PART I OF A SPECIAL SERIES OF REPORTS FROM

DIGESTIVE DISEASE WEEK 2007

May 19–24, Washington DC, USA

Digestive Disease Week (DDW) is considered the largest and most prestigious meeting in the world for the GI professional. This year close to 17,000 physicians, researchers and academics attended the meeting to learn about the latest advances in gastroenterology, hepatology, endoscopy and gastrointestinal surgery; prevention, diagnosis and treatment of digestive disorders; and cutting-edge technological advances. Each year DDW features about 2300 oral and 4000 poster presentations. The following report is part I of a series based on a selection of key sessions, with commentary by leading Australian specialists.

Controversies in colon polyp surveillance

Report by Associate Professor Peter Katelaris
Consultant Gastroenterologist, Concord Hospital; Clinical Associate, Professor, University of Sydney

Controversies in colon polyp surveillance were the subject of a clinical symposium comprising three parts. The first part dealt with medico-legal risk. The speaker, John Bond, focussed on the issue of interval cancer – cancer that arises between planned surveillance intervals. He cited the fallacies of colorectal cancer screening as:

(i) Proper screening prevents all death from colorectal cancer.

(ii) Colonoscopy never misses lesions.

(iii) Polypectomy prevents all colorectal cancer.

(iv) All colorectal cancers develop slowly over 10 years.

A number of papers have examined the likely prevalence of interval cancer and estimated it to occur between 1.7–2.4/1000 person years. One in 110 subjects screened are found to have a colorectal cancer within 3 years of the procedure (Lieberman 2005). Interval cancers are thought to arise for one of three reasons. The lesion was missed at the initial colonoscopy, a polyp was incompletely removed and cancer arose from the remaining adenomatous lesion or that a rapid *de novo* cancer arose after colonoscopy.

The issue of colonoscopy-missed rate was suggested to be between 6% and 12% for polyps greater than 1 cm (Rex 1997 and Pickhardt 2003). It was suggested that about 25% of patients might have faster growing tumours that can arise within 3 or 4 years. While this is predominantly in those with HPCC, it may occur in up to 15% of sporadic cancer. Moreover, some cancers are easier to miss at colonoscopy, particularly those that are flat.

Proceduralists will limit their medico-legal risk by making sure patient consent is truly informed, photographing landmarks, particularly the caecum, documenting the quality of the preparation and acting on the result (by either repeating examination of poorly prepared bowels or shortening the interval between surveillance procedures). The issue of adequate and careful withdrawal time has been highlighted and should be documented. The imperative of the endoscopist to assign follow-up in writing to either the patient and/or the referring doctor was highlighted.

Jerry Waye then shared his experience of difficult polypectomy. He offered a recipe for an inexpensive hyaluronic acid substitute for lifting flat polyps. He uses methylcellulose eye drops 2.5 mL together with 8 mL of saline and 2 drops of Methylene blue to achieve a longer lasting cushion prior to removing flat lesions.

The last speaker Phillip Schoenfeld dealt with the latest American guidelines for surveillance intervals (see textbox overleaf). He highlighted recent survey data that showed most gastroenterologists are either unaware of the guidelines or consciously do not adhere to them (Winawer 2003). Polyp surveillance tests now comprise a quarter of all colonoscopies done in the USA and this number is likely to rise. The magnitude of the problem can be appreciated from studies that have shown that 20% of women and 33% of men with a negative faecal occult blood test and no family history had one or more adenoma on screening (Schoenfeld 2005 and Lieberman 2000).

The context of the guidelines in Australia is the same as it is for the Americans. Faced with a rising demand for colonoscopy the test needs to be targeted for those most at risk, the unnecessary repeating of tests needs to be minimised and the quality of the test needs to be maximised.

Bond H *et al*. Minimising risks for the patient and endoscopist. Presentation 487. Wade JD. Advanced polypectomy – tricks of the trade. Presentation SP140. Schoenfeld PS. Simplyfying colon polyp surveillance – following the new guidelines. Presentation SP141.

