

LETTERS TO THE EDITOR

Liver disease and pulmonary hypertension

EDITOR.—I read with interest the leading article on hepatopulmonary syndromes (*Gut* 2000;46:1-4). The author describes explicitly the various associations between the liver and lung disorders. Several clinical studies and autopsy findings have demonstrated a 20% higher prevalence of pulmonary hypertension in patients with advanced liver disease and portal hypertension, the histological findings of which show features similar to those seen in pulmonary hypertension from other causes.^{1,2} However, the underlying mechanism(s) responsible for pulmonary hypertension in these patients is not known. It has been recently hypothesised that increased circulating levels of noradrenaline (NA) or increased activity of α_1 adrenergic receptors in the pulmonary arteries can produce excessive pulmonary vasoconstrictor and proliferative responses leading to pulmonary hypertension.³

It is generally believed that pulmonary hypertension results from defective hepatic elimination of a vasoconstrictive agent produced in the splanchnic territory which reaches the pulmonary arteries through porto-systemic shunts.⁴ The mesenteric organs produce about 50% of the total NA present in the human body⁵ which is rapidly metabolised by liver parenchymal cells to vanillylmandelic acid before it reaches the systemic circulation.^{6,7} Following hepatectomy, circulating levels of NA have been shown to be increased by up to 10-fold in experimental animals⁸ while patients with liver cirrhosis or those undergoing extracorporeal hepatic resection or liver transplantation have levels of circulating NA up to 2.6-fold greater.^{9,10} Increased pulmonary vascular resistance has often been observed during the anhepatic phase of liver transplantation⁸ while several studies have demonstrated that pulmonary hypertension often resolves completely in patients with liver cirrhosis following liver transplantation.¹¹ Formation of a portocaval shunt without liver cirrhosis has also been shown to produce severe pulmonary hypertension.¹² It has been demonstrated recently that hepatectomy produces a sharp increase in pulmonary vascular resistance which correlates positively with pulmonary arterial NA levels.⁵

Defective hepatic metabolism by diseased liver parenchymal cells could greatly increase circulating levels of NA. The resulting portal hypertension and porto-systemic shunt also transfers large amounts of NA directly from the mesenteric bed to the systemic and pulmonary circulation. High circulating levels of NA could then stimulate α_1 adrenergic receptors present in the pulmonary arteries to produce excessive pulmonary vasoconstrictor and proliferative responses leading to pulmonary hypertension. Increased NA levels could also explain the association of increased cardiac output noted in patients with portopulmonary hypertension. α_1 Antagonists or drugs that rapidly metabolise circulating lev-

els of NA could therefore prevent the development of pulmonary hypertension in patients with advanced liver disease and portal hypertension.

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UDCA, PBC, and biochemistry, what does normal mean?

EDITOR.—We read the commentary by Lindor (*Gut* 2000;46:8) with great interest and would like to raise the following points.

Lindor is not surprised that in our study¹ patients with primary biliary cirrhosis (PBC) who initially had less abnormal liver function tests responded more favourably to ursodeoxycholic acid (UDCA) than those who had initially greater abnormal liver function values. We believe this is interesting as it is known that patients with lower abnormal liver function tests respond less favourably (for example, chronic autoimmune hepatitis to treatment with glucocorticoids) and that values do not decrease in a linear manner. Furthermore, it is well known that UDCA in PBC does not cause normalisation of liver function tests in most patients, and to date there has been no extensive examination of full and incomplete responders. Only in one study was this area addressed but few liver parameters were studied and there was only a short follow up period.²

Lindor states that our finding of no correlation between the percentage of UDCA in serum bile acids and biochemical response is different from other reports. However, he quotes only one study.³ Based on data from the literature,⁴ we reported in our paper¹ that

it is improbable that a further increase in bile acid concentrations in serum and a shift from the more hydrophobic to a more hydrophilic bile acid pool could be responsible for a complete response to UDCA therapy. Further results are awaited.

Lindor speculates that in our study the high percentage of patients with early stage PBC could have been an artefact because there was no correlation between histological stage at entry and biochemical response. We started UDCA therapy for PBC in 1978/79. In that time we have had 120 patients under constant supervision and over this period of 21 years only three patients have undergone liver transplantation and two have died as a result of late stage liver disease. Furthermore, our patients underwent regular liver biopsies and some even laparoscopy. That we have seen no more deaths or complications can only be explained by the fact that patients were in the early stages of the disease and that they were treated continuously with UDCA.

