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Clinical and endoscopic predictors of cytological dysplasia or cancer in a prospective multicentre cohort study of large sessile serrated adenomas/polyps

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Aim: Sessile serrated adenoma/polyps (SSA/P) are recognized as an important precursor to colon cancer. The development of cytological dysplasia within an SSA/P (SSA/P-D) is thought to be a critical step along the pathway to malignancy. There are no studies describing the clinical and endoscopic characteristics of SSA/P-D. We aimed to examine the clinical and endoscopic characteristics of SSA/P ≥20mm resected by Wide Field Endoscopic Mucosal Resection (WF-EMR) and identify the characteristics and predictors of SSA/P-D.

Methods: Prospective multicentre data of large sessile colorectal polyps referred for resection by WF-EMR (September 2008 - May 2013) were analysed. Comprehensive patient and procedural data was collected including scheduled follow up at 14 days, 5 and 16 months. All histology was reviewed by expert gastrointestinal pathologists and classified according to the World Health Organisation criteria (2010).

Results: 268 SSA/Ps were found in 207/1546 patients (13.4%). SSA/P-D comprised 32.4% of SSA/Ps. Cancer occurred in 3.9%. On multivariable analysis, SSA/P-D was associated with increasing age (OR 1.69 per decade (1.19-2.40, p.004) and increasing lesion size (OR 1.90 per 10mm (1.30-2.78), p.001) an ‘adenomatous’ pit pattern (Kudo III, IV or V) (OR 3.98 95%CI (1.94-8.15), p<.001) and any 0-Is component within an SSA/P (OR 3.10 95%CI (1.19-8.12) p.021). Conventional type dysplasia was more likely to exhibit an adenomatous pit pattern than serrated dysplasia. HGD or cancer was present in 7.2% and on multivariable analysis, was associated with increasing age (OR 2.0 per decade; 95%CI 1.13-3.56) p.017) and any Paris 0-Is component (OR 10.2; 95%CI 3.18-32.4 p <.001).

Conclusion: Simple assessment tools allow endoscopists to predict SSA/P-D or HGD/cancer in SSA/Ps. Correct prediction is limited by failure to recognise SSA/P-D which may mimic conventional adenoma. Understanding the concept of SSA/P-D and the pitfalls of SSA/P assessment may improve detection, recognition and resection and potentially reduce interval cancer.
Chronic exposure to LPS induces goblet cell differentiation in human colonic organoids

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Aim: Modification of the intestinal microbiota results in marked changes in the properties of the intestinal epithelium. This response is believed to result from direct interaction between the microbiota and the intestinal epithelial cells (IEC), and changes induced by signals arising from the gastrointestinal immune system. Here we have used colonic organoids, which are primary cultures of human colonic intestinal epithelium, to investigate the effect of microbial stimuli on the development of the intestinal epithelium, independent of immune input.

Methods: Organoids were grown from crypts isolated from the transverse colon of healthy individuals and transferred to Matrigel and growth media for 15 days in the presence and absence of the lipopolysaccharide (LPS, 20 ng ml-1). Organoid structure was assessed by light microscopy and gene expression of proliferation, differentiation, maturation and stem cell activity markers was analysed by qPCR.

Results: After 15 days of culture a mixed population of organoids developed that consisted of 70% undifferentiated colonospheres and 30% colonoids. The colonoids had a well-differentiated epithelium consisting entirely of colonocytes with no evidence of goblet or enteroendocrine cells. The inclusion of LPS in the culture media had no effect on the growth of organoids or the relative proportions of colonoids or colonospheres. However, the number of goblet cells in the colonoids increased to 20±3% (P<0.05) of the total cells. Associated with this was an increase in the transcript levels of the goblet cell specific markers Muc2 (P < 0.005), trefoil factor 3 (P< 0.005) and the goblet cell specific transcription-factor KLF4 (P < 0.05).

Conclusions: LPS, a microbial agonist of the pattern recognition receptor TLR4, induced goblet cell differentiation in the colonic epithelium independent of immune modulation. This is consistent with direct cross-talk between the IECs and the microbiota and is likely to be important in epithelial homeostasis in the intestine.

Supported by a University of Otago Research Grant and Grants from the Dean’s Fund, Otago School of Medical Sciences, the Department of Physiology University of Otago and NZSG AbbVie Research Grant.

Infliximab and adalimumab trough concentrations and anti-drug antibodies correlate with response in inflammatory bowel disease

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Aims: The TNF-α antagonists infliximab (IFX) and adalimumab (ADA) are the most effective treatments for inflammatory bowel disease (IBD) but more than half of patient fail to respond, or lose response, by 12 months of treatment. Failed treatment may be due to low drug concentrations and/or presence of anti-drug antibodies. We aimed to measure trough concentrations of ADA and IFX, and antidrug antibodies, in patients with IBD, and correlate concentrations with disease activity.

Methods: Subjects included gastroenterology outpatients and inpatients at Christchurch Hospital with IBD treated with IFX or ADA. Blood samples were collected just prior to dosing, at least 12 weeks after treatment initiation. Disease activity indices for CD and UC were recorded at the time of...
sampling and at the time of treatment initiation. Drug and anti-drug antibody concentrations were measured by enzyme-linked immunosorbent assay (ELISA).

**Results:** Sixty-one patients were studied, including 33 on IFX (24 CD, 7 UC, 1 indeterminate) and 28 on ADA (all CD). Median (range) IFX and ADA concentrations were 7.9 (0-58) and 4.9 mg/L (0-59). Twenty-five patients had concentrations below 5 mg/L, a suggested threshold for drug activity. Crohn’s Disease Activity Index (CDAI) was significantly higher in patients with drug concentrations <5 versus >5mg/L (median 166 vs 89, p=0.007). ROC analysis suggested a threshold value of 5-7mg/L is appropriate. There was no correlation between treatment duration and trough drug concentrations (p=0.282). Of 10 patients with drug concentrations <1mg/L, 5 had detectable anti-drug antibodies (3 IFX and 2 ADA antibodies).

