

in the Australian Product Information for donepezil,<sup>4</sup> as the article by Rogers and colleagues<sup>2</sup> refers to rates of adverse events experienced by those on the 10 mg dose, after a forced titration after *only* one week on 5 mg. We presented data for adverse events at the 10 mg dose, as this was the dose recommended for donepezil given the findings of greater benefit on the higher dose. The Australian Product Information does not indicate whether the rates of adverse events refer to the 5 mg or 10 mg dose.

Usual clinical practice, which is to start with 5 mg daily and increase to 10 mg after 4–6 weeks, results in fewer adverse events. The figures of 11.3% for nausea, 7% for diarrhoea and less than 5% for vomiting presented in the Nordic study,<sup>5</sup> in which over 80% of patients were taking 10 mg of donepezil daily, with a more flexible titration schedule, appear to be more realistic.

1. Brodaty H, Ames D, Boundy KL, et al. Pharmacological treatment of cognitive deficits in Alzheimer's disease [review]. *Med J Aust* 2001; 175: 324-329.
2. Rogers SL, Farlow MR, Doody RS, et al. A 24-week, double-blind, placebo-controlled trial of donepezil in patients with Alzheimer's disease. *Neurology* 1998; 50: 136-145.
3. Rogers S, Friedhoff L. Long-term efficacy and safety of donepezil in the treatment of Alzheimer's disease: an interim analysis of the results of a US multicentre open label extension study. *Eur Neuropsychopharmacol* 1998; 8: 67-75.
4. Australian-approved Product Information for Donepezil. Sydney: Pfizer Pty Limited, 10 December 2001.
5. Winblad B, Engedal MD, Soininen H, et al. A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. *Neurology* 2001; 57: 489-495. □

### High prevalence of coeliac disease in a population-based study from Western Australia: a case for screening?

Jeremy Ryan

Gastroenterologist, Brighton Gastroenterology Associates, Suite 5, 2 Church Street, Brighton, VIC 3186. jeremy@brightongastro.com

**TO THE EDITOR:** I read with interest the recent article by Olynyk's group at Fremantle on the prevalence of coeliac disease in rural Western Australia.<sup>1</sup>

It is now increasingly realised that coeliac disease is underdiagnosed in adults because it may be clinically silent — but not necessarily asymptomatic. The symptoms, however, may be non-specific and not those traditionally associated with coeliac disease. In a recently reported small study from suburban Melbourne,<sup>2</sup> I demonstrated that about 5% of patients (5/97) undergoing gastroscopy had coeliac disease based on small-bowel biopsy results. In only one of

the patients was the disease suspected clinically.

I have used these figures to argue the case for routine duodenal biopsy at the time of gastroscopy, regardless of the indication. It is important to note that in my study none of the patients presenting with diarrhoea, and only one of six with anaemia, had coeliac disease — so that restricting biopsy to this group would have missed most patients with coeliac disease.

Timely diagnosis is important, as symptoms may be alleviated, presymptomatic nutritional deficiencies corrected, and the risk of cancer reduced by instituting a gluten-free diet. People presenting for gastroscopy represent a high-yield group for histological screening for coeliac disease in Australia.

1. Hovell CJ, Collett JA, Vautier G, et al. High prevalence of coeliac disease in a population-based study from Western Australia: a case for screening? *Med J Aust* 2001; 175: 247-250.
2. Ryan J. Case 5-2001: Unsuspected coeliac disease [letter]. *N Engl J Med* 2001; 344: 1950-1951. □

John K Olynyk,\* Digby J E Cullen,†  
Guy Vautier,‡ Judith A Collett,§  
Dominic F Mallon,¶ Chris J Hovell\*\*

\*Associate Professor; †Gastroenterologist, Fremantle Hospital, PO Box 480, Fremantle, WA 6959; ‡Registrar, Gastroenterology, Royal Defence Medical College, Gosport, UK; §Gastroenterologist; ¶Clinical Immunologist; \*\*Senior Registrar, Gastroenterology, Fremantle Hospital, Fremantle, WA. jolynyk@cylle.uwa.edu.au

**IN REPLY:** We agree with Ryan that coeliac disease is common in the Australian community, with a prevalence of 1 in 250.<sup>1</sup> Furthermore, all individuals positive for antiendomysial antibody who undergo small-bowel biopsy have typical features of coeliac disease.<sup>1</sup> Clearly, there is a need to increase awareness relating to coeliac disease and determine appropriate screening strategies for our population.

