PROFESSIONAL PRACTICE 08

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SYDNEY

GASTROENTEROLOGY EDUCATIONAL SYMPOSIUM

Janssen-Cilag's most successful Professional Practice Symposium to date was convened in April 2008, with more than 100 gastroenterologists gathering in Sydney for a mix of professional and clinical topics of interest. The Professional Practice Symposium has been held for four consecutive years now and this year's program proved the most popular yet. Featuring international guest Professor Kenneth McColl speaking on the acid pocket and implications of this in the increased incidence of upper gastrointestinal cancers, the program received glowing endorsements from attendees. For the first time in 2008, the symposium offered a hands-on PowerPoint lab for clinicians wanting to brush up on their presentation skills. Other highlights of the meeting included plenary sessions on Barrett's oesophagus ablation techniques and financial aspects of gastroenterology practice.

Gender the key to modifying GO junction cancer development

Keynote international speaker **Professor Kenneth McColl**
Gardiner Institute, Western Infirmary, Glasgow, Scotland

Professor Kenneth McColl explored the marked increase in gastro-oesophageal (GO) junction cancers in his plenary address at this year's Professional Practice Symposium.

Professor McColl discussed the possible roles of atrophic gastritis and *H. pylori* in the aetiology of GO junction cancer, as well as proposing certain environmental factors as key contributors.

In exploring the high incidence of GO junction cancers in north-west England, Professor McColl sought to identify the role of gastro-oesophageal reflux disease (GORD) in cardia cancer, as well as to describe two distinct aetiologies discernable at the time of presentation. He outlined the two subtypes as follows:

Type A
- similar to non-cardia cancer
- *H. pylori*-induced atrophic gastritis hypochlorhydria
- intestinal or diffuse histological subtype.

Type B
- similar to oesophageal adenocarcinoma
- healthy *H. pylori* negative acid secreting stomach
- associated with GORD
- intestinal histological subtype.

The role of nitrite as an important pre-carcinogen was discussed in the context of GO junction cancers. Professor McColl suggested that dietary nitrates could contribute to the high incidence of GO junction cancers, via acid nitrosation into nitric oxide in the upper GI tract. He also highlighted the fact that acid reflux generates nitric oxide in Barrett's oesophagus. An important parallel between the increase in fertiliser usage and GO junction cancer was also presented as a possible explanation for the increasing incidence of this type of cancer.

A gender phenomenon characterised by a marked male predominance in adenocarcinomas of the oesophagus and stomach was also discussed. Professor McColl's research identified that although this gender phenomenon was unrelated to the anatomical site of the cancer, the intestinal subtype appeared to play a role. A population study in the west of Scotland demonstrated that there was a 17-year delay in the development of cancers in females versus males. Professor McColl also indicated that this delaying process operates until 55 years of age at which point it disappears.

Professor McColl then questioned the factors influencing the nature or impact of the inflammatory process in males versus females prior to 55 years of age. He proposed that tissue iron status and reproductive hormones could be explanations for the difference in genders.

The high incidence of GO junction cancer warrants consideration of the gender phenomenon with respect to screening and disease modification options. Professor McColl said his findings cannot only be helpful in establishing an appropriate age for screening, but can also offer insight into the carcinogenic process in males versus females. He says that being able to modify this carcinogenic process to achieve the same 17-year delay in males as seen in females would be a favourable outcome. Modification of the carcinogenic process via hormonal intervention presents a more viable method of reducing the high incidence of GO junction cancer than attempting to modify other possible contributing environmental factors such as dietary nitrates.

Professor McColl's address prompted questions from attendees regarding the role of various other environmental factors such as alcohol and smoking, and he agreed that the rise in obesity could play a role. Obesity could also contribute to the gender phenomenon in some way, but this required further investigation.

In terms of clinical management, Professor McColl suggested that there is no single answer. He felt screening in patients with intestinal metaplasia was not a cost-effective option and that it created unnecessary angst in patients. However, in cases where dysplasia was detected, screening was worthwhile.

Should we measure azathioprine metabolites?