**Conclusions:** It is now possible to measure drug concentrations of IFX and ADA, and anti-drug antibodies to both drugs, in New Zealand. These results confirm published results showing that trough concentrations are correlated with disease control in IBD and that drug concentration and anti-drug antibody monitoring may aid in dosing decisions.

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**Annual incidence of IBD in the Otago region: an 18-year epidemiological analysis**

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University of Otago

**Background:** Recent research suggests that internationally the rates of IBD have been increasing, but in some areas may be beginning to plateau. While regions of New Zealand have among the world’s highest incidence rates of IBD, changes over time are unknown.

**Aims:** The aims of this study were to determine the annual incidence of IBD in the Otago region between 1996 and 2013, and to identify changes in phenotypic presentation of the disease between the 4-year period 1996-1999 and the 4-year period 2010-2013.

**Methods:** All NHIs with an IBD associated ICD code assigned between 1996 and 2013 were gathered into a master list. The earliest date of IBD diagnosis was confirmed by colonoscopy or histology or both. Demographics, IBD phenotype and IBD management data were extracted from the medical notes. Disease behavior was recorded using the Montreal classification. Annual incidence was age-standardised using the Otago region census population and the WHO world standard population.

**Results:** Of 1,089 ICD coded NHIs, 443 confirmed IBD diagnoses were made in the Otago region. There was an overall increase of 0.27 cases per 100,000 people per year in age-adjusted annual incidence for IBD, however this increase was not statistically significant. In 2012 the IBD incidence was highest at 23.67 cases per 100,000. Age-specific rates were highest between 15 to 40 years of age for all types of IBD. Besides disease location, the phenotypic presentation was consistent between the first and last four years of investigated cases.

**Conclusions:** Annual IBD incidence in the Otago region is high compared to the rest of the world but less than in other NZ regions. There has been a slight but non-significant increase in incidence over the past 18 years. There have been minimal changes in phenotypic presentation of the diseases over the past 18 years.
Deep mural injury and perforation associated with colonic endoscopic mucosal resection: classification, risk factors, management and outcomes

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**Aims:** Perforation is the most serious complication associated with Wide Field Endoscopic Mucosal Resection (WF-EMR) of large colonic lesions. We aimed to describe the spectrum of deep mural injury (DMI) following WF-EMR, determine associated patient and procedural factors, propose a classification system and examine clinical outcomes in relation to this system.

**Methods:** Prospective data for WF-EMR of colorectal sessile polyps $\geq 20$ mm (Feb 2010-July 2013) were analysed. Case notes and a comprehensive standardised photographic record were reviewed to confirm and further characterise DMI syndromes. A DMI classification score was proposed (Fig 1)

**Results:** WF-EMR was performed on 714 lesions (mean size 38.5mm, proximal colon 53.3%) in 625 patients (mean age 66.8 years). DMI features were identified in 57 patients (9.1%). Intraprocedural perforation occurred in 0.6%. A clinically significant perforation occurred in 1 patient. 86% of patients had same-day discharge, all without sequelae

On multivariable analysis, DMI types 3-5 were strongly associated with transverse colon location (OR 5.8 p.005), lesions with high-grade dysplasia (HGD) or submucosal invasive cancer (SMIC) (OR 3.6, p.008) and en-bloc excision (OR 2.9, p.029 95%CI 1.13-8.68)

**Conclusion:** After WF-EMR, DMI features are found in 9.1%. DMI is strongly associated with transverse colon location, HGD or SMIC and en-bloc excision. Defect classification guides the management of patients with DMI. The majority of patients can be safely discharged the same day.

![Sydney Classification of Deep Mural Injury (DMI) following WF-EMR](image)

Exclusive enteral nutrition and reintroduction of solid food affect faecal microbiota composition: results of a pilot study

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Support received from Laurenson Fund and New Zealand Society of Gastroenterology

**Aims:** Dietary intake is known to affect faecal microbiota composition. Individuals have a microbiota with distinct compositions. The aim of this study was to document faecal microbiota changes during 8 weeks of exclusive enteral nutrition (EEN) and upon reintroduction of solid food in a group of patients with active Crohn’s disease.
Methods: Patients aged 16 – 40 years old with newly diagnosed ileal or ileocolonic Crohn’s disease were recruited to undertake eight weeks of EEN. Stool samples were collected at weeks 0, 2, 4, 6, 8, 12 and 26. Faecal microbiota composition was analysed using 16S rRNA gene sequencing.

Results: The faecal microorganisms of 6 patients were analysed. The patients had microorganisms of unique bacterial compositions which changed while on EEN and again on reintroduction of solid food. The faecal microbiota of patients was grouped according to “community type”, at baseline four of the six patients had community type C whereas at week 8 all patients had community type C: absence of Prevotella, low abundance of Bacteroides and higher abundance of Faecalibacterium and Ruminococcaceae. Upon reintroduction of solid food, the faecal microbiota composition changed to a similar, but not identical, pattern to that seen at baseline. Despite individual microorganisms, bacterial species characteristic of EEN or solid food consumption were detected.

Conclusions: Based on the results of our pilot study faecal microbiota composition changed while on EEN and again on reintroduction to solid food but does not revert to original structure. Further research is required to ascertain the clinical significance of such changes.

