of Toronto, Toronto, ON, Canada; 3. Internal Medicine, University of Toronto, Toronto, ON, Canada

Background: There is a paucity of literature evaluating competence in advanced endoscopic modalities in the treatment of pancreatobiliary diseases. Traditionally, competency in endoscopy has been measured by procedural volume and adverse events. A formal curriculum has not been widely established to standardize proficiency in ERCP. It is clear, from both training and patient quality perspectives that defined outcomes for clinical competence at the conclusion of advanced endoscopic training needs to be established.
Aims: We propose to develop a competency tool for ERCP using a standardized Delphi Approach.
Methods: Delphi Panel Recruitment and Sample: Delphi methodology will be used to reach consensus amongst a panel of recruited international therapeutic endoscopy experts (Therapeutic Endoscopists, Surgeons, Endoscopy Nurses) to establish criteria for assessing ERCP competence.
Item Generation and Finalization of ERCP Competency Assessment Tool:
Systematic Literature review (ERCP Performance and Assessment) followed by open-ended survey of panel members with opportunity for expert panelist commentary and input. Structure surveys distributed according to Dilman's tailored design method.
Results: Initial Round:
a) Respondents identify the importance of each check-

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list and global rating item using an ordinal scale.
b) Respondents asked to list up to 10-additional check-list or global rating items not included they deeme to be important.

Checklist Items (Figure 2)
Divided into Pre-Procedure, Intra-Procedure and Post-Procedure domains. Procedure competency is further subdivided into Technical, Cognitive and Global Rating domains.

Analysis of Responses:
Descriptive statistics to establish mean rating with a 95% confidence interval within each category of ordinal scoring
Checklist or global item to be removed if mean rating < 4.0 and critical rating <5.0
Consensus to be established if homogeneity of opinion seen in 80% or more of respondents in any Delphi round following the introductory round.

Conclusions: No research to date has used trained raters using specifically designed assessment tools with direct observation or video recorded assessments. Rigorous continued assessment of a trainee's performance with a validated assessment tool is valuable, providing insight to individual learning curves in comparison to other learners in a standardized fashion. Delphi panel results to be complete by CDDW/GRIT.

A333
THE ROLE OF IMAGING IN DETERMINING PROGNOSIS FOR PRIMARY SCLEROSING CHOLANGITIS: A SYSTEMATIC REVIEW

D. Segal[4], B.M. Aljudaibi[3], P. Marotta[1], M. Mosli[5], B.G. Feagan[2]

1. London heatlh sciences Center, University of Western Ontario, London, ON, Canada; 2. Robarts Clinical Trials Inc, London, ON, Canada; 3. Gastroenterology, london health science centre, London, ON, Canada; 4. department of medicine, western university, London, ON, Canada; 5. King Abdulaziz University, Jeddah, Saudi Arabia

Background: Primary Sclerosing Cholangitis (PSC) is a chronic, progressive, inflammatory bile duct disease that causes fibrosis and stricturing. Resultant complications include life-threatening infection , progressive liver disease including cirrhosis, and malignant tumors. While diagnosis utilizes imaging studies extensively, the role of imaging in determining the clinical prognosis is less clear.

Aims:
The aim of this study was to systematically review existing imaging indices and features that predict PSC progression.

Methods: We performed a systematic review of imaging indices and features that predict PSC progression. PubMed, EMBASE (Ovid), MEDLINE (Ovid), and the Cochrane Library (CENTRAL) from inception to November 2015 were searched for relevant studies. Pertinent data was extracted and assessed.

Results: The search returned 2024 results. Of the resulting twenty-five pertinent studies selected for full text review, eight were included. The two imaging modalities studied were endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance imaging. Two imaging indices (ERCP based and MR based) have been described and partially validated. The ERCP index was validated in a second population by comparing predicted time to liver related death or liver transplant to actual outcomes. It was then updated to be more robust. The MRCP index determined via multivariate analysis for gadolinium and non-gadolium studies was found to only be predictive of transplant free survival for the non-gadolinium studies in a proof-of-concept cohort.