Dr Miles Sparrow
Director, Inflammatory Bowel Disease Clinical Trials
Department of Gastroenterology, Box Hill Hospital, Melbourne

Measurement of azathioprine metabolites offers an explanation for non-response in some patients, as well as a way to detect those at risk of leukopaenia, a rare but potentially fatal side effect of azathioprine.

Dr Miles Sparrow presented his views on azathioprine metabolite measurement at the Professional Practice Symposium. The two metabolites measured are 6-TGN (6-thioguanine nucleotides), levels of which correlate with drug efficacy, and 6-MMP (6-methylmercaptopurine), which instead correlates with hepatotoxicity. Patients in remission have higher levels of 6-TGN than those with active disease. 6-TGN induces apoptosis of T lymphocytes, and is also responsible for any leukopaenia associated with thiopurine immunomodulators. Dr Sparrow emphasised that the white cell count is still the most important measure for patients on thiopurines and should be continued for the duration of therapy, as patients can become leukopaenic at any time.

Dr Sparrow highlighted the value of azathioprine metabolite testing in the context of a new top-down approach to the management of inflammatory bowel disease (IBD) published recently in *The Lancet*, in which immunomodulators are used much earlier in the treatment of inflammatory bowel disease.

He said metabolite measures were useful in patients not responding to standard doses of thiopurines to help clarify the reason for non-response (which is defined as not being in a steroid-free remission). The tests helped identify four groups of patients:

- Non-compliant (metabolites are absent)
- Under-dosed (low metabolites)
- Thiopurine resistant (low 6-TGN, high 6-MMP)
- Thiopurine refractory (high metabolites).

In order to differentiate between non-compliant and under-dosed patients, it was important to note that the levels detected were indicative of the last 2–4 weeks. In those showing thiopurine "resistance" due to the preferential production of the inefficacious metabolite 6-MMP, an experimental strategy recently utilised has been the addition of low doses of allopurinol to reduced-dose immunomodulator therapy, which has been shown to increase thiopurine efficacy in this small subgroup of patients.

Alternative immunomodulators to azathioprine were discussed, but despite good outcomes, Dr Sparrow said these alternatives were limited by poor side effect profiles. He said thioguanine (TG) was associated with nodular regenerative hyperplasia and hepatic veno-occlusive disease leading to portal hypertension, and therefore its use cannot be currently recommended.

Many consider the cost of testing at approximately $200 for both metabolites expensive, but Dr Sparrow argued that this could be justified in thiopurine non-responders as a way to optimise dosage before otherwise switching to alternate agents such as methotrexate or infliximab. He said metabolite testing represents part of a current shift towards "personalised medicine" in which future patients will have their genetic and serological profiles established at baseline, and thereafter the management of their disease can be more individually targeted. He said metabolite testing offered a way of optimising the use of thiopurines and this testing sits well with current practice of the increasing role of immunomodulators in managing IBD.

Workshop explores role of acid pocket in GO cancer

Acid secretion in reflux disease is a contentious area, and one Professor Kenneth McColl tackled at the Professional Practice Symposium. Professor McColl described his work on the "acid pocket" as the source of reflux disease. He theorised that an acid pocket sitting at the top of the stomach bathes the distal oesophagus in acid following a meal. He said the meal distorts the lower oesophageal sphincter (LOS), exposing the squamocolumnar junction to acid, thereby resulting in acid reflux.

Professor McColl said the increase in the incidence of reflux, as well as adenocarcinomas could be attributed to many factors including diet, obesity and *H pylori* infection. He added that people's physiology had changed with the stomach maintaining high acidity well into old age, despite the fact that acid's protective role is largely obsolete in a modern, sterile world. "Reflux is a disease of the developed world, but we will see the epidemic spread as the westernised diet and lifestyle moves into other parts of the world," he said.

With only 1 in 20 oesophageal adenocarcinomas beginning as Barrett's oesophagus, screening was an ineffective management strategy. He said the asymptomatic oesophageal adenocarcinoma patient presented a great challenge and that effective management must also address the many environmental factors associated with the increasing incidence of gastro-oesophageal cancers.

