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Identification of single-nucleotide polymorphisms in inflammatory bowel disease patients on azathioprine therapy

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Background. Azathioprine is an immunosuppressant used in the treatment of inflammatory bowel disease (IBD). However, its side-effects have raised concern, as >20% of treated patients present with leukopenia or myelosuppression. Much of azathioprine's side-effect profile is linked to single-nucleotide polymorphisms (SNPs) in the thiopurine methyltransferase (*TPMT*) gene, which ensures the metabolism of azathioprine. Mutated *TPMT* alleles result in deficient *TPMT* levels which directly correlate to cytotoxicity when azathioprine is administered. *TPMT* SNP profiles of global populations have been studied, but little literature is available for the South African (SA) population. Azathioprine therapy is an affordable treatment for IBD, and while genetic testing is expensive, it outweighs the accumulation of hospitalisation and treatment costs associated with cytotoxicity. But is it essential to include 'early warning' SNP testing into common practice?

Methods. 40 patients with IBD and 40 controls were enrolled. After patient consent, 5 mL of blood was collected to determine the presence of *TPMT* allele SNP *3A, *3B or *3C using restriction fragment length polymorphism-polymerase chain reaction. Patient demographics, diagnosis, erythrocyte sedimentation rate, C-reactive protein and leucocyte counts prior to azathioprine dosing as well as 12 months post initial dosing were obtained.

Results. *TPMT* *3B/*3B was detected with statistical significance ($p < 0.001$) in 33/40 (82.5%) IBD patients, and *TPMT* 1/*3A was present in 7/40 patients (17.5%). Only 6 control patients presented as *TPMT* *3B/*3B.

Conclusion. A unique discovery of *TPMT* *3B/*3B was made that had not previously been detected in *TPMT* studies of any ancestry. This may be a result of the diverse and unique SA population. The *3B homozygosity was present in patients both with and without recorded azathioprine reactions. In future, the enzymatic effect of *TPMT* *3B/*3B should be studied in a larger sample size prior to recommending early warning SNP testing in IBD patients using azathioprine, as these results cannot be ignored.

Inflammatory bowel disease and HIV infection: Epidemiology and disease phenotype at a single centre in Cape Town

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Background. The development of new-onset inflammatory bowel disease (IBD) in patients with established HIV infection has been



reported. However, data evaluating the role of the CD4+ count in this scenario are scanty.

Objectives. To describe the characteristics of IBD in HIV-positive patients in order to determine the impact of HIV infection on IBD phenotype, severity and disease outcomes.

Methods. The study was a retrospective analysis of patients infected with HIV and diagnosed with *de novo* IBD in the gastroenterology unit at Groote Schuur Hospital, Cape Town, from January 2013 to May 2018.

Results. There were 63 patients who were HIV-positive with endoscopic and radiological features consistent with colitis; 14 (22.2%) subsequently had a confirmed histological diagnosis of IBD (Crohn's disease $n=2$, ulcerative colitis $n=10$ and IBD-unclassified $n=2$). The remainder had infectious colitis (cytomegalovirus, tuberculosis, *Clostridium difficile*) or colitis with features not typical for IBD or infection (nonspecific). Of the 14 IBD patients 78% were female, with a mean (standard deviation) age at IBD diagnosis of 36.5 (11) years. The median interval from HIV positivity to IBD diagnosis was 1.3 years (interquartile range 0.8 - 5), with a mean CD4+ count of 380 (269) cells/ μ L. Although the mean white cell count was within normal limits ($7.4 (0.82) \times 10^9/L$), the mean haemoglobin concentration (10.7 (2.3) g/dL) and albumin level (28.7 (10) g/L) were low and the mean C-reactive protein level was markedly elevated (61.6 (54.7) mg/L). On bivariate analysis the CD4+ count was not associated with the interval to diagnosis or severity of IBD. Eight of 14 patients were on antiretroviral therapy, 5 were treated with topical and oral 5-aminosalicylates, and 6 were treated with corticosteroids. Of the 2 patients with Crohn's disease, 1 required surgery and the second was treated with antibiotics. All but 3 of the patients responded well to medical treatment.

Conclusion. *De novo* IBD in HIV infection is becoming more common in clinical practice in our setting. The clinical features appear similar to those in immunocompetent patients. However, this phenomenon deserves further study in terms of characterising the clinical phenotype and understanding the underlying mechanisms.