Lindor says that improvement in liver histology in our patients treated with UDCA ($p < 0.05$) differs from the overall experience in other studies. However, in our study, we discriminated between incomplete and complete responders whereas in other trials complete and incomplete responders were evaluated together and compared with an untreated group.

In addition, Lindor is surprised that the histological progression reported in our series, even in incomplete responders, was slow. Based on modelling studies of untreated patients with PBC, he stated that substantially more patients developed histological progression. The difference between the studies cited by Lindor and ours is that we studied patients treated long term and not untreated patients, and it is well known that UDCA retards histological progression,⁵ as recently shown using the Markow model.

Our description of how the histological grading was performed was not sparse; it was presented carefully and in accordance with other studies. It is correct that the histological data are mentioned in a single sentence and are not tabulated or otherwise presented. But having been a pathologist myself, I am rather sceptical towards liver histology in a patchy disease. For example, in 1994 it was shown⁶ that in a focal disease such as PBC, nine liver biopsies were needed from one session to warrant a definitive histological diagnosis. As this is not possible for ethical reasons, histological findings should not be over interpreted. Clinical data, development of complications, outcome, etc, are more relevant.

The most important objection of Lindor is the question of the relation between normalisation of liver function tests and clinically relevant findings. This is in contrast with a statement by Lindor himself (personal communication, November 9, 1999, 5th Annual Meeting, AASLD, Dallas, Texas) where he told us that in his incomplete responders the disease progressed in 38% of patients and in full responders in only 5%. We believe our results are comparable. In common with Lindor, in full responders we found progression of the disease in 4% and in 11% of incomplete responders; in incomplete responders progression occasionally took place not only from one stage to the next, but to the next but one stage. As patient numbers were small in our study, we did not give percentage values. Hence it is clear from our results the significance of normalisation of liver function tests.

The most important findings in our study were that: (1) UDCA improved cholestatic indices in incomplete and full responders in a strictly parallel manner; (2) in incomplete responders, the curves levelled off after about 3–5 years and did not normalise; and (3) cholestatic indices in patients with anicteric early stages of PBC allowed differentiation between responders and incomplete responders. This parallelism of the curves may indicate that UDCA influences mainly cholestasis and that other reactions are secondary. Therefore, more potent choleric compounds or a combination of various choleric substances could further improve results in incomplete responders. As stated previously, we are about to conclude such a study and the results seem to support our hypothesis.

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Endoscopic gastrin test and *Helicobacter pylori* infection

EDITOR.—In their recent article in *Gut*,¹ Iijima and colleagues conclude that reduced acid secretion in gastric ulcer patients and gastric acid hypersecretion in duodenal ulcer patients were both normalised after *H pylori* eradication. We agree with the recovery of gastric secretory function in the former group of patients, who constantly bear chronic gastritis which improves greatly after disappearance of the germ, with subsequent restoration of gastric glandular tissue.^{2–4} However, we disagree with their conclusion regarding the latter group, because it is not supported by the experimental data they obtained. It is surprising that they found an increase in acid secretion (although not significant) in duodenal ulcer patients one month after eradication.

This finding is difficult to explain, because basal gastrin levels were significantly reduced compared with those before eradication in the same patients, and others have found a rapid decrease of acid output in relation to the decline of serum gastrin.^{5,6} The Japanese researchers state that this disparity may depend on the premature assessment of gastrin stimulated acid output (one month), because the same evaluation performed after seven months showed significantly decreased

values compared with those before eradication. It must be pointed out, however, that there is a tremendous overlap between acid outputs measured before and after seven months of eradication, and those pertaining to *H pylori* negative controls. Moreover, the rate of decrease of acid secretion after seven months was only 23% in their study.

This reduction is very low and similar to the level of 16% seen after six months of eradication by Parente *et al*,⁷ who themselves acknowledged in their paper that this small percentage casts doubt on the unique role of *H pylori* in determining the augmented acid secretion typical of duodenal ulcer. Although the data obtained by Iijima *et al* and Parente *et al* after cure of *H pylori* infection were significantly different from those before eradication, we believe that statistical significance does not mean physiological relevance in this case.