Factors associated with adverse outcomes of endoscopically excised malignant colorectal polyps

Sekra A, Ryniker E, Ogra R

Background and Aims: Management of patients following endoscopic excision of malignant colorectal polyps is debated. It is unclear whether they should have surgery or endoscopic surveillance. We aimed to assess factors associated with adverse outcomes of these polyps. Adverse outcomes were defined as endoscopic recurrence of cancer, cancer or nodal metastases in surgical specimen; or distant metastases on follow up.

Methods: Prospective database of endoscopically excised malignant polyps is maintained. Case notes were retrospectively reviewed.

Results: Complete data was available on 55 patients. Median age 73 years (range 46-90), 32/55 females.

26/55 proceeded to surgery. Surgical specimen of 10/26 with endoscopically negative margins showed no residual cancer. One had nodal metastases. This patient had lymphovascular invasion (LVI) on initial histology. Surgical specimen of remaining 16 with endoscopically positive margins showed cancer in 6/16. 2/16 had nodal metastases and 1/16 had distant metastases despite no cancer in surgical specimen. 7/26 died of unrelated cause with no recurrence after median follow up of 62 months. Remaining 9/26 had no recurrence after median follow up of 66 months.

29/55 did not have surgery. 22/29 had negative margins endoscopically. 1/29 had endoscopic recurrence after 6 months. This patient had positive margins endoscopically. 7/29 died of unrelated cause with no recurrence after median follow up of 45 months. Remaining 21 had no recurrence after median follow up of 78 months (range 4-133).

11/55 polyps had adverse outcomes. 8/11 had endoscopically positive margins (p=0.003), 1/11 had LVI (p=0.002), and 2/11 had both.

Conclusions: Factors associated with adverse outcomes of endoscopically excised malignant polyps are positive margins and LVI. These patients should undergo surgery. Patients who do not have these risk factors can be surveyed endoscopically.
Colonoids – a model of the colonic epithelium in IBD?

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**Aims:** Increased permeability may contribute to the pathogenesis of Inflammatory Bowel Disease (IBD), but inflammation also increases intestinal permeability. Therefore, whether the permeability changes in IBD are a cause or consequence of inflammation is unknown. In vivo, the influence of the microbiota and immune system prevent investigation of the intrinsic details of the epithelium. Therefore, the development of colonic organoids was characterised to determine their suitability as a model to investigate the inherent properties of the intestinal epithelium.

**Methods:** Organoids were grown from crypts isolated from transverse colonic biopsies from healthy and IBD patients and grown in Matrigel plus stem cell media. Organoid structure was determined by light and electron microscopy, transcript levels of tight junction (TJ) proteins by qPCR, and quantification and localization of TJ proteins by immunoblotting and immunofluorescent microscopy. Statistical significance was determined by unpaired Student’s t-test.

**Results:** After 4d only thin walled colonospheres were present, whereas after 15d colonospheres and thick walled colonoids were present. Colonospheres had an undifferentiated epithelium, whereas the colonoids had a well-developed polarised columnar epithelium, linked by TJs and consisting entirely of colonocytes without goblet cells. Despite the absence of polarisation, TJs were evident in colonospheres and the transcript levels of the TJ proteins, occludin, claudin-1-4, 7 and ZO-1, ZO-2, in colonospheres were not different from those in colonoids (n=6). Consistent with this there was no significant difference in the expression of occludin, ZO-1 and claudin-2 in colonospheres and colonoids. Furthermore, in both the colonoids and colonospheres there was punctate staining of occludin and ZO-1 localized to the apical pole of the epithelial cells (n=3). Similar results were obtained from IBD patients (n=3).

**Conclusion:** Spontaneously maturing colonoids provide a colonocyte model, but their use in investigating the effects of IBD on the colonic epithelium maybe limited by the absence of goblet cells.

Supported by a University of Otago Research Grant and Grants from the Dean’s Fund, Otago School of Medical Sciences and the Department of Physiology.

NKp30+ natural killer cells have enhanced cytotoxicity that protects blood transfusion recipients from acquiring hepatitis C infection

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We recently identified a rare cohort of individuals who received hepatitis C (HCV)-contaminated blood products but did not become infected. Protection from HCV infection has been described in injecting drug users but not in transfusion recipients.

**Methods:** Recipients of HCV-infected blood pre-1991 were identified from the English Lookback programme. Eight exposed but uninfected recipients (EUs) who tested negative for anti-HCV and HCV RNA following exposure to blood products from an HCV-positive donor were identified. We examined innate and adaptive responses in the 8 EUs and compared them with 10 healthy controls, 10 spontaneous resolvers and 10 chronic HCV patients.

**Results:** Of 1340 cases who received HCV-infected blood, we identified 8 who had verified exposure without developing infection. Five of the 8 EUs received blood from donors who transmitted HCV to at least 2 other recipients, one transfused before and one after the EU subject. In the other 3 EUs, each
received blood products from single donations that were split into different components and transfused to others who became infected.

EUs had higher percentages of circulating NK cells than healthy controls and those with chronic infection \((p<0.01)\). NK cells of EUs expressed higher levels of the activating receptor KIR2DL3 relative to other groups \((p<0.05)\). Expression of killer immunoglobulin-like receptor KIR2DL3 was also increased on CD56\(^{bright}\) NK cells of EUs relative to other groups \((p<0.05)\).

NK cells of EUs had enhanced cytotoxicity relative to healthy controls and chronically infected patients \((p<0.05)\). Cytotoxicity was correlated with the expression of NKp30 \((p=0.02)\). T cell responses to HCV antigens were minimal in EUs.

**Conclusion:** Protection from HCV infection is rare following transfusion-related exposure. NK cells of EUs are readily activated with increased NKp30 and enhanced cytotoxicity. T cell responses did not play a significant role. Innate immunity is key to conferring protection from HCV infection.