Gastrointestinal common variable immunodeficiency presenting with symptomatic hypocalcaemia: A case report

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Background. Common variable immunodeficiency (CVID) is a rare form of immunodeficiency with protean clinical manifestations. We describe an unusual presentation of CVID.

Case report. A 17-year-old woman with primary amenorrhoea presented with symptomatic hypocalcaemia. She had experienced paraesthesia and carpopedal spasms over the past 3 months, associated with episodic watery diarrhoea. On examination, she had a body mass index of 17 kg/m² and classic signs of hypocalcaemia

(Trousseau and Chvostek signs). Laboratory investigations confirmed hypocalcaemia with appropriately elevated parathyroid hormone levels, vitamin D deficiency, hypomagnesaemia, hypophosphataemia and iron deficiency anaemia. Albumin, folate and vitamin B₁₂ levels were normal. Stool tests were negative for enteric pathogens and parasites. Serological tests for coeliac disease and HIV were negative. The most striking finding at upper endoscopy was that of multiple nodules carpeting the duodenal mucosa with no discernible areas of normal mucosa. Histology showed villous blunting and atrophy with eosinophilia in the lamina propria. Initial treatment included electrolyte replacement, anthelmintics, intravenous iron and a gluten-free diet trial without success after 3 months. Repeat endoscopy demonstrated persistence of duodenal mucosal nodularity and histology now revealed giardiasis. Further investigations confirmed profound pan-hypoglobulinaemia. Subsequent treatment included metronidazole followed by monthly immunoglobulin infusions, corticosteroids and introduction of azathioprine once clinical and biochemical improvement became apparent.

Discussion. CVID affecting the gastrointestinal tract has variable clinical presentations mimicking better-known conditions. Histology may be nonspecific, with giardiasis infestation being a frequent finding and a paucity of plasma cells as a distinguishing feature from coeliac disease. Immunoglobulin replacement does not appear to be effective in gastrointestinal CVID. Immunosuppressive agents and antibiotics for recurrent giardiasis appear to be the mainstay of treatment.

Conclusion. To the best of our knowledge, symptomatic hypocalcaemia as the initial presentation of CVID remains undescribed. This case highlights an unusual presentation and endoscopic features of a rare condition.

Primary sclerosing cholangitis in a cohort of South African patients with inflammatory bowel disease at Charlotte Maxeke Johannesburg Academic Hospital

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Background. Primary sclerosing cholangitis (PSC) is a cholestatic liver disease that has a strong association with inflammatory bowel disease (IBD). The presentation of PSC may vary in different populations and its phenotype can be different to that in patients with underlying IBD. There is a dearth of information on this topic from Africa and specifically in the black South African (SA) population.

Objectives. To describe the features of PSC subjects from a single centre in SA and compare subjects with PSC and PSC-IBD.

Methods. A retrospective chart review of subjects with PSC and/or IBD attending the gastroenterology clinic at Charlotte Maxeke Johannesburg Hospital from 1 January 2008 to 31 May 2014. A structured data sheet was used to record information and captured using Microsoft Excel and Statistical Product and Service Solutions for statistical analysis.

Results. 305 charts were reviewed and 69 subjects with PSC were identified. There was an almost equal distribution between females (51%) and males (49%). In females, the average age at diagnosis was marginally higher (42 years v. 39 years).

The majority of the cohort was black African (68%), the rest comprising whites (15%), Asians (13%) and coloureds (4%). Cirrhosis was significantly more common in the non-black African groups. There was an almost equal number of subjects with PSC alone (49%)

and PSC-IBD (51%). At presentation, 60% had features indicative of PSC, 26% had IBD and the remainder had features of PSC-IBD. Demographic, clinical and radiological findings were similar. A significantly higher rate of isolated common bile duct involvement was observed in the PSC group. Smoking conferred a protective effect against the development of PSC.

Conclusion. In our setting, black African subjects with PSC have a similar profile to previously described Western cohorts. This study supports the observations of other studies that colonic inflammation is important for PSC development, particularly with ulcerative colitis.

Age is a predictor of significant endoscopic findings in dyspepsia patients in South Africa

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Background. Dyspepsia is the commonest indication for endoscopy. Current American guidelines recommend that all dyspepsia patients aged ≥60 years undergo endoscopy to exclude significant pathology.

