breast cancer and lytic bone lesions: A randomized controlled study. J Clin Oncol 1999;17:846-54.

- 6 Hortobagyi GN, Theriault RL, Porter L, Blayney D, Lipton A, Sinoff C, et al. Efficacy of pamidronate in reducing skeletal complications in patients with breast cancer and lytic bone metastases. N Engl J Med 1996;335:1785-91.
- 7 Conte PF, Latreille J, Mauriac L, Calabresi F, Santos R, Campos D, et al. Delay in progression of bone metastases in breast cancer patients treated with intravenous pamidronate: results from a multinational controlled trial. J Clin Oncol 1996;14:2552-9.
- 8 Tripathy D, Lichinitzer M, Lazarev A, MacLachlan SA, Apffelstaedt J, Budde M. On behalf of the MF 4434 Study Group. Oral ibandronate for the treatment of metastatic bone disease in breast cancer: efficacy and safety results from a randomized, double blind, placebo-controlled trial. *Ann Oncol* 2004;15:743-50.
- 9 Body JJ, Diel IJ, Lichinitzer M, Lazarev A, Pecherstorfer M, Bell R, et al. Oral ibandronate reduces the risk of skeletal complications in breast cancer patients with metastatic bone disease: results from two randomized, placebo controlled phase III studies. *Br J Cancer* 2004;90:1133-7.
- 10 Tubiana-Hulin M, Beuzeboc P, Mauriac L, Barbet N, Frenay M, Monnier A, et al. Double blinded controlled study comparing clodronate versus placebo in patients with breast cancer bone metastases. *Bull Cancer* 2001;88:701-7.
- 11 Kristensen B, Ejlertsen B, Groenvold M, Hein S, Loft H, Mouridsen HT. Oral clodronate in breast cancer patients with bone metastases: a randomized study. J Intern Med 1999;246:67-74.
- 12 Paterson AHG, Powles TJ, Kanis JA, McCloskey E, Hanson J, Ashley S. Double blind controlled trial of oral clodronate in patients with bone metastases from breast cancer. *J Clin Oncol* 1993;11:59-65.
- 13 Van Holten-Verzantvoort ATM, Kroon HM, Bijvoet OLM, Cleton FJ, Beex LVAM, Blijham G, et al. Palliative pamidronate treatment in patients with bone metastases from breast cancer. J Clin Oncol 1993;11:491-8.
- 14 Ross JR, Saunders Y, Edmonds PM, Patel S, Broadley KE, Johnston SRD. Systematic review of role of bisphosphonates on skeletal morbidity in metastatic cancer. BMJ 2003;327:469-75.
- metastatic cancer. BMJ 2003;327:469-75.
 15 Pavlakis N, Stockler M. Bisphosphonates for breast cancer. Cochrane Database Syst Rev 2004;4:CD00075320-100000000-02521.
- 16 Rosen LS, Gordon DH, Dugan W, Major P, Eisenberg PD, Provencher L, et al. Zolendronic acid is superior to pamidronate for the treatment of bone metastases in breast carcinoma patients with at least one osteolytic lesion. *Cancer* 2004;100:36-43.

- 17 Wong R, Wiffen PJ. Bisphosphonates for the relief of pain secondary to bone metastases. *Cochrane Database Syst Rev* 2004;3:CD00075320-100000000-01585.
- 18 Clemons M, Verma S. Should oral bisphosphonates be standard of care
- in women with early breast cancer? Breast Cancer Res Treat (in press).
 19 Major P, Cook R. Efficacy of bisphosphonates in the management of skeletal complications of bone metastases and selection of clinical end-points. Am I Clin Oncol 2002:25:s10-s18.
- end-points. Am J Clin Oncol 2002;25:s10-s18.
 20 Anderson PK, Gill RD. Cox's regression model for counting processes: a large sample study. Ann Stat 1982;10:1100-20.
- 21 Plunkett TA, Smith P, Rubens RD. Risk of complications from bone metastases in breast cancer: implications for management. *Eur J Cancer* 2000;36:476-2.
- 22 Verma S, Kerr-Cresswell D, Dranitsaris G, Charbonneau F, Trudeau M, Yogendran G, et al. Bisphosphonate use for the management of breast cancer patients with bone metastases: a survey of Canadian medical oncologists. *Support Care Cancer* 2004;12:852-8.
- 23 LoRusso P. Analysis of skeletal related events in breast cancer and response to therapy. *Semin Oncol* 2001;28(suppl 11):22-7.
- 24 Hillner B, Ingle JN, Chlebowski RT, Gralow J, Yee GC, Janjan NA, et al. American Society Of Clinical Oncology 2003 Update on the role of bisphosphonates and bone health issues in women with breast cancer. J Clin Oncol 2003;21:4042-57.
- 25 Clemons M, Enright K, Cesta A, Charbonneau F, Chow E, Warr D, et al. Do physicians follow systemic treatment and funding policy guidelines? A review of bisphosphonate use in patients with bone metastases from breast cancer. *Can J Clin Pharmacol* 2004;11:e168-e178.
- 26 Hillner B, Weeks JC, Desch CE, Smith T. Pamidronate in prevention of bone complications in metastatic breast cancer: A cost effectiveness analysis. J Clin Oncol 2000;18:72-9.
- 27 Clamp A, Danson S, Nguyen H, Cole D, Clemons M. Assessment of therapeutic response in patients with metastatic bone disease. *Lancet* Oncol 2004;5:607-16.
- 28 Brown JE, Thomson CS, Ellis SP, Gutcher SA, Purohit OP, Coleman RE. Bone resorption predicts for skeletal complications in metastatic bone disease. Br J Cancer 2003;89:2031-7.
- 29 Brown J, Cook R, Major P, Lipton A, Saad F, Smith M, et al. Bone turnover markers as predictors of skeletal complications in prostate cancer, lung cancer and other solid tumors. J Natl Cancer Inst 2005;97:59-69.

