(2) As is clearly shown in the table under fig 2, for patients with ALT $<0.5 \times$ upper limit of normal (ULN), the risk of development of complications was significantly different from those with ALT $0.5-1 \times$ ULN. Also, the risk of development of complications was significant lower than patients with ALT $>1-2 \times$ ULN and ALT $>2-6 \times$ ULN. Clearly, ALT levels $>1-2 \times$ ULN have the highest risk of complications.

We would like to stress that the "baseline HBV DNA levels" of the study of Yu *et al* were arbitrary,¹ taken at the particular time point the subjects were recruited on a completely random basis.

As for the study of Yang and colleagues,² hepatitis B e antigen (HBeAg) status was only measured on recruitment. It is not known what proportion of these patients had HBeAg seroconversion during the subsequent follow up of 92 359 patient years (that is, HBeAg/anti-HBe status was not known at the time of development of hepatocellular carcinoma).

(3) As for our specifically studying the late complications of cirrhosis, we consider this as one of the important and innovative aspects of our study, and not a flaw. Huo *et al* are wrong in saying that only the formation of cirrhosis or hepatocellular carcinoma is directly linked with chronic HBV infection. As the study of Liaw *et al* has elegantly shown, lowering viral replication can suppress the development of late complications of cirrhosis.³ In fact, this exactly confirms the proposal of our study.

M-F Yuen, C-L Lai

Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong

Correspondence to: Dr M-F Yuen, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong; mfyuen@hkumc.hku.hk

Conflict of interest: None declared.

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Mannan binding lectin (MBL) gene polymorphisms are not associated with anti-Saccharomyces cerevisiae (ASCA) in patients with Crohn's disease

Recently, an association between the presence of antibodies to *Saccharomyces cerevisiae* (ASCA) and mutations in exon 1 and the promoter region of the mannan binding lectin (MBL) gene was described in 58 patients with Crohn's disease (CD).¹ A possible link between ASCA and MBL mutations in patients with CD is plausible. MBL is a component of the innate immune system that can bind to *S cerevisiae* and the serum concentration of MBL depends on structural mutations in exon 1 and promoter polymorphisms.

Table 1 Different mannan binding lectin (MBL) variants and the presence of anti-Saccharomyces cerevisiae (ASCA)

	Prevalence of ASCA (%)	p Value (χ^2 test)	Titres of ASCA (EU/ml)*	p Value (Kruskal-Wallis or Mann-Whitney U)
MBL exon 1 (codons 52, 54, 57)		0.62		0.82
A/A	54		4.12 (1.12-11.88)	
A/O	58		4.48 (1.46-10.18)	
O/O	67		5.31 (0.95-8.23)	
MBL promoter C-225G		0.61		0.55
Y/Y	55		4.37 (1.32-11.81)	
Y/X	52		3.61 (1.05-9.87)	
X/X	71		5.61 (3.25-6.41)	
MBL		0.27		0.43
Sufficient (A/A+YA/O)	53		3.64 (1.23-10.32)	
Insufficient (XA/O+O/O)	63		4.96 (0.92-10.45)	

*Values are median (interquartile range).

Wild-type alleles are designated A (structural alleles) and Y (promoter -225 allele). Mutant alleles are designated O (structural alleles) and X (promoter -225 allele).

We previously found no association between structural mutations in exon 1 of the MBL gene and susceptibility to CD.² In view of the recent report of Seibold and colleagues,¹ we were interested to see if we could confirm the reported association between ASCA and MBL mutations in a larger and independent cohort of CD patients. Three point mutations in exon 1 (codons 52, 54, and 57) and one polymorphism in the promoter region (C-225G) of the MBL gene were genotyped using polymerase chain reaction-restriction fragment length polymorphism or ARMS in a cohort of 241 CD patients. Statistical analysis was performed using SPSS 12.0 for Windows. The results are summarised in table 1.

We found no association between the presence of ASCA and structural MBL mutations in exon 1 (codon 52, 54, and 57) ($p = 0.62$; χ^2). Similarly, we found no association between the presence of ASCA and MBL promoter polymorphism C-225G ($p = 0.61$; χ^2). Furthermore, no statistical difference was found between ASCA titre and MBL structural genotypes in exon 1 ($p = 0.82$; Kruskal-Wallis) and promoter polymorphism C-225G ($p = 0.55$; Kruskal-Wallis). Finally, no difference was found when we compared sufficient and insufficient MBL alleles towards either the presence or the titre of ASCA (see table 1).

