Pugh's grading in the classification of liver decompensation

EDITOR,—As a houseman on the Liver Unit at King's College Hospital, London, I benefited from a unique experience of acute medical care during the heady days of the emerging unit, from an absorbing exposure to active clinical research, and from the career motivation of early publication.1 It was the practice of the unit director to encourage the houseman in the collection of clinical data, under the supervision of the registrar or senior registrar.

The series of patients with bleeding oesophageal varices, which represented my particular assignment, interested me since the morbidity and mortality data did not conform that well to Child’s classification of A, B, and C.1 In particular, this system did not consider any bleeding tendency. An alternative classification that included reference to the prothrombin time was proposed in the report of these patients and an attempt was made to devise a numerical scoring system. It is apparent that this alternative system has stood the test of time, because of two major advantages: (a) it does not artificially place patients into a category of abnormality; (b) it results in a total score which provides a better index for statistical analysis.

Now, as a clinical epidemiologist working in an academic environment, I find it slightly amusing to reflect that a strictly scientific method was not adopted in formulating an alternative classification of liver decomposition. Rather, it was the adoption of a pragmatic response to a gut feeling that something more flexible was required to categorise these patients!

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3 MacDougall BRD, Westaby D, Blenkins LA. Portal hypertension—25 years of progress. Gut Supple-
ment 1991; 518–524.

Proliferation of human gastrointestinal epithelium

EDITOR,—The altered pattern of epithelial proliferation in familial adenomatous polyposis (FAP) noted by Potten et al1 must be interpreted carefully. In studying the upward shift of the proliferative compartment using the monoclonal antibody Ki-67, I have satisfied myself that this phenomenon occurs only within the context of adenomatous change, whether this is a macroscopically visible adenoma, a microadenoma, or an unusual adenoma (unpublished observations). This interpretation is not completely straightforward, because early adenomatous change in FAP appears to be familial from the outset. It is, however, important to establish whether the unicrypt adenoma is the first manifestation of the disease or whether there are ‘field changes’ detectable through cell kinetic disturbances or other functional alterations. For example, some workers have described mucin or lectin histochemical changes in the normal appearing mucosa in FAP that we have been unable to confirm in a carefully controlled study.2 The concept of ‘preneoplastic field change’ has been accepted widely but unretractly in relation to gastrointestinal epithelium.3

The observations of Potten et al are based on a very elegant series of experiments.1 Their demonstration of a negative correlation between cell kinetic indices and likelihood of malignancy will hopefully lead to a full reappraisal of the place of cell kinetics in our understanding of colorectal neoplasia.

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Cholestatic hepatitis associated with clavulanic acid

EDITOR,—We read with great interest the report by Larrey and colleagues regarding hepatitis associated with the combination of amoxicillin-clavulanic acid in Gut.4 With this in mind, we would like to add some observations on similar cases in Melbourne, Australia, as well as a single case of prolonged cholestasis following treatment with ticarcillin-clavulanic acid.4

Larrey and coauthors, as well as others,5 contend that a hypersensitivity reaction is the likely consequence with which we agree; in most of the cases reported by us, however, the patients were simultaneously taking oral corticosteroids, and so the manifestations of an immunological reaction, which we believe have been masked. Interestingly, three of the 15 patients reported by Larrey and coauthors were also taking oral corticosteroids; none of them exhibited skin rashes, hypeereosinophilia, or positive tests for autoantibodies associated with cholestatic liver disease.

In part, the relatively larger proportion of our reported cases receiving concurrent steroid treatment (6/8 with the amoxicillin-clavulanic acid group, 1/1 with ticarcillin-clavulanic acid) may reflect different prescribing practices; in Australia, amoxicillin-clavulanic acid is most often given to patients suffering from the infectious complications of chronic obstructive diseases, because of its efficacy in treating infection with the common respiratory pathogens, Haemophilus parainfluenzae (usually resistant to amoxicillin alone). These patients typically have severe airway disease and are often receiving corticosteroids at the same time. Other prescribed predosing factors, such as increasing age and prolonged duration of treatment, may also relate to this older group of patients who are most likely to be prescribed the amoxicillin-clavulanic acid combination for longer than usual.

Larrey and coauthors have contributed to the growing number of cases of cholestatic hepatitis associated with clavulanic acid combinations, and we hope that this will help to raise the practising clinician’s awareness of these agents as the cause of uncomfortable, often prolonged cholestasis. We recommend the reporting of suspected or confirmed cases to the appropriate national adverse drug reaction committee, to enable more accurate data regarding incidence to be gathered. Finally, we wish to reemphasise that consideration of the diagnosis of amoxicillin-clavulanic acid associated jaundice can save the patient from potentially hazardous investigations such as endoscopic retrograde cholangiopancreatography and liver biopsy.

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Superior mesenteric blood flow

EDITOR,—We read with interest the paper by Sieber et al in Gut.5 We cannot agree with their observation of a smaller proportion of superior mesenteric artery (SMA) blood flow with a carbohydrate meal rather than with a meal of fat or protein. These results are at odds with the findings of the late Dr Mohammed Qamar and others,6 and we cannot agree that these results are flawed by the lack of any consideration of gastric emptying. Qamar devoted an entire chapter of his PhD thesis to the role of gastric emptying in postprandial hyperamia.7 In unpublished work, using simultaneous transcutaneous Doppler ultrasound to measure SMA blood flow and gamma-camera scanning to measure the passage of a radiolabelled meal from the stomach into the duodenum in 12 healthy young subjects, he found no consistent difference between SMA blood flow rates following liquid and solid meals. He concluded that gastric emptying was the major physiological factor in regulating SMA blood flow. We believe the addition of polyethylene glycol (PEG) to the duodenal perfuse explains this unexpected result.

The absorption of glucose by the upper small intestine is reduced significantly by the addition of complex, non-absorbed polysaccharides such as guar gum and pectin8 and the resultant reduction in postprandial hyperglycaemia has an application in the management of diabetes.9 The precise mechanism by which this occurs is obscure but it seems likely that the addition of PEG — which is also a complex, non-absorbed carbohydrate — will reduce glucose absorption in a similar way. It therefore seems that the original observations9 — made without test meal additives — are correct.

We do not dispute the fact that meal composition is the chief determinant of postprandial hyperamia; the precise mechanisms by which this occurs is, however, still unknown, although our own unpublished data are in agreement with those of Sieber et al and others10 who have suggested that gut hormones have no role.

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