The 2008 Professional Practice Symposium offered a hands-on PowerPoint lab for clinicians wanting to brush up on their presentation skills

It runs in the family

Clinical Associate Professor Judy Kirk
Director, Familial Cancer Service, Westmead Hospital, Sydney

Family cancer clinics offer advice, early detection and prevention of cancer in patients with a family history. Associate Professor Judy Kirk discussed the nature of these clinics and identified some of the familial syndromes involved in gastrointestinal cancers at the Professional Practice Symposium.

Professor Kirk said it was important to acknowledge that genetic susceptibility to gastrointestinal cancers was rare, but in certain individuals genetic testing could aid risk reduction and influence cancer management – with a view to targeted therapies in the future. She said bowel cancer usually occurs as a result of a series of mutations in critical genes such as APC, KRAS, p53, and MMR, which control cell growth, and in rare cases, this type of genetic mutation may be familial. Patients with a germline (heritable) mutation present in all cells are at increased risk and usually have a strong family history of early onset bowel cancer.

Among the genetic syndromes associated with bowel cancer, is Lynch syndrome (also known as hereditary non-polyposis colon cancer [HNPCC]). This is attributed to a germline mutation in one of the mismatch repair (MMR) genes and is associated with a high risk of colorectal cancer and an increased risk of uterine and ovarian cancers.

Familial adenomatous polyposis (FAP) occurs due to a germline APC mutation, and in 70–80% of cases there is an affected parent. With a 100% risk of bowel cancer in these patients, prophylactic colectomy is standard in these patients. About 30% of individuals with polyposis that looks like FAP have no family history and have new germline mutations when tested. Others, despite showing clinical polyposis do not have APC mutations. Myh-associated polyposis (MAP) is a recessive inherited mutation that should be treated and followed up in the same manner as FAP patients.

The Peutz-Jeghers syndrome (LKB1/STK11) mutation is characterised by peri-oral freckling, multiple hamartomatous polyps in the small and large bowel and infers a 10–20 fold risk of cancer. This syndrome is positively associated with colon, small bowel and stomach cancers with an increased incidence of pancreas, breast, cervix and sex-cord tumours.

In juvenile polyposis syndrome (SMAD4 and BMPR1A), the risk of cancer varies 10–60% for gastrointestinal cancers and pancreatic cancer. Those at risk include patients with more than five juvenile polyps, or those with a family history who present with any juvenile polyps.

Hereditary diffuse gastric cancer (E-cadherin/CDH1) is responsible for 1% of diffuse gastric cancers. The lifetime risk is 70–80% and prophylactic surgery is associated with high levels of morbidity and mortality, making management of these patients difficult.

Professor Kirk summed up the current status of family cancer clinics by emphasising the importance of genetic counselling and testing where appropriate. She said these clinics offer the ability to calculate an individual's risk of cancer based on family history and apply an appropriate detection and prevention strategy based on that information.

"Genetic susceptibility to gastrointestinal cancers is rare, but in certain individuals genetic testing can aid risk reduction and influence cancer management."

Clinical Associate Professor Judy Kirk

A new endoscopic paradigm for Barrett's oesophagus

Associate Professor Ian Norton
Department of Gastroenterology, Royal North Shore Hospital, Sydney

Australia's high incidence of Barrett's oesophagus presents a clinical dilemma in terms of cancer risk and management. The debate over surgical versus endoscopic management has been invigorated by the introduction of improved technology and better endoscopic techniques. Associate Professor Ian Norton outlined some of those new techniques at this year's Professional Practice Symposium.

The high level of morbidity combined with a 5% mortality rate make oesophagectomy an unattractive option for many patients, regardless of whether or not a laparoscopic or open approach is taken. The range of new ablative therapies is increasingly seen as an alternate management option, particularly in poor surgical risk groups.

Photodynamic therapy is now available in Sydney and Melbourne, but is largely uncommonly used in Australia due to the prohibitive set-up costs and lack of local outcome data.

Capsule mucosectomy – often thought of as a "big biopsy" – has been largely outmoded by band-ligation mucosectomy. Band ligation is now commonly practised, but experience has shown that if the disease is circumferential, it is better to do the mucosectomy in two procedures to minimise the risk of stricture. The development of strictures remains a limitation of band ligation.