Objectives. To provide an epidemiological analysis of dyspepsia in the South African (SA) context and to determine whether age ≥60 is a predictor of significant endoscopic findings.

Methods. A retrospective chart review of 1 000 consecutive endoscopies done at Madadeni Provincial Hospital, KwaZulu-Natal, from 2014 to 2016 was performed. All patients with dyspepsia were identified and divided into age ≥60 and <60 cohorts. Demographic data, significant endoscopic findings (tumour, ulcer, stricture) and non-significant findings (gastritis, hiatus hernia, candidiasis, oesophagitis, normal) were recorded.

Results. Of the 1 000 endoscopies that were evaluated, 584 (58.4%) were done on patients who presented with dyspepsia. Among the 584 cases identified, the median age was 49 years (interquartile range 14 - 87). There were 142 males (24.4%) and 442 females (75.6%). There were 432 (74%) patients in the age <60 cohort and 152 (26%) in the age ≥60 cohort. In the age <60 cohort 6.7% (29/432) of patients had significant findings, in comparison with 17.1% (26/152) of patients in the age ≥60 cohort (odds ratio 2.8675, 95% confidence interval (CI) 1.6823 - 5.0498; *p*=0.0003). The overall prevalence of functional dyspepsia findings was 27.5% (*n*=161). There was a significantly higher percentage of functional dyspepsia in the <60 age group than in the ≥60 age group (31% v. 17.1%) (OR 2.2028, 95% CI 1.3786 - 3.5197; *p*=0.001).

Conclusion. Age ≥60 years is a predictor of significant endoscopic findings in dyspepsia patients in SA. We recommend that SA guidelines be amended to increase the age cut-off for endoscopy for dyspepsia from 45 years to ≥60 years.

Review: Direct-acting antiviral therapy for hepatitis C patients attending Tygerberg Hospital

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Background. The advent of direct-acting antiviral (DAA) therapy has changed the way we manage hepatitis C virus (HCV) infection, from a difficult-to-treat disease to a curable disease. Multiple

guidelines have been published describing various protocols in managing HCV infection using DAAs. Sofosbuvir, an NS5B protein inhibitor, in combination with ledipasvir, a viral NS5A inhibitor, has been successfully used to treat HCV at Tygerberg Hospital. We present the findings in a cohort of 10 patients who received DAA therapy at Tygerberg Hospital between 2016 and 2017.

Methods. A retrospective folder review of 10 patients commenced on DAAs was undertaken. We describe HCV genotype, patient demographics, HIV co-infection status and viral loads (pre and post treatment). Where possible, risk factors for obtaining HCV were noted and described.

Results. All 10 patients were virally suppressed after undergoing 12 weeks of treatment. 50% of our patients were of mixed ancestry, and the mean age was 47 years. The male-to-female ratio was equally distributed. Three of the patients in our cohort were co-infected with HIV and had already started antiretroviral therapy for HIV infection prior to being started on DAA therapy. The genotypes found on testing were 1a, 1b, 3a, 4a and 5a, with genotype 1a being the most common (40%). Viral loads taken at 12 weeks post DAA completion confirmed that 100% of our patients were virally suppressed.

Conclusion. DAA therapy for HCV patients, although costly, is an effective treatment with few side-effects. It is well tolerated, with a short duration of treatment. While sofosbuvir/ledipasvir is not considered a pan-genomic DAA, and is used for the treatment of genotype 1, our results have shown that it can be successfully used to treat other HCV genotypes. We conclude that with the advent of DAA therapy, HCV cure is now a reality.

Peroral endoscopic speaking valve insertion: A novel endoscopic approach

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Background. Many techniques for secondary puncture procedures for voice restoration have been described in the literature. Voice restoration is an important clinical outcome for patients undergoing curative total laryngectomy for laryngeal carcinoma. The gold standard in achieving voice restoration post laryngectomy is via insertion of a speaking valve prosthesis, thereby facilitating tracheo-oesophageal speech. The majority of patients undergo a primary procedure at which a speaking valve is inserted at the time of laryngectomy. Occasionally, a secondary (or delayed) procedure is performed in patients who require pharyngeal reconstruction via a free flap (jejunal or tubed anterior lateral thigh flap) or in cases where the tracheo-oesophageal fistula created at laryngectomy closes spontaneously.