Apart from the previously mentioned overlapping, some patients even show an increase in acid secretion after seven months, and others have found no change in maximal acid secretion 12 months after eradication of the bacterium.⁶ It is clear that the deregulation of gastric physiology in duodenal ulcer is caused by a combination of factors and *H pylori* is only one of them. In addition, it should not be forgotten that 20% of patients with duodenal ulcer have been shown to relapse despite ascertained *H pylori* eradication,⁸ and a high acid output has been found in patients with duodenal ulcer recurrence after the disappearance of *H pylori*.⁹

These findings seem to suggest that a genetic predisposition to secrete more acid is present at least in a subset of patients with duodenal ulcer, and is independent of *H pylori* status.¹⁰ Therefore, overenthusiastic statements that eradication of *H pylori* is followed as a rule by normalisation of gastric acid output are deceiving and should be attenuated.

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Losartan and renal sodium handling

EDITOR.—We read with great interest the paper by Girgrah *et al* (*Gut* 2000;46:114–120). Their report suggests that the subtle sodium retention that is characteristic of preascitic cirrhosis is improved by administration of low dose losartan. This is despite the paradoxical observation of an angiotensin concentration that is significantly lower in patients compared with healthy volunteers (mean (SEM) patients 6 (2); controls 40 (10) pmol/l). Our results of angiotensin II measurements are at variance with those published by Girgrah *et al* and are summarised in fig 1.^{1,2} Our studies suggest that there is a progressive increase in angiotensin II concentrations with increasing severity of sodium retention. In fact, this increase in angiotensin II is evident before any measurable derangement in systemic haemodynamic characteristics.³ The values measured in healthy volunteers are also significantly higher than those reported in the literature.⁴ We are not sure if these differences in measured values are the result of different patient populations, differences in the method of collection of the sample (Girgrah *et al*—EDTA and aprotinin; Newby *et al* and Helmy *et al*—0.5 ml of 0.45% O-phenanthroline and 1% disodium EDTA), or different assay techniques (were the samples extracted prior to the radioimmunoassay?).

The authors hypothesise that the increase in renal sodium excretion observed after administration of losartan was possibly due to its effect on intrarenal angiotensin II secretion. If this were true then, why was there a significant increase in plasma angiotensin II concentrations after administration of losar-

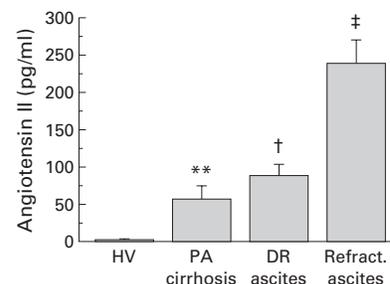


Figure 1 Measured angiotensin II concentrations in healthy volunteers (HV) and in patients with cirrhosis and varying degrees of severity of sodium retention (preascitic (PA) cirrhosis, diuretic responsive (DR) ascites, and refractory ascites). Our results are in pg/ml and the values reported by Girgrah *et al* are in pmol/l; 1 pg/ml is approximately equal to 1 pmol/l, taking the molecular weight of angiotensin II as 1046.2. ** $p < 0.01$ v controls; † $p < 0.05$ v preascitic cirrhosis and controls; + $p < 0.05$ v controls, preascitic cirrhosis, and refractory ascites.

tan? Values of angiotensin II observed in this study are contradictory to expected values. Indeed, in patients with severe heart failure, mean values of 60–70 pg/ml are reported and a value >10 pg/ml in patients given angiotensin converting enzyme inhibitors is considered high.^{4,5} These findings question the pathophysiological interpretation of the main results of the study by Girgrah *et al.* It is more likely that improvement in sodium excretion after administration of losartan was due to its effect on reducing portal pressure⁶ which in turn alters renal function through the hepatorenal axis.^{7–9}

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Reply

EDITOR.—We thank Drs Jalan and Newby for their comments on our recent study (*Gut* 2000;**46**:114–120). We understand that our findings of decreased angiotensin II levels in preascitic cirrhotic patients compared with normals are at variance with their findings of elevated levels in such patients.^{1,2} Before we comment on this, we will first address their second point that our results in healthy volunteers are higher than those previously reported.³ On reviewing the literature, we noted that our values were within the same “ballpark” as the reported reference values of 20 (7) pg/ml,³ whereas those from the Edinburgh group (3.2 (0.3) pg/ml¹) are on the low side. Furthermore, their angiotensin II levels in cirrhotic patients with ascites (238 (30) pg/ml¹) are several times higher than those reported in patients with severe heart failure.³ We believe the explanation for these disparate results in normals and patients is

laboratory variation, which is why each investigation needs its own reference values.

