- 1 Oxford Dictionary of Quotations. 4th Ed. Oxford: 1992: 638.
- 2 Lacy ER, Kuwayama H, Cowart KS, King JS, Deutz AH, Sistrunk S. A rapid, accurate, immunohistochemical method to label proliferating cells in the digestive tract: a comparison with tritiated thymidine. *Gastroenterology* 1991; **100**: 259-62.
- 3 Morstyn G, Pyke K, Gardner J, Ashcroft R, Fazio Ad, Bhathal P. Immunohistochemical identification of proliferating cells in organ culture using bromodeoxyuridine and a monoclonal antibody. *J Histochem Cytochem* 1986; **4**: 697-701.
- 4 Cahill RJ, O'Sullivan KR, Mathias PM, Beattie S, Hamilton H, O'Morain C. Effects of vitamin antioxidant supplementation on cell kinetics of patients with adenomatous polyps. *Gut* 1993; **34**: 963-7.
- 5 Sobhani JJ, Lhy T, Laurent-Puig P, Cadot G, Ruzniewski P, Mignon M. Chronic endogenous hypergastrinemia in humans: evidence for a mitogenic effect on the colonic mucosa. *Gastroenterology* 1993; **105**: 22-30.
- 6 Bartram HP, Gostner A, Scheppach W, Reddy BS, Rao CV, Dusel G, et al. Effects of fish oil on rectal cell proliferation, mucosal fatty acids, and prostaglandin E₂ release in healthy subjects. *Gastroenterology* 1993; **105**: 1317-22.
- 7 Potten CS, Kellett M, Roberts SA, Rew DA, Wilson GD. Measurement of in vivo proliferation in human colorectal mucosa using bromodeoxyuridine. *Gut* 1992; **33**: 71-8.
- 8 Scheppach W, Loges C, Bartram P, Christl SU, Richter F, Dusel G, et al. Effect of free glutamine and alanyl-glutamine dipeptide on mucosal proliferation of the human ileum and colon. *Gastroenterology* 1994; **107**: 429-34.
- 9 Mantell MP, Ziegler TR, Adamson WT, Roth JA, Zhang W, Frankel W, et al. Resection-induced colonic adaptation is augmented by IGF-I and associated with upregulation of colonic IGF-I mRNA. *Am J Physiol* 1995; **269**: G974-80.
- 10 Zhang W, Frankel WL, Adamson WT, Roth JA, Mantell MP, Bain A, et al. Insulin-like growth factor-I improves mucosal structure and function in transplanted rat small intestine. *Transplantation* 1995; **59**: 755-61.
- 11 Savage AP, Gornacz GE, Adrian TE, Ghatei MA, Goodlad RA, Wright NA, et al. Is raised plasma peptide YY after intestinal resection in the rat responsible for the trophic response? *Gut* 1985; **26**: 1353-8.
- 12 Goodlad RA, Plumb JA, Wright NA. Simultaneous measurement of intestinal crypt cell production rate and water absorption. *Gut* 1987; **28** (suppl 1): 189-92.
- 13 Goodlad RA, Plumb JA, Wright NA. The relationship between intestinal crypt cell production and intestinal water absorption measured in vitro in the rat. *Clin Sci* 1987; **72**: 297-304.
- 14 Goodlad RA, Savage AP, Lenton W, Ghatei MA, Gregory H, Bloom SR, et al. Does resection enhance the response of the intestine to urogastrone-epidermal growth factor in the rat? *Clin Sci* 1988; **75**: 121-6.
- 15 Hebel R, Stromberg MW. *Anatomy and embryology of the laboratory rat*. Worthsee: Biomed Verlag, 1986.
- 16 Shaw GB. *Maxims for Revolutionists*. Quoted in Best Quotations. Henry L ed. New York: Doubleday, 1964.

Experimental colitis is ameliorated by inhibition of nitric oxide synthase activity

EDITOR.—We congratulate Rachmilewitz and colleagues for their paper discussing the effects of nitric oxide synthase inhibition on experimental intestinal inflammation (*Gut* 1995; **37**: 247-55). Using a rat model of colitis induced by 30 mg trinitrobenzenesulphonic acid in 0.5 ml 50% ethanol (TNBS/E) we have similarly shown the importance of the L-arginine-nitric oxide pathway on mucosal inflammation.¹ L-arginine given by mouth, the biosynthetic precursor of nitric oxide, promoted the inflammatory response in experimental colitis. Addition of N^G-nitro-L-arginine methyl ester (L-NAME) to the arginine supplemented diet reduced both colonic inflammation and weight loss. In accordance with Rachmilewitz and colleagues, we have also found that oral administration of L-NAME alone, as an oral solution (500 mg/l) or as an enema, (1 g/l)

reduced colonic inflammation in this model of colitis.