Colon polyp surveillance recommendations

1. Patients with small rectal hyperplastic polyps should be considered to have normal colonoscopies, and therefore the interval before the subsequent colonoscopy should be 10 years; an exception is patients with a hyperplastic polyposis syndrome; they are at increased risk for adenomas and colorectal cancer and need to be identified for more intensive follow-up evaluation.
2. Patients with only 1 or 2 small (< 1 cm) tubular adenomas with only low-grade dysplasia should have their next follow-up colonoscopy in 5–10 years; the precise timing within this interval should be based on other clinical factors (such as prior colonoscopy findings, family history, and the preferences of the patient and judgment of the physician).
3. Patients with 3 to 10 adenomas, or any adenoma ≥ 1 cm, or any adenoma with villous features, or high-grade dysplasia should have their next follow-up colonoscopy in 3 years providing that piecemeal removal has not been performed and the adenoma(s) are removed completely; if the follow-up colonoscopy is normal or shows only 1 or 2 small tubular adenomas with low-grade dysplasia, then the interval for the subsequent examination should be 5 years.
4. Patients who have more than 10 adenomas at 1 examination should be examined at a shorter (< 3 years) interval, established by clinical judgement, and the clinician should consider the possibility of an underlying familial syndrome.
5. Patients with sessile adenomas that are removed piecemeal should be considered for follow-up evaluation at short intervals (2–6 months) to verify complete removal; once complete removal has been established, subsequent surveillance needs to be individualised based on the endoscopist's judgement; completeness of removal should be based on both endoscopic and pathologic assessments.
6. More intensive surveillance is indicated when the family history may indicate HNPCC.

Reference Winawer SJ *et al.* Guidelines for colonoscopy surveillance after polypectomy: A consensus update by the US Multi-Society Task Force on colorectal cancer and the American Cancer Society. *Gastroenterology* 2006;130:1872–1885.

Abstracts in review

Report by Associate Professor Peter Katelaris
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Eradication of *H. pylori* for the prevention of peptic ulcer rebleeding

This was a large confirmatory study of 400 patients who presented with *H. pylori*-associated bleeding ulcers and were given eradication therapy. NSAIDs were not used in this group. Follow-up was for 12 months with a total of 906 patient years of follow-up. Recurrent bleeding occurred in two patients at 1 year (incidence 0.2%/patient year of follow-up) and this occurred after NSAID use in both cases. This study confirms that peptic ulcer re-bleeding does not occur in patients with complicated ulcers after *H. pylori* eradication and therefore maintenance anti-secretory therapy is not necessary if eradication is achieved and NSAIDs are not used.

Gisbert JP *et al.* Eradication of *Helicobacter pylori* for the prevention of peptic ulcer rebleeding. Presentation T2065.

Colorectal cancer diagnosis following a negative colonoscopy

The authors reviewed 920 patients diagnosed with bowel cancer within the study time: 2.7% (25) of these patients had cancer diagnosed within 5 years of a prior negative colonoscopy. The mean interval between colonoscopy and diagnosis was 33 months. Negative colonoscopy in this study meant non-cancer – ie. either normal or adenomas only. The proportion here is similar to other data.

Quraishi ER *et al.* Colorectal cancer diagnosis following a negative colonoscopy. Presentation T2129.

Gastroesophageal reflux and endoscopic findings in patients presenting with dental erosions

This adds to the small literature relating reflux with dental erosions in a positive way. This was an observational study only. This adds substantially to the limited information and is supportive of the apparently real association between reflux and dental erosion.

Wilder-Smith C *et al.* Gastroesophageal reflux and endoscopic findings in patients presenting with advanced dental erosions. Presentation T1174.

EMR and ablation therapy for Barrett's oesophagus

Report by Dr Martin Weltman

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There were multiple presentations on endoscopic mucosal resection (EMR) and ablation therapy for Barrett's with high-grade dysplasia (HGD) in Barrett's oesophagus. Presentations focussed on the current available options – intensive surveillance, oesophagectomy and ablation or resection. Although HGD and early stage cancer can be treated with oesophagectomy, the inherent morbidity and mortality of oesophageal adenocarcinoma mean that there has been a significant increase in interest and research regarding alternative treatments such as ablative techniques and EMR. Endoscopic techniques for treatment of HGD in Barrett's and associated early neoplasia have become excellent alternatives to oesophagectomy for appropriately selected patients.

Dr Lightdale (Columbia University Medical Center) discussed the utilisation of photodynamic therapy (PDT) for HGD in Barrett's oesophagus, a technique that has been around for some time. Studies evaluated the role of biomarkers in predicting the likelihood of a responder to this intervention. In a prospective study of 30 patients, 15 responded to PDT. All of these 15 patients had intact tumour suppressor gene p16, with the 15 non-responders having inactivation of p16. Another prospective study including 104 patients with HGD reported similar results. Intact p16 (within Barrett's cells with HGD) therefore appears to be an important biomarker for predicting a successful response to PDT.