An emerging strategy involves the use of confluent radio frequency ablation of Barrett's mucosa ("Halo"). Available as Halo 360° and Halo 90°, this form of thermal ablation is performed under conscious sedation and may also offer a viable option for the "worried well" with long segment Barrett's. The Halo 90° can be used to "spot weld" lesions while the 360° provides circumferential ablation.

These new techniques provide more alternatives for high-risk surgery patients and also an opportunity to reassess the management of Barrett's oesophagus in Australia.

Fiji program offers chance to help out

Professor Finlay Macrae
Head, Colorectal Medicine and Genetics, The Royal Melbourne Hospital, Gastroenterological Society of Australia (GESA)

Australian gastroenterologists have put their hands up to assist the Fiji School of Medicine's GE training program via the GESA Fiji Training Team (GESAFiTT). In a presentation to the Professional Practice Symposium, Professor Finlay Macrae said 42 gastroenterologists have already volunteered their services for this GESA-endorsed initiative.

The program involves working at the Colonial War Memorial Hospital in Suva in a two-week block, delivering lectures and training to undergraduate, Diploma and Masters students. Ward rounds and scoping lists form part of this teaching, as well as providing a valuable service.

There is an emphasis on gastroscopy and colonoscopy training as well as lectures on a range of upper and lower gastroenterological diseases.

Professor Macrae welcomes more interest in GESAFiTT. To join, please contact finlay.macrae@mh.org.au

Associate Professor Thein Htut (left), Professor Finlay Macrae and Dr Joji Malani (right) in the Endoscopy Unit, Colonial War Memorial Hospital, Suva, Fiji

Structuring for financial gain

Terry McMaster, Financial Adviser, McMasters'

"Dr John" is a 38-year-old gastroenterologist in private practice. He earns a healthy income, but is he really optimising his financial situation? Terry McMaster presented this scenario at the Professional Practice Symposium, in a somewhat challenging case study.

Taking a step-by-step approach Mr McMaster outlined the value of setting up a specialist practice as a trust for maximum financial flexibility. He also challenged attendees to consider deferring their taxes and then borrowing to pay the eventual, rather substantial, tax bill. Working through a range of specialist-specific tax deductions, Mr McMaster had the audience captivated. From endoscopes to laptop computers, he outlined the applicable methods of purchasing and deducting tax on "tools of trade". Attendees over 50 years of age were particularly interested in his tips on superannuation and the favourable rules that apply to this group. Those with teenage children are now seriously considering employing them in their practices having learned of the financial advantages involved in this practice.

This session capped off a very full program of clinical and professional development content and left attendees pondering the positive changes they could make on return to their practices.

For more information on this topic, Mr McMaster invited attendees to visit www.mcmasters.com.au To access the tools on this website the following access codes are required: User ID: mcmclient, Password: welcome123

Proactivity minimises legal risk

Scott Chapman, Partner, TressCox Lawyers

The best strategy for avoiding litigation is to pre-empt issues and communicate effectively, according to Scott Chapman from TressCox Lawyers.

Mr Chapman said tort law reform had reduced the number of claims against practitioners, but there had been a corresponding rise in health complaints as a result of increased media scrutiny and government enquiries into the health system. Most cases never make it to court, but of those that do, certain practises can assist with a successful defence.

Accurate, contemporaneous accounts of consultations are not only required by law, but can also be crucial in mounting a defence against a claim. Mr Chapman said any notes or alterations to records should always be dated and that altering records in response to a claim was a misguided way to reduce medicolegal exposure and most often resulted in a lost case.

Considerable discussion around consent took place in the workshop, but Mr Chapman pointed out that the method of gaining consent was not particularly important, so long as this occurred appropriately and was sufficiently documented. He said most claims against gastroenterologists related to perforations or misdiagnosis and in those situations, sometimes a settlement was recommended. Bedside manner and communication went a long way towards diffusing potentially difficult matters and often patients just sought an apology from their physician. "Saying sorry is not an admission of liability," he said.

Mr Chapman wrapped the session up with some quick pointers on how to manage if, despite the various strategies he suggested, a claim was lodged against the physician:

- remain calm
- notify your insurer/MDO immediately
- don't alter your records
- be completely open with your MDO and lawyers (all information is protected by privilege and is needed to mount a defence), and
- be prepared to settle the case for a range of non-clinical reasons.

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