Objectives. To assess the efficacy of a novel approach to perform a secondary speaking valve puncture in laryngectomy patients using a gastroscop, under conscious sedation.

Methods. We describe a series of four patients who have undergone a secondary procedure for voice prosthesis (Provox Vega) insertion post laryngectomy by means of peroral endoscopic speaking valve insertion (PESVI) under conscious sedation with local anaesthesia.

Results. Four patients were included in the study. One patient underwent two failed attempts at speaking valve insertion using the conventional approach of rigid oesophagoscopy under general anaesthesia. Three of the four patients had jejunal interposition procedures at the time of laryngectomy. All patients had successful

phonation within hours of speaking valve insertion. There were no immediate complications following the procedure and patients were discharged on the same day.

Conclusion. To the best of our knowledge, the procedure described has not previously been reported in the literature. Our experience performing PESVI has shown that voice restoration can be achieved safely as an outpatient procedure, with an additional cost-savings benefit.

Tuberculous peripancreatic mass in a patient with inflammatory bowel disease

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Background. Owing to the high prevalence of tuberculosis (TB) in South Africa, clinicians should consider this condition in atypical presentations. We describe an unusual presentation of TB in a patient with inflammatory bowel disease (IBD) and highlight the role of endoscopic ultrasound (EUS) in establishing a definitive diagnosis.

Case report. A 23-year-old man with ulcerative colitis maintained on sulphasalazine since 2013 developed a perianal abscess and fistula in 2015. There was a satisfactory response to drainage and setons. In 2017, he reported recurrent fistula drainage, weight loss and a febrile episode. Endoscopic findings were indeterminate for ulcerative or Crohn's colitis. Computed tomography (CT) enterography revealed a multiloculated cystic mass in the region of the pancreatic head, small (<1 cm) para-aortic lymph nodes and no features of Crohn's disease. A chest radiograph was normal. Linear EUS showed a mixed echogenic 3 cm mass adjacent to the pancreatic head. EUS-guided fine-needle aspiration (FNA) obtained caseous material. Cytology showed no malignant cells and no acid-fast bacilli. Cultures were positive for drug-sensitive TB. A repeat CT scan after 9 months of anti-TB therapy confirmed resolution of the mass. During this period, the patient reported weight gain, fistula healing and a reduction in stool frequency. Subsequent colonoscopy and histology revealed mild ulcerative colitis, and the patient remained on sulphasalazine maintenance therapy.

Discussion. TB may develop in patients with IBD even in the absence of immunosuppressive therapy. An isolated peripancreatic or pancreatic mass is a rare presentation of TB. EUS-guided FNA is a minimally invasive procedure that may distinguish TB from neoplastic intra-abdominal masses. In TB-endemic regions, samples must be prepared for microbiology tests and cytology.

Conclusion. This case highlights the importance of EUS-guided FNA as a modality for establishing the diagnosis of a peripancreatic tuberculous mass.

Difference in the prevalence of clarithromycin-resistant *Helicobacter pylori* strains in public and private hospital settings in Johannesburg

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Background. The prevalence of *Helicobacter pylori* infections may differ between the public and private healthcare sectors.

Clarithromycin resistance in *H. pylori* has not been described in these two settings in Johannesburg. The polymerase chain reaction (PCR) has an advantage compared with culture for the detection of *H. pylori* and can detect clarithromycin resistance.

Objectives. To study *H. pylori* prevalence and clarithromycin resistance in two cohorts, one from Mediclinic Morningside (MM) and one from Chris Hani Baragwanath Academic Hospital (CHBAH).

Methods. A total of 167 gastric samples were collected, 131 (78.4%) from MM and 36 (21.6%) from CHBAH. These samples were submitted for routine histology and culture and were subjected to Amplidiag *H. pylori*+ClariR (Mobidiag, Finland), a commercial PCR.

Results. *H. pylori* was detected in 24/131 (18%) of gastric samples from MM, and 17/24 (70.8%) were clarithromycin resistant. In contrast, it was detected in 22/36 (61%) of gastric biopsies from CHBAH, and 3/22 (13.6%) were clarithromycin resistant.

