REVIEW ARTICLE
• Mortality, Surgical Therapy and Infected Necrosis in Acute Pancreatitis

CASE REPORTS
• Wilson Disease in a young Kenyan adult
• Nesidioblastosis and the selective arterial calcium stimulation test, a case report and review of the literature
• The value of microscopy in the diagnosis of colitis
• A case of severe vitamin B12 deficiency secondary to Helicobacter pylori gastritis
• A twist in the tale

THE GASTROENTEROLOGY FOUNDATION OF SOUTH AFRICA
The most dispensed omeprazole in South Africa

Omeprazole

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- Effective in maintaining remission of GORD
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References:

*GORD = Gastro-oesophageal Reflux Disease

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Editorial

IAP, ASSA, SAGES, VASSA, SASES, TSSA, BIGOSA, SACRS, CMSA, COSECSA, PAAS, SAGINS. Quite a jamboree of associations with something for everyone and a great deal for those with an interest in gastroenterology. A lot of thought and effort has gone into the program and being only on the periphery of the organizational effort I take my hat off to the LOC members from HPBASA, SAGES, and ASSA who have expended so much effort in liaising with the International Association of Pancreatology and other societies to put the meeting together.

There are the usual news items chronicling the activities and value of the GF Liver and IBD special interest groups. I would like to bring to your attention another GF initiative, championed by Wendy Spearman and Geoff Dusheiko, the introduction and hopefully roll out, with the African Union backing, of the Extension for Community Healthcare Outcomes (ECHO™) venture. A tele-mentoring project to facilitate the management of liver diseases in Africa.

I must also bring to your attention that events in Sudan are of great concern to me and I trust to all of us. I really hope the regime change driven and supported by the medical community of that country will be worth the expense of human life. I have strong personal links with senior gastroenterologists in Sudan through the WGO and the GF and they are longing for stability and re-engagement with gastroenterology and endoscopy training events we had planned from South Africa.

In my retirement I have cajoled several folk in the UCT GSH GI Unit to contribute to this issue. The intricacies of diagnosing and managing Nesidoblastosis are expounded eloquently. Amoebiasis, no longer a disease confined to KZN and we must always keep our eyes wide open when dealing with dysenteric illnesses. One of my article solicitations was related to my own involvement when I was dragged willingly from a challenging colonoscopy list at Victoria hospital to encounter a “tik” addict with an acute abdomen and participate in his surgical treatment. Turn to page 35 if you want an instant answer. The remaining case reports came from an unexpected source, my first supernumerary trainee Allan Rajula who works in AGA Khan Hospital in Nairobi. He found an unusual culprit in the diagnostic pursuit of B12 deficiency and a hereditary cause for a young jaundiced male, a diagnosis alas to late to make a difference. More importantly Allan rekindled his association with the unit. I also hope you enjoy an extract from Frank Anderson’s HIV Pancreatitis PhD literature review on dealing with the evolution of the role of surgery in acute pancreatitis and its effect on surgical mortality.

My other retirement activities are the development of an endoscopy service at False Bay Hospital. Editing the South African Journal of Surgery (there is a really good issue in your congress bag with lots of HPBology in it). Playing golf badly at Rondebosch and still winning (most of the time) and most enjoyable of all watching my gene pool double with the addition of two granddaughters Aila and Adelie.

Please enjoy this issue and the congress.

Sandie Thomson
EDITORIAL

Editorial

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REVIEW ARTICLE

Mortality, Surgical Therapy and Infected Necrosis in Acute Pancreatitis
F Anderson, S Thomson

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CASE REPORTS

Wilson Disease in a young Kenyan adult
I Jamal, AC Rajula

Nesidioblastosis and the selective arterial calcium stimulation test, a case report and review of the literature
J Lindemann, N Morse, E Jonas

The value of microscopy in the diagnosis of colitis
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A case of severe vitamin B12 deficiency secondary to Helicobacter pylori gastritis
C Mithi, D Atandi, A Mwirigi, A Rajula

A twist in the tale
N Leech, J Plaskett, SR Thomson

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GASTROENTEROLOGY FOUNDATION

IBD Interest Group Meeting
T Khan

Establishing an endoscopy service at False Bay Hospital

Launch of the Viral Hepatitis in sub-Saharan Africa ECHO program

Acute Liver Failure Symposium
F van der Schyff

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BE THE

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Reference: 1. IMS HEALTH, MIDAS Database, MAT Sep 2017 [IMS Health. Copyright 2017. All rights reserved].

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3 Omez 40. Each capsule contains omeprazole 40 mg. Reg. No. 34/11.4.3.0030.

DATE         Saturday 17th August 2019
TIME         17h30 - 19h15
VENUE       CTICC Room 1.40, Cape Town
RSVP        Please RSVP by 12 August 2019 to Bini Seale at Cornucopia Communications
            bini@global.co.za or 082 442 9779

This is a CPD accredited event.
Limited seating available.

TOPIC       The shades of grey in diagnosing GERD - case discussion
PANEL       Dr Debbie Nel, Dr Dion Levin, Dr Robert Nel

INTERNATIONAL SPEAKER

Dr Radu Tutuiian completed his medical training at the “Carol Davila” University of Medicine in Bucharest, Romania and obtained his PhD at the “Iuliu Hateganu” University of Medicine in Cluj-Napoca, Romania. He completed post-graduate medical education in Internal Medicine and Gastroenterology in the United States (Graduate Hospital Philadelphia, PA and Medical University of South Carolina, Charleston SC). During his training in the United Stated he was mentored by Prof Donald Castell. He returned to Switzerland and was appointed Head of the Gastrointestinal Function laboratory at the University Hospital in Zurich. He is currently academic member of the University of Berne and Zurich, Switzerland and Leitender Arzt Gastroenterologie in the University Clinics for Visceral Surgery and Medicine at the Inselspital Bern, Switzerland.
The Gastroenterology Foundation of Sub Saharan Africa presents
AASLD Hepatology Connect Program 2019

to be held at SAGES 2019:
Cape Town International Convention Centre
in association with IAP  HPBASA  ASSA  SAGES

Friday, 16 August 2019 | 08:30 – 17:30

The Gastroenterology Foundation welcomes you to attend the AASLD Hepatology Connect Program 2019, register at www.iap2019.co.za

Topics
• Management of cirrhosis complications
• Management of liver mass(es)
• HBV reactivation in patients receiving immunosuppressive therapy
• Acute liver failure
• Jaundice
• Treatment of HCC outside of Milan Criteria
• Curative therapies for HBV and HCV and their impact on HCC in SSA
• HCC: Resection vs transplant vs local ablation
• The dominant stricture in PSC disease
• Cholangiocarcinoma – new management frontiers
• Transplantation for malignancies other than HCC
• Panel discussions
• Meet the Professor Sessions

International Guest Speakers

Dr. Lewis R. Roberts is the Peter and Frances Georgeson Professor in Gastroenterology Cancer Research at the Mayo Clinic, where he directs the Hepatobiliary Neoplasia Clinic, is Associate Director of Pre-Doctoral Programs in the Center for Clinical and Translational Sciences, and Director for Research at Mayo Clinic Alix School of Medicine. He earned his medical degree from the University of Ghana Medical School, a PhD in Physiology and Biophysics from The University of Iowa, and completed postgraduate training in Internal Medicine, Gastroenterology and Hepatology, and Cancer Genetics at Mayo Clinic.

Dr. Roberts clinical practice is focused on liver and bile duct cancers. He has authored over 200 publications. Dr. Roberts currently serves as Deputy Editor of *Hepatology* and is on the Editorial Boards of *Liver Cancer* and *Hepatic Oncology*. He also serves as President of Africa Partners Medical, a non-profit organisation focused on improving health in Africa.

W. Ray Kim, MD, MBA, FAASLD, currently serves as Professor of Medicine and Chief, Division of Gastroenterology and Hepatology in the Department of Medicine at Stanford University. Dr. Kim received his MD degree from Seoul National University and his MBA from the University of Pennsylvania. He did his residency in internal medicine at the University of Arkansas, Little Rock followed by a fellowship in gastroenterology and advanced training in hepatology/liver transplantation at Mayo Clinic.

Following his training, Ray joined the staff at Mayo Clinic and the faculty of the Mayo College of Medicine. He rose to the level of Professor of Medicine while building a leading clinical research group making seminal observations in liver transplantation, especially concerning public policy around organ allocation. His research has been funded through NIH for many years.

Dr Kymberly Watt trained in Winnipeg, Manitoba 1997-2002 and previously worked in Dalhousie University in Hepatology and helped re-establish a Liver Transplant Program in Atlantic Canada from 2004-6.

She was recruited to Mayo Clinic in late 2006. She is the current Medical Director of Liver Transplantation at Mayo Clinic, Rochester, MN, Associate Professor of Medicine and clinician in a very busy hepatology practice and liver transplant program. Her clinical research interests center around long term outcomes after liver transplantation as well as NASH both in the transplant and non-transplant patients.

Gyongyi Szabo, MD, PhD is the Worcester Foundation for Biomedical Research Endowed Chair, Professor and Associate Provost at the University of Massachusetts Medical School. Dr. Szabo is an internationally recognized leader in the field of liver immunity and inflammation. Her clinical investigations focus on alcoholic hepatitis, non-alcoholic fatty liver disease and viral hepatitis. She is the lead investigator on an NIH-supported multicenter clinical trial in alcoholic hepatitis. Her laboratory studies the cellular and molecular mechanisms of inflammation and immunity in liver injury to identify therapeutic targets in liver diseases including non-alcoholic liver disease and NASH. Her investigations recently revealed the importance of micro-RNAs and extracellular vesicles in liver diseases. Dr. Szabo has received honorary degrees from the Semmelweis University and she is an elected member of the Hungarian Academy of Sciences. Dr. Szabo is Past President of the American Association for the Study of Liver Diseases (AASLD) and the inaugural Editor-in-Chief of Hepatology Communications.
Introduction
At the beginning of the 20th century mortality rates in acute pancreatitis (AP) reached 60%.1 The use of positive pressure ventilation in the 1940s resulted in a decline in mortality to 18%.2 In the period 1969-1979 a further reduction to 7.8% was observed. 3 Subsequently in the decade from 1984 to 1995 there was a decline from 9.1% to 6.6% despite an increase in the overall number of fatalities.4 These improvements in survival were associated with advances in respiratory, cardiac and renal support and, antimicrobial therapy in critical care settings (Figure 1).

Early and late mortality
Aetiology has not been demonstrated to influence mortality in most settings but a study from Korea demonstrated that an alcohol aetiology when compared to a biliary aetiology had a more severe course with pseudocyst formation (20% vs 7%), organ failure beyond 48 hours (24% vs 1%) and a significantly higher mortality (8% vs 0%).4 Death in acute pancreatitis occurs in two phases early (<2 weeks) or late (>2 weeks). Table 16-22 illustrates the proportion of early and late mortality in various trials and in previous studies from South Africa most (67-79%) mortalities were early within two weeks.6-25 The global trend is towards a greater proportion of mortality within two weeks. In a large study of 13727 patients 78% of early mortalities were in patients older than 60 years.4 Early mortality results from a severe SIRS and initial treatment is organ support in the ICU to lessen the risk of progression to multiple organ failure and death. Late mortality is a result of septic complications and organ failure and hence the management focus is on the need for intervention to address infected necrosis.26 Figure 1 not only depicts the timeline for the adjuncts and mortality improvements but shows how surgery has evolved with a better understanding of the pathophysiology of AP allowing one to better define how one has arrived at the current approach to the diagnosis and treatment of infected necrosis.