Conclusions: Two imaging indices, one ERCP and one MR based, have been described to predict prognosis. The ERCP index has been validated in a second cohort while the MRCP index requires external validation.

PEDIATRIC LIVER DISEASE

A335
BILIARY ATRESIA HOME SCREENING PROGRAM IN BRITISH COLUMBIA: EVALUATION OF FIRST TWO YEARS

J.P. Woolfson[1], R. Schreiber[1], A. Butler[2], J. MacFarlane[3], J. Kaczorowski[4], J. Collet[6], S. Bryan[5]

1. Division of Pediatric Gastroenterology, Hepatology and Nutrition, BC Children's Hospital, Department of Pediatrics, University of British Columbia, Vancouver, BC, Canada; 2. Division of Pediatric Gastroenterology, Hepatology and Nutrition, BC Children's Hospital, Vancouver, BC, Canada; 3. Perinatal Services BC, PHSA, Vancouver, BC, Canada; 4. Dept of Family and Emergency Medicine, Université de Montréal and CRCHUM , Montreal, QC, Canada; 5. School of Population and Public Health, University of British Columbia, Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute , Vancouver, BC, Canada; 6. Department of Pediatrics, University of British

Columbia, BC Children's Hospital Research Institute , Vancouver, BC, Canada

Background: Biliary atresia (BA), a rare newborn liver disease (1:19,000 births in Canada), is the leading cause of cirrhosis and liver related mortality in children. Early referral and timely surgical intervention (≤60 days of age) with a Kasai procedure (KP) offers the best chance for long-term survival without liver transplant. Taiwan has a universal BA screening program using infant stool colour cards (SCCs) with proven effective-ness. We report our experience following introduction of a similar BA screening program in BC.

Aims: To assess the BC provincial BA home screening program performance and cost during the first 2 years of operation.

Methods: The study period was from program launch April 1, 2014 to March 31, 2016. SCCs were distributed to families upon discharge from the maternity ward. Parents were instructed to monitor their infant's stool colour for the first month of life using photos of normal and abnormal stool colour on the SCC and contact the screening centre if concerned. Number of live births, BA cases and program costs were calculated. Frequency and reasons for contacting the centre were recorded. Card distribution was assessed by examining the num-ber of SCCs re-ordered by maternity units compared with their number of births. Also, BC Children's Hospital charts from four 2-week periods were randomly se-lected between July 2015 and June 2016 to determine SCC distribution rates based on nurse sign-off of the SCC box on the discharge sheet. Analyses of sensitivity, specificity, PPV and NPV of SCC performance were performed. The UBC IRB approved the study.

Results: There were 87,583 live births through the study period and 8 cases of BA (1:10,948)**.** Four BA cases were identified by the SCC and four were missed. The median age of KP in the identified and missed groups was 51 and 112 days respectively. The sensitivity of the SCC was 50%, specificity 99%, PPV 5% and NPV 99%. The false positive rate was 0.08%. 126 maternity units received SCCs. Eight sites did not reorder sufficient number of SCCs based on their num-ber of births, accounting for 2% of the provincial births. 1050 BCCH charts were reviewed. 63 did not contain a discharge record. Of the remaining 987 charts, 94% had the SCC signed off as a discharge item. Reasons for incomplete SCC sign off were early discharge and discharge sheets with multiple unsigned items. The total 2 year operational cost was $42,600 with the SCC cost per birth being $0.48.

Conclusions: This first report of the BC BA screening program showed SCC case identification was associ-ated with earlier age of KP. However, the SCC requires modification to improve its sensitivity. Specificity and distribution rates were high and program cost was low. Further assessment of the program after 5 years will provide additional information regarding outcomes and cost effectiveness.