Concerning the differences between our findings and those of Helmy *et al.* of increases in angiotensin II levels in preascitic patients, the Edinburgh group not surprisingly found an increase in plasma renin activity also. They acknowledge in their publications that this is at variance with much of the literature on the subject in which several studies found suppression of the renin-angiotensin-aldosterone system in preascitic patients in the supine position,^{4,8} the position the Edinburgh group used in their studies.^{1,2} In addition, their preascitic patients had normal levels of atrial natriuretic peptide, which is also at variance with much of the literature, as summarised in the review by Bernardi and colleagues.^{9,10} Hence how do we explain these differences? We cannot explain them in terms of decreased sodium intake as their patients were on a diet of 150 mmol of sodium per day. However, we noted that a significant percentage of their preascitic patients had primary biliary cirrhosis. These patients were cholestatic, giving rise to an unusually high mean serum bilirubin level (35 (12) μ mol/l) for a group of preascitic cirrhotics.¹ This in turn may have contributed to some of their preascitic patients being classified as Child B whereas such patients are generally in the Child A category.^{1,2} These cholestatic patients, with or without jaundice, also have elevated levels of serum bile acids which are vasodilators¹¹ and could be partly responsible for the decreased effective blood volume in the jaundiced patients, even in the absence of cirrhosis.¹² Relatively mild jaundice may also explain the reduced vascular responsiveness to angiotensin II found by the Edinburgh group.¹³

In general, we largely agree with much of the Edinburgh group’s findings. In particular, we agree with the increase in serum angiotensin II levels with deterioration of liver disease; with their findings after the TIPS procedure; and with the importance of liver function and portal hypertension in the pathogenesis of sodium retention in chronic liver disease. Therefore, we concur with their concluding remark that improvement in renal sodium handling found in preascitic cirrhotic patients after low dose losartan may well be due in part to the lowering effect of losartan on portal pressure.¹⁴

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Replication error phenotype in colorectal cancer

EDITOR.—The results presented in the article by Curran *et al.* (*Gut* 2000;**46**:200–204) may have been different if the authors had classified DNA microsatellite instability status as stable (MSS), low (MSI-L) or high (MSI-H), as recommended by a National Cancer Institute sponsored workshop.¹ Their “RER+” group included both MSI-H and MSI-L cancers. The finding of bandshifts in two of eight dinucleotide markers is not specific for MSI-H cancers and will pick up a proportion of MSI-L cases.^{2,3} Two of the three RER+ cancers with a K-ras mutation (study Nos 52 and 129) showed bandshifts at only two loci, were left sided, and were positive for nuclear p53. It would be interesting to know if these cancers are characterised by bandshifts at the mononucleotide markers BAT25, BAT26, or BAT40 (specific and sensitive for MSI-H) and/or show loss of expression of hMLH1.⁴ I expect these (and other cancers) will be found to be MSI-L. This would also explain the high frequency of p53 positivity, not seen by others.⁵ Their conclusions with respect to RER+ cancers regarding molecular profiles and prognostic significance only compound the confusion generated by earlier studies that failed to draw the fundamental distinction between MSI-L and MSI-H.

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Reply

EDITOR.—Jass has pointed out that the criteria we used to define microsatellite instability (MSI) status are not in accordance with the recommendations produced by the National Cancer Institute workshop on microsatellite instability.¹ We would point out that the conclusion of our study and submission of our manuscript were contemporaneous with the publication of these recommendations. It is clear that the criteria we used may have resulted in some MSI-L cases being included in the RER+ cohort for the purpose of the analysis. Clearly, the best way to address this issue would be to reassess our RER+ cohort using a mononucleotide repeat marker, BAT-25 or BAT-26^{2,3}; however, sufficient clinical material is no longer available to us.

We based our analysis on eight dinucleotide repeat markers and defined tumours as RER+ if two or more markers (that is, 25%) exhibited allelic shifts.^{4,5} This analysis categorised 14% of tumours (22 of 159) as RER+. The NCI recommendations for analyses involving greater than five markers were that MSI-H would be defined as having allelic shifts in >30–40% of markers.¹ This would suggest that our RER+ cohort must contain a number of MSI-L tumours but that, by the NCI criterion, the majority are likely to have been MSI-H. Therefore, while we readily concede that our study included a number of MSI-L tumours in the RER+ category, we believe that this number was small (in the context of a total patient cohort of 159) and does not completely invalidate our conclusions. Furthermore, as we have pointed out in our paper, we believe that our decision to include only patients who underwent potentially curative surgery for cancers which had penetrated beyond the bowel wall but which had not breached the peritoneal surface, spread to other organs or metastasised to lymph nodes or distant sites at the time of operation (T3, N0, M0), lends significant strength to our study in avoiding potentially confounding effects of tumour stage on microsatellite instability or other parameters.