Early approaches to AP management
Initially the majority of patients with acute pancreatitis (AP) were diagnosed intra-operatively and early surgical intervention was considered appropriate though only a few survived surgery. In 1889, Fitz reviewed the presenting symptoms, signs, aetiological associations, local complications and different pathological classifications.27 He set out the initial criteria for an antemortem diagnosis of acute pancreatitis. He initially considered surgery as unhelpful and later recognised some benefit in selected patients. In 1894 Werner Körte performed surgical drainage of an abscess complicating acute pancreatitis. He advocated delayed surgical intervention as early surgery was associated with poor outcome.28 Despite these conservative recommendations, a prolonged period of the primacy of surgery in acute pancreatitis followed in the early decades of the 20th century. Moynihan was convinced that recovery was unlikely without surgical intervention despite the lack of agreement on the nature of the intervention.29 He advocated debridement and drainage of the lesser sac. In 1927, Schmieden in a review of 1510 cases of acute pancreatitis found a mortality rate of 51%.
Mortality, Surgical Therapy and Infected Necrosis in Acute Pancreatitis

Frank Anderson¹, Sandie Thomson²

¹ Departmental Head of Surgery, Inkosi Albert Luthuli Central Hospital, University of KwaZulu Natal, Durban, South Africa
² Emeritus Professor Division of Gastroenterology, University of Cape Town, Cape Town, South Africa

Introduction

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Early and late mortality

Aetiology has not been demonstrated to influence mortality in most settings but a study from Korea demonstrated that an alcohol aetiology when compared to a biliary aetiology had a more severe course with pseudocyst formation (20% vs 7%), organ failure beyond 48 hours (24% vs 1%) and a significantly higher mortality (8% vs 0%).⁴ Death in acute pancreatitis occurs in two phases early (<2 weeks) or late (>2 weeks). Table 1²⁶ illustrates the proportion of early and late mortality in various trials and in previous studies from South Africa most (67-79%) mortalities were early within two weeks.⁶⁻²⁵ The global trend is towards a greater proportion of mortality within two weeks. In a large study of 13727 patients 78% of early mortalities were in patients older than 60 years.⁴ Early mortality results from a severe SIRS and initial treatment is organ support in the ICU to lessen the risk of progression to multiple organ failure and death. Late mortality is a result of septic complications and organ failure and hence the management focus is on the need for intervention to address infected necrosis.⁵ Figure 1 not only depicts the timeline for the adjuncts and mortality improvements but shows how surgery has evolved with a better understanding of the pathophysiology of AP allowing one to better define how one has arrived at the current approach to the diagnosis and treatment of infected necrosis.

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the 1278 patients subjected to surgery. He advocated early surgical intervention despite their findings of 24% and 65% mortality rates in the oedematous and necrotizing pancreatitis respectively. The introduction in 1929 of the biochemical marker serum amylase enabled the diagnosis of acute pancreatitis without the need for surgery. This allowed the clinical differentiation between mild and severe forms and the recognition that acute pancreatitis had a mild and self-limiting course in the majority of cases, that did not require surgery. The paradigm shift from frequent surgical intervention to initial non-operative intervention was strengthened by a 1948 analysis of a series of 307 patients that revealed a surgical mortality of 45% and a non-operative mortality of 28%. The management of pancreatic necrosis is dependent on local expertise and experience. Contrast-enhanced computed tomography (CECT) is of great value in assessing the degree of pancreatic and peripancreatic necrosis. Patients with necrosis of more than 50% of the pancreas are prone to infection and multiorgan failure. However, the relationship between pancreatic necrosis and organ failure is not linear and organ failure is found in only half of patients with pancreatic necrosis. The development and progression of organ failure and its relationship to pancreatic necrosis are not only the key determinants of morbidity and late mortality but guide the need for intervention to deal with the infected pancreatic and peripancreatic tissues. The diagnosis of infected necrosis is difficult as these patients are frequently in high dependency environments and physiologically unstable. Several diagnostic strategies have been reported, including the presence of gas on CECT and microbiological culture from fine needle aspiration. Diagnosing infected necrosis in the absence of gas on CECT is particularly challenging. In daily practice the decision to embark on an invasive intervention for suspected infected necrosis is based on clinical parameters such as fever and increased serum inflammatory markers. In particular CRP, PCT and IL-8 are markers currently under evaluation. A summary of the three recent studies is presented in Table 2. The morbidity rate for pancreatic fistula ranged between 14% and 88% and bleeding complications between 5% and 83%. The overall outcomes of open surgery and demonstrates mortality rates that range between 6% and 39% and that a rate of 15% has been achieved with all techniques in experienced centres.

### Table 1. Patterns of mortality in series of acute pancreatitis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Origin</th>
<th>Number</th>
<th>Deaths</th>
<th>Early</th>
<th>Late</th>
</tr>
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<tbody>
<tr>
<td>Renner6</td>
<td>1985</td>
<td>USA</td>
<td>405</td>
<td>100</td>
<td>25</td>
<td>76</td>
</tr>
<tr>
<td>Mann7</td>
<td>1994</td>
<td>England</td>
<td>631</td>
<td>57</td>
<td>9</td>
<td>44</td>
</tr>
<tr>
<td>McKay8</td>
<td>1999</td>
<td>Scotland</td>
<td>13727</td>
<td>1030</td>
<td>8</td>
<td>54</td>
</tr>
<tr>
<td>Lowham9</td>
<td>1999</td>
<td>England</td>
<td>105</td>
<td>6</td>
<td>6</td>
<td>100</td>
</tr>
<tr>
<td>Muttinga10</td>
<td>2000</td>
<td>USA</td>
<td>805</td>
<td>17</td>
<td>2</td>
<td>47</td>
</tr>
<tr>
<td>Ashley11</td>
<td>2001</td>
<td>USA</td>
<td>99</td>
<td>14</td>
<td>14</td>
<td>29</td>
</tr>
<tr>
<td>Gloor12</td>
<td>2001</td>
<td>Switzerland</td>
<td>106</td>
<td>10</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Appelros13</td>
<td>2001</td>
<td>Sweden</td>
<td>883</td>
<td>21</td>
<td>2</td>
<td>62</td>
</tr>
<tr>
<td>Carnovale14</td>
<td>2005</td>
<td>Italy</td>
<td>1150</td>
<td>55</td>
<td>5</td>
<td>51</td>
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<tr>
<td>Frey15</td>
<td>2006</td>
<td>USA</td>
<td>70231</td>
<td>4227</td>
<td>6</td>
<td>30</td>
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<tr>
<td>Mofidi16</td>
<td>2006</td>
<td>Scotland</td>
<td>759</td>
<td>45</td>
<td>6</td>
<td>51</td>
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<td>Fu17</td>
<td>2007</td>
<td>Taiwan</td>
<td>643</td>
<td>105</td>
<td>16</td>
<td>42</td>
</tr>
<tr>
<td>Bai18</td>
<td>2007</td>
<td>China</td>
<td>1976</td>
<td>233</td>
<td>12</td>
<td>79</td>
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<tr>
<td>Dellinger19</td>
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<td>Multicentre</td>
<td>100</td>
<td>19</td>
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<tr>
<td>Bumbasirevic20</td>
<td>2009</td>
<td>Serbia</td>
<td>110</td>
<td>59</td>
<td>54</td>
<td>25</td>
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<tr>
<td>Overall</td>
<td></td>
<td></td>
<td>76752</td>
<td>4746</td>
<td>9</td>
<td>43</td>
</tr>
<tr>
<td>Anderson21</td>
<td>2008</td>
<td>South Africa</td>
<td>322</td>
<td>28</td>
<td>9</td>
<td>79</td>
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<td>Anderson22</td>
<td>2017</td>
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<td></td>
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<td></td>
<td></td>
<td>77701</td>
<td>4816</td>
<td>9</td>
<td>58</td>
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</table>
Further studies are needed to clarify the clinical utility of these markers to decide on the need for antimicrobial treatment or surgical intervention.

However, diagnosed infected pancreatic necrosis requires intervention if it is associated with progressive organ failure. Traditionally open surgery techniques which included open packing, repeat laparotomy, closed packing and closed continuous lavage were utilised. Table 3 summarises the outcomes of open surgery and demonstrates mortality rates that range between 6% and 39% and that a rate of 15% has been achieved with all techniques in experienced centres. The morbidity rate for pancreatic fistula ranged between 14% and 88% and bleeding complications between 8% and 83%.

The high morbidity and mortality of open surgery resulted

### Table 2. Accuracy of serological predictors of infected pancreatic necrosis

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Test cut off</th>
<th>Duration assay</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>Rau40</td>
<td>1997</td>
<td>PCT (1.8 ng/ml)</td>
<td>1st 2 days</td>
<td>94</td>
<td>91</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td></td>
<td></td>
<td>IL-8 (112 pg/ml)</td>
<td></td>
<td>72</td>
<td>75</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Riche41</td>
<td>2003</td>
<td>IL-6 (&lt; 400 pg/l) + PCT (&lt; 2 ng/l)</td>
<td>1st 3 days</td>
<td>75</td>
<td>84</td>
<td>60</td>
<td>91</td>
</tr>
<tr>
<td>Rau42</td>
<td>2007</td>
<td>PCT ≥ 3.5 ng/ml</td>
<td>1st 2 days</td>
<td>93</td>
<td>88</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
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<td>CRP ≥ 430 mg/l</td>
<td></td>
<td>40</td>
<td>100</td>
<td>NS</td>
<td>NS</td>
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<tr>
<td></td>
<td></td>
<td>PCT ≥ 3.5 ng/ml</td>
<td>3rd and 4th day</td>
<td>79</td>
<td>93</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CRP ≥ 430 mg/l</td>
<td></td>
<td>36</td>
<td>97</td>
<td>NS</td>
<td>NS</td>
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### Table 3. Outcomes of surgery in infected pancreatic necrosis

<table>
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<tr>
<th>Procedure</th>
<th>Year</th>
<th>No</th>
<th>Infection (%)</th>
<th>Pancreatic</th>
<th>Enteric</th>
<th>Total</th>
<th>Haemorrhage (%)</th>
<th>Mortality (%)</th>
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<td>Open laparotomy</td>
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<td>1988</td>
<td>95</td>
<td>42</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>8</td>
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<tr>
<td>Fernandez-del Castillo-lo44</td>
<td>1998</td>
<td>64</td>
<td>56</td>
<td>53</td>
<td>16</td>
<td>69</td>
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<td>Branum45</td>
<td>1998</td>
<td>50</td>
<td>84</td>
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<td>16</td>
<td>88</td>
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<td>NS</td>
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<td>2013</td>
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<td>83</td>
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<td>Wronski49</td>
<td>2017</td>
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<td>32</td>
<td>36</td>
<td>68</td>
<td>29</td>
<td>27</td>
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</table>

Planned re-laparotomies

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Year</th>
<th>No</th>
<th>Infection (%)</th>
<th>Pancreatic</th>
<th>Enteric</th>
<th>Total</th>
<th>Haemorrhage (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarr49</td>
<td>1991</td>
<td>23</td>
<td>75</td>
<td>26</td>
<td>52</td>
<td>78</td>
<td>26</td>
<td>17</td>
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<td>Tsioitos51</td>
<td>1998</td>
<td>72</td>
<td>79</td>
<td>19</td>
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<td>18</td>
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</table>

Closed continuous lavage

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Year</th>
<th>No</th>
<th>Infection (%)</th>
<th>Pancreatic</th>
<th>Enteric</th>
<th>Total</th>
<th>Haemorrhage (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Farkas52</td>
<td>1996</td>
<td>123</td>
<td>100</td>
<td>13</td>
<td>1</td>
<td>14</td>
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<td>7</td>
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<tr>
<td>Farkas53</td>
<td>2006</td>
<td>220</td>
<td>100</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>8</td>
</tr>
</tbody>
</table>

Surgical step-up approach

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Year</th>
<th>No</th>
<th>Infection (%)</th>
<th>Pancreatic</th>
<th>Enteric</th>
<th>Total</th>
<th>Haemorrhage (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Brunschot54</td>
<td>2018</td>
<td>47</td>
<td>98</td>
<td>32</td>
<td>17</td>
<td>49</td>
<td>21</td>
<td>13</td>
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</tbody>
</table>
in a shift to a minimally invasive staged approach. Initial management accesses the collection and may provide definitive drainage or more usually act as a bridge to allow optimization of organ failure prior to further interventions. A number of techniques have been devised utilizing percutaneous drainage with saline flushes, laparoscopic drainage, video assisted retroperitoneal debridement (VARD) and transluminal endoscopic techniques. The results of these approaches are evaluated in Table 4.

The morbidity and mortality rates range widely between 10% and 88%, and 5% and 40% respectively due to the heterogeneity of the study populations.

