

PostScript

LETTERS

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Osteoporosis and liver disease: additional reasons for coeliac disease screening

We read with great interest the recently published guidelines on the management of osteoporosis associated with chronic liver disease (*Gut* 2002;50(suppl 1):i1-9). However, we would like to add a few words of comment. Associations between coeliac disease (CD) and primary biliary cirrhosis in particular and other autoimmune liver diseases in general have been reported.¹⁻³ In addition, it has been suggested that these individuals should be considered as an at risk group for whom serological testing for CD is indicated.¹ Patients with CD are at high risk of developing low bone mineral density and bone turnover impairment,¹ and it has been shown that adherence to a gluten free diet has a significant positive impact on these parameters.⁴ Thus we suggest that physicians caring for patients with the above mentioned liver diseases should screen them for CD in the presence of signs and symptoms suggestive of malabsorption such as osteoporosis. This seems a reasonable strategy as detection of CD will allow for a more rational therapeutic approach to the risks determined by this association. Complications due to the presence of CD, such as malnutrition, anaemia, and osteoporosis, may have a considerable impact on liver disease management and the need/success of transplantation.^{5,6}

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References

- 1 **Fasano A**, Catassi C. Current approaches to diagnosis and treatment of coeliac disease: An evolving spectrum. *Gastroenterology* 2001;120:636-51.
- 2 **Gogos CA**, Nikolopoulou V, Zolota V, *et al*. Autoimmune cholangitis in a patient with coeliac disease: a case report and review of the literature. *J Hepatol* 1999;30:321-4.
- 3 **Heathcote EJ**. Management of primary biliary cirrhosis. *Hepatology* 2001;31:1005-13.

- 4 **Scott EM**, Gaywood I, Scott BB, for the British Society of Gastroenterology. Guidelines for osteoporosis in coeliac disease and inflammatory bowel disease. *Gut* 2000;46(suppl 1):i1-8.
- 5 **Metcalf J**. Coeliac disease and primary biliary cirrhosis: a case for mutual screening. *Gut* 1998;42:9-10.
- 6 **Neuberger J**. PBC and the gut: the villi atrophy, the plot thickens. *Gut* 1999;44:594-5.

Caerulein induced pancreatitis

We have read with interest the article by Frossard *et al* (*Gut* 2002;50:78-83) entitled "Both thermal and non-thermal stress protect against caerulein induced pancreatitis and prevent trypsinogen activation in the pancreas". We have a few comments with regard to the interpretation of the data that were obtained in this experiment.

Previous experimental work by Frossard and others have implicated HSP70 as playing a protective role in caerulein induced acute pancreatitis. In the present study Frossard *et al* showed that thermal and non-thermal stress induced by injection of the β agonist isoproterenol upregulated HSP70 in the pancreas which is associated with amelioration of subsequently induced caerulein pancreatitis. The authors hypothesise that the protective effects on pancreatitis severity caused by thermal and non-thermal stress may be mediated by HSP70. We believe however that both heat shock stress and non-thermal stress can stimulate several other anti-inflammatory pathways which were not discussed in this study, all of which could be alternative explanations for the observations that were made.

It is widely established that catecholamines, both endogenously released during heat shock stress or by injection of isoproterenol, can influence activation of inflammatory pathways during inflammation and infection¹ (reviewed by van der Poll²). Evidence exists that catecholamines exert anti-inflammatory effects on a number of host mediator systems, such as the cytokine network and neutrophils, all of which are implicated in the pathogenesis of acute pancreatitis and the pancreatitis associated systemic inflammatory response syndrome. Catecholamines, either endogenously produced or exogenously administered, may act to dampen excessive pro-inflammatory pathways by mechanisms not related to enhanced production of heat shock proteins. Firstly, catecholamines exert anti-inflammatory effects on the cytokine network by inhibiting the production of proinflammatory cytokines such as tumour necrosis factor (TNF), interleukin (IL)-1 β , IL-12, and interferon γ (IFN- γ), of which TNF and IL-1 β have been implicated as mediators that play a proinflammatory role in acute pancreatitis.^{3,4} Secondly, in animal models of endotoxaemia, pretreatment with isoproterenol enhances the production of the anti-inflammatory cytokine IL-10 which has been shown to be protective in acute pancreatitis.^{5,6} Thirdly, in endotoxaemia models, β adrenergic stimulation results in reduction of levels of CC chemokines.⁷ Fourthly, neutrophil migration to the pancreas, one of the hallmarks of acute pancreatitis, towards chemotactic stimuli such as C5a and lipopolysaccharide (LPS) is reduced by administration of β agonists but also affects

LPS induced neutrophil degranulation in vivo. Fifthly, with regard to the hypothesis that HSP70 prevents the activation of trypsinogen in the pancreas, it must be noted that recent evidence suggests that neutrophils and possibly cytokines can also influence trypsinogen activation. Therefore, the reduction in trypsinogen activation shown in their study might be unrelated to HSP expression and may be explained by the reduction of inflammation due to β adrenergic effects.^{8,9}

Therefore, we believe that the conclusion by Frossard *et al* that the protective effects of thermal and non-thermal stress might be mediated by HSP70 is only one possible explanation and that their observations might also be explained by the immunomodulatory effects of catecholamines.

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References

- 1 **Won SJ**, Lin MT. Thermal stresses reduce natural killer cell cytotoxicity. *J Appl Physiol* 1995;79:732-7.
- 2 **van der Poll T**. Effects of catecholamines on the inflammatory response. *Sepsis* 2001;4:59-67.
- 3 **Severn A**, Rapson NT, Hunter CA, *et al*. Regulation of tumor necrosis factor production by adrenaline and beta-adrenergic agonists. *J Immunol* 1992;148:3441-5.
- 4 **Hasko G**, Szabo C, Nemeth ZH, *et al*. Stimulation of beta-adrenoceptors inhibits endotoxin-induced IL-12 production in normal and IL-10 deficient mice. *J Neuroimmunol* 1998;88:57-61.
- 5 **Hasko G**, Szabo C, Nemeth ZH, *et al*. Stimulation of beta-adrenoceptors inhibits endotoxin-induced IL-12 production in normal and IL-10 deficient mice. *J Neuroimmunol* 1998;88:57-61.
- 6 **Berney T**, Gasche Y, Robert J, *et al*. Serum profiles of interleukin-6, interleukin-8, and interleukin-10 in patients with severe and mild acute pancreatitis. *Pancreas* 1999;18:371-7.
- 7 **Hasko G**, Shanley TP, Egnaczyk G, *et al*. Exogenous and endogenous catecholamines inhibit the production of macrophage inflammatory protein (MIP) 1 alpha via a beta adrenoceptor mediated mechanism. *Br J Pharmacol* 1998;125:1297-303.