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Fibrosing colonopathy in an adult caused by over use of pancreatic enzyme supplements

EDITOR.—We read with interest the report by Bansi and colleagues (*Gut* 2000;46:283–285) describing fibrosing colonopathy secondary to high dose pancreatic enzyme therapy in an adult patient. Some details of the patient's history—cholangitis, pancreatitis, and pancreatic insufficiency—are strikingly similar to symptoms displayed by our adult patient with cystic fibrosis and fibrosing colonopathy described previously.¹ In this patient with cystic fibrosis, chronic cholangitis and cholelithiasis required repeated endoscopic retrograde cholangiopancreatography, and severe pancreatic insufficiency was the reason for high dose pancreatic enzyme supplementation. Bansi *et al* assume that their patient was not suffering from cystic fibrosis. As previously discussed in the commentary by Dodge in the same issue,² negative results after even extensive mutation analysis of the cystic fibrosis transmembrane regulator gene cannot rule out cystic fibrosis. Furthermore, as outlined by the Cystic Fibrosis Foundation Consensus Panel,³ sweat testing is the standard test for diagnosis of cystic fibrosis. In patients with typical clinical symptoms but normal or borderline sweat chloride concentrations and normal genetic findings, nasal potential difference measurements should be performed. The clinical symptoms of the patient described by Bansi *et al* are highly indicative of cystic fibrosis with exclusive involvement of the gastrointestinal tract. Moreover, the histopathology of the pancreatic tissue, showing glandular fibrosis and atrophy, is also typical of cystic fibrosis, as are frequent bowel actions.⁴

Proof of fibrosing colonopathy in a patient not suffering from cystic fibrosis may contribute considerably to a better understanding of the pathogenesis of fibrosing colonopathy which is still a matter of discussion.^{5,6} It would underline the aetiological impact of toxic effects of high dose pancreatic enzyme supplementation but caution against overestimating the contribution of factors possibly related to the cystic fibrosis transmembrane regulator gene mutation, such as increased intestinal absorption.² We would therefore be interested in the patient's sweat chloride concentration and, if normal, in the result of nasal potential difference measurements. This paper strongly advocates well thought out supplementation of pancreatic enzymes in adults who, like infants and children, are at risk of developing fibrosing colonopathy.

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Coeliac disease and unfavourable outcome of pregnancy

EDITOR.—We read with interest the paper by Martinelli *et al* (*Gut* 2000;46:332–335) in which the authors found that 12 of 845 (1 in 70) pregnant women were positive for antiendomysium antibody (AEA). We have conducted a similar study. We examined sera from 450 consecutive unselected pregnant women and 125 normal non-anaemic female blood donors as controls. We found that 2/450 and 0/125 women were AEA positive, respectively. Both AEA positive patients were anaemic (haemoglobin <11 g/dl). Hence in continuing the study we elected to examine only sera from anaemic pregnant women. Of a total of 216 consecutive samples, five were positive for AEA (1 in 43).

In the study of Martinelli *et al*, 9/12 women with AEA were anaemic by these criteria. The other three were associated with good outcome. In view of this and our own findings, we agree with the authors that pregnant women should be screened for coeliac disease but we would suggest that this could be made considerably more cost effective by screening only those who are anaemic. Women who are anaemic, whether pregnant or not, should be investigated for coeliac disease.¹

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- 1 Unsworth DJ, Lock RJ, Harvey RF. Iron-deficiency anaemia in premenopausal women. *Lancet* 1999;353:1100.

Reply

EDITOR.—We are pleased that Dr Unsworth and colleagues have had a similar experience of undiagnosed coeliac patients among pregnant women. Their rate of 2/450 women is not very different from that observed in our study. It is also surprising that so many cases have been found in a country where coeliac disease has recently been reported as “disappearing”!

We agree that anaemic women should be screened for coeliac disease.