### Table 4. Series of minimally invasive necrosectomy reporting outcomes

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Year</th>
<th>No</th>
<th>Infect- ed</th>
<th>Procedure completed</th>
<th>Sepsis ↓</th>
<th>Morbidity</th>
<th>Mortality</th>
</tr>
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<tbody>
<tr>
<td><strong>Percutaneous</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Freeny55</td>
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<td>34</td>
<td>100</td>
<td>47</td>
<td>74</td>
<td>0</td>
<td>12</td>
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<tr>
<td>Echenique56</td>
<td>1998</td>
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<td>100</td>
<td>100</td>
<td>NS</td>
<td>50</td>
<td>0</td>
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<tr>
<td>Gouzi57</td>
<td>1999</td>
<td>32</td>
<td>81</td>
<td>65</td>
<td>NS</td>
<td>59</td>
<td>15</td>
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<tr>
<td><strong>Retroperitoneal laparostomy</strong></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Fagniez58</td>
<td>1989</td>
<td>40</td>
<td>97</td>
<td>NS</td>
<td>NS</td>
<td>50</td>
<td>33</td>
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<tr>
<td>Villazon59</td>
<td>1991</td>
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<td>NS</td>
<td>NS</td>
<td>38</td>
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<tr>
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<td>100</td>
<td>NS</td>
<td>NS</td>
<td>65</td>
<td>25</td>
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<td>Raraty61</td>
<td>2010</td>
<td>137</td>
<td>64</td>
<td>86</td>
<td>NS</td>
<td>55</td>
<td>19</td>
</tr>
<tr>
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<td>2012</td>
<td>22</td>
<td>64</td>
<td>NS</td>
<td>71</td>
<td>45</td>
<td>5</td>
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<td><strong>Laparoscopy</strong></td>
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<tr>
<td>Zhu238</td>
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<td>0</td>
<td>90</td>
<td>NS</td>
<td>NS</td>
<td>10</td>
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<td><strong>Retroperitoneoscopy</strong></td>
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<td></td>
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<tr>
<td>Gambiez64</td>
<td>1998</td>
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<td>65</td>
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<td>van Brunschot54</td>
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<td><strong>Endoscopic</strong></td>
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<td>100</td>
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<td>90</td>
<td>100</td>
<td>NS</td>
<td>25</td>
<td>18</td>
</tr>
</tbody>
</table>

**References**

Heterogeneity of the study populations.

10% and 88%, and 5% and 40% respectively due to the shift to a minimally invasive staged approach. Initial

REVIEW


45. Branum G, Galloway J, Hichowitz W, Pendley M, Hunter J. Pancreatic necrosis: results of necrosectomy, packing, and...
Wilson Disease in a young Kenyan adult

Imran Jamal1, Allan Rajula2
1 Internal Medicine Resident, Aga Khan University Hospital, Nairobi, Kenya
2 Consultant Gastro-enterologist, Aga Khan University Hospital, Nairobi, Kenya

Introduction
Wilson disease (WD) is a rare cause of chronic liver disease. It is an autosomal recessive disease resulting in a systemic accumulation of copper. The prevalence is approximately 1 in 30,000.1 WD was first described in Senegal2 and has been previously documented in only 4 countries in subSaharan Africa.3,4 This is the first case report of WD in Kenya. Although WD is a rare diagnosis in SubSaharan African adults, it should be considered in the differential diagnosis of chronic liver disease, especially if no obvious cause has been found.

Case Report
A 21 year old male university student presented to the gastroenterology clinic with a two month history of painless bilateral lower limb and hand swelling associated and periorbital oedema. He also experienced recurrent abdominal pain during this period, associated with nausea and melena stools. There was no history of fever or weight loss or any significant travel history. His father suffered from an unknown liver condition, otherwise his family history was unremarkable. He denied alcohol intake or cigarette smoking. A review of systems revealed joint pains at the knees, right shoulder and lower back.

On physical examination, he had jaundice, gynaecomastia and loss of axillary hair. Abdominal examination revealed a reduced liver span of 5 cm and splenomegaly. His musculoskeletal examination did not reveal any features of synovitis. The rest of his examination was unremarkable. He denied alcohol intake or cigarette smoking. A review of systems revealed joint pains at the knees, right shoulder and lower back.

His laboratory evaluation revealed thrombocytopenia (83 x 10⁹/L). His estimated GFR of 101 ml/min/1.73m² was in the normal range. Computed tomography (CT) of the abdomen and pelvis showed splenomegaly and a shrunken liver with diffuse nodularity of the liver parenchyma indicative of macronodular liver cirrhosis. There was also evidence of portal hypertension with recanalization of the umbilical vein and gastro-esophageal collateral formation and uncomplicated cholelithiasis. A presumptive diagnosis of liver cirrhosis was made.

Hepatitis A, B and C viral serology was negative as was his achistosoma antibody test. His transferrin saturation (TSAT) was elevated at 81.3 %. An autoimmune profile including antinuclear (ANA), antismooth muscle (ASMA), antimitochondrial (AMA) antibodies and serum caeruloplasmin level was requested at this time to assess for other causes of liver cirrhosis.

Approximately 1 month later, he was admitted with jaundice, diffuse muscle cramps and pains. His parents also noted that he had drooling from the left side of the mouth and progressive difficulty in walking. His abdominal examination revealed asterixis and bilateral pitting pedal edema, but was otherwise largely unchanged from his previous review. There was no abdominal tenderness and no features to suggest ascites. He was mildly dysarthric. His motor exam of upper and lower limbs revealed generalized hyperreflexia and hypertonia. His gait was also noted to be ataxic. An ophthalmology review was conducted after which perirelbral granular deposits (Kayser-Fleischer rings) were identified in the anterior segment of both eyes. There were no sunflower cataracts noted during slit-lamp examination.

His laboratory evaluation revealed thrombocytopenia (83 x 10⁹/L) with normal hemoglobin (14 g/dL). He also had a raised ferritin of 2873 ng/mL with a TSAT of 89 %. His liver function tests were relatively unchanged from his previous evaluation are shown in Table 1. He also had worsening coagulopathy with an INR of 3.05. A creatine phosphokinase level in serum was mildly dysarthric. His motor exam of upper and lower limbs revealed generalized hyperreflexia and hypertonia. His gait was also noted to be ataxic. An ophthalmology review was conducted after which perilimbral granular deposits (Kayser-Fleischer rings) were identified in the anterior segment of both eyes. There were no sunflower cataracts noted during slit-lamp examination.

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| Table 1. Results of the Patients Liver Function Tests before and during hospitalization |
| **Liver Function Tests** | **Clinic Visit** | **Hospital Admission 1 month after clinic visit** |
| | **First week** | **Second week** |
| ALP (U/L) | 337 | 142 | 143 |
| GGT (U/L) | 78 | 67 | 121 |
| AST (U/L) | 73.6 | 75.2 | 60.4 |
| ALT (U/L) | 40.8 | 32.6 | 57.6 |
| Bilirubin (Total) (µmol/L) | 77.4 | 80.4 | 115.6 |
| Bilirubin (Direct) (µmol/L) | 53.9 | 42.8 | 55.9 |
| Protein (g/L) | 74 | - | - |
| Albumin (g/L) | 25.5 | - | 22.3 |
| INR | 2.42 | 3.05 | 2.88 |

Correspondence
Allan Rajula
email: allanrajula@yahoo.com
He was initiated on rifaximin, lactulose, furosemide 40 mg daily and spironolactone 100 mg daily. Two days after admission, he complained of numbness and paraesthesiae of both feet. Nerve conduction studies of all limbs revealed features suggestive of asymmetrical mixed sensory-motor demyelination and radiculopathy of all limbs. An MRI of the cervical spine revealed mild straightening of the cervical spine likely secondary to muscle spasms. An MRI brain with contrast, done to further evaluate the cause of his upper motor neurone signs, revealed the findings shown in Figures 1-4:

**Figure 1. T1 pre- (left) and post-contrast (right) images illustrating hyperintensity in the globus pallidus bilaterally (white arrows)**

**Figure 2. T2/FLAIR images showing hyperintensity in the head of the caudate nuclei (Black arrows)**

**Figure 3. Restricted diffusion (image on the right) and low ADC (image on the left) shown in the caudate nuclei and putamen bilaterally – shown with black arrows**
The most commonly reported initial MRI abnormality in WD is T1 hyperintensity in the lentiform nuclei and mesencephalic region with T2 hyperintensities involving the basal ganglia and the thalamus. In addition to these findings, we also demonstrated the characteristic ‘face of the giant panda’ sign on T2 (FLAIR)-weighted images, which is highly suggestive of WD.

By this time, his serum ceruloplasmin results were found to be low (5.48 mg/dL). Serum copper levels were also low at 40.6 µg/dL (Reference range: 74 – 130 µg/dL). Given the results of his iron studies, we conducted DNA sequencing to detect HFE mutations (C282Y and H63D), which were negative. A liver biopsy revealed features of liver cirrhosis (Figure 4-6). Copper quantification could not be done in our facility due to lack of appropriate equipment.

His Leipzig score11 (detailed in Table 2) was 8, which confirmed the diagnosis of WD. His MELD score was 27 with a Child-Pugh class of C. His sister consented as a living related donor and he was referred for liver transplant in India. On arrival at the transplant centre, he decompensated and developed status epilepticus, requiring endotracheal intubation and transfer to the intensive care unit. He further deteriorated and died shortly afterwards.
appropriate equipment.

quantification could not be done in our facility due to lack of HFE mutations (C282Y and H63D), which were negative. A liver 40.6 µg/dL (Reference range: 74 – 130 µg/dL). Given the results to be low (5.48 mg/dL). Serum copper levels were also low at region with T2 hyperintensities involving the basal ganglia is T1 hyperintensity in the lentiform nuclei and mesencephalic

CASE REPORT

Table 2: Leipzig Criteria for Wilson Disease

<table>
<thead>
<tr>
<th>Clinical and Laboratory Findings</th>
<th>Points</th>
<th>Patient Level</th>
<th>Patient Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kayser-Fleischer (KF) rings</td>
<td>2</td>
<td>Present</td>
<td>2</td>
</tr>
<tr>
<td>Neurologic symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2</td>
<td>Severe</td>
<td>2</td>
</tr>
<tr>
<td>Mild</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum Ceruloplasmin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.1-0.2 g/L</td>
<td>1</td>
<td></td>
<td>0.0548 g/L</td>
</tr>
<tr>
<td>&lt;0.1 g/L</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coombs-negative hemolitic</td>
<td>1</td>
<td>Not evaluated</td>
<td>0</td>
</tr>
<tr>
<td>Liver copper</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;5 x ULN (&gt;4micromol/g)</td>
<td>2</td>
<td>Not evaluated</td>
<td>0</td>
</tr>
<tr>
<td>No cholestasis</td>
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<td></td>
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</tr>
<tr>
<td>0.8-4 micromol/g</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rhodanine-positive granules</td>
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<tr>
<td>Normal (&lt;0.8 micromol/g)</td>
<td>-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary copper no acute hepatitis</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1-2 x ULN</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;2 x ULN</td>
<td>2</td>
<td>(2.9 x ULN)</td>
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</tr>
<tr>
<td>Normal, but &gt;5 x ULN after D-penicillamine</td>
<td>2</td>
<td></td>
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</tr>
<tr>
<td>Mutation analysis</td>
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</tr>
<tr>
<td>On both chromosomes detected</td>
<td>4</td>
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<tr>
<td>On one chromosome detected</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
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<td></td>
<td>8 points</td>
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</table>

Discussion

Several cases of WD have been described in North Africa. However, there is no literature describing WD in other parts of Africa. This discrepancy may be due to the higher rate of consanguinity in North Africa.

WD is a monogenic, autosomal recessive condition resulting in systemic copper overload. It was first described as a syndrome by Kinnier Wilson in 1912. It is a result of a mutation of the ATP7B gene (on chromosome 13), which encodes a copper-transporting P-type ATPase. The ATP7B transporter functions to transport copper into the trans-Golgi compartment into the bile and incorporate copper into ceruloplasmin. Defective ATP7B function results in systemic overload of copper, which is the major cause of tissue pathology and clinical symptoms in patients.

Most patients with WD are diagnosed between the ages of 5 and 35 years of age. Liver disease is the first clinical manifestation in approximately 40-50% of patients. Initial neurological presentation occurs in 40-60% of patients. The spectrum of liver disease in WD is varied, ranging from asymptomatic forms with elevated liver enzymes or hepatomegaly, chronic hepatitis with steatosis and fibrosis to liver cirrhosis and chronic liver failure.