**Ethnic disparity in incidence and outcome of biliary atresia in New Zealand children**

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**Background:** Biliary atresia (BA) is the commonest liver disease in infancy. Incidence in Europe and North America is approximately 1/20,000 live births but commoner in Taiwan (1/8000) and French Polynesia (1/3000). Corrective Kasai portoenterostomy can prevent or delay the need for liver transplantation (LT) but is most successful if performed before 6-8 weeks of age.

**Aim & methods:** To investigate the incidence of BA in children presenting to Starship Hospital 2002-2013 using casenote review and comparison to Statistics New Zealand birth rate data for Auckland-born children. Ethnicity was recorded according to parental report. Outcomes for Kasai success (bilirubin < 20 mmol/L by 6 months), need for liver transplantation and overall survival were calculated overall and according to ethnicity.

**Results:** 75 children (36M; 39F) presented with BA. Ethnicity was European in 25 (33%), Maori in 31 (41%), Pacific in 12 (16%), South East Asian in 4 (5%) and Other in 3. Overall incidence was 1/8,002 but 1/17,893 for European babies and 1/5,430 for Maori children. Maori babies presented earlier than European babies (median 31 days versus 46 days), were more likely to have a successful outcome following Kasai (62% successful versus 20%) and proceeded to LT later (4.8 years compared to 0.8 years). Need for LT was high overall with transplant-free survival being 70%, 49% and 30% at 1, 2 and 5 years of age respectively but overall survival was 92%, 87% and 86% at these timepoints.

**Conclusions:** BA is commoner in New Zealand likely due to an excess incidence in Maori children who have better outcomes related to earlier presentation and operation. It is important that Maori infants with prolonged jaundice are promptly investigated for BA.

*Hayley Wong received a Summer Studentship from the University of Auckland for her participation in this project*
Rising incidence of hepatitis C-related hepatocellular carcinoma and impact of surveillance

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Aims: To determine rates of hepatocellular carcinoma (HCC) in patients with chronic hepatitis C (HCV) and impact of regular surveillance on treatment outcomes and overall survival.

Methods: A retrospective analysis of all HCC patients referred to NZLTU from 1999-2014.

Results: 1326 new HCCs were diagnosed, of whom 286 were HCV-related. Number of HCV-HCCs increased from 1/27 (3.7%) in 1999 to 47/183 (25.7%) in 2013. 126 (44.06%) HCV-related HCCs were detected by surveillance whilst remaining 160 (55.94%) were diagnosed incidentally or following onset of symptoms. Of 160 symptomatic or incidentally picked up cases, 31 were not known to have prior diagnosis of HCV, 76 were diagnosed with HCV and known to have cirrhosis but lost to follow-up and 53 were diagnosed with HCV but thought to be non-cirrhotic. Of the 53 non-cirrhotic patients, 35 never underwent staging with either biopsy or a fibroscan. At most recent staging of remaining patients 6/18 had severe fibrosis (F3 or LSM>9.5 kPa), 8/18 had moderate fibrosis (F2 or LSM>7.1 kPa) and 4/18 had mild fibrosis (F0/F1 or LSM<7.1 kPa).

At time of detection, 101/126 (80.1%) screen-detected HCCs were suitable for curative interventions compared to 63/160 (39.3%) not detected through screening.

Conclusions: HCV has become the leading cause of HCC in New Zealand. Unfortunately, more than half HCCs are only diagnosed following onset of symptoms or incidentally, when advanced stage precludes curative intervention and reduces survival. More frequent staging with a liver biopsy or fibroscan is needed with regular surveillance in all HCV cirrhotic patients.

Survival from diagnosis

![](image)

p<0.0001 (Log-rank)
Hepatitis B e-Antigen (HBeAg) loss with antiviral therapy in South Auckland population: a large retrospective analysis

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New Zealand Liver Transplant Unit, Auckland City Hospital, Auckland

Background and aim: HBeAg loss and the development of Anti-HBe antibodies (seroconversion) is an important event during the course of chronic hepatitis B virus (HBV) infection. Loss of HBeAg is typically associated with a sustained fall in viral load and resolution of hepatic inflammation. HBeAg seroconversion rates after one year of anti-viral therapy have been reported in 12% to 21%. We aimed to assess HBeAg seroconversion rates in the South Auckland population.

Methods: A prospective database of all the patients with chronic HBV infection has been maintained since 1998. Data on patients who were HBeAg positive at baseline were obtained retrospectively for this audit.

Results: We identified 597 patients with positive HBeAg serology. HBeAg loss was detected in 328/597 (55%) patients after median follow-up of seven years. 235 (72%) of those who had HBeAg loss had raised ALT and received anti-viral treatment. Median time to HBeAg loss was 9 months in this group. 80/235 discontinued anti-viral therapy after median of 2 years following HBeAg loss. 77 (96%) remain HBeAg negative off therapy after median follow up of 6 years. 69/80 patients had follow up HBV DNA levels and all were <2000 IU/ml.

93/328 (28%) with normal ALT had spontaneous HBeAg loss with median time to HBeAg loss of 13 months. 83/93 (89%) remain HBeAg negative after median follow up of 6 years.

Conclusion: HBeAg relapse rates are low with or without treatment. Patients who have sustained HBeAg loss on antiviral therapy for two years can be considered for cessation of anti-viral therapy.

Tumour secretion of integrated hepatitis B surface antigen post transplant: case series

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Department of Anatomical Pathology, Auckland City Hospital

Aims: Prior to highly effective antiviral prophylaxis, reappearance of serum Hepatitis B surface antigen (HBsAg) following liver transplantation for HBV was often accompanied by recurrence of hepatocellular carcinoma (HCC) suggesting that HCC recurrence is a direct consequence of HBV reinfection. This hypothesis is challenged by recent observations that HBV DNA remains undetectable in serum.