(Accepted 29 January 2005)

Lesson of the week Atypical presentation of coeliac disease

R M Furse, A S Mee

Adult coeliac disease is usually associated with a presentation of weight loss, diarrhoea, and malabsorption of nutrients. We are now seeing, however, increased numbers of silent, or subclinical, cases, which are often picked up by the finding of an unexplained anaemia.¹ Despite this change, few clinicians would expect obesity to be part of the presentation. Here we describe four cases that show that we should not be dissuaded from a potential diagnosis of coeliac disease on the basis of a patient's body weight. This is especially pertinent in today's society, where 22% of men and 23% of woman in the United Kingdom are now obese (body mass index > 30).²

Case histories

Case 1

A 53 year old woman was referred to the gastroenterology department with an 18 month history of diarrhoea and a background of almost lifelong irregular bowel habit. She had always been overweight, and there had been no recent change. She weighed 131 kg (body mass index 47). Routine blood tests gave normal results apart from mild iron deficiency. She had a test for endomysial antibodies as part of her investigations,

BMJ VOLUME 330 2 APRIL 2005 bmj.com

and the result was positive. Duodenal biopsies confirmed partial villous atrophy. A bone density (dual energy x ray absorptiometry) scan could not be done because of her weight.

She was put on a strict gluten-free diet and within four months had lost 17 kg. She continued to lose 6.5 kg over the next six months. Her diarrhoea resolved completely.

Case 2

A 51 year old woman was referred by her general practitioner with longstanding dyspepsia and reflux worsened by alcohol and bread. She had always been overweight but had recently noticed a large gain. She weighed 116 kg (body mass index 41) at referral. Results of routine blood tests were normal, other than a vitamin-B12 concentration of 139 (normal 163-490) pmol/l. A test for endomysial antibodies was positive. Duodenal histology confirmed partial villous atrophy, and a bone density scan showed no abnormality.

She was treated with a gluten-free diet and a proton pump inhibitor for her grade 3 reflux oesophagitis. Her weight remained unchanged at follow up, but her symptoms resolved completely. Editorial by Watson and p 775

The presence of obesity does not exclude coeliac disease

Department of Gastroenterology, Royal Berkshire Hospital, Reading RGI 5AN R M Furse *locum specialist registrar* A S Mee *consultant gastroenterologist* Correspondence to: A S Mee

anthony.mee@ rbbh-tr.nhs.uk

BMJ 2005;330:773-4

Case 3

A 51 year old woman with a chronic leg ulcer attended the gastroenterology clinic after her general practitioner had picked up microcytic anaemia (haemoglobin 4.5 mmol/l, mean corpuscular volume 67.4 fl) after routine blood tests. She was asymptomatic and had no alteration in her bowel habit. She had a good dietary iron intake and the remainder of her medical history was non-contributory.

Examination showed no abnormality, although she was obese, weighing 103.7 kg (body mass index 42). Endoscopy showed an abnormal looking duodenal mucosa with scalloped folds suggestive of villous atrophy, and this was confirmed by biopsy. Her anaemia resolved with a gluten-free diet and iron supplements. Her weight increased to 107 kg (body mass index 44).

Case 4

A 36 year old woman was referred because of fatigue, bloating, and an irregular bowel habit. She was passing loose stools up to four times a day. She denied any weight loss and weighed 111 kg (body mass index 38). All of her routine blood tests gave normal results, but on further questioning it became apparent that her father had recently had coeliac disease diagnosed. An endomysial antibody test was therefore ordered. The result was positive, and subsequent duodenal histology confirmed subtotal villous atrophy. She was treated with a gluten-free diet and her symptoms resolved.