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BOOK REVIEWS

What Should I Do? Ulcerative Colitis Health Management Guide. Edited by A Kennedy, D Robinson (Pp 80; illustrated; £12.50) UK: RTFB Publishers, 1999. ISBN 9 781902 983073.

A booklet a little larger than the size of a two column review may seem unimportant. But this is an exception. This publication is for patients with ulcerative colitis and such sources of information should be the concern of gastroenterologists. It has been written by Andrew Robinson, whose self management programme for patients with colitis leads to fewer outpatient visits, more rapid treatment of relapse, and improved patient satisfaction (*Gut* 1999;44:A12) and Anne Kennedy, a research fellow in primary care. They have been assisted by a professional writer and sensibly had the guide endorsed by the Plain English Campaign.

The guide consists of two booklets in a single plastic folder. Part One includes an overview of ulcerative colitis, tests, treatment and surgery. Part Two is an individual patient record. There is much to be commended, with detailed information helpfully summarised in coloured boxes ("Things to Remember"), or treatment options discussed ("Your Choice") and anecdotes from patients that give a personal appeal. Clinical views and opinions are, on the whole, well balanced, and I could see this guide being a valuable contribution to patient information. Faults, however, qualify this commendation. The surgical subsection on ileorectal anastomosis for ulcerative colitis is wholly inappropriate and there is confusion in terminology in the section on pouch surgery. Factual errors (such as a "2% risk" of ulcerative colitis in offspring, or "5-mercaptopurine") and statements such as "immunosuppressants may make your baby very small and can lead to abnormalities" are simply misleading. Indeed the whole section on pregnancy is poor, with two anecdotes from patients advising cutting down or stopping maintenance therapy. It was surprising that there was no information for adolescents, or on osteoporosis, and little mention about the dilemmas of coexisting irritable bowel syndrome or the implications of differentiating ulcerative colitis from Crohn's colitis. A brief mention of new therapies on the horizon would have suited the aim of the book, if only to highlight the importance of clinical and basic science research, which were simply ignored.

The patient record booklet is a good idea, but constructed in a bizarre manner: only three pages for clinic visits, but four sections for documenting "usual treatment when well" and fully five boxes for details on "what to do in the event of a relapse"! A two centimetre space is allotted for recording the results of monitoring steroid or azathioprine therapy when a whole record page, to document the dates and results of blood

monitoring, would have been helpful—bearing in mind that treatment with azathioprine often extends for several years. It is this sort of detail, along with the errors in the main text, that gives an impression of clinical inexperience.

Nevertheless, these points are correctable and if asked by a patient, I would broadly recommend the guide. There is nothing else like it on the market and it gives far more useful information than can be readily gleaned from the internet or from pharmaceutical sponsored freebies. I hope that the authors will stand by their commitment to update the guide every two years. This means that they should be working on the 2001 edition now.

S P L TRAVIS

Development of the Gastrointestinal Tract. Edited by Ian R Sanderson and W Allan Walker (Pp 324; illustrated; £105.00) Canada: BC Decker Inc, 2000. ISBN 1-55009-081-X.

When I was a fellow with Allan Walker fifteen years ago, gut development was a topic of interest to a handful of researchers worldwide. A classic review by Grand, Watkins and Torti published in *Gastroenterology* in 1976, and Koldovsky's monograph *Development of the Functions of the Small Intestine in Mammals and Man* in 1969, brought together much of what was then known about the ontogeny of the human gut. Developmental biologists were beginning to recognise the opportunities offered by this rapidly differentiating organ to understand the interactions of genetic endowment and environmental influences in early life. The focus of much research was on the process of adaptation to milk feeding. With the survival of ever more preterm infants the function of the immature gut and its capacity to deal with enteral feeds prematurely, were questions of increasing practical concern.

I had the grand idea at that time to produce a short book bringing the field all together. But I quickly realised that not only was it growing too fast, but that a full understanding of gut development and function also required an understanding of the composition and properties of human milk and the metabolism of the newborn. The developing gastrointestinal tract and lactating mammary gland are complementary organs, jointly involved in the transfer of nutrients and other substances from mother to infant. Until weaning, the neonate is an extra-gestate fetus, and breast and gut are analogous to the uterine-placental interface.