Methods: At NZLTU, 55/478 adult liver transplants were performed for HBV-related HCC, of whom 6 developed recurrent HCC. In 4 cases, HCC recurrence was accompanied by reappearance of HBsAg in serum without detectable HBV DNA. These cases have been studied in detail.

Results: The first 2 cases presented >6 years posttransplant with symptomatic advanced tumour and both died within 3 months. The remaining 2 cases presented <3 years with palpable subcutaneous masses, reflecting pretransplant seeding at the site of percutaneous procedures (needle track from a diagnostic biopsy and laparoscopic RFA). Both were treated with local resection and switch to sirolimus. Serum HBsAg disappeared following resection. The recent patient, the excised tumour stained positive for HBsAg. Molecular studies are ongoing to determine whether tumour tissue...
contains the HBs gene, closed circular (ccc) DNA, HBV replicative intermediates, HBsAg mRNA and integrated HBsAg DNA.

**Conclusions:** This case series demonstrates for the first time that the reappearance of HBsAg in serum following recurrence of HBV-related HCC is not due to recurrent HBV infection. Rather, this reflects expression of HBs protein from transcription of integrated HBs gene within tumour tissue. This observation may help improve tumour surveillance post-liver transplantation for HBV related HCC.

![Image of cytoplasmic Orcein positivity in a perinuclear location within tumour cells, consistent with HBsAg production.](http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2015/vol-128-no-1408/6424)

**Fig 1:** Cytoplasmic Orcein positivity in a perinuclear location within tumour cells, consistent with HBsAg production

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**Growth, body composition & bone density post paediatric liver transplant**

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^ University of Auckland, Faculty of Medical & Health Sciences

*Research grant obtained from the New Zealand Society of Gastroenterology*

**Aims:** Cholestatic liver disease and consequent liver failure is the most common indicator for paediatric liver transplant (LT). These patients are often vitamin deficient & malnourished pre-transplant, with significant corticosteroid exposure post-transplant. There are no long-term studies assessing bone acquisition post-transplant. There is also increasing evidence of obesity and metabolic syndrome post-LT. Our study aimed to assess growth, body composition and bone density in patients post-paediatric LT.

**Methods:** Body composition and bone densitometry scans were performed on 21 patients (12 male). Pre and post-transplant anthropometric data were analysed on all patients. Physiological bone health was assessed using serum alkaline phosphatase, calcium, phosphate & procollagen-I N-peptide levels. Median age at transplant and at this assessment was 2.7 and 10.6 years respectively. Indications for LT included cholestatic liver disease (16/21), acute liver failure (3/21), paracetamol overdose (1/21) & metabolic disorders (1/21).

**Results:** Physiological markers of bone health were normal in all patients. 2 patients (transplanted for ALF) had reduced bone density; 19 were normal.
### Anthropometrics

<table>
<thead>
<tr>
<th>Metric</th>
<th>Pre-transplant median z-score (range)</th>
<th>Post-transplant median z-score (range)</th>
<th>Delta Median (range)</th>
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<tbody>
<tr>
<td>Weight</td>
<td>0.6 (-0.52 to 2.17)</td>
<td>0.58 (-1.53 to 2.68)</td>
<td>-0.28 (-1.76 to 2.01)</td>
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<tr>
<td>Height</td>
<td>-0.85 (-3.62 to 2.81)</td>
<td>0.09 (-2.01 to 1.95)</td>
<td>0.87 (-2.35 to 3.71)</td>
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<tr>
<td>Body Mass Index</td>
<td>1.8 (-0.19 to 3.93)</td>
<td>0.76 (-0.76 to 3.08)</td>
<td>-0.53 (-3.25 to 2.03)</td>
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### Total Body Fat % Post-transplant

<table>
<thead>
<tr>
<th>Category</th>
<th>Number (percentage)</th>
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<tbody>
<tr>
<td>Underweight (&lt;2nd centile)</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Normal (2nd – 85th centile)</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Overweight (&gt;85th centile)</td>
<td>5 (23.1)</td>
</tr>
<tr>
<td>obese (&gt;98th centile)</td>
<td>6 (28.6)</td>
</tr>
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</table>

### Conclusions:
Bone density is preserved post paediatric LT despite significant corticosteroid exposure, with good catch-up growth, particularly height, which is reassuring. However, 11/21 patients (52%) were either overweight or obese post-transplant potentially placing them at an increased risk of developing metabolic syndrome and its sequelae in later life. Further studies are required to corroborate these findings.

### Association of NOD2 mutations with disease phenotype in an Otago cohort of patients with Crohn’s disease

**Lim MH**, Phipps-Green M², Merriman T³, Schultz M¹,³

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**Background:** The presence of NOD2 mutations in patients with Crohn’s disease (CD) has been associated with a younger age of disease onset, ileal involvement and stricturing/penetrating disease as well as surgery.

**Aim:** To document the NOD2 prevalence and analyse the association with phenotypic characteristics.

**Methods:** CD patients in Otago were prospectively recruited between 01.03 – 31.05.2014. Blood (10mL) was collected from each patient for DNA extraction and genotyping for the three most common NOD2 mutations i.e. R702W (rs2066844), G908R (rs2066845) and 1007fs (rs2066847) using Taqman PCR. Phenotypic data was obtained retrospectively using paper and electronic medical records. Patients were phenotyped according to the Montreal classification. Disease severity was judged according to prescription of immunomodulators and surgery.

