

the Insider

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Since 1985, GastroIntestinal Endoscopy (GIE) has provided an efficient 'Open Access' service for colonoscopy and upper gastrointestinal endoscopy.

GIE provides an enviable level of medical experience. Our eight Gastroenterologists possess a broad base of clinical expertise in their varied speciality areas of interest. Currently, GIE operates an 'Open Access' service from four centres:

- **Brisbane Endoscopy Services** – a Day Endoscopy Centre located at the McCullough Centre, Sunnybank which is owned and operated by the GIE partners;
- **Chermside Day Hospital** at Chermside;
- **North West Private Hospital** at Everton Park;
- **The Wesley Hospital** at Auchenflower.



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www.gastros.com.au

The Insider scopes coeliac vaccine

With news that a coeliac therapeutic, Nexpep's Nexvax2, is being developed and is already in Phase 1 clinical trials, *The Insider* investigates coeliac disease, uncovers some facts about the developing therapeutic and reports on how the patients can learn more about coeliac disease and its management.

Coeliac disease is a lifelong digestive disorder that currently affects up to 1% of the Australian population – a statistic that is common across most of the western world. There is a genetic factor involved in this autoimmune disorder and there is a one in 10 chance of being affected if a first degree relative has the disease. Research has found that the HLA-DQ2 and HLA-DQ8 genes cover 99.6% of all coeliac sufferers, compared to about 30-40% of the general population. In coeliac disease, an immune-mediated toxic reaction occurs in the small intestine when people consume food containing gluten. However, coeliac disease is widely undiagnosed because most patients present with non-gastrointestinal symptoms, such as tiredness and often have iron deficiency. In addition to lethargy and fatigue, patients may present with nausea, abdominal pain, bloating, and diarrhoea.

Coeliac disease frequently has an association with other medical problems including thyroid disease, Type 1 diabetes, other autoimmune conditions, osteoporosis and infertility. At present, a gastroscopy with a biopsy of the distal duodenum is the only definitive diagnosis for coeliac disease.

Currently, the only management is a strict lifelong gluten-free diet (i.e. no wheat, barley, rye, oats or spelt) and to treat specific vitamin deficiencies. This restrictive diet often forces sufferers to forgo foods such as standard wheat flour-based pastas, cakes and biscuits and be extremely vigilant in avoiding contamination of food shared with people on a normal diet. The Walter and Eliza Hall Institute of Medical Research in Melbourne has been the home to gastroenterologist Dr Bob Anderson, who has lead the research leading to the 'coeliac vaccine'.

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Above right: Dr Bob Anderson, Nexpep CEO and Chief Scientist, and Dr Rod Roberts GIE gastroenterologist discuss the coeliac vaccine.



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Dr Anderson is the co-founder of Nexpep Pty Ltd and his research into the disease hopes to change the way coeliac disease is managed, by creating a peptide-based immunotherapy designed to desensitise the patient's immune system to gluten derived toxic peptides and give coeliac sufferers the ability to replace a gluten-free diet with the Nexpep vaccine treatment.

Further information

For more information regarding the developments in the coeliac vaccine trials, general information about coeliac disease or other helpful coeliac related websites please follow the links through the new and improved GIE website – www.gastros.com.au.

There is a wealth of information relating to all gastroenterology related illness both for doctors and patients and our own GastroIntestinal Endoscopy doctors have also provided their own research for viewing on the webpage.

Did you know?

General Practitioners can now download GIE referral stationary through Medical Director or PractiX programs, or contact staff at one of the Brisbane locations for delivery of forms to your site.

Side effects of Proton Pump Inhibitors

By Dr Alistair Cowen/Dr Rod Roberts

Proton Pump Inhibitors (PPI) are prescribed worldwide in vast quantities and have proved to be remarkably effective and largely free of serious side effects. However, adverse reactions do occur, and some are either not widely appreciated or have only recently been described.

Initial concern that reduced acid secretion would lead to intra gastric bacterial proliferation with production of nitrosamines and the stimulation of gastric cancer development has not been confirmed. However, long-term proton pump inhibitors do increase the rate of *Helicobacter* migration from the antrum toward the fundus. Potentially this could shorten the time for the development of chronic atrophic gastritis, which is known to have pre-malignant potential. For this reason we believe all patients being considered for long-term PPI therapy should be tested for *Helicobacter pylori* and if this organism is present it should be eliminated.

Common PPI side effects include gastrointestinal tract upsets, both diarrhoea and constipation, as well as bloating and abdominal discomfort. Headache and rash can occur. Uncommon side effects include hepatic dysfunction, dizziness, paresthesiae, insomnia and unusual skin rashes and malaise.