This book goes a long way to recognising this. Each chapter (essentially a stand alone review) is written by a leading figure or group expert in its field. Together they cover the major aspects of gut development and function but, apart from a short preface, there is no overview or attempt to synthesise the book's contents. It would be impossible for one author to write this book now. The impact of molecular biology has moved the subject from an essentially descriptive science, with some experimental work in vivo, to the level of the cell and gene. This has shifted it away from the womb, breast, or incubator and into the laboratory. This book is a valuable starting point for students or researchers wishing to get up to date with the basic biology of human gut development, but it will be of little interest to the practising

neonatologist struggling to define rational approaches to feeding the preterm neonate.

Medicine is fast becoming a major branch of biology, concerned with the application, often experimentally, of novel therapies based on insights and new understanding of biologic processes. However at a time when the biological sciences are advancing so rapidly, and manipulation of genes within cells, including those of the embryo is possible, the gap between the worlds of medicine and biology is widening rather than narrowing.

The last century saw the integration of medicine and science, and a determination to base the practice of the former on the latter. At the beginning of this century we are struggling to define a core of knowledge, skills, and ideas to teach our medical students. The wide scope of what we currently regard as the province of medicine now includes sociology, psychology, epidemiology, etc, and the basic sciences have been squeezed. We may be making a mistake in failing to equip medical students and young doctors with a firm understanding of the "new biology"—embracing genetics, molecular medicine, and developmental biology. This book deals with these things and, although its subject is a small part of the totality of human biology, it is dealt with in depth by recognised leaders. Ian Sanderson and Allan Walker must be congratulated for bringing their research together.

Development of the Gastrointestinal Tract is also provided as a CD-ROM, but this offers little more than the facility to read it on screen. It has no search tools, nor is it possible to cut and paste sections (for those wishing to produce a review article overnight). However, the opportunity to print out chapters will abolish the tedium of photocopying, and will also preserve the spine of this handsome and well produced book.

L WEAVER

A Colour Handbook of Gastroenterology. Edited by Hodgson HJF, Boulton R, Cousins C, *et al.* (Pp 208; illustrated; £29.95). London: Manson Publishing Ltd, 2000. ISBN 1 87454 555 3.

To paraphrase Mark Twain, reports of the impending demise of the print media have been greatly exaggerated—a trainee can still spend hours browsing new editions in a medical bookshop and, usually during frantic preparation for higher exams while fulfilling DSM-IV criteria for anxiety disorder, part with large sums of money on illustrated texts. There also seems to have been a small explosion of abridged versions of textbooks and specialty handbooks, although some of these "handbooks" can weigh in at more than 500 pages, and entail some serious fitness training if carried around in a coat pocket.

Almost qualifying for the cruiserweight division at just over 200 pages, *A Colour Handbook of Gastroenterology* provides a concise, richly illustrated summary of clinical gastroenterology. Apart from oesophageal varices and ascites, hepatological conditions are not included. The book contains about 90 subjects organised into 10 colour coded anatomical sections. Each section starts with a short discussion of the relevant anatomy and physiology, as well as techniques for imaging, and functional assessment. Most major areas of gastroenterology are covered, although the level of detail is sometimes a little uneven. For example, seven pages are devoted to vascular

disorders of the small bowel and colon, but the less visually glamorous conditions of constipation and irritable bowel syndrome are relegated to a single page or less. The text on disease management is usually limited to a few lines on each subject, so that a trainee will still need to consult more detailed references when making treatment decisions. There is also a paucity of newer imaging techniques, including magnetic resonance imaging and endoscopic ultrasonography, two technologies that are beginning to revolutionise our approach to patients with suspected gastrointestinal disorders.

Perhaps the main attraction of this book for the visually inclined, busy trainee is that the text is structured, succinct, and richly illustrated with over 300 high quality radiographs, colour photographs, and tables. Given the increasing availability of electronic textbooks and medical images, one wonders about the future of such handbooks—although, unlike any other medical text on my computer or bookshelf, it was certainly easy to read from cover to cover. The preface states that it is directed towards junior doctors who are preparing for higher qualifications in gastroenterology and general medicine, but it will also appeal to financially solvent medical students who are keen to learn more about gastroenterology.

S P PEREIRA

NOTES

Sir Frances Avery Jones British Society of Gastroenterology Research Award 2001

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 2001 Award. Applications (TWENTY COPIES) should include:

- A manuscript (2 A4 pages ONLY) describing the work conducted
- A bibliography of relevant personal publications
- An outline of the proposed content of the lecture, including title
- A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

Entrants must be 40 years old or less on 31 December 2000 but need not be a member of the Society. The recipient will be required to deliver a 30 minute lecture at the Annual meeting of the Society in Glasgow in March 2001. Applications (TWENTY COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St

Andrews Place, London NW1 4LB by 1 December 2000.