The neurologic manifestations are also variable, and characterized by cumulative motoric dysfunction. Clinical signs include a wing beating tremor, dysarthria, dysphagia, ataxia, dystonia, choreoathetosis, parkinsonism, impaired concentration and cognition, hypersalivation and drooling. Psychiatric manifestations include personality changes, mood disorders, anxiety and uncommonly psychosis.

Other organs/organ systems that can be affected include the eyes (sunflower cataract, KF rings), the genitourinary system (amenorrhea, ovarian dysfunction, infertility, and abortion), the musculoskeletal system (stiffness, back pain, osteoarthritis, and osteoporosis), the renal system (tubular dysfunction and Fanconi syndrome), the heart (cardiomyopathy, arrhythmias), the hematologic system (hemolytic anemia) and the gastrointestinal system (pancreatitis, gallstones).

The initial approach to a patient suspected to have WD involves determination of serum ceruloplasmin concentration, an ocular slit-lamp examination and a 24-hour urinary copper excretion. If these investigations are suggestive of WD, no further tests are required for diagnosis. The Leipzig score was created to help determine the need to continue with diagnostic testing for WD and determine the certainty of diagnosis. A score of 4 or more makes the diagnosis of WD highly likely, while a score of 1 or less makes WD unlikely (Table 2). Quantitative hepatic copper determination (2250 µg/g dry weight) remains the best biochemical evidence for WD, but may not be readily available in low resource settings. Neuroimaging (preferably magnetic resonance imaging) should be considered before treatment of patients with neurologic WD. The ‘face of the giant panda’ sign is highly suggestive of WD. In addition, a ‘face of a panda cub’ may be seen in the dorsal pons. Both of these are collectively referred to as the ‘double panda sign’.

Initial management of symptomatic patients is copper
chelation (D-penicillamine or trientine) and avoidance of foods and water with high concentrations of copper. Oral zinc causes malabsorption of copper, and is relatively more accessible than D-penicillamine. It can be used for maintenance therapy following chelation or less commonly as primary therapy with chelation. Zinc provides an alternative for patients unable to tolerate chelation therapy. Our patient did not receive penicillamine as he was in acute liver failure and was too ill. Patients with acute liver failure should be referred for liver transplantation immediately. In those patients receiving chelation therapy, routine monitoring of serum copper and ceruloplasmin, liver function tests, INR, complete blood count and urinalysis should be performed regularly. The 24-hour urinary excretion of copper should also be performed annually.18

Hemochromatosis is characterized by iron overload with extensive deposition in multiple tissues (notably the skin, liver, pancreas, thyroid and heart). The diagnosis of hereditary hemochromatosis (HH) requires demonstration of iron overload (Transferrin saturation of ≥45% and/or elevated ferritin) and a positive HFE genotype.19 Our patient had a transferring saturation (TSAT) of 89% with an elevated ferritin of 2873ng/mL. However, genomic analyses for C282Y/H63D mutations were negative. The presence of WD and HH in the same patient has been documented only in 4 cases.20-22 Moreover, iron overload without features of hereditary hemochromatosis has been described in 6 cases 23-25 to date. This is the seventh case of Wilson’s disease with documented iron overload, although we did not perform a liver biopsy to quantify the amount of tissue iron, given the invasive nature of the investigation and the clinical state of our patient. There are 3 possible mechanisms of iron overload in WD: Hemolysis, very low caeruloplasmin levels and hereditary hemochromatosis. The prognosis of WD is good except in those with advanced disease, rapidly progressive liver failure and hemolysis. We believe that our patient would have had a better outcome if he had presented to our facility earlier.

References
described in 6 cases 23-25 to date. This is the seventh case of without features of hereditary hemochromatosis has been ferritin) and a positive HFE genotype.19

hereditary hemochromatosis (HH) requires demonstration of with extensive deposition in multiple tissues (notably the iron, given the invasive nature of the investigation and the did not perform a liver biopsy to quantify the amount of tissue Wilson's disease with documented iron overload, although we.

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primary therapy with chelation. patients unable to tolerate chelation therapy , routine monitoring of serum receiving chelation therapy ,

The prognosis of WD is good except in those with advanced disease, rapidly progressive liver failure and was in acute liver failure did not receive penicillamine as he was in acute liver failure for patients unable to tolerate chelation therapy . Our patient.

CASE REPORT

1. Huster D. Wilson disease. Best practice & research Clinical


5. Longe AC, Glew RH, Omene JA. Wilson's disease:

3. Abdelghaffar TY, Elsayed SM, Elsobky E, Bochow B, Buttner

2. Dumas M, Girard PL, Jacquin-Cotton L, Konate S. [1st case of

1. Bull PC, Thomas GR, Rommens JM, Forbes JR, Cox DW . The


24. W alshe JM, Cox DW . Effect of treatment of Wilson's disease

23. Shiono Y, W akusawa S, Hayashi H, Takikawa T, Y ano M,


18. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson

17. Ferenci P , Caca K, Loudianos G, Mieli-Vergani G, Tanner S,


13. Bull PC, Thomas GR, Rommens JM, Forbes JR, Cox DW . The

10. Jacobs DA, Markowitz CE, Liebeskind DS, Galetta SL. The

9. Hegde AN, Mohan S, Lath N, Lim CC. Differential diagnosis

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- Intravenous Pyelograms (IVP)
- Bowel Evacuation
- Abdominal X-Ray Examinations
- Surgery
- Colonoscopy

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CASE REPORT

Correspondence
Eduard Jonas
email: eduard.jonas@uct.ac.za

Nesidioblastosis and the selective arterial calcium stimulation test, a case report and review of the literature
Jessica Lindemann1, Nicole Morse2, Eduard Jonas1

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2 Pathologist, Lancet Laboratories, Cape Town, South Africa

Introduction
Nesidioblastosis, a rare cause of persistent hyperinsulinemic hypoglycaemia (PHH), originates from the Greek words nesidion meaning islet and blasto meaning bud or sprout. First described by Laidlaw in 1938, it is an entity most often diagnosed in neonates.1, 2 Nesidioblastosis in adults is an exceedingly rare condition, with approximately 100 cases reported in the literature to date.3, 4 Several authors have estimated that it comprises between 0.5 – 7% of all cases of PHH, although precise estimates do not exist.3-8 In addition to being a rare disease, nesidioblastosis is often challenging to diagnose. We present a patient with symptoms consistent with PHH who underwent selective arterial calcium stimulation testing (SACST) that localized the overproduction of insulin to the body/tail of the pancreas which was successfully managed with a spleen-preserving left pancreatectomy.

Case presentation
A previously healthy 39-year-old female presented with an 18-month history of dizziness and weakness that improved after eating sugar-rich foods. She also reported a 10 kg weight gain over the last year. Laboratory investigations revealed a fasting insulin level of 59.5 mIU/L (normal range: 2.6 - 24.9 mIU/L) and a C-peptide value of 4.6 ug/L (normal range: 1.1 – 4.4 ug/L). With the working diagnosis of a possible insulinoma, a pancreas protocol CT, an MRI/MRCP and an EUS were performed, none of which could identify a tumour. To assist with tumour localization, a SACST was performed.

Selective arterial calcium stimulation test
The use of the SACST allows for characterization of the gradient of insulin production throughout the pancreas and aids in determining the regional localization of the source of insulin over-production (head versus body/tail).9 The specificity of the SACST for localization of an occult insulinoma has been found to be greater than 90% in several studies. 10-12 A recent study found a sensitivity of 81% and a specificity of 77% for differentiating between insulinoma and nesidioblastosis.13 The technique for SACST used in the described patient is shown in Figure 1. 11 The femoral vein is cannulated, and a sampling catheter is passed into the right hepatic vein via the inferior vein cava. The femoral artery, usually on the opposite side is cannulated and the superior mesenteric artery (SMA), gastroduodenal artery (GDA) and splenic artery (SA) are selectively isolated in sequence for administration of a 10% calcium gluconate solution. A weight based dose of 0.025 mEq of calcium per kg for normal weight patients and 0.01 mEq of calcium per kg for obese patients is injected into the targeted artery after fluoroscopic confirmation of the position of the catheter tip.9 Blood samples from the right hepatic vein are taken at baseline (prior to injection) and then at 20, 40, 60 and 90 seconds after calcium injection. This is then repeated for each of the three arteries. The change in insulin concentration in hepatic venous blood over time is plotted to localize the site of greatest insulin production within the pancreas, based on the pancreatic arterial blood supply (Figure 1).

Angiographic images from the selective cannulation of the SMA, GDA and SA of the patient are displayed in Figure 2. An anomalous dominant supply to a large transverse pancreatic artery from the SMA supplying the body and tail of the pancreas was seen (Figure 2c). Results of the patient’s SACST are shown in Figure 3. There was a dramatic increase in hepatic insulin concentration between 20 and 40 seconds after calcium injection into the SMA and SA which decreased, but remained significantly elevated, at 90 seconds post-injection. The changes in hepatic insulin concentration were much less pronounced after injection of calcium into the GDA. This suggested that the greatest production of insulin by the pancreas came from the body and tail region. Based on this information, the decision was made to perform a spleen-preserving left pancreatectomy. Intraoperative ultrasound did not demonstrate a distinct mass lesion. The patient tolerated the procedure well with no intraoperative or post-operative complications. There was a dramatic decrease in insulin levels observed from a post-operative day one level of 60.2 mIU/L to 28.3 mIU/L by post-operative day four (Figure 4). The histology showed features in keeping with nesidioblastosis (Figure 5).

CASE REPORT

Nesidioblastosis and the selective arterial calcium stimulation test, a case report and review of the literature

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Introduction
Nesidioblastosis, a rare cause of persistent hyperinsulinemic hypoglycaemia (PHH), originates from the Greek words nesidion meaning islet and blasto meaning bud or sprout. First described by Laidlaw in 1938, it is an entity most often diagnosed in neonates.¹, ² Nesidioblastosis in adults is an exceedingly rare condition, with approximately 100 cases reported in the literature to date.³, ⁴ Several authors have estimated that it comprises between 0.5 – 7% of all cases of PHH, although precise estimates do not exist.³-⁸ In addition to being a rare disease, nesidioblastosis is often challenging to diagnose. We present a patient with symptoms consistent with PHH who underwent selective arterial calcium stimulation testing (SACST) that localized the overproduction of insulin to the body/tail of the pancreas which was successfully managed with a spleen-preserving left pancreatectomy.

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Selective arterial calcium stimulation test
The use of the SACST allows for characterization of the gradient of insulin production throughout the pancreas and aids in determining the regional localization of the source of insulin over-production (head versus body/tail).⁵ The specificity of the SACST for localization of an occult insulinoma has been found to be greater than 90% in several studies.¹⁰-¹² A recent study found a sensitivity of 81% and a specificity of 77% for differentiating between insulinoma and nesidioblastosis.¹³ The technique for SACST used in the described patient is shown in Figure 1.¹¹ The femoral vein is cannulated, and a sampling catheter is passed into the right hepatic vein via the inferior vein cava. The femoral artery, usually on the opposite side is cannulated and the superior mesenteric artery (SMA), gastroduodenal artery (GDA) and splenic artery (SA) are selectively isolated in sequence for administration of a 10% calcium gluconate solution. A weight based dose of 0.025 mEq of calcium per kg for normal weight patients and 0.01 mEq of calcium per kg for obese patients is injected into the targeted artery after fluoroscopic confirmation of the position of the catheter tip.¹³ Blood samples from the right hepatic vein are taken at baseline (prior to injection) and then at 20, 40, 60 and 90 seconds after calcium injection. This is then repeated for each of the three arteries. The change in insulin concentration in hepatic venous blood over time is plotted to localize the site of greatest insulin production within the pancreas, based on the pancreatic arterial blood supply (Figure 1).