- 8 **Gukovskaya AS**, Gukovsky I, Zaninovic V, *et al.* Pancreatic acinar cells produce, release, and respond to tumor necrosis factor- α . Role in regulating cell death and pancreatitis. *J Clin Invest* 1997;**100**:1853–62.
- 9 **Gukovskaya AS**, Vaquero E, Zaninovic V, *et al.* Neutrophils and NADPH oxidase mediate intrapancreatic trypsin activation in murine experimental acute pancreatitis. *Gastroenterology* 2002;**122**:974–84.

Authors' reply

We thank van Westerloo *et al* for their interest in our paper and their comments on the interpretation of our data. They are of the opinion that besides heat shock proteins both thermal and non-thermal stress can stimulate several other anti-inflammatory pathways that in turn could be responsible for the protective effects observed in the study. Secondly, catecholamines can exert anti-inflammatory effects independent of heat shock proteins.

When we embarked on this project, we were also concerned that all the stresses that result in the induction of HSP70 may have other non-HSP related effects and did mention this in our discussion. At that point we did not have the tools to show the crucial protective role played by HSP70.

To prove that a cause-effect relationship exists between HSP70 expression and protection against pancreatitis, we adopted the antisense oligonucleotide approach in another recently published experimental study¹ to indicate unequivocally that the thermal stress induced protection of intrapancreatic trypsinogen activation and protection against caerulein induced pancreatitis are mediated by HSP70. Furthermore, our studies have shown that HSP70 induction that occurs during the evolution of pancreatitis in non-thermally stressed rats acts to limit the severity of pancreatitis.

Using antisense oligonucleotides to HSP70, Nisoli and colleagues² have also shown that the protective effects of noradrenaline against tumour necrosis factor α induced apoptosis in cultured rat brown adipocytes is due to nitric oxide induced HSP70 expression. In fact, catecholamines have been used in the past to induce heat shock proteins in several experimental systems.^{3,4}

Westerloo *et al* have cited examples wherein exogenous or endogenous catecholamines inhibit the production of inflammatory cytokines and enhance the production of interleukin 10 (IL-10), an anti-inflammatory cytokine that has been shown to limit the severity of pancreatitis. Unfortunately, in the studies cited expression of HSP70 was not monitored. It is entirely possible that prior thermal or non-thermal stress induce HSP70 which may in turn lead to the enhanced production of anti-inflammatory factors and attenuation of proinflammatory cytokines. Indeed this has

been shown to be the case in many experimental systems, including animal models of sepsis (reviewed by Bruemmer-Smith and colleagues⁵). Moreover, mycobacterial HSP70 has been shown to prevent adjuvant arthritis and induce IL-10 producing T cells.⁶

The mechanism(s) by which HSP70 might protect against caerulein induced pancreatitis is not yet known. Experiments examining the relationship between HSP70 and the inflammatory cascade induction during caerulein induced pancreatitis are currently underway.

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References

- 1 **Bhagat L**, Singh VP, Song AM, *et al.* Thermal stress-induced HSP70 mediates protection against intrapancreatic trypsinogen activation and acute pancreatitis in rats. *Gastroenterology* 2002;**122**:156–65.
- 2 **Nisoli E**, Regianini L, Bulbarelli A, *et al.* Protective effects of noradrenaline against tumor necrosis factor- α -induced apoptosis in cultured rat brown adipocytes: role of nitric oxide-induced heat shock protein 70 expression. *Int J Obes Relat Metab Disord* 2001;**10**:1421–30.
- 3 **Matz JM**, LaVoi KP, Blake MJ. Adrenergic regulation of the heat shock response in brown adipose tissue. *J Pharmacol Exp Ther* 1996;**277**:1751–8.
- 4 **Meng X**, Brown JM, Ao L, *et al.* Norepinephrine induces cardiac heat shock protein 70 and delayed cardioprotection in the rat through α 1 adrenoceptors. *Cardiovasc Res* 1996;**32**:374–83.
- 5 **Bruemmer-Smith S**, Stuber F, Schroeder S. Protective functions of intracellular heat-shock protein (HSP) 70-expression in patients with severe sepsis. *Intensive Care Med* 2001;**12**:1835–41.
- 6 **Wendling U**, Paul L, van der Zee R, *et al.* A conserved mycobacterial heat shock protein (hsp) 70 sequence prevents adjuvant arthritis upon nasal administration and induces IL-10-producing T cells that cross-react with the mammalian self-hsp70 homologue. *J Immunol* 2000;**164**:2711–17.

Pathology and cost effectiveness of endoscopy surveillance for premalignant gastric lesions

We read with great interest the article by Whiting *et al* (*Gut* 2002;**50**:378–81). The Birmingham experience shows how the prevalence of gastric cancers detected at an early stage is significantly higher in the endoscopically surveyed population than in non-surveyed patients. As a result, this study demonstrates that, in the secondary prevention of gastric malignancy, the “once in a lifetime” strategy (suggested for colorectal cancer) is

not cost effective while repeated endoscopies (in selected patients) seem most appropriate. This conclusion however raises two cardinal questions. Firstly, are there “special” requirements (that is, a protocol of gastric biopsy sampling) to be satisfied when carrying out the upper endoscopy procedure? Secondly, are there evidence based criteria for selecting patients to be included in surveillance programmes?

The authors do not provide detailed information on the number of biopsy samples obtained per endoscopy. We believe that a standardised protocol of biopsy sampling is a leading part of any upper endoscopy procedure, and mucosal “abnormalities” should be considered the targets of additional sampling.¹ Taking into account that 46% of the cancers referred to in Whiting’s study were discovered within 13 months from the second last procedure, we agree with the authors who considered these cancers endoscopically missed.