Bacteria, bacterial products, and cytokines may all promote induction of calcium independent nitric oxide synthesis in the colonic mucosa. There is evidence that enteric bacteria and their products can penetrate the gut mucosal barrier in patients with inflammatory bowel disease (IBD) and in experimental models of colitis.^{2,3} Increased faecal concentrations of tumour necrosis factor have also been shown in both IBD and TNBS/E induced colitis.^{4,5} In addition we have recently shown that administration of an anti-tumour necrosis factor antibody reduces the inflammatory response in this model of colitis.⁶ It is therefore possible that these bacterial products and cytokines may exert a pro-inflammatory action in patients with IBD by the induction of nitric oxide synthesis.

We agree with the authors that modulation of nitric oxide synthase activity may have therapeutic potential in IBD. As shown by Rachmilewitz and colleagues L-NAME given by mouth has potent hypertensive effects, which may limit its usefulness in the treatment of patients with chronic IBD. Topical administration, however, may confer beneficial anti-inflammatory effects with reduced cardiovascular complications.

P J D NEILLY
K R GARDINER
B J ROWLANDS
Department of Surgery,
The Queen's University of Belfast,
Grosvenor Road, Belfast BT12 6BJ

- 1 Neilly PJD, Kirk SJ, Gardiner KR, Anderson NH, Rowlands BJ. Manipulation of the L-arginine-nitric oxide pathway in experimental colitis. *Br J Surg* 1995; **82**: 1188-91.
- 2 Gardiner KR, Halliday MI, Barclay GR, Milne L, Brown D, Stephens S, et al. Significance of systemic endotoxaemia in inflammatory bowel disease. *Gut* 1995; **36**: 897-901.
- 3 Neilly PJD, Gardiner KR, Kirk SJ, Jennings G, Anderson NH, Elia M, et al. Endotoxaemia and cytokine production in experimental inflammatory bowel disease. *Br J Surg* 1995; **82**: 1479-82.
- 4 Braegger CP, Nicholls S, Murch SH, Stephens S, MacDonald TT. Tumour necrosis factor alpha in stool as a marker of intestinal inflammation. *Lancet* 1992; **339**: 89-91.
- 5 Neilly PJD, Campbell GR, Anderson NH, Gardiner KR, Kirk SJ, Rowlands BJ. Faecal and systemic tumour necrosis factor in experimental inflammatory bowel disease. *Surgical Research Communications* 1995; **18**: 11-7.
- 6 Neilly PJD, Gardiner KR, Kirk SJ, Jennings G, Anderson NH, Elia M, Rowlands BJ. Anti-TNF α antibody reduces the systemic inflammatory response in experimental colitis. *Gut* 1995; **37** (suppl 2): A16.

Heartburn in patients with achalasia

EDITOR.—We were interested to read the thought provoking paper on heartburn in patients with achalasia, in which the authors hypothesised that the heartburn described by 48% of achalasia patients eligible for review was related to gastro-oesophageal reflux disease (GORD) and documented on manometry a relative reduction in basal lower oesophageal sphincter pressure in such patients (*Gut* 1995; **37**: 305-8).

They themselves note that there are many alternative causes for heartburn in patients with achalasia and performed no pH monitoring to support what they admit remains speculation. However, if such a group of patients did exist and could be reliably selected they would clearly be candidates for an antireflux procedure at the time of treatment by surgical myotomy.

Following an initial study examining the need for an antireflux procedure during laparoscopic Heller's cardiomyotomy,¹ we have prospectively evaluated patients with achalasia undergoing such surgery with a protocol that includes pre and postoperative 24 hour pH monitoring.

The 12 patients who have undergone preoperative pH monitoring had a median composite DeMeester score² of 0.45 (range 0.2-16.8) (upper limit of normal 14.72 at pH threshold <4) only one patient showed abnormal oesophageal acidity at this stage. Postoperatively in 10 patients the median score increased to 6.00 (range 0.2-19.6) with two patients lying outside the normal range, one of whom had probably had an inadequate myotomy.

Preoperatively significant reflux was extremely uncommon and these results do not support the hypothesis that the heartburn experienced by patients with achalasia is due to acid reflux. Even after a myotomy completely dividing the lower oesophageal sphincter very few patients showed significant GORD despite their aperistaltic oesophagus and it seems likely that factors such as the crural fibres of the diaphragm³ continue to effectively prevent reflux in most patients. A review of 75 papers reporting 5002 patients with achalasia gave an average incidence of postoperative GORD of 8.6%.⁴ It is improbable therefore that large numbers of such patients refluxed significantly before the development of their achalasia as speculated by our authors.