Rare side effects include stomatitis, mental confusion, agitation, aggression, as well as encephalopathy and liver failure in patients with pre-existing severe liver disease. Photosensitivity and Stevens-Johnson syndrome together with hypersensitivity reactions have been reported very rarely. Some studies looking at long-term side effects have reported increased respiratory infection rates, while others have not. PPIs should be used with caution in patients with 'volume reflux' symptoms including episodes of aspiration and recurrent chest infection.

Recurrent pneumonia associated with reflux is a clear indication for surgery.

PPI side effects which are under-recognised or only recently described include:

- **Interstitial nephritis** This can be caused by numerous drugs including PPIs. In one report over 50% of drug induced cases of interstitial nephritis related to PPIs. All PPIs available in Australia have been associated with interstitial nephritis. Unfortunately, complete recovery on cessation of the PPI is NOT usual.
- **Osteoporosis and increased risk of fracture** Three large retrospective studies have reported an association between long-term PPI therapy and bone fractures. One study reported increased hip fractures in those exposed to PPI for five years and even higher risk after seven years. Similar increase in hip fracture rates have been reported from Denmark and from England.
- **Interaction with anti platelet agents** Clopidogrel (Plavix and Iscover) may be less effective in certain patients due to genetic polymorphism or drug interactions. Clopidogrel is metabolised by the cytochrome P450 system, particularly CYP2c19. Genetic polymorphism reducing CYP2c19 function has been identified in some patients. Drugs known to inhibit CYP2c19 may reduce the effectiveness of clopidogrel. It has been suggested PPIs may reduce clopidogrel effectiveness by this mechanism.

At the moment it is unclear whether this interaction is a class effect and so applies to all PPIs or whether there are differential effects. Until further studies are completed it is safest to assume a class effect. Patients on clopidogrel who require PPI therapy should continue both.

There is a theoretical benefit to giving the PPI in the morning and the clopidogrel in the evening, given the half-lives of these medications. Where an effective alternative exists, including H2 receptor antagonists, prokinetics and antacids, this could be considered. The new agent prasugrel is also metabolised by the cytochrome P-450 system but more efficiently. The extent of any interaction between PPIs and prasugrel is currently unknown.

- **Increased incidents of infections** There are several studies showing an increased risk of community acquired pneumonia in patients on PPIs but no similar increase in incidence of nosocomial pneumonia.

Long-term PPI use may be associated with decreased iron absorption. Certain patients with haemochromatosis require fewer venesections while on PPI therapy. However, iron deficiency should never be attributed to PPI use without excluding other more likely and more important causes.



Dr Alistair Cowen

Frequently asked questions

Dr Alistair Cowen, Gastroenterologist, *respondant*

Q. When a GP considers coeliac disease as part of the 'a differential diagnosis', what blood tests are useful as part of the patient's work-up? Does this vary depending on the patient's age?

A. All coeliac screening serology tests have false positives and negatives. If there is a strong clinical indication, or the patient requires certainty as to the diagnosis of coeliac disease, then a small gut biopsy should be performed. It is probably useful to do endomysial antibodies (EMA) and tissue transglutaminase autoantibodies (TGAA – can also be referred as coeliac serology / antibodies) as well. If one or both of the antibody tests and the small bowel biopsy is positive, the patient has confirmed coeliac disease. If the antibodies are positive, and the biopsy normal, then the patient may be at risk of developing clinical coeliac disease at some future date. If the antibodies are negative and the biopsy shows villous atrophy, then other causes of malabsorption may have to be considered (e.g. tropical sprue).

If there is a low probability of coeliac disease, or the tests are being performed as a screening measure, then the autoantibodies (EMA and TGAA) and total serum IgA levels should be conducted. If all tests are negative then coeliac disease is unlikely, but certainly not impossible. If TGAA or EMA are positive, or there is IgA deficiency, then small bowel biopsy should be undertaken.

A much wider spectrum of disorders causing villous atrophy (usually partial) occurs in very young children.

Q. Should a patient diagnosed with coeliac disease have follow-up upper GI endoscopes?

A. Follow-up endoscopy is not necessary in patients who respond clinically to a gluten-free diet. If there is any doubt about the diagnosis, or an incomplete clinical response, follow-up biopsy is required at three months. Recurrence of symptoms, unexplained weight loss or diarrhoea occurring after initial response also requires re-biopsy.