We found no association between the presence of ASCA and polymorphisms/mutations in the MBL gene in a large cohort of CD patients and conclude that the occurrence of ASCA is not related to MBL polymorphisms/mutations. This is in contrast with a previous report in which such an association was suggested.¹ Therefore, we consider the relationship between ASCA and MBL highly controversial.

S Joossens, M Pierik

Department of Gastroenterology, University Hospital Gasthuisberg, Leuven, Belgium

A Rector

Laboratory of Clinical and Epidemiological Virology, University Hospital Gasthuisberg, Leuven, Belgium

S Vermeire

Department of Gastroenterology, University Hospital Gasthuisberg, Leuven, Belgium

M V Ranst

Laboratory of Clinical and Epidemiological Virology, University Hospital Gasthuisberg, Leuven, Belgium

P Rutgeerts

Department of Gastroenterology, University Hospital Gasthuisberg, Leuven, Belgium

X Bossuyt

Laboratory of Medicine, University Hospital Gasthuisberg, Leuven, Belgium

Correspondence to: Dr S Joossens, Department of Gastroenterology, University Hospital, Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium; sofie.joossens@uz.kuleuven.ac.be

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Dyspepsia is distinguishable from heartburn

This systematic, original, and large study from the Leuven group (*Gut* 2005;**54**:1370-6) proves what experienced physicians have appreciated for many years: that heartburn is a specific symptom that is easily identifiable by careful history or validated questionnaire; that heartburn is predictive of abnormal oesophageal acid exposure in approximately 75% of people with the symptom; and that it occurs in a minority of patients with typical or "true" dyspepsia, especially when the latter syndrome consists of symptoms other than pain or burning which occur after meal ingestion.

The heartburn prevalence of $<20\%$ in the typical dyspepsia group of Tack and colleagues (*Gut* 2005;**54**:1370-6) is consistent with the high rate of somatic symptoms in these patients and it is likely that it represents

"background noise". In a community based study of uninvestigated dyspepsia, the prevalence of heartburn was similar, and somatisation scores (SCL-90) and somatic symptom checklist scores were higher than in community controls.¹

Data from this important study suggest that the subgroup of reflux-like dyspepsia (for example, in Rome I criteria) should be discarded, that studies demonstrating efficacy of acid reduction in dyspepsia are generally uninformative in the context of true dyspepsia, and that inclusion criteria for true dyspepsia studies can be tightened by using a questionnaire to exclude heartburn rather than requiring laborious and costly 24 hour pH monitoring or upper gastrointestinal endoscopy.

The implications of this study are very significant and they should be embraced by practising physicians, regulatory agencies, and those who write consensus documents on symptom based criteria for functional gastrointestinal disorders.

M Camilleri

Correspondence to: Professor M Camilleri, Clinical Enteric Neuroscience Translational and Epidemiological Research (CENTER) Group, Mayo Clinic, Charlton 8-110, 200 First St SW, Rochester, MN 55905, USA; camilleri.michael@mayo.edu

Conflict of interest: None declared.

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BOOK REVIEWS

Evidence-based Gastroenterology and Hepatology, 2nd Edn

Edited by J W D McDonald, A K Burroughs, B G Feagan. London: BMJ Books, 2004, £125, pp 624. ISBN 072791751X

"Facts are stubborn things; and whatever may be our wishes, our inclinations, or the dictates of our passions, they cannot alter the state of facts and evidence", John Adams

We owe it to our patients to know the facts and implement them accurately for improving their quality of lives. This obligation imposes formidable challenges to a modern practicing physician often struggling with information overload, demands of revalidation, and a maze of regulatory requirements. The second edition of this very successful and well known volume is a superb way of updating gastroenterology and hepatology evidence and facts encapsulated within one manageable volume. The "Introduction" is a concise assembly of the science behind collating, dissecting, and interpreting evidence, itself now a major medical specialty. The second edition has gained important chapters such as microscopic and collagenous colitis, antibiotic associated diarrhoea, oesophageal motility disorders, Barrett's

oesophagus, non-alcoholic steatohepatitis, management of obesity, management of viral hepatitis after liver transplantation, and acute colonic pseudo-obstruction. The volume admirably covers all priority areas within gastroenterology and hepatology, perhaps with the exception of constipation, hidden in the chapter on irritable bowel syndrome. The volume can be used both as a reference textbook and as a real confidence boosting update to be read from cover to cover. The contents will cover 95% of patients an average general gastroenterologist would expect to care for, both in acute wards and in outpatient clinics. Coverage of infectious gastroenteritis, including that in the immunocompromised host, may make subsequent editions more appealing to a wider readership worldwide. Authorship across the Atlantic divide gives a rare balance to the volume and should appeal to all English-reading physicians.