Ryan suggests that patients presenting for upper gastrointestinal endoscopy represent a group in whom a high diagnostic yield of coeliac disease is expected.<sup>2</sup> However, clinical expression of the disease is variable.<sup>1</sup> In this setting, we believe that it is important to determine the cost-effectiveness of the various screening strategies before introducing broad-based screening.<sup>3</sup> There is no doubt that treatment of symptomatic patients who present with coeliac disease is appropriate, but there are limited data on outcomes for asymptomatic patients who are discovered in population-based screening programs.

As we stated in our article, we recommend screening by serology and small-bowel biopsy if the clinical suspicion is high or the patient is in a high-risk group.

1. Hovell CJ, Collett JA, Vautier G, et al. High prevalence of coeliac disease in a population-based study from Western Australia: a case for screening? *Med J Aust* 2001; 175: 247-250.
2. Ryan J. Case 5-2001: unsuspected coeliac disease [letter]. *N Engl J Med* 2001; 344: 1950-1951.
3. Navab F. Case 5-2001: unsuspected coeliac disease [letter]. *N Engl J Med* 2001; 344: 1951-1952. □

### Megadose vitamin C in treatment of the common cold: a randomised controlled trial

Luis Vitetta,\* Avni Sali,† Bill Paspaliaris,‡  
Nicola J Reavley§

\*Director of Research; †Professor and Head of School; ‡Senior Research Fellow; §Research Assistant, Graduate School of Integrative Medicine, Swinburne University of Technology, 9 Frederick St, Hawthorn, Melbourne, VIC 3122. LVitetta@medicine.swin.edu.au

**TO THE EDITOR:** There is much conflicting evidence that increased intake of vitamin C enhances the natural protective mechanisms of the body and decreases both the incidence and severity of the common cold.<sup>1</sup>

It is regrettable that the study by Audera and colleagues failed to show a significant therapeutic effect of megadose vitamin C in treatment of the common cold.<sup>2</sup> The groups compared had, on average, similar composition after randomisation. However, the viral infections that cause the common cold and its progression to ill health, as evidenced by multiple symptoms, are affected by many factors, while symptom severity is well known to vary greatly. Therefore, the study's reliance on respondents' self-diagnosis of symptom severity and onset is a significant weakness in design.

Randomisation of participants to the treatment groups may have been insufficient to override this design deficit, thereby significantly biasing the outcome. A better design might have combined patient self-report of symptom severity with physical examination, thus allowing independent and professional assessment of severity. Also, proper assessment of previous history of severity of cold symptoms is crucial for proper randomisation to treatment groups. If Audera and colleagues' study failed to control for this history, then randomisation may have also failed to balance its effect equally between treatment groups, significantly compromising the study's validity to detect any therapeutic benefit of vitamin C. Cold symptoms also vary diurnally, while severity varies with alcohol use and smoking status,<sup>3,4</sup> which also affect vitamin C absorption.<sup>5,6</sup> No information was provided on study participants' alcohol consumption and smoking status.

Finally, the study did not assess stress, which may constitute a further, important uncontrolled bias. A recent cohort study of stress and the common cold concluded that all four dimensions of stress investigated — stressful life events, negative affects, positive affects and perceived stress — were significantly related to occurrence of the common cold.<sup>7</sup> Stress may also have significantly affected symptom severity and participants' perception of their symptoms.

Certainly, the trend observed in the placebo group of shorter duration of some symptoms and lower mean severity could have been due to less severe symptom history, compounded by a lower degree of overall stress.