Conclusion. Despite the lower detection rate of *H. pylori* infection at MM, clarithromycin resistance rates were high. Possible contributing factors to the higher resistance rate include previous antibiotic exposure and strain variation. At MM, *H. pylori* clarithromycin susceptibility testing should be performed before including the drug in an antibiotic regimen. PCR is an improvement on culture testing for *H. pylori*. Further studies are needed to explore regional differences in susceptibility.

Wilson's disease: A case series at a transplant unit

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Background. Wilson's disease is a rare autosomal recessive condition affecting copper metabolism. The most common clinical presentations are liver disease, including fulminant hepatitis, and neuropsychiatric manifestations. There are no typical or diagnostic presentations.

Methods. We retrospectively reviewed the records of patients with a diagnosis of Wilson's disease at the Wits Donald Gordon Medical Centre liver clinic between 2012 and 2017.

Results. A total of 11 patients were identified, 7 males and 4 females; 4 were white, 3 Indian, 3 black and 1 coloured. Their ages ranged from 7 to 59 years. *Clinical presentation:* All 11 patients had hepatic involvement, 5 had neuropsychiatric symptoms, 5 had Coombs-negative haemolysis and 6 had confirmed Kayser-Fleischer rings. *Investigations:* 7 patients had a serum copper test, with 4/7 below the reference range; 6 patients underwent 24-hour urine copper measurement, with 6/6 elevated; 2 patients had elevated quantitative liver copper; 10 patients had a low serum caeruloplasmin level; and 8 patients had a magnetic resonance imaging scan, with 4/8 showing radiological features in keeping with Wilson's disease. Interestingly, only 7 patients had a Leipzig score of ≥ 4 . A further 4 patients fulfilled criteria for fulminant Wilson's disease. Finally, 7 patients required liver transplantation; 6 of these patients had a poor prognostic index score of >11 , which indicates fatal disease without liver transplantation. *Patient outcomes:* Of the 7 transplanted patients, 6 are alive and 1 died. The remaining 4 patients have stable liver disease and continue regular follow-up.

Conclusion. Wilson's disease is a rare cause of liver disease. We are presenting 11 patients seen at a transplant unit, of whom 7 have undergone liver transplantation. The inconsistency of clinical findings is in keeping with international literature.

Relevance of thiopurine methyltransferase mutation screening in patients with inflammatory bowel disease in Cape Town

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Background. Azathioprine (AZA) and 6-mercaptopurine (6-MP) are potent immunosuppressive drugs, well established in the treatment of inflammatory bowel disease (IBD). Thiopurine methyltransferase (TPMT) mutation testing identifies patients at risk of thiopurine-related adverse drug reactions (ADRs); prior testing for TPMT mutation in all patients with IBD on thiopurines is therefore recommended (ECCO guidelines).

Objectives. To describe the frequency of TPMT mutation and its correlation with ADRs and disease outcomes in our IBD population.

Methods. A retrospective descriptive analysis of adult IBD patients who were tested for TPMT mutation between 2008 and 2017.

Results. 53 records were analysed; 58% patients were female, 21% were smokers and 64% had Crohn's disease (24% with penetrating disease). The median age of the cohort and age at IBD diagnosis were 51 years (interquartile range (IQR) 40 - 58) and 38 years (IQR 22.5 - 47), respectively. The mean (standard deviation) weight was 70 (19.7) kg. The majority were treated with AZA (66%), 9% were treated with 6-MP, and although presumptively tested for TPMT, 24% did not require therapy. The mean maximum dose of AZA was 123 (54) mg. Median time to thiopurine treatment was 10 months (IQR 10 - 60). Only 2 patients (3.7%) had TPMT mutation; both were heterozygous and Caucasian. The main reason for stopping treatment was side-effects (62.5%), mainly gastrointestinal intolerance, non-compliance (18.7%), sepsis (6.3%) and failure to control disease (12.5%). Notwithstanding, TPMT genotype was not associated with ADRs, stopping therapy, drug dose or duration.

Conclusion. Although this is a small sample, TPMT mutations were infrequent and did not correlate with thiopurine-related treatment and complications. The majority (70%) of patients on AZA were under-dosed. In low- and middle-income countries, TPMT testing needs evaluation in terms of clinical relevance v. economic cost. More data are needed.