Q. How long does it take for the small intestine to recover from villous atrophy once a patient diagnosed with coeliac disease commences on a gluten-free diet?

A. Usually after six weeks on a gluten-free diet there is very substantial improvement or return to normality of the biopsy. It has previously been suggested that up to 5% of coeliac patients will fail to respond to a gluten-free diet alone. In recent years, this percentage seems much lower; this may partially be due to the fact that much milder cases of the disease are being diagnosed. Currently, it seems that 1-2% of adult patients will fail to respond to a gluten-free diet and may require a course of steroids to trigger a response.

Q. What other testing should be done for patients newly diagnosed with coeliac disease and for their family members?

A. Newly diagnosed coeliac patients require full blood count, red blood cell, folate levels and ELFTs. DEXA scans for osteoporosis should be considered in adult women. Any clinical suggestion of connective tissue disease, thyroid disease or Addison's disease should trigger appropriate investigation because of the known association with coeliac disease. Conversely, a diagnosis of recurrent miscarriage, Type 1 diabetes, collagen disorder, autoimmune thyroid disease, female osteoporosis, lymphocytic and cholangitis, colitis and cerebellar ataxia should cause the clinician to consider the possibility of associated coeliac disease.

Routine screening testing of first degree relatives of coeliac patients is controversial. If screening is to be undertaken it should include TGAA, EMA and serum IgM. Certainly, any family member with possible coeliac symptoms or disease known to be associated with coeliac disease should be screened.

Q. What are the best resources to best educate a patient newly diagnosed with coeliac disease to cope with a gluten-free diet?

A.

1. The newly diagnosed coeliac patient should be referred to an accredited practice dietician (information available on 1800 812 942 or on the Dietician Association of Australia Website www.daa.asn.au, where patients can search for dieticians with an interest in coeliac disease).
2. Coeliac patients will benefit from joining their state Coeliac Society (details from the National Office on 02 9411 4100 or for Queensland residents, the Queensland Coeliac Society has excellent information www.qld.coeliacsociety.com.au or 07 3839 5404).
3. A comprehensive information guide is available on the GUT Foundation website, 'Coeliac Disease, Food Allergy and Intolerance' – www.gut.nsw.au (Publications – Information booklets – coeliac disease – assets/documents/coeliac text.pdf).

Another excellent resource for patients and GPs is the interactive CD Rom created by Dr Bob Anderson *Coeliac Disease: New Directions for General Practitioners and people with coeliac disease*. The CD Rom is available from the Queensland Coeliac Society.

25th Anniversary for Gastrointestinal Endoscopy

Queensland's first open access endoscopy service will celebrate 25 years in 2010.

To celebrate, GIE will be holding education evenings for general practitioners and specialists that will provide topical information and insight into open access procedures.

Keep your eye out for further updates in coming issues of *The Insider*.



GIE practice locations and contact details

For all appointments, call 1300 4 GASTRO (Ph: 1300 4 427876)