The second point of concern is the rationale for a surveillance protocol. Any cost effective strategy of secondary cancer prevention requires the risk of cancer to be higher within subjects undergoing surveillance than in the general population. In the Birmingham study, such a prerequisite does not seem to have been assumed in the study design. Endoscopy surveillance definitively included the whole spectrum of abnormalities described in gastric carcinogenesis,^{2,3} from regenerative changes (with a nearly null cancer risk) to non-invasive neoplasia (which carries, by definition, predisposition for progression to invasion and metastasis). As a consequence of (i) cancers missed at endoscopy and (ii) shortness of the follow up period, the results shown in their table 3 may be misleading. The association of intestinal metaplasia (regardless of its histochemical phenotype) with the highest risk of cancer evolution is not only biologically questionable but, and this is even worse, it may result in inappropriate patient management. While intestinal metaplasia represents the most common background of stomach cancer,^{4,5} “gastric intestinalisation” per se does not carry the phenotypic and genotypic alterations pre-carrying invasive neoplasm. Most importantly, the high prevalence of metaplastic lesions within subjects who will never develop adenocarcinoma exclude (non-extensive) intestinal metaplasia as the proper target of surveillance programmes.

In the natural history of epithelial tumours, the term dysplasia identifies a lesion that carries biological alterations comparable with those of full fledged cancer but lacking stromal invasion.² Recently, the term “dysplasia” has been replaced by “non-invasive neoplasia”, which more clearly identifies such a lesion as the most advanced alteration antecedent to invasive adenocarcinoma.⁶ Since 1985, we have prospectively followed up a

Table 1 Invasive cancer detected during follow up of non-invasive gastric neoplasia

Histology at enrollment	Gastric cancer detected after follow up longer than 12 months			Gastric cancer detected within 12 months from initial diagnosis				
	Follow up (months)*	EGC	AGC	GC-nos	Follow up (months)*	EGC	AGC	GC-nos
Low grade non-invasive neoplasia (99 cases)	48 (38–80)	5	1	2	1.5 (1–2)	1	1	0
High grade non-invasive neoplasia (25 cases)	30 (13–72)	7	1	3	2 (1–4)	6	3	0
Total	35 (13–80)	19			1.7 (1–4)	11		

EGC, early gastric cancer (that is, UICC pathological stage I); AGC, advanced gastric cancer (that is, UICC pathological stages II-III); GC-nos, gastric cancer of unknown pathological stage.
*Mean [range].

series of patients with low and high grade gastric non-invasive neoplasia.⁴ The follow up schedule was differentiated a priori, depending on the cancer risk presumably associated with each grade of lesion.⁷ The number of patients enrolled in each diagnostic category, follow up time, and number of cancers detected are shown in table 1. It is worth emphasising the high prevalence of early gastric cancers (77%) among the 30 cases of cancer detected in our prospective follow up study. The 19 cases of cancer detected in the long term follow up support the premalignant significance of non-invasive neoplasia while the 11 cases detected within one year from the original endoscopy fully demonstrated that non-invasive neoplasia frequently coexists with advanced cancer. Both of these observations could represent valid foundations in drawing a surveillance programme aimed at secondary gastric cancer prevention.

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References

- Dixon MF, Genta RM, Yardley JH, *et al.* Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol* 1996;**20**:1161-81.
- Correa P, Shiao YH. Phenotypic and genotypic events in gastric carcinogenesis. *Cancer Res* 1994;**54**:1941-3.
- Rugge M, Correa P, Dixon MF, *et al.* Gastric dysplasia: the Padova international classification. *Am J Surg Pathol* 2000;**24**:167-76.
- Rugge M, Leandro G, Farinati F, *et al.* Gastric epithelial dysplasia. How clinicopathologic background relates to management. *Cancer* 1995;**76**:376-82.
- Rugge M, Baffa R, Farinati F, *et al.* Epithelial dysplasia in atrophic gastritis. Biopsical follow-up study. *Ital J Gastroenterol* 1991;**23**:70-3.

6 **Fenoglio-Preiser C**, Carneiro F, Correa, *et al.* Gastric carcinoma. In: Hamilton SR, Aaltonen LA, eds. *Pathology and genetics, tumors of the digestive system*. Lyon: IARC Press, 2000:39-52.

7 **Rugge M**, Farinati F, Baffa R, *et al.* Gastric epithelial dysplasia in the natural history of gastric cancer: a multicenter prospective follow-up study. Interdisciplinary Group on Gastric Epithelial Dysplasia. *Gastroenterology* 1994;**107**:1288-96.

Adult height in patients with early onset of Crohn's disease

Alemzadeh *et al* (*Gut* 2002;**51**:26-9) reported that adult height, compared with the general Dutch population, was reduced by a mean of -0.9 SDS (95% confidence interval -1.55 to -0.28) in 15 Crohn's patients with prepubertal onset of symptoms. However, the calculated deviation from "target" height (based on parental height) did not reach statistical significance and the authors have speculated that familial short stature, and not Crohn's disease, may be a factor in this group. Furthermore, no height deficit was found in those with postpubertal onset of symptoms.

We are currently undertaking a review of those with childhood onset diseases attending our paediatric and adult IBD clinics. In the majority of cases parental height was measured by trained auxologists, although in some, details were not available in the case notes to discern the method of measurement and may therefore have included self reported parental heights. We calculated SDS scores from the revised British Longitudinal standards¹ using the method described by Alemzadeh *et al* (mean British male adult height of 176.0 cm (SD 6.3) and female adult height of 163.6 (SD 5.7)). "Target height" was calculated for male patients by (paternal height + (maternal height + 13))/2 and for female patients by (maternal height + (paternal height - 13))/2 (cm). "Prepubertal" children were defined as males and females with onset of symptoms at <13 and <11 years, respectively. We defined the upper limit of "postpuberty" as 16 years, in contrast with Alemzadeh *et al* who used 22 years. The population we serve is ethnically diverse and therefore we have confined this analysis to Caucasians, as per the Dutch study.