A bleeding 'tail' of haemosuccus pancreaticus

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Background. Haemosuccus pancreaticus is an obscure cause of gastrointestinal haemorrhage. As it is potentially life-threatening, the diagnosis should not be missed. The intermittent nature of the associated symptomatology may prove to be unreliable in establishing a diagnosis, so there is heavy reliance on imaging modalities to confirm this diagnosis.

Case report. We describe a young woman with resolving pancreatitis, who presented with intermittent gastrointestinal bleeding. Despite being severely anaemic, she remained haemodynamically stable, and following negative endoscopic procedures an aetiology remained elusive. Computed tomography of the abdomen was then performed, revealing cystic lesions at the tail of the pancreas; notably no vascular abnormalities were evident. It was only on visceral angiography that the diagnosis was confirmed, and bleeding cessation occurred

following coil embolisation of a pseudoaneurysm involving a branch of the splenic artery. Our case highlights the difficulty in making a diagnosis of haemosuccus pancreaticus and further emphasises the importance of having a high index of suspicion.

Off-label drug use in inflammatory bowel disease in The Netherlands

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Background. In daily clinical practice, drugs are commonly prescribed outside the terms of product licence, also known as off-label prescribing. Off-label drugs create alternative treatment options, but may be associated with unknown safety risks since they are under-evaluated for unlicensed indications. Data on the number of off-label prescriptions for the management of inflammatory bowel disease (IBD) are absent.

Objectives. To assess the characteristics of off-label prescribing for IBD in tertiary care in The Netherlands.

Methods. The Parelsnoer Institute database, a prospective Dutch national database of IBD patients from all university hospitals in The Netherlands, was used to collect data on drug prescriptions for IBD and demographics. Drugs were classified as off-label if they were unlicensed for Crohn's disease and/or ulcerative colitis as an indication.

Results. Data on drug prescriptions were available for 4 601 patients with IBD (59% were female and 62% had Crohn's disease). Of these IBD patients, 1 248 (27%) were exposed to ≥ 1 off-label drug/s, including mercaptopurine in 66%, beclomethasone in 19%, thioguanine in 13%, allopurinol in 11%, cyclosporine in 8%, tacrolimus in 7%, methotrexate in 6%, mycophenolate mofetil in 2%, certolizumab pegol in 2%, thalidomide in 1%, natalizumab in 1% and tofacitinib in 0.2%. Off-label prescriptions were more common in ulcerative colitis (28%) and IBD-unclassified (27%) compared with Crohn's disease (24%; $p < 0.05$). Patients in the off-label group were more likely than those without off-label prescriptions to be exposed to ≥ 5 types of drugs during their disease course (71% v. 23%; $p < 0.001$).

Conclusion. Approximately 30% of patients with IBD were exposed to ≥ 1 off-label drugs. Future studies are needed to evaluate the consequences of off-label prescriptions for the management of IBD.

Hydatid cyst/hepatitis B co-infection: A case report

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Background. Hepatitis B and echinococcal infections are both endemic in South Africa (SA).

Case report. A 13-year-old girl was referred to our outpatient clinic for management of hepatitis B infection. She presented with a 1-week history of worsening jaundice, malaise, fatigue and increasing abdominal pain. Physical examination confirmed a fever, deep jaundice and significant fluctuant abdominal distension. Her symptoms and physical findings were initially attributed to portal hypertension as a consequence of cirrhosis. An abdominal ultrasound scan revealed features consistent with a complex hydatid cyst. This was confirmed by positive serology for echinococcal disease. The cyst was surgically decompressed, and the patient was discharged on long-term albendazole treatment.

Discussion. Hydatid cyst and hepatitis B co-infection is rare. The literature reports three cases of hepatitis B and hydatid liver co-infection. All the cases were from outside SA.

Conclusion. Chronic hepatitis B infection is regarded as an immunosuppressive disease. The extent to which the disease progression or management of one of the conditions affects the other is unknown.

A retrospective analysis of the overlap syndromes of the autoimmune liver diseases: A study from Charlotte Maxeke Johannesburg Academic Hospital

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Background. Overlap syndromes (OSs) of the autoimmune liver diseases (AILDs) are characterised by the coexistence of features of autoimmune hepatitis (AIH) with those of primary biliary cirrhosis (PBC) and primary sclerosing cholangitis (PSC). There is a paucity of information characterising these OSs in the South African context.