A336
PREVALENCE AND RISK FACTORS FOR TRANSIENT NEONATAL CHOLESTASIS IN A MOTHER AND CHILD TERTIARY UNIVERSITY CENTER

M. Chartier[1], M. Paganelli[1], F. Alvarez[2]

1. Gastroenterologie, Hépatologie et Nutrition, CHU Ste-Justine, Montreal, QC, Canada; 2. CHU-Sainte Justine, Montreal, QC, Canada

Background: Neonatal cholestasis has an incidence of 1/2500 in term infants and can be caused by various disorders. Since the list of genetic diseases associated with neonatal cholestasis is continuously expanding, it is thought that transient neonatal cholestasis (TNC) is decreasing. TNC is characterized by an early onset cholestasis, normalisation of clinical and biochemical parameters at follow-up, and has been associated with neonatal adverse events.
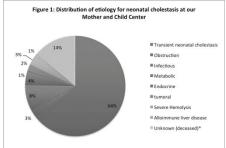
Aims: The primary objective was to determine the prevalence of diverse disorders causing neonatal cholestasis and particularly TNC, in our Mother and Child Hospital in Montreal. The secondary objective was to determine if there were factors that could predict the diagnosis of TNC over other diagnosis for cholestasis.

Methods: This was a retrospective study that included all patients born between January 1, 2011 and December 31, 2013, who presented with cholestasis in the first 90 days of life. All data were obtained from an electronic neonatal database and through medical chart review.

Results: 113 patients were diagnosed with neona-tal cholestasis during the 3-year study period. Of those, 74 (64%) had a diagnosis of TNC, 3 (3%) had an obstructive cause (biliary atresia, non-syndromic paucity of bile ducts), 9 (8%) had an infection (TORCH, pyelonephritis), 4 (4%) had a metabolic disorder (ga-lactosemia, cystic fibrosis, Dubin-Johnson), 1 (1%) had an endocrine cause (panhypopituitarism), 2 (2%) had a tumor (liver infiltration of juvenile myelomonocytic leukemia, hemangioendothelioma), 3 (3%) had inspis-sated bile syndrome from severe hemolysis, 1 (1%) had alloimmune liver disease and 16 (14%) died before the cholestasis was resolved or before the etiologic evaluation was completed. The prevalence of neonatal cholestasis in our NICU was 2.4% and the prevalence of TNC was 1.5%. The majority of patient with TNC had ≥2 risk factors compared to the group with other combined causes for cholestasis; prematurity < 32 weeks in 55% vs 0% (p=<0.0001), parenteral nutrition > 7 days in 82% vs 26% (p=<0.0001), NEC in 23% vs 0% (p=0.0099) and sepsis in 47% vs 22% (p=0.0323) respectively. The mean maximum total bilirubin was lower in the TNC group compared to the group with other causes for cholestasis; 128 umol/L vs 256 umol/L respectively (p=0.008). The average duration of cholestasis was 82 days in the TNC group compared to 85 days in the

group with other causes for cholestasis (p=0.8849). However in the latter group, the duration was variable according to the etiology.

Conclusions: This study highlights that in a large mother and child hospital, the most likely etiology for cholestasis in infants under the age of 90 days, is TNC, despite advances in diagnostic techniques for metabolic and genetic disorders. This can be explained by the high-risk pregnancies being followed at this tertiary hospital.

Figure 1: Distribution of etiology for neonatal cholestasis at our Mother and Child Center

Funding Agencies: None

A337
RESULTS OF PILOT HEPATITIS C SCREENING PROGRAM IN INFANTS BORN TO HIGH RISK MOTHERS

S. Gander[1], D. Webster[2], D. Smyth[2], S. materniak[2]

1. Paediatrics, Horizon Health, Saint John, NB, Canada; 2. Centre for Research, Education and Clinical Care of At-Risk Populations (RECAP), Saint John, NB, Canada

Background: Hepatitis C (HCV) is a global health concern with an estimated 2-3 % of the general population infected. It is estimated that the vertical transmission rate of mother-to-child is 5.8%. Due to the placental transfer of maternal antibodies, confirmation of hepatitis C infection is often delayed until the baby is 12-18 months of age, however many centres across North America screen earlier in order to ensure screening.