The chapters are conventionally arranged and are rigorously evidence based, with evidence grades prominently shaded. Some recommendations, such as lifestyle changes in alleviating gastro-oesophageal reflux, refer to studies of variable robustness without evidence grades. Most chapters are extensively referenced, some with over 300 references, a notable exception being functional dyspepsia with 58 references, clearly missing some pivotal works. Coverage of hepatology is extensive and superb, with a rich list of topics related to liver transplantation. This is especially welcome "bucking the trend" as most textbooks now separate into gastroenterology and hepatology, while most gastroenterologists continue to manage a wide spectrum of liver disorders. Oesophageal diseases, ulcer disease, and *Helicobacter*, inflammatory bowel diseases, including microscopic colitis, irritable bowel syndrome, and acute pancreatitis are very well covered. Colon cancer is perhaps less well covered and topics on nutritional support are scant.

The textbook comes bundled with a convenient CD-ROM which should be an essential travel companion in every gastroenterologist's laptop carry case. What about a PDA version in the future? Evidence ages rapidly, and a very welcome feature is the update section available from a designated website. Each of the chapters present comprehensive evidence as well as expert interpretation. Most chapters clearly delineate where evidence is lacking and further research is required. I have no doubt that this is an essential acquisition for all practising gastroenterologists, including gastrointestinal surgeons and gastroenterology departments. Trainees too should familiarise themselves with the CD-ROM as a convenient way of knowing evidence filtered through experts. A list of trials, systematic reviews, and meta-analysis can be daunting but there is no better user friendly access to evidence for gastroenterologists. I foresee the volume going through many editions and becoming a classic.

"The facts are always friendly, every bit of evidence one can acquire, in any area, leads one that much closer to what is true" Carl Rogers

S Ghosh

Meta-analysis in Medical Research. The Handbook for the Understanding and Practice of Meta-analysis

G Leandro. Oxford: Blackwell Publishing, 2005, £39.50, pp 98. ISBN 1405127333

I should declare a conflict of interest at the outset of this review. This handbook is intended for those in the medical profession seeking to carry out meta-analysis in their chosen area of research and provides a manual of practical advice together with an accompanying program (on CD-ROM) to enable them to get started. My conflict arises as co-ordinating editor for one of The Cochrane Collaboration review groups in gastroenterology. The Collaboration does itself produce a plethora of training materials on how to do systematic reviews and meta-analyses along with its own software (Revman) and this can all be downloaded free of charge to anyone, whether or not they are involved in producing Cochrane reviews. The Cochrane products, which have been collectively developed by hundreds of users over 15 years, set the standard against which one offs, such as this handbook from Leandro, need to be evaluated. It is a bit like comparing a foreign language phrase book with an intensive multimedia language course. The former may enable you to order a meal on holiday whereas the latter should make it possible to learn a new language.

The main selling point has to be the meta-analysis program supplied on CD (sometimes called META and sometimes METANALYSIS) and the rest of the handbook is really little more than a manual on how to use the program. There is a very short introductory section on the importance of meta-analysis in medical research together with brief notes on how to plan a meta-analysis, problems of bias, and the common statistics that are output. The concept of conducting a systematic literature review, which should form an essential prelude to any meta-analysis, is touched upon only minimally. The complexity of methodologies for several aspects of the systematic review process (for example, bibliographic searching for randomised trials) is hardly mentioned and one gets an impression that the handbook may be adopted most enthusiastically by those seeking shortcuts to the required rigour of reviews.

The program itself is easy to install and run and does have one or two nice features not available within the Cochrane software (for example, the ability to produce cumulative meta-analyses over time and to output alternatives to the standard Forest plot (such as Galbraith and L'Abbe plots)). There are however some glaring deficiencies of which the most apparent is that the Forest plot study point estimates of effect are not graphically represented by a square that is proportional in size to the precision of the study. It is also not possible to meta-analyse continuous outcome measures. In places the program is a little clunky and it is necessary to scrutinise the handbook quite closely to structure commands in the correct order. There are also occasions when menus and comments switch from English to Italian.

The author is described as a gastroenterologist and biostatistician and, for readers of *Gut*, his use of examples from gastroenterology