Methods. This was a retrospective study at Charlotte Maxeke Johannesburg Academic Hospital. We compared the demographics, clinical characteristics, diagnosis, treatment and outcomes between the two OS groups.

Results. There were 20 OS patients, 10 in the AIH/PBC OS group and 10 in the AIH/PSC OS group. There was a significant racial difference between the two groups: 70% ($n=7$) of the AIH/PBC group were white and 60% of the AIH/PSC group were black. The autoimmune serology profiles also differed between the two groups: 30% of the patients with AIH/PBC were positive for anti-mitochondrial antibodies (AMA), whereas none of those with AIH/PSC were positive for AMA. Cytoplasmic anti-neutrophil cytoplasmic antibodies (c-ANCA) were positive in 30% of the AIH/PSC group and negative throughout the AIH/PBC group. The minimal presence of concomitant diseases (only 10%) across both groups of patients with OSs was an unexpected finding. The majority of patients in the AIH/PBC OS group (70%) and half the patients in the AIH/PSC OS group were treated with a combination of azathioprine, ursodeoxycholic acid and prednisone. The AIH/PSC OS group had better outcomes and a lower complication rate than the AIH/PBC group. The number of deaths was equal in each group.

Conclusion. Arguably the most significant finding from this retrospective study was the racial disparity in the two OS groups, possibly reflecting a previously undocumented genetic predisposition. The autoimmune profiles are consistent with the literature. Genetic studies in our patient population may provide clues to an association between race and OSs of the AILDs.

The Inflammatory Bowel Disease Registry: Tuberculosis incidence and risk factors for development in Cape Town

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Background. Inflammatory bowel disease (IBD) is a global disease with an increasing incidence in low- and middle-income countries

including South Africa (SA), where tuberculosis (TB) is endemic. Immunosuppressive therapy in IBD, in particular steroids and anti-tumour necrosis factor therapy, increases the risk of TB.

Objectives. To determine the frequency of and identify risk factors for TB in a local IBD cohort. This will aid in the formulation of guidelines appropriate for TB-endemic countries.

Methods. Consenting patients in the SA Inflammatory Bowel Disease Registry were included. Individuals who developed TB after their IBD diagnosis were identified. The incidence rate was calculated as the number of cases divided by disease-free person-time of observation from date of IBD diagnosis to date of TB diagnosis, death or last follow-up. The following variables were collected: gender, smoking history, immunosuppressive therapy, HIV status, IBD type, TB type, and mode of TB diagnosis. Appropriate statistical tests identified relevant variables as potential risk factors for TB.

Results. Of the 1 045 consenting registry patients, 635 (60.7%) were women. 487 (46%) had ulcerative colitis, 527 Crohn's disease and the remainder IBD-unclassified. The median age at IBD diagnosis was 36.5 years (interquartile range 26.6 - 50.8). 536 (51%) had ever smoked and 113 (11%) had a positive family history of IBD. 42 patients (4%) had TB, 33 with pulmonary and 9 with extrapulmonary disease. TB diagnoses were confirmed mainly by microscopy. The crude incidence of TB was 332 per 100 000 person-years follow-up. Statistically significant risk factors for TB development were smoking ($p=0.026$), HIV ($p=0.004$), Crohn's disease ($p=0.02$) and previous IBD surgery ($p=0.01$).

Conclusion. The incidence rate of TB in our IBD cohort is among the highest in the world. Subjects at risk should be considered for TB prophylactic strategies when immunosuppression is instituted.

The clinical spectrum and G516T CYP2B6 single-nucleotide polymorphism in efavirenz drug-induced liver injury

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Background. Efavirenz (EFV) is a frequently used antiretroviral drug. We have previously described clinicopathological patterns of EFV drug-induced liver injury (DILI). The G516T CYP2B6 single-nucleotide polymorphism (SNP) is associated with EFV toxicity by slowing metabolism. No data exist on a possible relationship between this SNP and EFV DILI.

Objectives. To determine the prevalence and possible influence of this SNP in EFV DILI.

Methods. Patients with causality criteria for EFV DILI were prospectively enrolled. A RUCAM score was calculated, liver biopsies were obtained and plasma EFV levels were measured. The G516T GG (wild type), GT (heterozygous) and TT (mutation) genotypes were determined by polymerase chain reaction amplification.