G S M ROBERTSON
P S VEITCH
Departments of Surgery
and Gastroenterology
Leicester General Hospital NHS Trust,
Gwendolen Road, Leicester LE5 4PW

- 1 Robertson GSM, Lloyd DM, Wicks ACB, de Caestecker J, Veitch PS. Laparoscopic Heller's cardiomyotomy without an antireflux procedure. *Br J Surg* 1995; **82**: 957-9.
- 2 DeMeester TR. Prolonged oesophageal pH monitoring. In: Read NW, ed. *Gastrointestinal motility: which test?* Petersfield: Wrightson Biomedical, 1989: 41-52.
- 3 Peck N, Callander N, Watson A. Manometric assessment of the effect of the diaphragmatic crural sling in gastro-oesophageal reflux: implications for surgical management. *Br J Surg* 1995; **82**: 798-801.
- 4 Andreollo NA, Earlam RJ. Heller's myotomy for achalasia: is an added anti-reflux procedure necessary? [review]. *Br J Surg* 1987; **74**: 765-9.

BOOK REVIEWS

Atlas of Clinical Hepatology. By N Gitlin, R M Strauss. (Pp 183; illustrated; £92). Philadelphia: W B Saunders, 1995. ISBN 0-7216-4356-6.

The explosion in information technology has revolutionised the way knowledge is sought and processed, but in a manner that reduces the impact of pictorial images on education. The role of the classic textbook as pivotal to teaching is increasingly challenged by

computer generated information. Clinical education is also less reliant on bedside teaching and intensive exposure to patients. Gitlin and Strauss have compiled an atlas of clinical, pathological, and radiological features of liver disease over many decades in their hope that this will provide a useful adjuvant to the study of hepatology. The extent to which it does so remains to be seen, but the need for such a book was never greater. The book is attractive and well produced. The layout in the main follows recognised disease categories, but it could possibly be improved by greater integration of the imaging chapter into the sections dealing with the relevant diseases. This would reduce the need for cross referencing and facilitate its use in a multimodality educational process.

The strength of this atlas lies very much in the arena of conventional hepatology, which is covered quite comprehensively. The paucity of text is an essential feature of this type of presentation, but the legends tend to be succinct and informative. The authors grappled with the changing terminology in some areas of hepatology, but in the area of chronic hepatitis they fell between two stools by describing the new terminology while continuing to use terms such as chronic active hepatitis, chronic persistent hepatitis, and piecemeal necrosis in the text. In that respect the book probably accurately reflects the position of most hepatologists. Many of the illustrations of end stage liver disease are extreme examples and hopefully will soon serve as a reminder of what was inevitable in the pre-transplant era. The illustration of the Budd-Chiari syndrome was especially good. Another highlight is the intriguing illustration of the imperfections of blind liver biopsies even when the liver is almost completely replaced by metastatic deposits.

Hepatology has been subjected to great change as a consequence of the impact of liver transplantation on the treatment of most liver diseases. This has also resulted in the new discipline of transplant hepatology, which has thrown up new diseases and different perspectives on established conditions. The section on liver transplantation is a token gesture, which recognises the procedure rather than attempts to deal with this expanding area with the same degree of authority as applies to the rest of the book.

J O'GRADY

Textbook on Interventional Radiology of the hepatobiliary system and gastrointestinal tract. Edited by A Adam, R N Gibson. (Pp 210; illustrated; \$95). London: Edward Arnold, 1994. ISBN 0-340-551666.

This practical guide has been written by 10 experts in the field of interventional radiology and describes both the basic procedures as well as the more specialised interventions. The general chapters cover percutaneous biopsy and cytology and aspiration of fluid collections while specific chapters deal with transjugular liver biopsy, gastrointestinal fistulas, and strictures. These latter disorders may become more frequent as the number of complex abdominal surgical interventions increases. The potential of radiological management for these indications should be widely known as there are guidewires and catheters now available that permit the treatment of the most complex situations. Treatment of oesophageal strictures is described in a separate chapter but concentrates mainly on balloon dilatation. The interventional

radiology in the biliary tree is the cornerstone of the book. Percutaneous drainage techniques, stent placement in malignant and benign conditions, and percutaneous approach to the gall bladder are extensively described, with reference to patient selection, complications, and their prevention and management. Percutaneous extraction of residual gall stones is detailed in one chapter. Plastic stents are still abundantly mentioned although the superiority of metal stent seems evident. The angiographic section includes discussion of such techniques as TIPS, embolisation, treatment of Budd-Chiari syndrome, embolisation of vascular lesions and liver lesions as well as peripancreatic vascular interventions. This chapter seems to summarise the potential of vascular interventional radiology but does not focus on the detail of specific techniques.