British Society of Gastroenterology Hopkins Endoscopy Prize 2001

Applications are invited by the Endoscopy Committee of the British Society of Gastroenterology who will recommend to the Council the recipient of the 2001 Award. Applications (TEN COPIES) should include:

- A manuscript (2 A4 pages ONLY) describing the work conducted
- A bibliography of relevant personal publications
- An outline of the proposed content of the lecture, including title
- A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

An applicant need not be a member of the Society. The recipient will be required to deliver a 20 minute lecture at the Annual meeting of the Society in Glasgow in March 2001. Applications (TEN COPIES) should be made to the Endoscopy Section Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2000.

Joint Meeting of Oesophageal Section of the BSG and Association of Upper GI Surgeons

There will be a joint meeting of the Oesophageal Section of the British Society of Gastroenterology and the Association of Upper GI Surgeons exploring some important issues in oesophageal disease at the Royal College of Surgeons of England, Lincoln's Inn Fields, London WC2 on Wednesday 1 November 2000. The meeting will take the form of four debates on:

- 1 The place of chemotherapy in the management of cancer of the oesophagus
- 2 The appropriate management of high grade dysplasia
- 3 Identifying the role of anti-reflux surgery in the current management of gastrooesophageal reflux disease and
- 4 The relevance of helicobacter pyloridis in oesophageal disease.

Further information from: WJ Owen, Hon Secretary, Oesophageal Section of the BSG, Suite 406 Emblem House, London Bridge Hospital, 27 Tooley Street, London SE1. Tel: (0)20 7403 3814; fax: (0)20 7403 3814.

Gluten Sensitivity Symposium

The Gluten Sensitivity Symposium meeting, sponsored by SHS International, will be held at the Natural History Museum, London, on Friday 20 October 2000. Speakers include Professor Paul Ciclitira, Dr Tony Ellis, Dr Geoff Holmes, Professor Markku Maki, Dr

Marios Hadjivassiliou, Professor Lionel Fry, Dr Gerd Michaelsson and Professor Tom MacDonald. Further information: Debbie Jones at SHS International. Tel: +44 (0)151 228 1992; email: djones@shsint.co.uk.

Food Allergy and the Gut

The Allergy Research Foundation presents Food Allergy and the Gut, to be held at the Royal Society of Medicine, London on 29 November 2000. Further information: Philip N Goddard, Executive Secretary, The Allergy Research Foundation, PO Box 18, Aylesbury, Bucks HP22 4XJ, UK. Tel & fax: +44 (0)1296 655818.

13th European Intensive Course of Digestive Endoscopy

This course will be held in Strasbourg, France on 18 and 19 December 2000. Further information from Professor G Gay, Service de Médecine Interne J, Hôpital de Brabois, Allée du Morvan, 54511 Vandœuvre-lès-Nancy Cedex, France. Tel & fax: +33 (0)3 83 15 35 49.

Joint Meeting of the American Pancreatic Association and the International Association of Pancreatology

This meeting will be held in Chicago, Illinois, USA on 1–5 November 2000. Symposia, posters, scientific sessions, "Pancreatology at the Millennium". Further information: Peter A Banks, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA. Tel: +1 617 732 6747; fax: +1 617 566 0338.

36th Annual Meeting of the European Association for the Study of the Liver (EASL)

This meeting will be held in Prague, Czech Republic on 18–22 April 2001. Abstract deadline: 27 November 2000. EASL will offer 10 travel bursaries to selected young investigators and 30 to Eastern European, pending on submission of an abstract. In addition, first authors under 35 years of age, and in training, who submit abstracts will have free registration. Further information: EASL Liaison Bureau, c/o Kenes International, 17 rue du Cendrier, PO Box 1726, CH-1211 Geneva, Switzerland. Tel: +41 22 908 0488; fax: +41 22 732 2850; email: info@easl.ch; website: www.easl.com

15th International Workshop on Therapeutic Endoscopy

This workshop will be held in Hong Kong on 5–7 December 2000. Further information: Miss Claudia Mak, Endoscopy Centre, Prince of Wales Hospital, Shatin, N.T., Hong Kong. Tel: +852 2632 2233; fax: +852 2635 0075; email: info@hksde.org