There was no deficit in height of the parents (48 mothers and 46 fathers) of children with childhood onset Crohn's disease compared with the general population. Furthermore, there was no deficit in height when examined by onset of their child's Crohn's disease: mean "prepubertal" parental SDS 0.00 (SD 1.11) and mean "postpubertal" parental SDS 0.08 (SD 1.12) (n=70 and n=24, respectively; p=0.34). In addition, we found no significant

sex difference: mean paternal SDS -0.20 (SD 0.98) and mean maternal SDS 0.03 (SD 1.22) (n=46 and n=48, respectively; p=0.94).

In 27 cases (18 males, nine females) children of these parents are now aged more than 16 years (mean age 19.3 (SD 2.6) years). An analysis of final height is presented in table 1. A separate analysis was also carried out using the nomogram of the Child Growth Foundation² which corrects height until the age of 22, but this did not alter our findings and the data are therefore not presented.

In the majority of patients (85% (23/27); p=0.008, χ^2 test) final height was less than "target height", and in 22% (6/27) the final height deficit was more than 10 cm. For those aged over 18 years the values were 88% ((14/16); p=0.022, χ^2 test) and 25% (4/16), respectively.

In this sample of patients with childhood onset Crohn's disease we found no evidence of a familial basis for short stature. Our data confirm the findings of others that mean adult height of patients with onset of symptoms before the age of 16 is reduced.^{3,4} Using age of onset of symptoms as a proxy for puberty, we found no significant difference in final height between those with pre- and postpubertal onset of symptoms. This is in contrast with the findings of Alemzadeh *et al* and may be because of differences in the upper age limit of "postpuberty" (16 versus 22 years).

Growth failure remains a concern to our British Crohn's patients and although the mean deficit of 5-6 cm from target height may be considered by some to be clinically inconsequential this includes a subset with much more significant growth impairment. A better understanding of the mechanisms underlying growth failure is required to determine whether there is an identifiable group of children that may benefit from early and more intensive immunosuppression and/or nutritional therapy.^{5,6}

We agree with Alemzadeh *et al* that only larger (population based) studies will have the power to determine the effect of factors such as site of disease activity and therapeutic intervention.

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Table 1 Final height of Caucasian Crohn's patients with pre and postpubertal onset of symptoms

	All	Prepubertal	Postpubertal	Pre v post (t test)
>16 years at last height				
SDS	-0.68 (-1.17 to -0.19)	-0.57 (-1.16 to 0.02)	-1.01 (-1.86 to -0.16)	p=0.41
Deficit (cm)	-5.9 (-8.2 to -3.4)	-5.5 (-8.6 to -2.4)	-7.0 (-8.8 to -5.3)	p=0.62
n	27	20	7	
>18 years at last height				
SDS	-0.73 (-1.42 to -0.04)	-0.65 (-1.48 to 0.18)	-1.07 (-2.12 to -0.02)	p=0.58
Deficit (cm)	-5.3 (-8.6 to -2.0)	-5.1 (-8.9 to -1.38)	-6.2 (-11.08 to -1.38)	p=0.84
n	16	13	3	

Data are mean (95% confidence interval).

References

- 1 **Buckler J**, Tanner J. *Revised British Longitudinal Standards*. Hertfordshire: Castlemead Publications Ltd, 1995.
- 2 **Freeman JV**, Cole TJ, Chinn S, *et al*. Cross-sectional stature and weight reference curves for the UK. *Arch Dis Child* 1995;**73**:17–24.
- 3 **Hildebrand H**, Karlberg J, Kristiansson B. Longitudinal growth in children and adolescents with inflammatory bowel disease. *J Pediatr Gastroenterol Nutr* 1994;**18**:165–73.
- 4 **Griffiths AM**, Nguyen P, Smith C, *et al*. Growth and clinical course of children with Crohn's disease. *Gut* 1993;**34**:939–43.
- 5 **Ballinger AB**, Azooz O, El-Hajj T, *et al*. Linear growth retardation in experimental colitis is induced through a decrease in insulin-like growth factor-1 which is independent of malnutrition. *Gut* 2000;**46**:695–700.
- 6 **Ballinger AB**, Camacho-Hubner C, Croft NM. Growth failure and intestinal inflammation. *Q J M* 2001;**94**:121–5.

Author's reply

I think that this study is clear. We agree with the authors that the differences are possibly caused by the other "end point" of puberty and the small population in both studies. Another difference could be that the authors did not calculate the corrected height SDS (height SDS target height SDS); this may be lower for the prepubertal group compared with the postpubertal group. Furthermore, they used another formula for target height. This formula does not include a correction for secular trend which will underestimate the deficit. Also, there is no information on the effect of corticosteroid use.

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Underdiagnosis of hereditary haemochromatosis: reflects lack of clinical not biochemical penetrance

In their paper, Ryan *et al* (*Gut* 2002;**51**:108–12) reported that 78% of men (mean age 42 years) and 36% of women (mean age 39 years) who were identified to be C282Y homozygotes by family screening had evidence of biochemical iron overload. They concluded that underdiagnosis of hereditary haemochromatosis may be the result of failure to diagnose the phenotype in patients with iron overload.

In Glasgow, the prevalence of the C282Y homozygous state is high at approximately 1 in 180 of the population, of whom only 5.1% had been diagnosed by August 2001.¹ Of these known cases we identified 42 (20 males) C282Y homozygotes who had been diagnosed by predictive genetic testing of family members of affected probands. At diagnosis, all 20 males (mean age 46) had evidence of biochemical iron overload, defined as a transferrin saturation of $\geq 45\%$ (transferrin detected immunochemically) or a serum ferritin of $\geq 300 \mu\text{g}$. Both parameters were elevated in 15 (75%) individuals, with three having an isolated elevated transferrin saturation and two an isolated elevated ferritin.

Of the 22 females (mean age 44) identified, 18 (81%) had evidence of biochemical iron overload at diagnosis, with 10 (45%) having raised transferrin saturation and ferritin, as defined above. A further seven patients had an isolated elevation in transferrin saturation

and one had an elevated ferritin alone. Only four (9.5%) C282Y homozygotes identified by family testing had no evidence of biochemical iron overload. All of these individuals were female (age range 17–48 years). Unfortunately, due to the retrospective nature of the analysis, it was not possible to assess symptoms at diagnosis.