**Results:** 71 CD patients (34 female) were recruited, mean age of diagnosis was 32 years (range 2-73). 64 patients (90%) had immunomodulators prescribed and 37 patients (52%) had surgery. 12 patients (17%) were NOD2 positive (11 simple heterozygotes, 1 compound heterozygote). Allelic frequencies for R702W and G908R were 0.063 and 0.028 respectively. None of the patients had the 1007fs mutation. Mean age of diagnosis was significantly younger for CD patients with NOD2 mutations (26 versus 34 years old, p=0.003). There was no statistically significant difference between NOD2 positive and negative groups for more severe outcomes although there was a trend towards...
stricturing/penetrating disease (67% versus 51%, p=0.16) and having had bowel resection (58% versus 37%, p=0.11) for NOD2 positive CD patients. There was no difference in immunomodulator prescription between the two groups.

Conclusion: Allelic frequencies for R702W and G908R were comparable with previous NOD2 studies in New Zealand. NOD2 positivity was associated with a younger age at diagnosis and a trend towards more complicated disease behaviour and patients having had bowel resection in our small cohort of CD patients.

Does computerised cognitive behavioural therapy help people with inflammatory bowel disease? A randomized controlled trial

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Background and Aims: Psychotherapy, especially cognitive behavioural therapy (CBT), may be a useful intervention for at least some inflammatory bowel disease (IBD) patients, especially those with psychiatric comorbidities. However, CBT can be financially and practically difficult to access. These difficulties can be overcome by computerised CBT (CCBT). This is a randomized controlled trial of a CCBT intervention for IBD patients. It is hypothesised that CCBT completers will have an improved health-related quality of life (HRQOL), anxiety, depression, stage of change, coping strategies, perceived stress, and IBD symptoms relative to people not allocated to the CCBT.

Methods: IBD patients were randomly allocated to CCBT (n=113) versus treatment as usual (TAU; n=86). Inflammatory bowel disease questionnaire (IBDQ) at twelve weeks after baseline was the primary outcome while generic HRQOL, anxiety, depression, stage of change, coping strategies, perceived stress, and IBD symptoms were the secondary outcomes. Outcomes were also measured at six months after baseline.

Results: Twenty-nine CCBT participants (25.7%) completed the CCBT. IBDQ was significantly increased at twelve weeks in CCBT completers compared to TAU patients (F=6.38, p=0.01). SF-12 mental (F=5.00, p=0.03) and the action stage of change (F=4.86, p=0.03) were also significantly better in CCBT compared to TAU patients at twelve weeks. These outcomes were no longer significant at six months after baseline.

Discussion: Improvements in IBDQ scores at twelve weeks after baseline were not maintained at six months. The high dropout rate from the CCBT was of concern and future research should aim to improve adherence rates.

New scoring systems on factors predictive of requirement for endoscopic therapy in patients presenting with upper gastrointestinal haemorrhage: a prospective study in Waikato Hospital

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Introduction: Endoscopic treatment of high-risk lesions reduces mortality in upper gastrointestinal haemorrhage (UGIH). The Rockall score and Blatchford score predict mortality and need for in-hospital treatment (transfusion, endoscopic or operative intervention inclusive) respectively.

New scoring systems have been derived to specifically predict requirement for endoscopic therapy (RET) in UIGH, assisting in triaging endoscopy.1
Aim: To validate the mentioned scoring systems in predicting RET.

Methods: Prospective data collection on all UGIH cases presenting to Waikato Hospital from 01/01/2014 to 31/05/2014. Patients with known cirrhosis or previous bleeding event(s) during study period were excluded. The scoring systems were applied (Simple Score: fresh haematemesis=2, fresh melaena=2, haemoglobin <130=2, urea >10=1, BP <100=1, male sex=1, history of peptic ulcer disease=1).

Results: 69 patients were identified, 47 were male, 19 were Maori, median age was 71 (range 21-97). 22 cases exhibited RET, rates were 11.8% (4/34) and 51.4% (18/35) for Simple Scores \( \leq 4 \) and \( >4 \) respectively. Lesions included 12 peptic ulcerations with stigmata of recent haemorrhage, 10 vascular lesions and no varices.

Conclusions: Interim results parallel with reported trend of requiring endoscopic intervention once Simple Score >4, longer period of study and external validation are warranted for statistical analysis.

1Irwin J, et al. *Frontline Gastroenterology* 2014;5:2-9

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An overview of upper gastrointestinal bleeding and assessment of referrals to endoscopy unit at BOP DHB

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Aims: Acute upper gastrointestinal bleeding (UGIB) is a common medical emergency with significant morbidity and mortality risks. In this audit, we assess our local cohort’s characteristics and referrals made by other services for urgent endoscopy.

Method: A prospective audit of all referrals made for urgent endoscopy between June and December 2013. Patients’ demographics, inpatient vs new admission, medications, comorbidities, Glasgow-Blatchford Score, time to endoscopy, diagnosis, endotherapy, length of stay, rebleed rate, transfusions and mortality were recorded. Referral forms were assessed for whether Glasgow-Blatchford Score, medications and blood results were fully documented by referring team.
Results: 95 cases were identified; 70.5% male, average age of 73.2 and 53.7% were already inpatients. 25.3%, 19%, 45.3% and 18.9% were on PPI, NSAIDs, anti platelets and anti coagulation treatment respectively. Peptic ulcer disease (PUD) was the commonest cause (33.7%) followed by gastritis, oesphagitis and variceal disease (8.4%, 8.4% and 3.2% respectively). Rebleeding was noted in 5.3% of which 80% were new admissions, had Glasgow score of >10 and had transfusions on admission. Overall, 22% of patients required endoscopic treatment and only 1 case required surgical intervention. Average time to endoscopy was 1.2 days; average length of stay was 10.2 days. Mortality rate of 6.3%; the majority were current inpatients.