With the advent of newer ablation resection techniques, the main advantage of PDT over other ablation therapies appears to be the depth of ablation (through the submucosa). This may confer an advantage in that up to 30% of patients with Barrett's oesophagus have co-existing localised cancers of the oesophagus. Disadvantages of PDT include photosensitivity, high rate of stricture formation (up to 39%), and post-procedure nausea, chest pain and fever. PDT also appears to be a treatment alternative for those patients with an early cancer of the oesophagus who are either unfit for or refuse oesophagectomy. PDT is effective in ablating HGD and/or intramucosal cancers complicating Barrett's oesophagus in the majority of cases. It also seems to be quite effective in treating T1b/limited T2 carcinomas.

A newer tool, the HALO360 System, utilises an endoscopic balloon-based ablation device. The ablation depth is dose related and extends to the *muscularis mucosae* only, but this appears sufficient for most patients. This permits ablation of the Barrett's in its entirety and the risk of complications, in particular stricture formation, is low and complete resection of the Barrett's tissue is achievable. Furthermore, there is no evidence of buried glandular mucosa.

Endoscopic mucosal resection (EMR)

EMR is now widely used to treat localised HGD and early cancers arising in Barrett's mucosa. One of the main advantages of this technique is that it provides histology for evaluation of depth of invasion, lymphovascular invasion and margins of resection. Two systems are available: (i) EMR-cap and (ii) Duette system. The EMR-C permits an increased size of tissue resection. The study presented by Dr Wang (Mayo Clinic) evaluated 466 patients utilising 832 EMR sessions: 64% had HGD, 23% had cancer. There was 6% stricture formation and 1% significant bleeding. Complications were more common using the EMR-C system. EMR may be combined with photodynamic therapy (PDT) to treat all of the mucosa at risk for neoplastic progression. EMR monotherapy for HGD or early cancer in Barrett's oesophagus is associated with recurrent lesions in up to 30% of treated patients and hence some presenters felt the addition of ablative therapy may be useful in specific patents.

Lightdale CJ. Endoscopic ablation: who, how and when. Presentation SP211. Lightdale CJ. Summary lecture: endoscopic treatment for Barrett's esophagus with high-grade dysplasia. Presentation SP304. Wang KK. Ablation therapies for Barrett esophagus. Presentation SP393.

Sacral nerve stimulation for constipation: an international multicentre study

Report by Dr Sanjay Nandurkar
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Patients with severe refractory constipation have limited treatment options. The standard medical therapy currently comprises combination therapies involving osmotic and stimulant laxatives with stool softeners. Currently, there is dearth of effective and safe promotility agents to complement the laxative regimen.

Consequently, in severe cases, the efficacy is variable and quality of life is considerably compromised. Not surprisingly, alternative cleansing therapies such as colonic irrigation have flourished despite its attendant risks. Colectomy, although a seemingly drastic measure, is required in certain cases.

Histopathogical analyses of the bowel in patients with constipation have revealed that there is a loss of interstitial cells of Cajal (which are the intestinal pace maker cells) along with disruption of the neural wiring. Conceptually, manipulation of the neural control of colon and pelvic floor via sacral nerve stimulation does have physiological underpinnings. Although this technique has been around for the best part of 10 years, the earlier studies focussed mainly on urinary and faecal incontinence. Most of the studies relating to constipation were very small and of limited duration.

The current study is a well-designed prospective study with large numbers and with a two-year follow-up period. The study convincingly shows that there is a significant improvement in all the primary outcomes measured such as improved frequency of defecation, decreased straining and diminished abdominal pain. Although improvement in transit time would have been expected, it is difficult to reconcile that colonic transit would have "normalised" in 50% of the subjects, as reported by the authors and further confirmation from other studies would be helpful.

Nevertheless, some of the key domains of quality of life appeared to have improved such as vitality and social and physical functioning. It must be noted that infection at the surgical site required removal of one apparatus and lead revision was required in another seven subjects. Furthermore, unexplained or unexpected pain in the buttock region or down the legs was also reported with this therapy.

This study has compelling data to suggest that use of permanent sacral nerve stimulation has a role in the long-term management of selected patients with severe refractory constipation.

Dudding TC *et al.* Sacral nerve stimulation for constipation: an international multi-centre study. Presentation 198.