Angiographic images from the selective cannulation of the SMA, CDA and SA of the patient are displayed in Figure 2. An anomalous dominant supply to a large transverse pancreatic artery from the SMA supplying the body and tail of the pancreas was seen (Figure 2c). Results of the patient’s SACST are shown in Figure 3. There was a dramatic increase in hepatic insulin concentration between 20 and 40 seconds after calcium injection into the SMA and SA which decreased, but remained significantly elevated, at 90 seconds post-injection. The changes in hepatic insulin concentration were much less pronounced after injection of calcium into the GDA. This suggested that the greatest production of insulin by the pancreas came from the body and tail region. Based on this information, the decision was made to perform a spleen-preserving left pancreatectomy. Intraoperative ultrasound did not demonstrate a distinct mass lesion. The patient tolerated the procedure well with no intraoperative or post-operative complications. There was a dramatic decrease in insulin levels observed from a post-operative day one level of 60.2 mIU/L to 28.3 mIU/L by post-operative day four (Figure 4). The histology showed features in keeping with nesidioblastosis (Figure 5).
CASE REPORT

Diagnosis of nesidioblastosis
The diagnosis of nesidioblastosis is notoriously difficult. Patients present with typical features of hypoglycaemia ranging from dizziness, confusion, headaches, or visual disturbances to rarely, seizures or coma. Hypoglycaemia sensed by the central nervous system results in significant catecholamine release and stimulation of the autonomic nervous system which can present with sweating, tremors, palpitations, paraesthesia and hunger, in addition to the hypoglycaemia symptoms.1, 14 The constellation of hypoglycaemic symptoms, a plasma glucose level ≤ 2.2 mmol/L, and relief of symptoms after administration of glucose are referred to as Whipple’s Triad and are often present in patients who present with hyperinsulinemic hypoglycaemia of various causes, including insulinoma and nesidioblastosis.1, 14 Clinically and biochemically, it is not possible to distinguish between the two pathologies.15,16

Standard initial evaluation is identical to that performed for diagnosis of insulinoma and aims to exclude spurious causes hypoglycaemia. Investigations include simultaneously measured blood glucose and insulin levels, C-peptide, proinsulin, beta-hydroxybutyrate, and sulfonylurea metabolites measured in the plasma and/or urine.14 Low C-peptide levels in the presence of elevated insulin and proinsulin suggest exogenous insulin overdose as the cause of hypoglycaemia, whereas elevated sulfonylurea metabolites indicate either misuse or impaired clearance of sulfonylurea agents commonly used in the management of diabetes. The classic “gold standard” test for establishing the diagnosis of insulinoma is the 72-hour fast.13 Often, there is no identifiable mass on cross-sectional or endoscopic imaging at which point the SACST can be useful as a diagnostic investigation both to confirm the pancreas as the source of hyperinsulinemia and also to localize excessive insulin production within its anatomic regions.8

The diagnostic criteria for nesidioblastosis include Whipple’s Triad, a negative 72-hour fast, negative preoperative imaging studies, a positive SACST and findings of islet cell hypertrophy on pathology.14 The major histopathologic diagnostic criteria include macroscopic, microscopic and immunohistochemical exclusion of an insulinoma, multiple beta cells with enlarged and hyperchromic nuclei and abundant clear cytoplasm in majority of the islets, islets with normal spatial distribution, regular hormone expression patterns of the pancreatic cell types, and no proliferative activity of the Ki-67 antigen.5

Management of nesidioblastosis
Nesidioblastosis occurs either as a primary idiopathic disease or in patients who have undergone upper gastrointestinal (GI) surgery, most commonly a Roux-en-Y gastric bypass, although other operations including subtotal oesophagectomy, subtotal gastrectomy, Billroth I partial gastrectomy and Billroth II gastric bypass operations have also been implicated.17,19 The recommended management strategy varies based on the underlying pathology. For adult patients with idiopathic nesidioblastosis the definitive treatment is surgical resection.6 Surgical options include a left, extended or near-total pancreatectomy.1 Left pancreatectomy as an initial operation, followed by an extended left pancreatectomy (70% resection) if still symptomatic is one recommended approach to avoid post-operative insulin-dependent diabetes.2 If patients remain symptomatic, a near-total (90%) resection of the pancreas or even a total pancreatectomy is suggested, despite the risks associated with insulin-dependent diabetes.5

However, for patients diagnosed with nesidioblastosis following upper GI surgery, medical management should be
attempted first, with the understanding that surgical resection of a portion of the pancreas may be required in severe cases that do not respond to initial medical therapy. The most commonly used medication is diazoxide, a potassium channel agonist that inhibits insulin release. Diazoxide can also be used in patients after partial pancreatectomy who remain symptomatic. Other medication options include somatostatin analogues, glucocorticoids and calcium channel blockers (verapamil and nifedipine). Studies also suggest changing to a low-carbohydrate diet in addition to medical therapy to protect against hypoglycaemic episodes. Outcome after treatment of nesidioblastosis

The cause of primary nesidioblastosis in adults is unknown. Unlike in neonates, there have been no isolated genetic mutations associated with adult nesidioblastosis, although a genetic cause is suspected. There is also no evidence to date that dysregulation of the pancreatic islet cells resulting in the hyperinsulinemic hypoglycaemia of nesidioblastosis is a neoplastic process. For that reason, in patients treated with left, extended or near-total pancreatectomies, the spleen is preserved and treatment is targeted at managing symptoms. The precise risk of post-operative insulin-dependent diabetes is unknown given the small number of patients surgically treated for nesidioblastosis. In one series, 40% of patients after near-total pancreatectomy developed insulin-dependent diabetes. In the same study, a left pancreatectomy of 60-80% of the pancreatic tissue resulted in cure for approximately 50% of patients with an additional 19% achieving normoglycemia with medications and only an 8% rate of developing post-operative insulin-dependent diabetes. To date, there is too little data to accurately predict recurrence.

**CASE REPORT**

**Figure 3.** Selective arterial calcium stimulation test results. Hepatic blood insulin concentration at time zero, 20, 40, 60 and 90 seconds after calcium gluconate injection into the selectively isolated superior mesenteric, splenic and gastroduodenal arteries. There was a dramatic increase in insulin concentration in the SMA and SA blood supply territories in the pancreas.

**Figure 4.** Post-operative insulin levels. Serum insulin concentration on post-operative day one through day four. Intravenous fluids were stopped on post-operative day two. There was a consistent, downward trend in serum insulin concentration post-operatively.

SMA – superior mesenteric artery, GDA – gastroduodenal artery, SA – splenic artery

**Figure 5a-f.** Histology. Figures 5a-e represent haematoxylin and eosin stained slides. Foci composed of sclerotic stroma with proliferation of both ducts and islets between 2 and 3mm are seen (5a). In the surrounding pancreas numerous irregularly shaped islets are seen (5b) with ductular insular complexes (5c), ectatic vascular spaces (5d) and scattered hyperchromatic and enlarged nuclei with surrounding clear cytoplasm (5e). Synaptophysin immunolabel shows proliferation of islets within the tail of the pancreas (5f).
rates of hypoglycaemia after surgical resection.4

Conclusion
In summary, nesidioblastosis is an exceedingly rare condition that clinically and biochemically is indistinguishable from an insulinoma. When cross-sectional imaging is negative for a discrete mass, SACST is recommended to aid in the diagnosis and localization of insulin hypersecretion. In our patient, there was a clear regional increase in insulin secretion in the distal pancreas, which aided in the decision to perform a left pancreatectomy. The patient made an uneventful recovery with resolution of hypoglycaemic symptoms by post-operative day four and remains asymptomatic and normoglycaemic on routine follow-up.

References
5. Babi
2. Laidlaw GF. Nesidioblastoma, the islet tumor of the pancreas.
1. Davi MV, Pia A, Guarnotta V, Pizza G, Colao A, Faggiano A.

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Thania Kahn
Correspondence

tachycardic and pyrexial (39°C). His abdomen was soft with no palpable masses or organomegaly. Initial investigations revealed an inflammatory stool sample, with numerous (3+) leucocytes and 2+ erythrocytes. He demonstrated an iron-deficiency anaemia with a haemoglobin of 7.8g/dL, MCV of 80fL and transferrin saturation of 11% and C-reactive protein of 750mg/L. His HIV ELISA was negative, as were all blood cultures.

Colonoscopy demonstrated an extensive patchy colitis with ulceration from the rectum to caecum, with a normal terminal ileum on intubation. Histology displayed features of chronic active colitis with PAS-positive free-lying amoebae (Figure 3). The patient responded well to oral metronidazole, at a dose of 750mg TDS for 10 days. A repeat endoscopy showed marked improvement, but not complete healing. He was referred to the Department of Gastroenterology at Groote Schuur Hospital, where a full intestinal series was performed, including an ileocolonoscopy, which revealed no further evidence of pathology. The patient was discharged on a course of oral metronidazole (400mg TDS for 10 days) and instructed to follow up for a repeat endoscopy in 1 month, feeling well, with full resolution of his symptoms.

We present a case of colitis in a young male in the Western Cape, while progressing through the ambit of establishing a definitive diagnosis. We would like to highlight the value of microscopy which led to the specific diagnosis and subsequent management. The value of microscopy

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The value of microscopy in the diagnosis of colitis

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SUMMARY
We present a case of colitis in a young male in the Western Cape, while progressing through the ambit of establishing a definitive diagnosis. We would like to highlight the value of microscopy which led to the specific diagnosis and subsequent directed treatment.

Consent was obtained from the patient prior to publication

Clinical Case
A recently imprisoned 37-year-old male polysubstance user who had lived in Cape Town since birth, presented with a 5-week history of bloody diarrhoea. His stool frequency was 20 per day, with associated abdominal pain, and a 10kg weight loss. Prior to this he was well, with no chronic illnesses nor any family history of relevance and no travel history outside of the Western Cape.

On admission, he was wasted and though normotensive was tachycardic and pyrexial (39°C). His abdomen was soft with generalized tenderness and no organomegaly. Initial investigations revealed an inflammatory stool sample, with numerous (3+) leucocytes and 2+ erythrocytes. He demonstrated an iron-deficiency anaemia with a haemoglobin of 7.8g/dL, MCV of 80fL and transferrin saturation of 11% and C-reactive protein of 310mg/L. His HIV ELISA was negative, as were all blood cultures drawn throughout his illness.

CT abdomen showed evidence of a colitis with dilated ascending and transverse colon and a distended splenic flexure (Figures 1 and 2).

Colonoscopy demonstrated an extensive patchy colitis with ulceration from the rectum to caecum, with a normal terminal ileum on intubation (Figure 3). Histology displayed features of chronic active colitis with PAS-positive free-lying amoebae (Figure 4). The Entamoeba histolytica ELISA ratio of 4.3 was positive and diagnostic.

The patient responded well to oral metronidazole, at a dose of 750mg TDS for 10 days. A repeat endoscopy showed marked interval improvement, but not complete healing. He was reviewed at our clinic 1 month later, feeling well, with full resolution of his symptoms.

Discussion
Amoebiasis is caused by the protozoan parasite E. histolytica, and globally accounts for an estimated 100,000 deaths per year.2 Symptomatic intestinal infection has a spectrum of manifestations, most commonly amoebic dysentery. The majority of E. histolytica infections are asymptomatic, with only 10-20% of cases progressing to symptomatic disease, and its wide spectrum of both intra- and extra-intestinal manifestations. The spectrum of intestinal amoebiasis includes amoebic colitis, fulminant colitis, perforation, peritonitis, intra-abdominal abscesses and haemorrhage, amoebomas, structures and peri-anal cutaneous amoebiasis.3 Extra-intestinal sites of infection may manifest as liver abscesses, pleuro-pulmonary and pericardial involvement, or via haematogenous spread to the CNS and genito-urinary systems. The most common presenting symptom of amoebic colitis is a bloody diarrhoea, which may be accompanied with abdominal pain, weight loss and fever, the course of which may be acute or gradual.4 This patient presented with the typical bloody diarrhoea, and displayed a colitis on endoscopy, involving his caecum and ascending colon, with no manifestations of extra-intestinal disease.