The prevalence of biochemical iron overload in our predominantly Celtic population is high and comparable with that reported from Dublin by Ryan *et al*. However, the proportion that will develop clinical "disease" related to hereditary haemochromatosis remains uncertain. Ryan *et al* proposed that underdiagnosis of hereditary haemochromatosis might be due to the non-specific nature of the symptoms early in the disease. They noted that fatigue, arthropathy, and male impotence were common complaints in these C282Y homozygotes identified by family screening. However, they provided no evidence that these symptoms were due to iron excess as they appeared to be as common in their biochemically non-expressing control group. It would be interesting to know whether any of these non-specific symptoms improved with phlebotomy.

In a recent large population screening study from the USA, Beutler *et al* reported the prevalence of biochemical iron overload in C282Y homozygotes to be similar to that observed by the Dublin group and ourselves. However, they found no evidence of more frequent symptoms in C282Y homozygotes compared with controls, even if biochemical iron overload was present.² It appears that these individuals have iron overload and a number of unrelated non-specific symptoms, similar to those seen in the general population. Prospective longitudinal studies are required to establish the proportion of C282Y homozygotes who will eventually exhibit the clinical phenotype of hereditary haemochromatosis.

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References

- 1 **Thorburn D**, Cook A, Spooner R, *et al*. Genetic haemochromatosis: where are all the patients? *Gut* 2002;**50**(suppl 11):A34.
- 2 **Beutler E**, Felitti VJ, Koziol JA, *et al*. Penetrance of 845G→A (C282Y) HFE hereditary haemochromatosis mutation in the USA. *Lancet* 2002;**359**:211–18.

Gastrointestinal epithelial neoplasia

We read with interest the viewpoint "Gastrointestinal epithelial neoplasia: Vienna revisited" by Dixon (*Gut* 2002;**51**:130–1).

For many years Western gastrointestinal pathologists have followed the recommendations of British gastrointestinal pathologists. We learned that terms such as *carcinoma in situ* should be banned from the diagnostic terminology as it could lead to misinterpretation by surgeons and to unnecessary surgical intervention.

The Vienna classification¹ has introduced new avenues to the understanding of the

process of carcinogenesis in the gastrointestinal tract. For some Western pathologists in the Vienna group who also received histopathological training in Japan, the concept of intraepithelial carcinoma (that is, carcinoma in situ) and of intramucosal carcinoma appeared natural. Although during the first day of discussions other Western pathologists appeared reluctant to accept such controversial notions, the discussion became less intense during the second day, and at the end a consensus was reached, gaining finally the pages of this journal.¹

The Vienna classification¹ dismembered the concept of dysplasia from that of carcinoma in its earlier forms. After many years of studying adenomas we now know that low grade dysplasia may progress to high grade dysplasia. On the other hand it remains elusive whether carcinoma in situ is preceded by high grade dysplasia or develops without a prodromic phase. By the same token we do not know whether carcinoma in situ antedates intramucosal carcinoma. If those microscopic realities of colorectal carcinogenesis are being ignored, how are we going to learn in a correct sequential fashion the intricate molecular footsteps that telescope from dysplasia to submucosal carcinoma? As that Pandora box is being presented to pathologists we should treasure it by opening it little by little.

One criticism of the Vienna classification¹ may be that although various categories of neoplasia were listed, the histopathological criteria for each one of the lesions were not verbalised, thus postponing the opportunity for its worldwide acceptance. Notwithstanding, some Western pathologists have started to herald the new "doctrine" by providing histopathological descriptions (criteria) for each one of the various categories proposed in Vienna.²

"To see or not to see" is not the question, as all lesions are there. As an example, dysplasia can be differentiated from carcinoma in situ.² Dysplasia in the glandular gastrointestinal mucosa is characterised by spindle or cigar shaped, elongated, pleomorphic, hyperchromatic nuclei, and regular nuclear membrane whereas carcinoma in situ displays large vesicular nuclei, irregular conspicuous nucleoli, and scalloped nuclear membranes. Bridges of nucleolus associated chromatin reaching irregular chromatin deposits are seen along the nuclear membrane. Bridges of chromatin are also seen connecting angular chromatin clumps. The nuclear polarity is disrupted, and marked cell pleomorphism and aberrant mitosis are present. Structural alterations may occur such as budding or branching crypts or tubules, with epithelial septa and back to back glands, and cribriform growth of epithelial cells in clusters and sheets. Those structures are confined to the basement membrane of the epithelial layer.² But surprisingly, despite those differences, high grade dysplasia and carcinoma in situ are still being regarded as synonyms in the Western literature.

The present discussion is beyond the usefulness of the Vienna classification as a tool for proper treatment; the discussion aims to point out our present lack of knowledge regarding the histogenesis of lesions represented by categories 4.2, 4.3, and 5.1 of Vienna¹ and their correct identification for future molecular research.

The viewpoint of Dixon appears to be in concert with the desire of many Western pathologists who are willing to embrace this new "doctrine" in order to acquire accurate information on the histological steps followed

by early neoplastic lesions of the gastrointestinal tract. Only then will we be able to translate such events into molecular terms.

Perhaps the spirit of Johan Strauss has succeeded in orchestrating not only fiddlers but also workers engaged in the microscopic diagnosis of gastrointestinal epithelial neoplasias.

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References

- Schlemperer RJ, Riddell RH, Kato Y, et al. The Vienna classification of gastrointestinal epithelial neoplasia. *Gut* 2000;**47**:251–5.
- Rubio CA, Jaramillo E, Lindblom A, et al. Classification of colorectal polyps: Guidelines for the endoscopist. *Endoscopy* 2002;**34**:226–36.

BOOK REVIEWS



Dynamic Radiology of the Abdomen: Normal and Pathologic Anatomy, 5th edn

M A Meyers. Germany: Springer-Verlag, 2000. ISBN 0-387-98845-9

This is the fifth edition of *Dynamic Radiology of the Abdomen: Normal and Pathologic Anatomy*, a book that has become essential reading for all those aiming to be expert at abdominal imaging. Previous editions have been published in Italian, Japanese, Portuguese, and Spanish.