Only 62.1%, 56.8%, 67.4% and 39% of referrals had Glasgow-Blatchford score, blood results, patients’ medications and a coagulation screen documented respectively.

Conclusion: UGIB remains a common condition with relatively high mortality and significant length of stay especially amongst inpatients. Our data correlates with international studies e.g. BSG audit of UGIB in 2011. Poor information on referral forms limits proper triaging of urgent endoscopies.

High dose vitamin D therapy in children with IBD is effective and safe

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Aims: Vitamin D deficiency is commonly seen in children with IBD. Intermittent high dose (STOSS) therapy has not previously been evaluated in paediatric IBD. This retrospective study aimed to assess the impact of STOSS therapy upon vitamin D status and disease activity.

Methods: The records of children with IBD were reviewed to determine those with Vitamin D deficiency managed with STOSS therapy. Children were administered up to 800,000 units of Vitamin D as a single dosage according to an age based protocol. The background characteristics of the children, response to therapy, side-effects and requirement for repeated dosing were reviewed. Disease activity was also noted.

Results: 76 children with IBD were identified to have had a total of 99 STOSS treatments (22 children had more than one course) with no toxicity noted. Mean 25-OHD levels were 40.8 (7.5) nmol/L at baseline, rising to 145.6 (51.8) nmol/L 1 month following STOSS therapy. All subjects had a 25-OHD level greater than 50nmol/L at 1 month, whilst this level was seen in 96.6% at 3 months and 76.4% at 6 months. Paediatric Crohn disease activity index (PCDAI) scores reduced from a mean of 10 [0-47.5] to 2.5 [0-85] after 6 months (p=0.0013). Albumin and haemoglobin levels also improved.

Conclusions: Single high-dose therapy for children with IBD effectively and safely corrects vitamin D deficiency in children with IBD. Clarification of dosage and timing for scheduled repeat dosing requires further evaluation. Optimised vitamin D status may be associated with better disease control: further prospective studies are required.
Evolving endoscopic management options for symptomatic stenosis (SS) post-laparoscopic sleeve gastrectomy (LSG) for morbid obesity: CMDHB experience

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Background and Aims: SS is an increasingly recognised complication following LSG to treat obesity with a reported prevalence between 0.1 and 3.9%. There are no clear guidelines on management of this. We aimed to determine the prevalence and management options for SS after LSG.

Methods: A total of 857 patients underwent LSG at CMDHB between May 2008 and June 2013. All cases referred for management of SS after LSG were recorded.

Results: SS developed in 26/857 (3.03%) following LSG confirmed by barium swallow. 3/26 patients developed a fixed stenosis in proximal stomach. These were all successfully treated by one dilatation of controlled radial expansion (CRE) balloon of <20 mm. 23/26 had a fixed stenosis at incisura angularis. 7/23 had short strictures (<3cm). 6/7 were successfully dilated by a CRE balloon and one improved after 30mm achalasia balloon dilatation. 16/23 had long strictures (>3cm). 9/16 were initially dilated with CRE balloon with symptomatic improvement noted only in 1 patient. Out of remaining 8 symptomatic patients, 6 were successfully dilated with achalasia balloon and 2/8 had self-expandable metal stent (SEMS) with resolution of symptoms. CRE balloon failure with long strictures was 89% (p<0.002). 7/16 were dilated with 30mm achalasia balloon directly with symptomatic improvement in 5/7 patients. Remaining 2 had temporary SEMS with resolution of symptoms. None of the 26 patients required a surgical procedure to correct their stenosis.

Conclusions: Use of a 30mm achalasia balloon and SEMS is an effective and safe treatment for patients with SS post-LSG who do not respond to standard dilatation. Achalasia balloon could be the first-line treatment in patients with longer stricture (>3cm) at the incisura angularis.

The cytological diagnostic yield of endoscopic ultrasound (EUS)-guided fine needle aspiration/biopsy (FNA/B)

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Aims: To determine cytological diagnostic yield (CDY) of EUS-FNA/B and compare to International Standards.

Methods: Retrospective analysis of pathology and endoscopy databases of all EUS FNA/B cases 2008-2014 was performed. Data collected included: site of lesion, endosonographic diagnosis, needle used, number of passes, and final histological diagnosis. Where available and relevant, data referring to corresponding radiology, tumour markers, and follow up was obtained.

Results: 218 EUS-FNA/Bs were undertaken (110 male, 108 female). The mean age of patients was 62.8 years (range 25-88). 170 EUS-FNA/Bs were of solid lesions; 48 were of pancreatic cysts. Needle gauges were 19, 22 or 25. The mean number of passes was 3 (range 1-8).

Figure 1 below shows the breakdown of EUS FNA/Bs by site, positive CDY as well as malignant diagnosis.
For solid lesions, 53.5% of all diagnoses were malignant. 17.1% were inconclusive, non-diagnostic, non-specific, or morphologic cytological descriptions only. 0.6% were insufficient, with no histology available for 1.2%. Overall, the positive CDY was 80%.

CDY for major lesion groups were: mediastinal lymph nodes 91%, pancreatic cysts 27%, solid pancreatic lesions 80%, left adrenal lesions 83%.

Conclusions: This data is in keeping with the limited published series from major international EUS centres. It is also above the standards of Quality Performance Indicators for EUS upheld by the ASGE and JAG, and proposed for New Zealand.

Increased colorectal cancer risks during follow up in patients with serrated polyposis syndrome (SPS): a single centre study

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Background and aims: Patients with SPS follow an accelerated pathway to develop colorectal cancer (CRC). The optimal surveillance interval for colonoscopy is still debated. We aimed to review our patients with SPS and timing of development of interval CRC.