E. histolytica is an infection of low-income countries, particularly in the tropical regions and areas with poor sanitation and inadequate hygiene.5 Transmission occurs after ingestion of infectious cysts, most commonly from faecal contaminated food or water. In South Africa, E. histolytica infection has been shown to be endemic in KwaZulu-Natal and North West provinces.6,7 Data on prevalence for the rest of the country is limited and traditionally the Western Cape is considered to be an amoebic free zone, however there have been 5 recent clinical presentations of this disease to the department of gastroenterology at Groote Schuur Hospital in the past year. The transmission modes may be similar to those in developed countries with a low endemicity where, the majority of cases are due to travellers or immigrants returning from endemic areas. More recently sexual exposure especially in men who have sex with men (MSM), has been highlighted as a form of transmission.8,9 Studies in Asia have shown increasing rates of invasive amoebic infection in MSM, although the HIV status was not declared.10 By comparison in the Western Cape, where the HIV prevalence in MSM is high, the risk of developing amoebiasis has not been shown to be increased.11 Our patient offered no travel history of note, and denied any sexual contact whilst in prison. We were unable to illicit any definite causative transmission in our patient, however his recent imprisonment may be noted as a risk factor.
When trying to elucidate the infection pathway it is important to understand the pathogenesis. There are many Entamoeba species that infect humans, of which 3 are morphologically indistinct from the pathogenic E. histolytica and E. moshkovski, which cause dysentery. E. dispar and E. bangladeshi are presumed to be non-pathogenic. There are only 2 stages to the life cycle of E. histolytica, namely excystation to trophozoites in the small intestine, followed by migration to the large intestines and further cyst multiplication. The trophozoites are passed in the stool, or may disseminate to extra-intestinal sites, such as the liver and lungs. Cytotoxicity, inflammation and tissue invasion are the hallmarks of pathological E. histolytica infection. The parasite has developed a number of mechanisms to evade host inflammatory defences and cause tissue destruction, including programmed cell death, phagocytosis and trogocytosis, a process whereby the enterocytes are “nibbled to death”. Gal/GalNAc lectin adhesion molecules facilitate adherence and access to the liver and lungs.

Several diagnostic modalities are available to evaluate patients for amoebic causes in any case of colitis, irrespective of the geographical location. Superseded stool microscopy, but is expensive and not freely available, remains the simplest diagnostic test. Antigen detection has become more popular but at expense limits its use in resource-limited settings. Stool cultures and microscopic examination may be useful in excluding the disease. These include stool cultures and microscopic examination, however, the sensitivity may be limited. All cases that are positive for E. histolytica with histology of amoebic colitis should have endoscopy to confirm the diagnosis. Chronic ulcers was seen on histology. This necrotic material lining the mucosa with an obvious dilated splenic flexure may cause diarrhoea. This was not possible in our patient as we were able to confirm the diagnosis on endoscopy. The treatment of amoebic colitis includes an amoebicidal agent and a luminal cytocidal agent. Asymptomatic patients with amoebic colitis may be treated with paromomycin 100mg/kg/day to eradicate the dormant oocytes. Paromomycin should be used with caution in patients with renal impairment.

A retrospective study from India, compared the endoscopic and histological findings in a group of patients with amoebic colitis and IBD. They noted that the endoscopic appearance of amoebic colitis is more severe in the IBD group. Inflammation extending to the deep mucosa and architectural ulcers was not a prominent feature in the IBD cases. Chronic ulcers was seen on histology. This necrotic material lining the mucosa with an obvious dilated splenic flexure may cause diarrhoea. This was not possible in our patient as we were able to confirm the diagnosis on endoscopy. The treatment of amoebic colitis includes an amoebicidal agent and a luminal cytocidal agent. Asymptomatic patients with amoebic colitis may be treated with paromomycin 100mg/kg/day to eradicate the dormant oocytes. Paromomycin should be used with caution in patients with renal impairment.

In the context of the above, we present a case of fulminant amoebic colitis diagnosed in a 70 year old male who presented with a 3 day history of bloody diarrhoea and colicky abdominal pain. He was admitted to the hospital with a diagnosis of non-IBD colitis. His clinical condition deteriorated quickly and he was intubated and ventilated. When trying to elucidate the infection pathway it is important to understand the pathogenesis. There are many Entamoeba species that infect humans, of which 3 are morphologically indistinct from the pathogenic E. histolytica and E. moshkovski, which cause dysentery. E. dispar and E. bangladeshi are presumed to be non-pathogenic. There are only 2 stages to the life cycle of E. histolytica, namely excystation to trophozoites in the small intestine, followed by migration to the large intestines and further cyst multiplication. The trophozoites are passed in the stool, or may disseminate to extra-intestinal sites, such as the liver and lungs. Cytotoxicity, inflammation and tissue invasion are the hallmarks of pathological E. histolytica infection. The parasite has developed a number of mechanisms to evade host inflammatory defences and cause tissue destruction, including programmed cell death, phagocytosis and trogocytosis, a process whereby the enterocytes are “nibbled to death”. Gal/GalNAc lectin adhesion molecules facilitate adherence and access to the liver and lungs.

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the host epithelium.\textsuperscript{5,6} *E. histolytica* forms a homolog with the proinflammatory cytokine macrophage migration inhibition factor (EMIF), the levels of which were recently found to correlate with intestinal inflammation in patients with amoebic colitis.\textsuperscript{7} The effect of this EMIF-induced inflammation is an increase in matrix metalloproteinases (MMPs), which in turn break down the extracellular matrix. Certain MMPs are reported to be overexpressed in patients with amoebic colitis and have been shown to be necessary for *E. histolytica* tissue invasion.\textsuperscript{8}

The differential diagnosis for this presentation includes other infectious causes, including bacteria, such as *Salmonella spp.*, *Shigella spp.*, *Campylobacter spp.*, entero-hemorrhagic *E. coli*, enteroinvasive *E. coli*, *C. difficile*; viruses; tuberculosis; and non-infectious causes, for example Inflammatory Bowel Disease (IBD), ischaemic colitis and colon carcinoma. A simple stool specimen for microscopy and culture often excludes these differentials.

Several diagnostic modalities are available to evaluate patients with suspected amoebiasis. Often it is a combination of these tests that establishes the diagnosis. These include stool microscopy, antigen detection, PCR molecular diagnosis, serology and endoscopy with histology. The most widely available test globally is stool microscopy, which requires a fresh stool sample, but has a poor sensitivity and specificity, and should not be used if other tests are available.\textsuperscript{1,9} However, if positive remains the simplest diagnostic test. Antigen detection has superseded stool microscopy, but is expensive and not freely available in resource-limited areas, with poor sensitivity and specificity in low-endemic areas. Stool PCR is the current gold standard for the diagnosis of amoebiasis, with excellent sensitivity and specificity. Its expense limits its use in resource-limited settings.\textsuperscript{1,9} We do not have access to this modality which largely remains a research tool in endemic areas. Serology, in the form of serum antibodies, can be detected in <70% of patient with colitis. Antibodies may remain positive for up to 5 years, so may be less useful in distinguishing between active or past infection, and may require repeat testing in 7-10 days, if initially negative. A negative result has a strong NPV, and therefore useful in excluding the disease.\textsuperscript{3,4}

Our patient’s diagnosis was confirmed on endoscopy, specifically the histology, which displayed *E. histolytica* with histochemical staining. Endoscopy allows for tissue histology, which often shows the characteristic flask-shaped ulcers and trophozoites may be identified using periodic acid-Schiff or immunoperoxidase staining with specific antibodies. The ascending colon and caecum are most commonly affected and may show friable colon with diffuse ulceration. A retrospective study from India, compared the endoscopic and histological findings in a group of patients with amoebic colitis and IBD.\textsuperscript{5} They noted the ulcers with amoebic colitis to be smaller (<2cm diameter), with normal intervening mucosa, and necrotic material mixed with mucus, proteinaceous exudate and blood clot lining the ulcers was seen on histology.\textsuperscript{7} This necrotic material lining the ulcers was not a prominent feature in the IBD cases. Chronic inflammation extending to the deep mucosa and architectural alteration were described as mild in the amoebic group and more severe in the IBD group.\textsuperscript{5}

The treatment of amoebic colitis includes an amoebicidal tissue-active agent and a luminal cytocidal agent.\textsuperscript{4} Asymptomatic patients need only a cytocidal agent to avert invasion and transmission. Available amoebicidal agents include the nitroimidazoles, metronidazole and tinidazole, which are both effective at trophozoite eradication. Tinidazole appears to be better tolerated, however metronidazole may be administered intravenously if oral tolerance is poor. The standard dosing regimen for amoebic colitis is oral Metronidazole 750mg three times daily for 5–10 days or Tinidazole 2g daily for 3–5 days. This is then followed by the luminal agent Paromomycin 25–35 mg/kg/day to eradicate the dormant oocytes. Paromomycin should not be given synchronously with nitroimidazole treatment as it may cause diarrhoea. This was not possible in our patient as this drug is not stocked in Groote Schuur Hospital. The use of loperamide and other anti-motility agents should be avoided in cases of amoebic colitis, based on a number of case reports suggesting that use of this drug may lead to the development of toxic dilatation.\textsuperscript{10,11}

There is still no vaccine for the prevention of amoebiasis and current preventative efforts focus on correct hand hygiene, food and water safety to minimise faecal-oral transmission. A thorough travel history should be sought in all patients, bearing in mind that fulminant amoebic colitis can occur years after travel.\textsuperscript{9} Newly diagnosed cases of IBD with a travel history to endemic areas should be screened for amoebiasis, as the administration of corticosteroids or other immunosuppressive therapy may progress to a fulminating colitis and misdiagnosis.\textsuperscript{12} This case highlights the importance of considering all infectious causes in any case of colitis, irrespective of the geographical location, as well as the merit of histology in establishing a definitive diagnosis and appropriate treatment, specifically the identification of the haematophagous amoeba.

\textbf{References}

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A case of severe vitamin B12 deficiency secondary to Helicobacter pylori gastritis

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Summary
Helicobacter pylori (H. pylori) is a gram-negative bacterium that colonizes the human stomach and is a major gastric infection worldwide. Approximately over 50% of the adult population in developed countries and 80% in developing countries are infected with this bacterium.1 2 H. pylori infection is invariably associated with gastritis, and triggers autoantibodies by a mechanism of molecular mimicry. It may play an important role in the impairment of vitamin B12 absorption leading to pernicious anaemia. This case report highlights H. pylori as a causative agent in vitamin B12 deficiency. H. pylori treatment reverse the underlying pathogenesis and corrects the vitamin B12 deficient state in selected individuals.

Case Report
A 31 year old non-vegetarian male, presented with a 9 month history of abdominal pain, and unintentional weight loss of 7kg. Laterally these symptoms were associated with 3 weeks of diarrhea and a decreased appetite. He was pale and not jaundiced. His abdominal examination was normal, with no hepatomegaly or ascites. There were no features of peripheral neuropathy.

Laboratory investigations revealed a pancytopenia with macrocytosis (normal range in brackets): hemoglobin 6.6 g/dL, MCV 111.8 fl (77-93 fl), MCH 38.80 pg (27-33 pg), red cell count 1.70 x 1012 / L (4.5-6.5 x 1012 / L), white cell count 2.42 x 109/L (4-10 x 109/L), platelet count 94 x 109/L (150 - 400 x 109/L). He was found to have severe vitamin B12 deficiency with a level of 59 pg /ml (191-663pg/ml) with normal folate levels of 14.08 ng/ml (7.2- 15.4 ng/ml) and ferritin levels of 361 ng/ml (30-400ng/ml).The peripheral blood smear revealed a macrocytic blood picture with marked anisopoikilocytosis with numerous fragments, macrocytes with elongated and tear drop cells.

Liver function tests revealed a mild indirect bilirubinemia: total bilirubin 10.80 µmol/L(normal range 0-2.5 µmol/L), but was otherwise normal (total proteins 60g/L, serum albumin 38g/mL, albumin/globulin ratio 1.7, aspartate transaminase 27 U/L and alanine transaminase 34 U/L). The haptoglobin was < 8 mg/dL (normal range 30-200 mg/dL). The patient had negative Coomb's test, and negative for Coombs test. The direct Coombs test was positive, while the direct Coombs test was negative.

Serology for pernicious anemia was equivocal; pancreatic islet cell antibodies and parietal cell antibody were weakly positive, but the intrinsic factor antibody was negative. For completion, hemoglobin electrophoresis was carried out, showing no evidence of beta thalassemia or hemoglobinopath.

A diagnosis of severe vitamin B12 deficiency was made and the patient commenced on hydroxy cobsalamin 1mg IM once a day for 3 days, then 1mg IM alternate days for 4 doses, then 1mg once a month for 3 months. The patient was initiated on H. pylori eradication therapy (Levofloxacin 500mg, Amoxicillin 1000mg, and Esomeprazole 40mg) and completed a two course.