Results. 92 patients, median age 33 years (interquartile range (IQR) 29 - 39) were included, the majority (94.5%, $n=87$) female and 83% ($n=76$) black, with 40% ($n=32$) initiating antiretroviral therapy (ART) during pregnancy. The median ART duration was 6 months (IQR 4 - 8) and the median CD4+ count 531 cells/ μ L (IQR 360 - 737). Among patients biopsied ($n=74$), patterns of injury included submassive necrosis (SMN) in 78%, mixed cholestatic hepatitis in 14% and severe nonspecific hepatitis (NSH) in 8%. The median RUCAM score was 8 (IQR 7 - 8) and the median international

normalised ratio at presentation was 1.67 (IQR 1.43 - 2.35). The TT genotype was observed in 13% of patients ($n=12$) and the GT and GG genotypes in 43.5% ($n=40$) each. The median plasma EFV level was 2.95 mg/L (IQR 1.0 - 4.4) with non-significant but elevated levels in those with the TT v. the GG genotype (3.92 (IQR 2.8 - 7.5) and 1.9 (IQR 0.8 - 4.3), respectively; $p=0.12$). On logistic regression analysis, a CD4+ count >350 cells/ μ L predicted for the SMN pattern (odds ratio (OR) 4.7, 95% confidence interval (CI) 1.7 - 13.3; $p=0.0043$) but no G516T genotypes did. In the NSH group, the TT genotype was predictive (OR 13.6, 95% CI 2.8 - 67; $p=0.0014$). The mortality rate was 11% ($n=10$).

Conclusion. EFV DILI has substantial mortality. The G516T genotype distribution is comparable to existing data from populations of similar demographics. Plasma EFV levels were higher in the TT genotype. The influence of additional CYP2B6 SNPs and other metabolising enzymes warrants analysis.

Post-endoscopic retrograde cholangiopancreatography pancreatitis

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Background. The major risk of endoscopic retrograde cholangiopancreatography (ERCP) is post-ERCP pancreatitis (PEP). This may be self-limiting and mild, but it can also be severe and require hospitalisation. It is rarely fatal. There are two techniques for access to the bile duct during ERCP. To prevent PEP, the technique in which a guidewire is used to probe the papilla accessing the bile duct is favoured over the traditional technique of inserting a catheter directly into the papilla and injecting to the bile duct.

Objectives. To study the risk factors for PEP.

Methods. Prospective cohort study on ERCP procedures performed by a single endoscopist.

Results. There were 275 patients, with a mean age of 47 years. The indications for ERCP were gallstones ($n=169$), sclerosing cholangitis ($n=26$), chronic pancreatitis ($n=3$), bile leak ($n=18$), malignancy ($n=36$), hepatitis ($n=1$), biliary pancreatitis ($n=20$) and giant duodenum diverticulum ($n=2$). Techniques of access to the bile duct were guidewire assisted ($n=206$, $n=204$ successful) and contrast/dye injecting ($n=69$, $n=66$ successful) ($p=0.86$). Therapeutic procedures were endoscopic sphincterotomy ($n=185$), stenting ($n=59$), pre-cut ($n=6$) and balloon dilatation ($n=1$). There were 9 cases of PEP, 6/206 in the guidewire-assisted group and 3/69 in the dye-injecting group ($p=0.57$). Further details on these cases are as follows: PEP after inadvertent pancreatic duct (PD) cannulation $n=7$, PEP with no inadvertent PD cannulation $n=2$; PEP in patients with a body mass index (BMI) <35 2/121, PEP in patients with a BMI >35 7/54 ($p=0.0035$); PEP after inadvertent PD cannulation in patients with a BMI <35 0/40, PEP with no inadvertent PD cannulation in patients with a BMI <35 2/81 ($p=0.9$); and PEP after inadvertent PD cannulation in patients with a BMI >35 7/37, PEP with no inadvertent PD cannulation in patients with a BMI >35 0/17 ($p=0.17$).

Conclusion. PEP risk in dye injection and inadvertent PD cannulation is not statistically significant. Inadvertent PD cannulation in patients with a BMI >35 increases the risk of PEP, and a BMI >35 is a statistically significant risk factor for PEP.