The continued aim of the author is to present a systematic application of anatomical and dynamic principles to aid our understanding of the characteristic appearances and modes of spread of intra-abdominal disorders. Dissections and cross sectional views of cadavers are used in conjunction with a full range of imaging modalities, including plain radiographs, contrast studies, computed tomography (CT), ultrasound, magnetic resonance imaging (MRI), and endoscopic, laparoscopic, and intraoperative ultrasound.

This edition has been extensively updated with six new chapters, 180 additional pages, and more than 520 new illustrations. Subjects that are included for the first time include clinical embryology in relation to disorders that become clinically apparent in the adult, TNM staging of gastrointestinal cancers, and the manifestations of free intraperitoneal air. There are now 11 other contributing authors, but Morton Meyers is solely responsible for about three quarters of the book and many of the cases illustrated are reproduced from his own numerous publications.

This book is well written, superbly illustrated, and comprehensively referenced. The illustrations, particularly the extensive use of cross sectional spiral CT images, make it easier for the reader to understand the complex anatomical arrangement of the abdominal

organs and spaces and how they are modified by disease processes. The normal and pathological anatomy of the different parts of the gastrointestinal tract, the other abdominal organs, and the extraperitoneal spaces is described in detail. There are excellent descriptions of the intraperitoneal spread of infections and of malignancies. There is also a chapter on internal abdominal hernias. Pancreatic disorders and their mode of spread are described in detail; the diverse locations of pancreatic pseudocysts are well illustrated.

CT is now used to show the many places where free intraperitoneal air can collect in the abdomen. In recent years Cho and Baker have used this information to reassess the radiological appearances of free intraperitoneal air on the supine abdominal radiograph and have also described a number of new signs. They have brought this information together in their chapter and the result is an excellent and well illustrated contribution, providing information on an important subject that is not widely available elsewhere.

This edition of *Dynamic Radiology of the Abdomen* lives up the reputation established by previous editions. It should be of interest to all doctors who wish to learn more about the abdomen, particularly radiologists, oncologists, and surgeons. Radiologists who perform any type of abdominal imaging should find this latest edition invaluable and registrars training in radiology should become acquainted with it early in their career. In the preface to the first edition, Lloyd Nyhus commented on the innovative nature of this work and stated that it was an important reading source for surgeons; it likely that he would be equally enthusiastic about the latest edition.

D Nolan

Artificial Nutrition Support in Clinical Practice, 2nd edn

Edited by J Payne-James, G Grimble, D Silk. Greenwich Medical Media, £125. ISBN 1-90015-97-9

The provision of nutritional support for patients in hospital and in the community has derived from a heightened awareness of the impact of malnutrition on patient outcome and quality of life. Attention has focused on the prevalence of disease related malnutrition, both in terms of weight loss and weight for height, but also in terms of micronutrient deficiencies. Drives to enhance awareness of undernutrition in the community have followed efforts to improve nutrition in hospitals through food improvement, supplement provision, and artificial feeding. The need for routine nutritional assessment in clinical practice, especially in chronic disease, and its careful documentation has become ever more appreciated, particularly among gastroenterologists.

It is widely acknowledged that the approach to nutritional care is best made via a multiprofessional team which combines the skill and knowledge of dieticians, nutrition nurse specialists, pharmacists, and doctors. Teams like this are the key to excellent patient centred nutritional care and lead to overall hospital strategies for nutritional support which seamlessly combine, in a cost effective way, the use of food and supplements with artificial feeding to provide nutrients by the simplest safest route acceptable to the patient. Such teams need to develop more in the community too.

As the more enlightened hospitals form teams, a demand develops for a comprehensive textbook. This one is widely seen as one of the best and it now enters its enlarged second edition. It is an edited collation in which British authors dominate but it also includes contributions from key players from continental Europe making it representative of much of what goes on in the more Anglophone corners of ESPEN. As such it unsurprisingly contains some excellent chapters and others which are a little more patchy. But the collations is comprehensive, with a sensible mixture of the practical and the theoretical, the general and the more specialist. I would recommend it as a sound basis and as a useful resource for further reading.

J Powell-Tuck

Dyspepsia

M J Lancaster Smith, K L Koch. UK: Health Press, 2000, \$14.00. ISBN 1-899541-92-6

We all have a word of advice and the general practitioner is a handy person to give it to. Getting it packaged right can be a challenge, not least when the front cover states that it is an "Indispensable guide to clinical practice". In this unusual transatlantic collaboration, two distinguished gastroenterologists have made a worthy effort to reach out and have successfully condensed most gastroenterological scenarios faced by the jobbing clinician into an attractive and accessible package. This little book packs a lot—while seeming to be a handy reference it is in fact a repository of facts and information and I confess to dipping into it often to confirm matters or to cull material for a presentation. For example, a map indicating the worldwide prevalence of *Helicobacter pylori* and tracings illustrating lower oesophageal pressures during swallowing enliven concepts glossed over in other publications.

None the less, the pedigree of the authors does tell on them in some of the sections. Hardly has the invisible ink (from the primary care practitioner's viewpoint) dried on the Rome II definitions before the one is being exhorted in the chapter on "Functional dyspepsia" to differentiate, on clinical grounds, ulcer-like and dysmotility-like dyspepsia. This is accompanied by advice on tailored regimens based on acid suppression or dysmotility agents. In real life, successful management, one fears, is more likely to be related to serendipity than acumen but there can be no harm in thinking constructively. The "Functional dyspepsia" chapter did rather throw me: the first line defines it as discomfort or pain centred in the epigastrium; luckily I kept at it and further down the page was informed that this only applies where "common or uncommon structural, biochemical or infectious agents have been excluded". Actually, this angst, and that of further subdividing functional dyspepsia, applies only to those who have heard of Rome II. Most primary care practitioners can thus relax. So can our gastroenterology colleagues who might otherwise be requested to confirm an exact diagnosis of functional dyspepsia in younger patients. Avoiding endoscopy here also avoids opprobrium; alas, the diagnosis of functional dyspepsia must remain in the mind rather than in the investigation suite.

This is the kind of handy book which one needs to receive gratis although I do recommend its purchase if necessary. It is eminently suited to distribution through the good will

and thoughtfulness of a pharmaceutical company and I trust that someone will come forward to do this. I do not plan to part with my copy, despite continuing references to prokinetic drugs which are no longer, or were never, available in the UK.