At clinic review a fortnight later, the pancytopenia had markedly improved; the hemoglobin count had risen to 10.2 g/dL, white cells to 4.5 x109/L and platelets to 550 x109/L. Hematocrit was 34.30%, mean corpuscular volume 96.30 fl and mean corpuscular hemoglobin 28.70 pg. A month later his blood panel revealed a hemoglobin of 13.7 g/dL, white blood cells of 4.1 x10^9/L, platelets of 282 x10^9/L and a mean corpuscular volume of 79 fl (77-93fl). He was noted to have significant weight gain of 5 kilograms over this period. At six months he remains well with a normal hemoglobin.

Discussion
H. pylori infection is strongly associated with chronic antral gastritis. The colonization of the gastric mucosa with H. pylori causes a chronic local and systemic immune response leading to antral gastritis, destruction of the gastric parietal...
cells, peptic ulcer and gastric atrophy.\(^4\)\(^5\)

_H. pylori_ infection triggers autoantibodies by a mechanism of molecular mimicry and can stimulate an autoimmune process against the gastric parietal cells and α, β subunits of the proton pump, which causes impairment in gastric acid and pepsin secretion.

The destruction of the gastric parietal cells, and induction of apoptosis, leading to atrophic gastritis, leads to reduced availability of intrinsic factor (IF).\(^4\)\(^5\) IF forms the IF-B12 complex, and mediates vitamin B12’s transport and absorption in the ileum. Lack of the IF therefore causes an interference with vitamin B12 absorption, thus leading to vitamin B12 deficiency and its clinical manifestations.

It has been proposed that pernicious anemia may represent the final phase of a process that begins with _H. pylori_ associated gastritis and evolves through progressive levels of atrophy until parietal cell mass is entirely lost.\(^5\)

Parietal cell antibody may be weakly positive in these cases of severe gastritis.

In a study by Raut et al, vitamin B12 levels in patients with _H. pylori_ positive gastritis were significantly lower than those with _H. pylori_ negative gastritis.\(^7\) It has been found that eradication of the infection restores acid secretion even in patients with severe atrophy.\(^8\)

The diagnosis of severe vitamin B12 deficiency in our case was confirmed by low serum vitamin B12 and the appearance of the peripheral blood smear examination. Additionally, our patient had weakly positive antibodies against the parietal cell. Eradication of _H. pylori_ infection and replacement of the Vitamin B12, successfully resolved the patient’s pancytopenia and symptoms.

**Conclusion**

There is a strong pathogenic link between _H. pylori_ and gastritis,\(^3\) and as such _H. pylori_ has been postulated to be one of the causative factors in the development of vitamin B12 deficiency. Eradication of _H. pylori_ infection may correct vitamin B12 levels and improve anemia in these patients, and investigation for this should be considered in patients who present with severe vitamin B12 deficiency with atypical clinical or laboratory features.

**References**


**CASE REPORT**

Figure 1a: Micrograph showing gastric antrum with features of gastritis; two active germinal centres are seen within the lamina propria (hematoxylin-eosin, original magnification x20)

Figure 1b: High power view of the lamina propria expanded by a mixed inflammatory infiltrate composed of plasma cells, lymphocytes, neutrophils and eosinophils (hematoxylin-eosin, original magnification x40)
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A 38-year-old male presented with a one-day history of worsening abdominal pain and distension. He reported no nausea or vomiting and had a bowel movement a few hours before admission. He had no significant past medical history except that he was a known chronic methamphetamine user, having indulged his habit in the past 48 hours. On physical examination, he was haemodynamically stable and apyrexial. His abdomen was distended and diffusely tender with no rebound or guarding. The rectum was empty on digital examination. An arterial blood gas revealed a pH of 7.37, a lactate 1mmol/L, a standard bicarbonate 22.6mmol/L and a base excess -2.9mmol/L. His white cell count was 29.72.

A plain abdominal radiograph (Figure 1) showed non-specific, dilated large bowel, with air in the rectum. No mass was identified in the stool sample. Biopsies of colonic mucosa were obtained, and showed a non-specific acute colitis. A provisional diagnosis of indeterminate colitis was made. The patient was started on intravenous metronidazole, due to his elevated white cell count and marked distension. A colonoscopy was performed on the day of admission and showed marked inflammation involving the sigmoid and descending colon, without ulceration. The procedure was abandoned at 80cm due to marked discomfort. A provisional diagnosis of ischaemic colitis, an infective colitis or an atypical large bowel obstruction was considered. The patient underwent an urgent laparotomy, and a complex caecal volvulus with pneumatosis coli (Figure 2) was identified. An emergency laparotomy was performed, and a right hemicolectomy was performed for an ileocecal obstructing caecal volvulus. Despite a delay in diagnosis, the patient recovered to live to fight another day.

SUMMARY

Three days post admission, his abdomen became massively dilated and hypertensive, with a palpable mass in the right iliac fossa. An urgent CT scan revealed a large bowel obstruction due to a caecal volvulus. The patient had undergone multiple unsuccessful attempts at reduction of the volvulus. The clinical presentation of patients with caecal volvulus is usually non-specific and can be highly variable. Common signs and symptoms include: generalised abdominal tenderness, abdominal distension, constipation/obstipation, fever, tachycardia, and worsening hypotension. Laboratory findings may include leukocytosis, metabolic acidosis, and non-specific elevations in liver function tests. Abdominal radiography is the first line investigation that offers the most value in diagnosing a caecal volvulus. It can result in splanchnic vasoconstriction causing acute hypertension, tachycardia and even myocardial ischaemia. Methamphetamine use results in the sustained release of norepinephrine. This can cause arterial vasoconstriction via alpha-1 receptors. Although more common for mesenteric infarction of the colon, without infection. These features were consistent with the clinical diagnosis of volvulus. Histopathology showed transmural ischaemia, with no infection identified in the stool sample. Biopsies of colonic mucosa were obtained, and showed a non-specific acute colitis. A provisional diagnosis of indeterminate colitis was made. The patient was started on intravenous metronidazole, due to his elevated white cell count and marked distension. A colonoscopy was performed on the day of admission and showed marked inflammation involving the sigmoid and descending colon, without ulceration. The procedure was abandoned at 80cm due to marked discomfort. A provisional diagnosis of ischaemic colitis, an infective colitis or an atypical large bowel obstruction was considered. The patient underwent an urgent laparotomy, and a complex caecal volvulus with pneumatosis coli was identified. An emergency laparotomy was performed, and a right hemicolectomy was performed for an ileocecal obstructing caecal volvulus. Despite a delay in diagnosis, the patient recovered to live to fight another day.

References:
3. SIMPONI® Solution for Injection package insert (May 2013).
4. SIMPONI® Solution for injection. Each 0.5 ml single use pre-filled syringe or pre-filled pen contains 50 mg of golimumab. Reg. No. 43/50/1/0808.
5. For full prescribing information refer to latest package insert (May 2013).
A young male presented with worsening abdominal distension and pain. Initial investigations were inconclusive, and an urgent colonoscopy revealed an active colitis, presumed to be due to methamphetamine induced mesenteric ischaemia. No bacterial or parasites were identified in the stool sample. Biopsies of colonic mucosa were obtained, and showed a non-specific acute colitis.

Case Report

A 38-year-old male presented with a one-day history of worsening abdominal pain and distension. He reported no nausea or vomiting and had a bowel movement a few hours before admission. He had no significant past medical history except that he was a known chronic methamphetamine user, having indulged his habit in the past 48 hours. On physical examination, he was haemodynamically stable and apyrexial. His abdomen was distended and diffusely tender with no rebound or guarding. The rectum was empty on digital examination. An arterial blood gas revealed a pH of 7.37, a lactate 1mmol/L, a standard bicarbonate 22.6mmol/L and a base excess -2.9mmol/L. His white cell count was 29.72 x 10^9/L. A plain abdominal radiograph (Figure 1) showed non-specific, dilated large bowel, with air in the rectum. No classical features of volvulus were identified. The differential diagnoses initially considered were amphetamine-induced ischaemic colitis, an infective colitis or an atypical large bowel obstruction.

Stool and blood samples were obtained for microscopy, culture and sensitivity. A colonoscopy was performed on the day of admission and showed marked inflammation of the sigmoid and descending colon, without ulceration. The procedure was abandoned at 80cm due to marked discomfort. A provisional diagnosis of indeterminate colitis was made. The patient was started on intravenous metronidazole, due to his elevated white cell count and suspicion of an infective colitis. No bacterial or parasites were identified in the stool sample. Biopsies of colonic mucosa were obtained, and showed a non-specific acute colitis.

Three days post admission, his abdomen became markedly distended, tympanic and tender. An urgent CT scan showed features of a large bowel obstruction due to a caecal volvulus with pneumatosis coli (Figure 2). An emergency laparotomy was performed, and a complex caecal volvulus involving the sigmoid colon was found (Figure 3). The sigmoid colon was staple transected to gain access to the mesentry of the ileo-caecal volvulus which was necrotic but not perforated. A right-hemicolectomy with a stapled, side-to-side anastomosis was performed. Continuity of the sigmoid volvulus was restored in a similar manner. His post-operative course was complicated by a prolonged ileus and contained anastomotic leak, requiring percutaneous drainage. The patient was discharged in a stable condition 21 days after admission. The patient was lost to follow up and did not return for clinical assessment. Histopathology showed transmural infarction of the colon, without infection. These features were consistent with the clinical diagnosis of volvulus.

Discussion

This case presented a diagnostic dilemma due to the non-specific nature of the clinical and radiological signs, further confounded by the history of recent methamphetamine use. Methamphetamine use results in the sustained release of norepinephrine. This can cause arterial vasoconstriction via alpha-1 receptors. Although more common for methamphetamine to have cardiac side-effects, such as hypertension, tachycardia and even myocardial ischaemia, it can result in splanchnic vasoconstriction causing acute mesenteric ischaemia. This diagnostic possibility was to some degree supported by the findings of mucosal inflammation seen on colonoscopy and these factors contributed to the delay in arriving at a diagnosis in need of surgical intervention.

The clinical presentation of patients with caecal volvulus is usually non-specific and can be highly variable. Common signs and symptoms include: generalised abdominal tenderness, abdominal distension, constipation/obstipation, and vomiting. Other presentations may include intermittent releting abdominal pain eased by the passage of flatus to outright peritonitis and septic shock. For this reason, the diagnosis is seldom made on the basis of clinical examination findings alone, with radiography and CT being important adjuncts in formulating a definitive diagnosis.

Abdominal radiography is the first line investigation that offers the most value in diagnosing a caecal volvulus. A massively dilated caecum, air fluid level in the caecum, small
bowel dilatation, and absence of distal bowel gas are usual radiographic findings. 1,2 CT is considered to be more sensitive and specific in evaluating caecal volvulus. The coffee-bean sign, bird beak sign, and whirl sign can be indicative of a volvulus of the caecum. 1,3,2 Caecal volvulus is an uncommon cause of bowel obstruction in Southern Africa. The condition is commoner in Europe, the United States and in parts of India, with the average age of presentation being 53 and 33 in the Western World and India respectively. 1,4,5 There is a paucity of literature regarding the incidence of caecal volvulus from Africa,1 where sigmoid volvulus is much commoner.

It is evident that making the diagnosis of caecal volvulus with certainty in young adults presenting with features suggestive of large bowel obstruction can be difficult. Early imaging, in the presence of a patient with intestinal obstruction, can prove vital in expediting definitive management. Ultimately, an early diagnosis could avoid the sequelae of an ischaemic and perforated caecum.

References
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References

The IBD Interest Group Meeting was held at the Vineyard Hotel in Cape Town, on a sunny winter’s Saturday in June. This was the 13th Inflammatory Bowel Disease (IBD) interest group meeting, hosted once again by the Gastro Foundation.

The focus of this meeting was aimed at improving the clinical management of IBD patients in our Sub-Sahara African setting, as well as reviewing some important topics in Gastroenterology.