Discussion

These cases are unusual but show that not all patients with coeliac disease will be thin or have lost weight at presentation. Coeliac disease is characterised histologically by total or subtotal villous atrophy. These changes tend to be greatest in the proximal small bowel.3 4 Our patients were probably able to compensate for proximal malabsorption by using intact absorptive mechanisms more distally. It is also known that an individual's coefficient for fat absorption remains relatively static and so the ability to maintain energy intake is preserved.4

This theory seems to be confirmed by studies in children. Two reports have been published of adolescents with known coeliac disease who became obese despite being malnourished as babies.^{5 6} This obesity had developed despite the persistence of villous atrophy on jejunal biopsy. It is postulated that as the surface area of the small bowel increases with age,

children develop the ability to ingest adequate compensatory energy.4 Children whose energy intake is excessive will become obese.

Gluten-free diet

The question arises whether obese patients with coeliac disease should be started on a gluten-free diet because of the assumption that they will gain more weight. In one case report of an obese 18 year old with silent coeliac disease, a gluten-rich diet was used to control his weight.⁶ Clearly, such an approach risks complications in later life, including not only the consequences of nutrient deficiencies but also small bowel lymphoma. The risk of such complications seems to be reduced by strict adherence to an exclusion diet.7

In fact, weight gain on treatment is not borne out by our cases. It is not clear why the patient in case 1 lost weight on a gluten-free diet. It may have been due to more sensible eating habits and a general reduction in dietary intake of refined carbohydrates. An increased feeling of wellbeing and a reduction in depression (which is common in coeliac disease) may also have reduced comfort eating.4

The heterogeneity of presentation of coeliac disease is increasing. It is not certain why only a few patients are overweight, but it probably reflects an underlying tendency to obesity in some individuals.⁴ We recommend that all patients with suggestive symptoms, nutrient deficiencies, or positive family history have serological testing for coeliac disease irrespective of their body weight.

Contributors: All patients included in the paper are under the care of ASM, who had the original idea for the report and provided collaboration and editorial input. RMF researched and wrote the article. ASM is guarantor.

Competing interests: None declared.

- Bottaro G, Cataldo F, Rotolo N, Spina M, Corazza GR. The clinical pattern of subclinical/silent celiac disease: an analysis on 1026 consecu-
- pattern of submittal shell cellad usease: an analysis on 1020 consecu-tive cases. Am J Gastroenterol 1999;94:691-6.
 Department of Health. Choosing health? A consultation on improving people's health. Obesity factsheet. London: DoH, 2004. www.dh.gov.uk/assetRoot/ 04/07/60/80/04076080.pdf (accessed 14 Dec 2004).
 Owen DA, Thorlakson TK, Walli JE. Celiac disease in a patient with morbid obesity. Arch. Intern. Med 1980;140:1380-1.
 Semperson LA, Browick UW, Gradedi D, Ohesinix in acting arms. J. Clin.
- 2
- 4 Semeraro LA, Barwick KW, Gryboski JD. Obesity in celiac sprue. J Clin Gastroenterol 1986:8:177-80. Conti Nibali S, Magazzu G, De Luca F. Obesity in a child with untreated
- coeliac disease. Helv Paediatr Acta 1987;42:45-8. 6 Czaja-Bulsa G, Garanty-Bogacka B, Syrenicz M, Gebala A. Obesity in an
- 18-year-old boy with untreated celiac disease [letter]. J Pediatr Gastroenterol Nutr 2001;32:226.
- Loftus CG, Loftus EV Jr. Cancer risk in celiac disease. Gastroenterology 2002:123:1726-9
- (Accepted 1 December 2004)

Submitting articles to the BMJ

We are now inviting all authors who want to submit a paper to the BMJ to do so via the web (http://submit.bmj.com).

Benchpress is a website where authors deposit their manuscripts and editors go to read them and record their decisions. Reviewers' details are also held on the system, and when asked to review a paper reviewers will be invited to access the site to see the relevant paper. The system is secure, protected by passwords, so that authors see only their own papers and reviewers see only those they are meant to.

Anyone with an internet connection and a web browser can use the system.

The system provides all our guidance and forms and allows authors to suggest reviewers for their paper. Authors get an immediate acknowledgment that their submission has been received, and they can watch the progress of their manuscript. The record of their submission, including editors' and reviewers' reports, remains on the system for future reference.

The system itself offers extensive help, and the BMJ Online Submission Team will help authors and reviewers if they get stuck.

Benchpress is accessed via http://submit.bmj.com or via a link from bmj.com