1. Douglas RM, Chalker EB, Treacy B. Vitamin C for preventing and treating the common cold. *Cochrane Database Syst Rev* 2000; 2: CD000980.
2. Audera C, Patulny RV, Sander BH, Douglas RM. Mega-dose vitamin C in treatment of the common cold: a randomised controlled trial. *Med J Aust* 2001; 175: 359-362.
3. Smith A, Tyrrell D, Coyle K, et al. Diurnal variation in the symptoms of colds and influenza. *Chronobiol Int* 1988; 5: 411-416.
4. Cohen S, Tyrrell DA, Russell MA, et al. Smoking, alcohol consumption, and susceptibility to the common cold. *Am J Public Health* 1993; 83: 1277-1283.
5. Pamuk E, Byers T, Coates R, et al. Effect of smoking on serum nutrient concentrations in African-American women. *Am J Clin Nutr* 1994; 59: 891-895.
6. Kleszczewski T, Kleszczewska E. FIA of vitamin C in blood serum in humans at increasing ethanol concentration. *J Pharm Biomed Anal* 2001; 25: 477-481.
7. Takkouche B, Regueira C, Gestal-Otero JJ. A cohort study of stress and the common cold. *Epidemiology* 2001; 12: 345-349. □

**Carmen Audera,\* Roger V Patulny,†  
Beate H Sander,‡ Robert M Douglas§**

\*Lecturer; †Research Assistant; ‡Research Assistant; §Visiting Fellow (corresponding author), National Centre for Epidemiology and Population Health, Australian National University, GPO Box 4, Canberra, ACT 2601. bob.douglas@anu.edu.au

**IN REPLY:** Precisely because of the temporal variation in symptom severity described by Vitetta and colleagues, we judged that medical professionals are not as well able, in a variably timed interview, to quantify patients' cold symptoms as the patients themselves can do on a continuing basis. Therefore, we consider that our study<sup>1</sup> would have been no more valid if the detailed symptom severity cards had been supplemented by one or more physical examinations. In that respect, we are in good company with others who have studied the common cold over many years.<sup>2</sup>

We agree that double-blind randomisation does not necessarily distribute all relevant variables equally. That is why, in Box 2 of our study report, we presented four variables — age, sex, mean number of colds in the previous year, and mean number of days unwell with colds in the previous year.<sup>1</sup> The likelihood that stress,

smoking and alcohol status would have been sufficiently maldistributed in this large group to mask a significantly beneficial effect in even one of the three groups which received high-dose vitamin C seems vanishingly small. Nevertheless, we acknowledge that the study would have been stronger if we could have reported the distribution of these three potential confounders.

We contest the view of Vitetta and colleagues that the evidence from randomised controlled trials of vitamin C in treating the common cold conflicts significantly (see Box 1 of our article<sup>1</sup>). The overview finding — that mega-doses of vitamin C for prophylaxis produce a relatively trivial reduction in cold severity but no reduction in incidence<sup>3</sup> — was the stimulus for our own study. No community studies of this issue have been flawless, but the mounting collective evidence suggests that we should look elsewhere for a cold panacea.

1. Audera C, Patulny RV, Sander BH, Douglas RM. Mega-dose vitamin C in treatment of the common cold: a randomised controlled trial. *Med J Aust* 2001; 175: 359-362.
2. Tyrrell DJ, Craig JW, Meade TW, White TA. A trial of ascorbic acid in the treatment of the common cold. *Br J Prev Soc Med* 1977; 31: 189-191.
3. Douglas RM, Chalker EB, Treacy B. Vitamin C for preventing and treating the common cold (Cochrane Review). In: *The Cochrane Library* 3, 2001. Oxford: Update Software. □

## Evolving evidence and continuing uncertainties for eating disorders

**Janice D Russell,\* Suzanne F Abraham†**

\*Director, Eating Disorders Program, Northside Clinic, 2 Greenwich Road, Greenwich, NSW 2065, and Clinical Associate Professor, Department of Psychological Medicine, University of Sydney; †Codirector, Eating Disorders Program, and Associate Professor, Department of Reproductive Medicine, University of Sydney. jrussel1@mail.usyd.au

**TO THE EDITOR:** We are writing in response to the editorial of Ben-Tovim et al.<sup>1</sup> Although we agree that more research into treatment efficacy in eating disorders is needed, we believe that the study to which reference is made<sup>2</sup> is seriously flawed. The study should not be presumed to provide evidence about the effect of treatment on outcome, particularly as the majority of patients studied received no treatment. The high death rate (3/95 [3.2%] among patients with anorexia nervosa and 2/37 [5.4%] among patients with "eating disorders not otherwise specified") in such mildly ill patients (few of whom would have warranted hospitalisation on the basis of their weight) approximates that of seriously