P Hungin

Reconstructive Surgery of the Esophagus

M K Ferguson. Futura Publishing, 2001, \$105, pp 344. ISBN 0-87993-494-8

Oesophageal disease brings together many disciplines within the field of gastroenterology and the book is aimed primarily at the specialist oesophageal surgeon. Reconstruction of the oesophagus following resection for benign or malignant disease is one of the most challenging surgical procedures currently performed, and the oesophagus being such an unforgiving organ increases that challenge. Rather surprisingly, this is the first truly authoritative and evidence based volume to be devoted completely to this topic.

Mark Fergusson was trained at the University of Chicago under doyens of oesophageal surgery including Skinner, Belsey, and DeMeester, and has continued the tradition of that fine school. He is therefore well qualified to write this specialist tome. The historical chapter regales the courage of the pioneers of oesophageal surgery in the first half of the twentieth century, in which great British oesophageal surgeons including Grey Turner, Ivor Lewis, Allison, and Belsey are afforded due prominence. Following general sections on the philosophy of and indications for oesophageal replacement and the choices available of the oesophageal substitute and route to bridge the gap, a chapter is then devoted to each of the principal reconstructive techniques using stomach, colon, and jejunum, as well as the use of prosthetic tubes. Each of the chapters goes into considerable detail about relevant surgical anatomy, physiology, operative technique, and complications and their management.

Reconstructive Surgery of the Esophagus is clearly and succinctly written. While it draws heavily on the author's considerable experience, one of the attractions of this book is that it is clearly evidence based, and as well as being liberally referenced, the key references and their conclusions are highlighted in tabular form in each chapter. Another strong point for its predominantly surgical audience is the wealth of line drawings, which clearly depict surgical anatomy and technique. Overall, this is an excellent book, which takes its place well between existing tomes on oesophageal disease. I can recommend it wholeheartedly as an essential reference volume for both trainees and consultants in oesophageal surgery and indeed gastroenterologists might usefully dip into it occasionally so as to appreciate the many challenges facing their oesophageal surgeons in this fascinating branch of gastrointestinal surgery.

A Watson

The Pelvic Floor: Its Function and Disorders

Edited by J H Pemberton, M Swash, M M Henry. Harcourt, 2002, £79.95, pp 487. ISBN 0-7020-2307-8

In my clinical practice, I have felt for a long time that the knowledge acquired in coloproctology should be more frequently shared with

specialists in obstetrics, gynaecology, urology, neurology, etc. Therefore, I enjoyed receiving this book where the contributors range between at least 10 specialities which concern pelvic floor disorders. Each chapter is written by a leading figure or a group expert in this field. The book is a valuable starting point for gastroenterologists who wish to become up to date with data concerning the clinical problems of the pelvic floor, associating the anterior and posterior components, including physiology, anatomy, diagnostic imaging, surgery, nursing, and psychology.

The previously published book by these authors was entitled *Coloproctology and the Pelvic Floor*—coloproctology has disappeared from the title of their new book, indicating that it is no longer possible to approach the posterior pelvic floor disorders without studying the pelvic floor as a whole. In this way, this new title by itself is a very strong message. However, the reader might be a little disappointed if he looks for how to treat, for example, a patient suffering from both anal and urinary incontinence, or a patient complaining of urinary stress incontinence and posterior pelvic floor dysfunction inducing straining at stools. The book contains a number of excellent algorithms concerning pathogenesis, investigations, and treatment of the pelvic floor disorders. However, these algorithms have been constructed to treat either the anterior pelvic floor or the posterior pelvic floor, but not to treat a patient who complains simultaneously of the two parts of the pelvic floor. It was perhaps because the book was initially so promising and the subsequent chapters so interesting that I was hoping for a little more specific detail from the authors!

Nevertheless, the psychological characteristics of the pelvic floor disorders are very well described, suggesting that the impact of social factors, such as sexual abuse for example and psychological distress, on the expression of pelvic floor symptoms should be taken into account. To date it has not been very easy to suggest guidelines indicating how to achieve a balance between identifying the pathophysiology of pelvic floor disorders and understanding psychological factors. There is no doubt that the algorithms given at the beginning of the book will be very useful for the reader. However, they would have been even more useful if the experts had suggested at which step(s) of their algorithms they felt the need to investigate the psychological profile of their patients.

As C Norton wrote in the book, "there is a small but growing movement to create multidisciplinary pelvic floor clinics, where urogynecologists, colorectal surgeons, specialist nurses, physiotherapists, neurologists, psychiatrists . . . work together to improve the management of pelvic floor disorders". While we are waiting for these future multidisciplinary clinics of "perineology", it was probably not the time to furnish algorithms in this particular edition of *The Pelvic Floor* concerning investigations and management of associated symptoms of the anterior and posterior pelvic floor, integrating the psychological profiles of the patients. JH Pemberton, M Swash, and MM Henry must be acknowledged and congratulated for bringing together the knowledge of all the specialities involved in the pelvic floor.

P Denis

Clinical Governance in Gastroenterology

G Rubin, R Jones, J Price, *et al.* Radcliffe, 2000, B/W, pp 101. ISBN 1-85775-438-7

Can external control drive clinical standards? In the meantime we have clinical governance. What this actually means, how it is meant to operate, and whether governance guidelines will become yardsticks for judging performance also remain open. But at least it sounds like a good thing, and one glib but hopefully sensible answer is that clinical governance might ensure "uniform standards" across heterogeneous NHS practices, reassure the public and, in any case, it seems here to stay—at least for the moment.

It still baffles me as to what differences there are between excellent clinical practice and practice by clinical governance—presumably the latter is not meant to be quite as good, but will do. There seems to be a clamour for "acceptable" standards and this handbook, from a group of eminent UK general practitioners, fills a gap for primary care. The authors are members of the Primary Care Society for Gastroenterology, an organisation that has made significant contributions in knocking down barriers between primary and secondary care and has advocated cogent seamless care. The publication covers a series of problems from dyspepsia to colon cancer and includes an interesting section on horizon scanning, an example of new NHS speak, evidence that the authors have their ear to the ground, shifting though it may be.