The first session was opened with a welcome talk from Prof C Kassianides. This was followed by a much-anticipated talk by Prof G Watermeyer on the emerging novel biologics. Over the last 15 – 20 years anti-tumour necrosis factors (TNFs) have revolutionised the management of IBD and now biosimilars of Humira (Adalimumab) and Remicaide (Infliximab), have become available. These products have proven highly similar to the reference product with no significant clinical difference in safety, quality or efficacy, and with the main benefit of a significant reduction in cost. This talk provided an interesting synopsis of the development of these newer agents, specifically Remsima, their comparison to the originators and their future in the management of IBD.

A few interesting case studies were presented, including a review of amoebic colitis. Traditionally, the Western Cape is thought to be an amoebic-free zone, however there have been 5 cases of amoebic colitis treated at Groote Schuur Hospital this year. This serves as an aide-memoire to considering this infectious cause in the differential diagnosis of any acute or chronic colitis, irrespective of the geographical area, as well as the importance of both a recent and distant travel history.

Dr T Machiridza, our gastroenterology fellow from Zimbabwe, presented an interesting case of a patient with Crohn’s Disease (CD), complicated by Primary Sclerosing Cholangitis (PSC) and pyoderma gangrenosum, requiring high doses of corticosteroids and immunosuppressive therapy (azathioprine). The patient then developed a liver lesion with accompanying loss of weight, which was thought to be a cholangiocarcinoma, due to her background of PSC. However, this diagnosis was not confirmed via a biopsy/histology. Subsequent to this, her condition deteriorated, with the development of new chest lesions (lung mass, pleural effusions), the biopsy of which confirmed the true diagnosis of tuberculosis (TB), for which the patient was treated.
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marked improvement. The case highlights the increased risk of opportunistic infections, in particular TB, in our immunosuppressed patients, as well as the importance of continual review of diagnoses in these patients.

Dr Daniel Surridge, from the Department of Colorectal surgery at Baragwanath Hospital in Johannesburg, provided a concise account of optimising our IBD patients for surgery, highlighting the importance of a multi-disciplinary approach, early involvement of the surgical team, the importance of pre-operative resuscitation, and the functionality of the Enhanced Recovery After Surgery (ERAS) protocol.

Prof G Watermeyer and Dr E Deetlefs reviewed common mistakes in the management of both severe Crohn’s Disease and Acute Severe Ulcerative Colitis (ASUC). The latter is a common medical emergency we regularly encounter, and if inadequately treated, carries a high mortality. The presentation included a review of the great mimics of this condition, its complications, the importance of early and aggressive medical therapy, and the problem of unnecessary delays in referrals to specialist centres.

The guest speakers were Dr Adegoke and Prof Ojo from Nigeria who gave us some insight to their experiences as pathologists in the field of IBD, highlighting the increasing hospital prevalence of IBD over recent years and the clinical diagnostic and management limitations in their setting.

Prof M Setshedi offered us a preview of their highly anticipated research into the statistics of a Sub-Saharan IBD cohort. The presentation highlighted the paucity of data in our setting, the reasons for this including underreporting of cases and the lack of specialist services in remote areas. Possible solutions to these issues should involve the institution of IBD registries, improving awareness and education and publishing already accrued data to benchmark the temporal epidemiological trends and outcomes from the diseases in the public and private sectors in South Africa and neighbouring states.

The final presentation of the day was delivered by Prof M Sonderup on IBD and the liver, with a focus on PSC, Hepatitis B reactivation and drug-induced liver injury (DILI). Important discussion points included the premalignant nature of PSC, and the problems of screening for associated cholangiocarcinoma. He supported the use of ursodeoxycholic acid, and discussed current investigative agents being trialled in this setting. Effective screening programs for PSC-related malignancies have been shown to improve outcomes.

In addition, Prof Sonderup provided valuable insight into Hepatitis B reactivation. He highlighted the frequency of occurrence, the impact of immunosuppressive agents used in IBD, and the expected outcomes and the efficacy of prophylactic antivirals, namely Lamivudine. He took us back to basics with an approach to the frequent occurrence of deranged liver function tests in our IBD patients, emphasising drug interactions and toxicity as the major culprits to be considered and managed accordingly.

The day included a delicious breakfast and brunch spread, against the backdrop of Table Mountain. A thank you to the sponsors Abbvie, Janssen, Adcock Ingram, Equity, Ferring and Takeda. These meetings would not be possible without their generous support. The meeting was a great success for my gastroenterological education and I believe was valuable and appreciated by all sixty-five gastroenterologists who attended, both young and old.
The beneficial health effects of probiotics can only be attributed to the strain tested. Probiotics must be alive, specified by genus and strain (research on specific probiotic strains cannot be applied to any product marketed as a probiotic), shown to be effective in controlled human studies and delivered in a dosage based on human studies showing a health benefit. This is exactly what Quatroflora offers. This 4-in-1 product stands out in the medical fraternity thanks to its high level of documentation and because of its well-researched positive effect on intestinal health. It survives stomach acid and bile, with resultant high activity in the intestine where it is needed. In addition, Hansen has developed a polysaccharide matrix for the probiotic capsules to further protect the bacteria from acidic influence.

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Establishing an endoscopy service at False Bay Hospital

In my last few years in as the Chair of the Department of Gastroenterology I introduced several initiatives to improve the standard of endoscopy in the GI unit at Groote Schuur and in the country in general. This is against the background of several reports on endoscopy services, most recently from KwaZulu Natal but also from the Western Cape province and from a SAGES initiative that the provision of endoscopy services in the state sector are woefully short of demand both in terms of personnel and equipment.

My passion for teaching and improving the standards of the practice of endoscopy to build capacity for an improved service has extended into my retirement. I have become involved at Victoria District Hospital with providing a colonoscopy service as the result of forward thinking Head of Surgery Jeremy Plaskett and Belinda Thomson, the long serving GI sister and past president of SAGINS. False Bay Hospital was using Victoria Hospital as an open access endoscopy service resulting in volume of requests that were simply not able to be processed in a reasonable time frame. The solution was obvious, provide an endoscopy service at False Bay Hospital. A meeting was set up between management for an in principle agreement and this was received by both management groups enthusiastically. The first step was to be able to free up an endoscopy stack and a gastroscopy. This was possible with the acquisition of new equipment to run their Victoria Hospital Service. Secondly, there was a need to train an established medical officer as an endoscopist. Adrian Morom was duly identified as an individual who was keen to develop the service and he began regularly attending the Monday gastroscopy list at Victoria where I mentored him on an individual basis through his first 50 gastroscopies.

In conjunction with this it was essential that we also identified a nursing sister who would be responsibility for running the nursing side of the endoscopy service and in particular take on the tasks of reprocessing and disinfecting the instrument. The initial sister identified moved on to pastures new before we could induct her into training but fortunately the new appointee, Sister Arendse, stepped into the breach. Now all the ducks had fallen into place and we were in a position to set up the service at False Bay.

The logistics of this task were in the capable hands of Belinda Thomson who recruited her long term associate Luanne Strydom who has been in the endoscopy business for many years and is currently the senior sales representative in Cape Town for Ascendis Health. They duly transferred the equipment and off we went on the June 3rd to False Bay to set up the reprocessing and disinfection logistics, organise the endoscopy room and provide logistic support for their initial 4 cases. The enthusiasm was infectious and the old grey haired man taking the pictures could only marvel at what a little bit of support and not too much red tape could set up inside 9 months. I hope this venture encourages this type of activity elsewhere and good luck to my fellow enthusiasts where ever you are.

Sandie Thomson

References

The logistics experts “the real trainers” Belinda Thomson (left) and being “endoscoped” Luanne Strydom (right)

The first patient who just happened to have Barrett’s oesophagus

The False Bay Team and their trainers

Left to right: Andrea Arendse, Katu Ramulumbi, Adrian Morom, Belinda Thomson, Diane Matthys, Brigitte van der Merwe, Luanne Strydom, Genevieve Witbooi
The launch of the Viral Hepatitis in sub-Saharan Africa ECHO program

The “Viral Hepatitis in sub-Saharan Africa” ECHO program was launched on 23 May 2019 from the Liver Unit at the University of Cape Town and Groote Schuur Hospital. This is a supranational model involving five countries:

- **South Africa**: Professors Wendy Spearman and Mark Sonderup
- **Nigeria**: The University of Lagos, Lagos led by Prof Funmi Lesi
- **Ghana**: Kwame Nkrumah University of Science and Technology, Kumasi led by Prof Mary Afihene
- **Ethiopia**: Addis Ababa University Medical School led by Prof Abate Shewaye
- **United Kingdom**: UCL Institute of Liver and Digestive Disease and Kings College Hospital. Active support and ongoing guidance from Prof Geoff Dusheiko

This TeleECHO program will encourage secondary level hospitals and community-based healthcare providers to participate in sub-Saharan Africa’s first viral hepatitis ECHO program to expedite delivery of appropriate treatment for Hepatitis B and C. The Liver Unit at the University of Cape Town and Groote Schuur Hospital will initially function as the Hub with the centres in Nigeria, Ghana and Ethiopia becoming their own Hubs over the next 6-12 months and developing their own spokes thereby rapidly increasing access to care for viral hepatitis within their regions.

Within South Africa, we plan initially to set up spokes at the secondary level hospitals in George, Port Elizabeth and East London where we already have well established patient referral pathways. Over time, this would be expanded to include other spokes at more hospitals throughout South Africa.

We look forward to actively interacting with healthcare providers across Sub-Saharan Africa and thereby improving linkage to care for hepatitis B and C.
Finding ways out of the conundrum that is acute liver failure management:

Many an experienced clinician will find him or herself daunted by the presentation of a patient in acute liver failure. Accurate goal-directed management strategies are paramount to ensuring a good outcome in a patient at very high risk of mortality. Erroneous decision-making often closes the small window of opportunity to save these patient’s lives and knowing where to turn for help and advice could make all the difference.

In view of the above the concept of hosting an acute liver failure management symposium was born. Input and advice from leaders in the field were presented in a concise, practically applicable manner covering topics from basics to experimental approaches in dealing with the patient in fulminant liver failure.

The meeting was held at the Radisson Gautrain hotel on 11 May 2019. Prof Chris Kassianides, one of the founding members of the Gastro Foundation, opened the morning with a warm welcome to all and the morning got underway with an opening talk by Prof Adam Mohammed on the diagnosis and local patterns of aetiology of acute liver failure in Southern Africa.

Dr. Tim de Maayer followed with an enlightening presentation on pediatric liver failure, covering common ground with its adult counterpart, and highlighting important differences between adult and pediatric liver failure. The intensive care management is often one of the most challenging aspects of the care of these patients. Dr. Lliam Brammingham provided clear guidelines on how to deal with common problems faced by these critically ill patients in the intensive care setting. A presentation given by Dr. Bilal Bobat on the concept of acute on chronic liver failure rounded off the session. The latter gave way to some lively debate amongst the delegates and after important consensus was reached the group broke for refreshments.

Following a delicious brunch and an opportunity to greet old friends and colleagues, the second session of the morning got underway. Prof. Jean Botha started by presenting guidelines on when to refer patients in acute liver failure for transplantation. Owing to the intricacies of managing these patients, the principle of referring early to a center with experience in the management of acute liver failure, with transplant capabilities was emphasized.

Dr. Sharan Rambarran followed with a very intriguing and stimulating talk on the current state and future direction of bridging therapies in liver failure and Prof Graham Paget tackled the issue that is ABO incompatible liver transplantation.

The group enjoyed a refreshment break after which Prof Jonas presented a talk on the controversial topic of alcohol induced liver failure. Dr. Greg Johnson gave the last talk of the day with insight given into the challenges of managing the psychological aspects of patients and families who survive acute liver failure.

In one morning a huge number of important issues surrounding the care of patients with acute liver failure got addressed and discussed. Important networking occurred between clinicians who often work in isolation and clear channels of communications were established. This is critical to ensure improved survival of these very challenging patients.

Francisca van der Schyff
Surgical Transplant Fellow
Wits Donald Gordon Medical Center
Treatment and maintenance of remission in ulcerative colitis

**DOSAGE:**
500 mg Suppositories
One suppository to be inserted rectally up to three times daily after defaecation.
Cipla is committed to delivering medicines to meet the needs of patients and families affected by gastrointestinal symptoms.

**Nesopram**
Esomeprazole 20 mg; 40 gm
Reg. No. 45/11.4.3/0123, 0124

**Prazoloc**
Pantoprazole 20 mg; 40 mg
Reg. No. 45/11.4.3/1147, 1148