This book is a practical guideline to those who want to use interventional radiological procedures, particularly residents in radiology. The illustrations and drawings are outstanding and technique is emphasised throughout the book.

R F DONDELINGER

Clinician's Manual on Helicobacter Pylori. Edited by J J Misiewicz, A Harris. (Pp 42; illustrated; £6.95). London: Science Press, 1995. ISBN 1-85873-063-5.

Helicobacter pylori is a troublesome spirochaete, which has turned much of gastroenterology on its head in the past decade. We can no longer adhere to Schwartz's dictum 'no acid, no ulcer' when we recognise that these organisms themselves adhere to the submucous regions of the gastric antrum and cause untold problems to the underlying mucosa. With foregut gastroenterology in the grip of helicomania, it is comforting to find a little book that provides an entirely sane and acceptable account of the role of helicobacter in upper gastrointestinal disease and describes, with great clarity, the methods available to identify and treat the organism.

This is an unusual publication. It is small, cheap, clearly written, authoritative, even handed, and comprehensible. It is elegantly produced, beautifully illustrated, and sparingly referenced. It also contains a number of tables and illustrations which, copyright law permitting, would form the basis of an extremely serviceable lecture on the place and management of helicobacter in upper gastrointestinal disease. Not only does it provide concise information for generalists, including general practitioners, but is also likely to represent a useful consensus statement for gastroenterologists. Moving from pathophysiology, through diagnosis to treatment and the indications for eradication therapy, the authors hardly put a foot wrong. My only concern is that they do not address the current vogue for using near-patient testing for helicobacter, principally in general practice, as an indicator for the empirical prescription of eradication therapy. Instead, the authors suggest that dyspeptic patients who are helicobacter positive are referred for endoscopy; this is at odds with a developing, although unevaluated, trend in primary care, and they would have done well to discuss the pros and cons of this strategy.

At £6.95, this book could usefully be purchased and distributed by Family Health Service Authorities or Health Commissions as a state of the art guide to the helicobacter problem. The authors emphasise the

importance of using effective eradication therapy, almost certainly using three drugs, rather than the more commonly used dual therapy, although their recommendations for follow up breath testing to confirm eradication may not be justified on either clinical or cost effectiveness grounds.

This publication raises a number of more fundamental questions about the links between research evidence and clinical practice, and the best way of communicating new data to practitioners. On the one hand, by the time this book is in wide circulation, it may be out of date. On the other, there is a clear mismatch between current practice and publication in peer reviewed journals. The answer might be to provide the information contained in this book in electronic form, which can be updated at intervals, and recommendations for treatment modified in the light of new evidence and accepted practice. If we are to embrace the concept of evidence based medicine, we are probably looking for solutions that transcend both the paper publication of primary research data and the subsequent publication of review material of this kind.

R JONES

Gastroenterology and Liver Disease. By P C Hayes, K J Simpson. (Pp 120; illustrated; £8.50). Edinburgh: Churchill Livingstone, 1995. ISBN 044-304-9556.

'What is the use of a book', thought Alice 'without pictures or conversation.'

Alice would have liked this book. The pictures are excellent. A series of colour prints with a brief accompanying text guide the reader through the wonderful world of gastroenterology and hepatology. Designed primarily as an introductory white coat book for students, it succeeds admirably. The book is just short enough to be read and just cheap enough to be bought by the average student. However the more specialist reader will find the brevity of the text somewhat disconcerting. For example the treatment of hepatic encephalopathy is discussed in two lines, and the aetiology of inflammatory bowel disease in four, with no mention of the importance of genetic factors. The staging of colonic cancer was also neglected. Perhaps more surprisingly, considering the impact of HIV disease on the gastroenterologist's time and practice, there were only two cursory references to this disease. These omissions should not detract from the authors' and publishers' achievements. Both should be congratulated on the quality of the illustrations. In particular the prints of radiological abnormalities are clearer than in many more expensive specialist tomes. Gastroenterology certainly lends itself to this illustrated format and I would have no hesitation in recommending this book as an introductory guide. The best introductions will stimulate readers to explore further and deeper. Whether it is good enough to provoke Alice's celebrated response of 'curiouser and curiouser!', only time will tell.

S BRIDGER

Role of Gut Bacteria in Human Toxicology and Pharmacology. Edited by M J Hill. (Pp 286; illustrated; £49). London: Taylor and Francis, 1995. ISBN 0-7484-0110-5.

The roles of gut microflora on the pharmacology and toxicology of drugs and environmental chemicals are among the cinderellas of