Brisbane Endoscopy Services

Suite 16-18
McCullough Centre
259 McCullough Street
Sunnybank QLD 4109

Phone: 07 3344 1844

Fax: 07 3344 2739

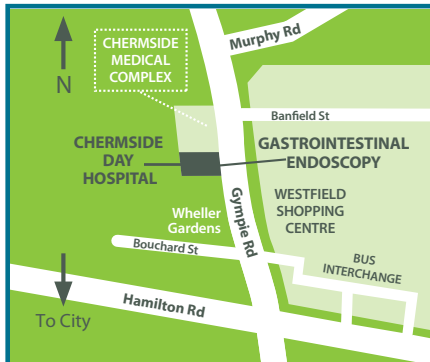


Chermside Day Hospital

Chermside Medical Complex
Level 1, 956 Gympie Road
Chermside QLD 4032

Phone: 07 3120 3407

Fax: 07 3120 3443

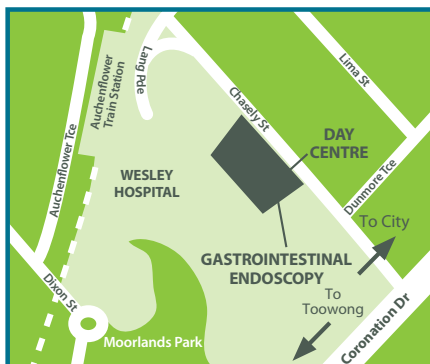


The Wesley Hospital

3rd Floor, Day Centre
451 Coronation Drive
Auchenflower QLD 4066

Phone: 07 3870 3799

Fax: 07 3870 5069

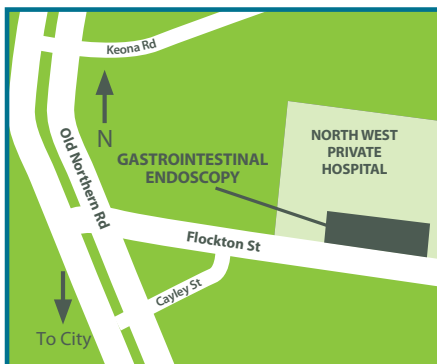


North West Private Hospital

Endoscopy Unit
137 Flockton Street
Everton Park QLD 4053

Phone: 07 3353 3322

Fax: 07 3353 9325



Private practice locations, contact details and special interests

<p>Dr Andrew Bryant MB BS FRACP Dip Av Med (Otago) Main Rooms: Level 2, 33 North St, Spring Hill QLD 4000</p>	<p>T: 3831 7238 F: 3831 7261</p>	<p>SI: Endoscopy, endoscopic mucosal resection, advanced polypectomy and hepatology C: Spring Hill, Sunnybank, North West Ramsay Place and Prince Charles Hospital Private Practice Clinic P: Sunnybank, Chermside Day Hospital</p>
<p>Dr Alistair Cowen MB BS (Hons) MD FRACP Does NOT Privately consult. Open Access procedures only</p>	<p>T: 3353 3322 F: 3350 4143</p>	<p>P: North West Private Hospital, The Wesley Hospital, Sunnybank, Chermside Day Hospital</p>
<p>Dr Benedict Devereaux MB BS MPhil FAGC FRACP Main Rooms: Holy Spirit Northside Hospital Level 1, Medical Centre, 627 Rode Rd, Chermside QLD 4032</p>	<p>T: 3861 4866 F: 3861 4897</p>	<p>SI: Gastroenterology, ERCP, EUS, therapeutic endoscopy, IBD and polyp surveillance C: Holy Spirit Northside, Manor Apartments – City, Chermside Day Hospital P: Chermside Day Hospital, North West Private Hospital</p>
<p>Dr Michael Miros MB BS (1st Class Hons Qld) FRACP Main Rooms: 66 Bryants Rd, Loganholme QLD 4129</p>	<p>T: 3801 5200 F: 3801 5212</p>	<p>SI: Barrett's oesophagus, gastric intestinal metaplasia, polyp surveillance, capsule endoscopy C: Loganholme (Limited consulting – endoluminal gastroenterology only) P: Sunnybank</p>
<p>Dr Roderick Roberts MB BS FRACP AGAF Main Rooms: Level 2, Suite 62, Ballow Chambers 121 Wickham Terrace, Brisbane QLD 4000</p>	<p>T: 3831 2704 F: 3835 1069</p>	<p>SI: IBD, coeliac disease, drug induced liver disease and polyp surveillance C: Wickham Terrace, Sunnybank, North West Ramsay Place, Chermside Day Hospital P: Sunnybank, Chermside Day Hospital, North West Private Hospital, The Wesley Hospital</p>
<p>Dr William Robinson MB BS FRACP Main Rooms: Level 4, Suite 85, Sandford Jackson Building 30 Chasley St, Auchenflower QLD 4066</p>	<p>T: 3870 7433 F: 3870 7466</p>	<p>SI: Gastroenterology and parental nutrition C: The Wesley Hospital and Strathpine Specialist Centre P: Sunnybank, Chermside Day Hospital, North West Private Hospital, The Wesley Hospital</p>
<p>Dr Neville Sandford BSc (Med) MB BS (1st Class Hons) FRACP AGAF Main Rooms: Brisbane Clinic, 79 Wickham Tce, Brisbane QLD 4000</p>	<p>T: 3270 4593 F: 3270 4588</p>	<p>SI: Gastroenterology and hepatitis treatment C: Wickham Terrace, North West Specialist Centre P: Sunnybank, Chermside Day Hospital, North West Private Hospital, The Wesley Hospital</p>
<p>Dr Patrick Walsh BSc MB ChB FRACP Main Rooms: Holy Spirit Northside Hospital Level 1, Medical Centre, 627 Rode Rd, Chermside QLD 4032</p>	<p>T: 3861 4866 F: 3861 4897</p>	<p>SI: Gastrointestinal malignancy, endoscopic ultrasounds, advanced polypectomy, polyp surveillance C: Holy Spirit Northside, St Andrew's Hospital P: Sunnybank, Chermside Day Hospital, The Wesley Hospital</p>

SI: Special Interests C: Consults P: Procedures