There are limited centres in Canada with a formal infant screening program and limited data regarding the rate of HCV transmission. Many primary care physicians and pediatricians do not have the awareness of when to implement a screening initiative for these at-risk babies. Identifiable factors in addition to maternal HCV-positive serostatus include illicit drug use and peri-natal methadone maintanence therapy (MMT) which is common in our community yet we do not screen mother nor babies.

Aims: 1. Does a formal targeted program improve screening and identify children with HCV?
2. What is the mother-to-child transmission rate observed in our community?
3. What are the barriers to screening?

Methods: At risk mothers (HCV positive, on MMT, con-

firmed/suspected illicit drug use) are identified at the time of delivery and a referral for follow-up sent to both the research team primary care provider explaining the need and timing for screening and the details around data collection for the purposes of this study. The family doctor or research team then contacts the family to arrange screening. Patient results and/or reasons for not screening are documented and monitored.

Results: A total of 26 infants were included in the pilot program conducted between January 2015 and February 2016. Babies were screened at an average of 10.8 months (range 1.7-17.9 months). Of the mothers, 11/27 (42.3%) were HCV positive, the remaining 15 (57.7%) infants had mothers with other high risk behaviours for HCV acquisition but an unknown HCV status. Six (23.1%) of babies have been screened for HCV as of October 12, 2016. All were found to be negative.

Conclusions: There remains a lack of data regarding the vertical transmission rate and outcome of infant HCV in Canada. There are many barriers to screening including patients lost to follow-up and screening refusal due to venipuncture. A longer prospective study is now underway to look for patient friendly alternatives to screening including point of care buccal swab tests being used in other countries. We also hope to follow patients once they are identified to be HCV positive in order to document clearance rates and/or possible treatment success. Also an infant screening program will serve to educate those on the importance of identifying HCV in pregnant mothers since treatment of the mother following delivery is safe and well tolerated.

Funding Agencies: None

A338
SEVERE POSTINFANTILE GIANT CELL HEPATITIS IN AN ADOLESCENT MALE RESPONDING TO IMMUNOSUPPRESSIVE THERAPY DESPITE NEGATIVE AUTOIMMUNE MARKERS

J. Jeong[1], M. Brundler[2], L. McKenzie[1]

1. Pediatric Gastroenterology, University of Calgary, Calgary, AB, Canada; 2. Pediatric Pathology & Laboratory Medicine, University of Calgary, Calgary, AB, Canada

Background: Giant cell hepatitis, characterized by extensive giant cell transformation of hepatocytes and variable inflammation, is commonly seen in newborn liver disease. Postinfantile Giant Cell Hepatitis (PIGCH) is a very rare pathologic finding in older children and adults. Thought to be due to a regenerative hepatocyte response to harmful stimuli, PIGCH is associated with drugs, viral infection, autoimmune diseases and other etiologies.

Aims: We describe a case of severe, chronic PIGCH in an adolescent male with no identifiable etiology despite exhaustive investigations. Ultimately, he responded to corticosteroids despite negative autoimmune markers.

Methods: A case of unexplained PIGCH in an adolescent male was reviewed. The literature on PIGCH was explored and summarized.

Results: A previously healthy 15-year-old male presented with a 2.5-month history of jaundice and hepatitis (ALT/AST > 2500 U/L, ALP 667 U/L, total bilirubin 64umol/L and INR 1.1). There was no history of travel, toxins, or medication use. A thorough infectious work up was negative. Metabolic causes such as Wilson's disease and alpha-1-antitrypsin were excluded. IgG levels were normal (12 g/L) and an extensive autoimmune hepatitis antibody panel was negative. A liver biopsy demonstrated severe lobular inflammation with abundant multinucleate giant cells and early bridging fibrosis.