Methods: A prospective database of all patients with SPS was maintained and reviewed retrospectively. Endoscopy and histopathology reports were collected to evaluate frequency of endoscopic surveillance and to obtain information regarding polyp and presence of CRC.

Results: In 40 patients with SPS, 1398 polyps were identified during a median follow up of 1.5 years. The median duration of surveillance colonoscopy was 19.6 months. In 13 (32.5%) patients CRC was detected of which 8 (20%) at index colonoscopy. CRC was detected during surveillance in 5 patients (cumulative incidence: 12.5%) after a median follow up of 10 years and a median surveillance colonoscopy interval of 5 years. The cumulative risk of CRC under surveillance was 7.5% at 5 years. An increasing number of sessile serrated polyps (SSP) (OR 3.79, 95% CI 1.6-9.2; p=0.001) was significantly associated with CRC presence. Increasing number of proximal SSP (OR 1.73, 95% CI 1.05-2.97, p=0.01) was significantly associated with interval CRC development.

Conclusions: SPS patients have risk of developing interval CRC despite being on surveillance. Increasing number of proximal SSP is strongly associated with interval CRC development. The number of serrated adenomas is positively correlated with presence of CRC in SPS, thus supporting a “serrated pathway” to CRC. To prevent development of CRC adequate detection and excision of these polyps is important. If this is not feasible then surgical resection should be considered.

Association between obesity and colonic adenoma

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Study was supported by Nurturing Clinician Scientist and Khoo Pilot awards

Aims: Colon cancer is the number 1 cancer in Singapore with mortality rates comparable to the West. Colon carcinoma is related to obesity and physical inactivity. Regular exercise can reduce the likelihood of colon carcinoma. Epidemiological evidence supports an association between obesity & colon carcinoma. We seek to determine in a pilot study the relationship between colon adenoma status and obesity (as defined by Asian BMI of 27.5 or more) in a Singaporean cohort.
Methods: Consecutive outpatients aged 45-70 years scheduled for colonoscopy were prospectively interviewed by a trained research coordinator. Anthropometric measurements and detailed medical histories were obtained. Validated questionnaire (IPAQ) was administered to characterize their physical activity patterns. Colonoscopy findings were prospectively obtained. Standard statistical methods were used to determine the relationship between colonic adenoma and obesity.

Results: 121 patients were studied. 31 were excluded because of poor bowel preparation (Boston bowel preparation score of less than 6). 90 patients were analysed. 49 were males (54.4%) Median age was 57.5 years (range 46-69). 19 patients (21.1%) had colonic adenoma. Median BMI is 23.4 (range 18-37). 15.6% were obese.

The prevalence of adenoma in obese patients was non-significantly higher than in the non-obese (28.6% vs 19.6% p =0.34%).

Conclusion: The prevalence of colonic adenoma is associated with obesity status in a non-significant manner. Larger studies are needed to clarify the association.

Management of chronic pancreatitis at CMDHB: inter-rater agreement of management between surgeons and gastroenterologists and comparison with American Pancreatic Association (APA) guidelines

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Background and Aims: Chronic pancreatitis is an inflammatory condition resulting in impairment of exocrine and endocrine function. We aimed to analyse agreement of management between surgeons and gastroenterologists at CMDHB and compare adherence with APA guidelines.

Methods: Cases were identified retrospectively by searching clinical coding database for ICD-10 codes for chronic pancreatitis from 1/1/2008 to 31/12/2013. Their demographics, symptoms, and management strategies were recorded. Kappa coefficient was measured to express agreement of management between surgeons and gastroenterologists. Adherence to APA guidelines was calculated.

Results: 125 patients were identified. Mean age was 57 (range 25-98 years). 63% were male. 44/125 managed by gastroenterologists and 81/125 by surgeons. Results are summarised below.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>APA guidelines</th>
<th>Management at CMDHB</th>
<th>Adherence to APA guidelines</th>
<th>Kappa coefficient (agreement between surgeons and gastroenterologists)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Management</td>
<td>Tramadol should be first line opiate</td>
<td>37/58</td>
<td>64%</td>
<td>0.148 (poor)</td>
</tr>
<tr>
<td>a) Opiate use</td>
<td>0/58</td>
<td>0%</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>b) Gabapentin use</td>
<td>8/81</td>
<td>10%</td>
<td>0.39 (fair)</td>
<td></td>
</tr>
<tr>
<td>c) Pancreatic enzyme replacement therapy (PERT)</td>
<td>Should be used in patients who use opiates chronically Should not be used for pain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol cessation advise</td>
<td>For all with alcoholic pancreatitis</td>
<td>62/64</td>
<td>97%</td>
<td>-0.06(poor)</td>
</tr>
<tr>
<td>Smoking cessation advise</td>
<td>For all smokers</td>
<td>61/68</td>
<td>90%</td>
<td>0.01 (poor)</td>
</tr>
<tr>
<td>Steatorrhoea management</td>
<td>Not necessary Everyone should have it</td>
<td>14/19 had faecal testing</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>a) Stool fat measurement</td>
<td>10/19</td>
<td>52%</td>
<td>0.184 (poor)</td>
<td></td>
</tr>
<tr>
<td>b) PERT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dietician referral</td>
<td>Everyone should be referred</td>
<td>58/125</td>
<td>46%</td>
<td>0.248 (fair)</td>
</tr>
</tbody>
</table>
Conclusions: There was a significant discrepancy in the management of chronic pancreatitis at CMDHB and there was poor adherence to APA guidelines. There is a need for establishment of guidelines for standard and consistent care of these patients.