It would be deluding to assume that all we know about gastroenterology, and that which matters to patient care can be compressed into 94 pages, but there is sufficient to keep governance types well busy. The information is well accessible but this is, of course, not a textbook. The chapter on stomas begins "A stoma is an artificial opening of the bowel on to the external skin", sheer gold dust to the doctor who forgot to attend the surgery lectures or to the non-clinical manager now anticipating being in charge of ensuring we do our jobs properly and services are commissioned effectively. There are one or two omissions—for example, the lack of mention of varices as a cause of acute bleeding—but each chapter does have a section on health economics for those hopefully traversing the quagmire of costs, effectiveness, care, and quality. Word has it that this book is selling well; the authors have got that aspect of health economics correct and timely.

P Hungin

Gastroenterology Highlights 2001–02

Edited by E Quigley. Health press, 2002, £15.00, colour, pp 84. ISBN 1-903734-12-6

Gastroenterology Highlights 2001–2 is attractively presented in good quality four colour format. This slim volume of 84 pages comprises 10 chapters written by a panel of international experts. Topics covered range from diseases of the oesophagus, liver, pancreas, and small bowel, to complications of liver disease, endoscopy, and colorectal cancer prevention and screening. The aim is to discuss key papers and put them into context. In most chapters, about 20 papers are reviewed but the actual numbers range from 16 to 30. Most chapters also review one or two abstracts. The

vast majority of papers covered were published in 2001 or 2000.

The *Fast Fact Highlights* series aims to "keep its readers abreast of the latest innovations" in each specialty. The flyer states that the information is presented "in an accessible style, comprehensively illustrated and fully indexed". Have these aims been met? Certainly the style is easy to read. However, there are only three figures in the whole book. Two of these are world maps showing geographical variations in colorectal incidence and mortality, while a third figure is a rather pointless flow chart of "preventive steps" for patient groups at average, moderate, and high risk from colorectal cancer. The steps are identical for the first two groups: change in lifestyle, chemoprevention and screening, and early diagnosis. These steps are again repeated for the high risk group, with preventive surgery added. There is no subject index.

I like the table in each chapter stating what are "in", what are "out", what are contentious, and what are still needed. However, it is irritating that many of the items mentioned as "in" or "out" have neither been discussed in the text nor referenced.

In the discussion on endoscopic treatment of gastro-oesophageal reflux, the EndoCinch and implantation of microspheres were discussed, but not the Stretta procedure. Both Freedman's study on the association between cholecystectomy and oesophageal adenocarcinoma as well as Schnell's report on non-surgical management of Barrett's oesophagus with high grade dysplasia, were reviewed in the oesophagus chapter and again in the chapter on gastrointestinal cancer. Tighter editing could have avoided this duplication as space in this book is clearly at a premium. I was surprised to read that "rectal examination as the only test for colorectal cancer" was "out". This statement was not referenced!

These brief reviews cannot by their nature be comprehensive. While this volume covers more ground than the short literature review booklets sponsored and distributed free by pharmaceutical companies, only about 20 papers are reviewed per topic. This can only represent a small selection of the many advances over a one to two year period, and

falls far short of the excellent reviews in the *Current Opinions in Gastroenterology* series. It is probably unsuitable for a library collection, and is not a book I would myself keep for reference. I am uncertain who may wish to purchase this volume, even though it is modestly priced at £15. While it is an easy read, I suspect that few consultant gastroenterologists would want to buy this book. I doubt if many trainees would either.

J Y Kang

CORRECTION

In the paper by Higham *et al* (*Gut* 2002;**50**:460–4) the heading for table 4 should read "Number of items (thousands) prescribed in England from 1990 to 1999. Prescription Cost Analysis system (Department of Health)".

NOTICES

38th EASL Annual Meeting

The European Association for the Study of the Liver will be holding its 38th annual meeting on 29 March–1 April 2003 in Istanbul, Turkey. Further information can be found on the website www.easl.ch/easl2003.

Falk Workshop—Inflammatory Bowel Disease: Turning New Advances into Practice

This will be held on 3 April 2003 in Berne, Switzerland. Further details: Falk Foundation e.V., Congress Division, PO Box 6529, Leinenweberstr. 5, 79041 Freiburg/Br, Germany. Tel: +49 761 15 140; fax: +49 761 15 14 359; email: symposia@falkfoundation.de; website: www.falkfoundation.de

International Symposium on Viral Hepatitis and Liver Disease

This conference will take place on 6–10 April 2003 in Sydney, Australia. Further infor-

mation: ISVHLD 2003 Congress Managers, GPO Box 128, Sydney NSW 2001, Australia. Tel: +612 9262 2277; fax: +612 9262 3135; email: isvhld@tourhosts.com.au; website: www.tourhosts.com.au/isvhld

Prague Hepatology Meeting

To be held on 5–7 June 2003 in Prague, Czech Republic. Leading speakers from Europe and the USA will present new ideas and suggestions on pathophysiology, diagnostics, and therapy of liver diseases in ten programmes blocks. Further details: Ms Veronica Revicka. Tel: +420 241 445 759; fax: +420 241 445 806; email: veronika@congressprague.cz

Falk Symposia—New Findings on Pathogenesis and Progress in Management of IBD

Two symposia and a workshop will be held on 10–14 June 2003 in Berlin, Germany. Further details - see Falk Workshop details above.

Gastroenterology and Endotherapy: XXIst European Workshop

This will be held on 16–18 June 2003 in Brussels, Belgium. Further details: Nancy Beauprez, Administrative Secretariat of the Workshop, Gastroenterology Department, Erasme Hospital, Route de Lennik 808, B-1070 Brussels, Belgium. Tel: +32 (0)2 555 49 00; fax: +32 (0)2 555 49 01; email: beauprez@ulb.ac.be

The Association of Coloproctology of Great Britain & Ireland

This annual meeting will be held on 7–10 July 2003 in Edinburgh, UK. Further details: Conference Secretariat, The ACPGBI at the Royal College of Surgeons of England, 35–43 Lincoln's Inn Fields, London WC2A 3PE. Tel: +44 (0)20 7973 0307; fax: +44 (0)20 7430 9235; email: acpgbi@asgbi.org.uk; website: www.acpgbi.org.uk