Due to ongoing severe hepatitis, the patient was started on prednisone despite negative autoimmune markers and by 48 hours, his liver enzymes improved dramatically. Azathioprine and ursodiol were introduced following prednisone initiation, which led to normalization of his liver enzymes. However, follow up liver biopsies at 10 and 24 months demonstrated ongoing mild chronic hepatitis with only occasional giant cells and progression to severe fibrosis. Transient elastography values increased over two years, suggesting ongoing fibrosis. Currently the patient is asymptomatic and is maintained on budesonide, azathioprine and ursodiol. All autoimmune markers remain negative.

Conclusions: PIGCH due to an underlying autoimmune etiology accounts for approximately 40% of all reported PIGCH cases, and presents with typical autoimmune markers such as elevated IgG, ANA, and ASMA. Autoimmune PIGCH has a generally poor prognosis, with only about 20% responding well to treatment and the rest progressing to cirrhosis or death. We describe an individual with PIGCH who had no autoimmune markers but biochemically responded to steroid therapy, suggesting prednisone should be considered in patients with no identifiable cause of their PIGCH. Even though our patient had symptomatic and biochemical improvement with immunosuppressive therapy, concern remains over ongoing inflammation and possible progression to cirrhosis as described in most other individuals with autoimmune PIGCH.

Funding Agencies: None

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The Product Monograph is also available by calling us at 1-866-384-1314.

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1. Bressler B, et al. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: the Toronto consensus. *Gastroenterology.* 2015;148:1035–1058.
2. CORTIMENT®MMX Product Monograph, Ferring Pharmaceuticals, June 2016.

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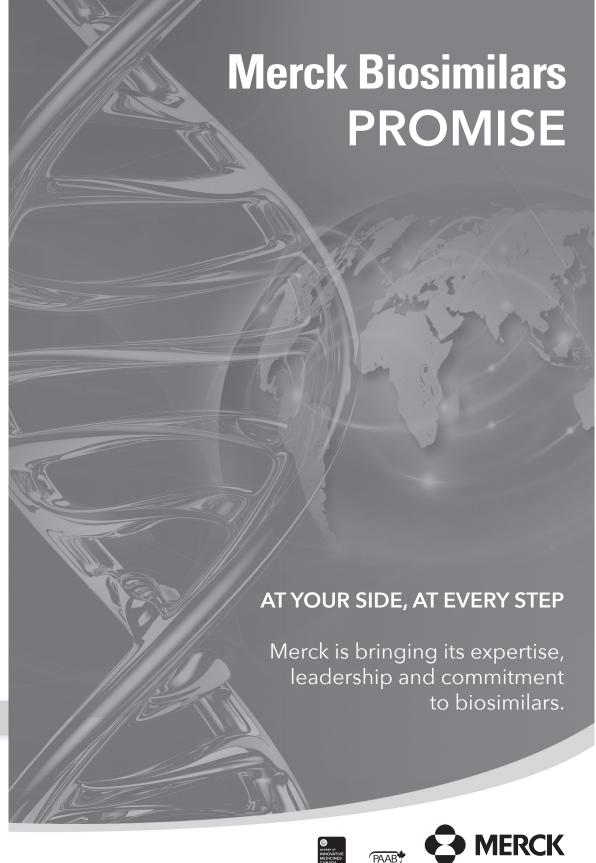
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Indication & Clinical Use:

EPCLUSA (sofosbuvir/velpatasvir) is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adults without cirrhosis or with compensated cirrhosis. EPCLUSA is also indicated in combination with ribavirin for the treatment of chronic HCV infection in adults with decompensated cirrhosis.

Safety and efficacy has not been established in pediatric patients

Contraindications:

• When used in combination with ribavirin, the contraindications to ribavirin are applicable to the combination regimen

Relevant Warnings and Precautions:

• Data to support the treatment of patients with decompensated cirrhosis who are infected with HCV genotype 2 or genotype 4 are limited, and there are no data for genotype 5 and genotype 6 HCV infected patients with decompensated cirrhosis. The indication for treatment of these patients is based on extrapolation of relevant clinical and in vitro data

• Should not be administered concurrently with other medicinal products containing sofosbuvir

• Should not be used with potent P-glycoprotein (P-gp) inducers and/or moderate to potent inducers of CYP2B6, CYP2C8, or CYP3A4

• Coadministration with amiodarone is not recommended due to risk of serious symptomatic bradycardia. If EPCLUSA is administered with amiodarone, patients should be counseled about the risk of symptomatic bradycardia. Cardiac monitoring is recommended in an in-patient setting for the first 48 hours of coadministration, after which outpatient or self-monitoring of heart rate should occur on a daily basis, through at least the first 2 weeks of treatment. Patients discontinuing amiodarone just prior to starting EPCLUSA should undergo similar cardiac monitoring

• Safety and efficacy has not been established in patients with severe hepatic impairment (Child-Pugh Class C)

• Safety and efficacy has not been established in patients with severe renal impairment (eGFR < 30 mL/min/1.73m^2) or end stage renal disease requiring hemodialysis

• Efficacy has not been established in patients who have previously failed treatment with other regimens that include an NS5A inhibitor

• Pregnancy and breastfeeding should be avoided

• If coadministered with ribavirin, the pregnancy and contraception warnings of ribavirin, in particular the pregnancy avoidance warning, apply to the combination regimen

• Safety and efficacy has not been established in patients with recurrent HCV infection after liver transplant

• Safety and efficacy has not been established in HCV patients co-infected with hepatitis B virus (HBV) or human immunodeficiency virus (HIV)

• Concomitant use with tenofovir DF, particularly in those at increased risk for renal dysfunction, requires monitoring for tenofovir-associated adverse reactions

• Co-administration with an efavirenz-containing regimen is not recommended

• Monitoring of liver function including direct bilirubin is recommended in patients with decompensated cirrhosis

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STUDY PARAMETERS

** The efficacy of EPCLUSA was evaluated in three Phase 3 trials with data available for a total of 1035 patients with genotype 1 to 6 chronic HCV infection without cirrhosis or with compensated cirrhosis. Primary endpoint was SVR12. The demographics and baseline characteristics for the patients in each study were balanced across the treatment groups.

ASTRAL-1: Phase 3, randomized, double-blind, placebo-controlled, multicentre study evaluating patients with GT 1, 2, 4, or 6 HCV infection. Patients (n=740) were randomized 5:1 to treatment with EPCLUSA (n=624) or placebo (n=116) for 12 weeks. Patients with GT 5 were enrolled in the EPCLUSA group. Randomization was stratified by HCV GT (1, 2, 4, 6, and indeterminate) and the presence or absence of cirrhosis. Primary endpoint was SVR12.

ASTRAL-2: Phase 3, randomized, open-label, multicentre study evaluating patients with GT 2 HCV infection. Patients (n=266) were randomized 1:1 to treatment with EPCLUSA (n=134) for 12 weeks or SOF + RBV (n=132) for 12 weeks. Randomization was stratified by the presence or absence of cirrhosis and prior treatment experience (treatment-naïve vs treatment experienced). Primary endpoint was SVR12.

ASTRAL-3: Phase 3, randomized, open-label, multicentre study evaluating patients with GT3. Patients (n=552) were randomized 1:1 to receive treatment with EPCLUSA for 12 weeks (n=277) or SOF+RBV for 24 weeks (n=275). Randomization was stratified by the presence or absence of cirrhosis and prior treatment experience (treatment-naïve vs treatment experienced). Primary endpoint was SVR12.

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