Correspondence

Comparative radiological and morphological study of human pancreas

SIR—It is a pity that the authors of this recent paper (*Gut* 1985; 26: 406) did not allude to the classical work of Birnstingl¹ on the same subject. Both studies show the low specificity of pancreatographic abnormalities – particularly minimal-change-pancreatitis (MIP) – in diagnosing chronic pancreatitis. This low specificity accounts for the poor positive predictive value (high false positive rate) of endoscopic pancreatography in the context of chronic pancreatitis.² The interpretation of MIP is facilitated by studying pancreatic exocrine function in the same patients: quantitative changes in 'early' disease include increased synthesis and secretory rates of enzymes; while qualitative changes include increased ratios of lysosomal to digestive hydrolases, anionic to cationic trypsinogen, lactoferrin to digestive hydrolases and hydrolases to trypsin inhibitor. By the time of presentation, the well recognised feature of the disease: reduced post-secretin bicarbonate output, is found in about half the patients whose pancreatograms are normal or show MIP.³

The functional changes of 'early' chronic pancreatitis reflect the ultrastructural alterations in acinar and, later, in ductal cells⁴⁻⁶ – proliferated endoplasmic reticulum and Golgi, increased numbers of lysosomes, microvesicular fat and deposits of lipofuscin (indicating lipid peroxidation) – changes that are also found in liver biopsies from patients with idiopathic, or alcohol related disease.⁷ An explanation is provided by the recent discovery that the pancreas contains phenobarbital-inducible and hydrocarbon-inducible mono-oxygenases,^{8,9} and our functional studies showing induction of the 'drug-metabolising-enzymes'¹⁰⁻¹² in most patients with chronic pancreatitis, including those with 'idiopathic disease', who constitute 50% of the total. While induction results in expansion of the endoplasmic reticulum and thereby, at least initially, increased production of transportable proteins (thus explaining the relationship between hypertriglyceridaemia and hepatic induction), it is known that prolonged induction promotes lipid peroxidation because increased amounts of oxygen free radicals are generated whilst antioxidants stores are simultaneously depleted. The corollary may be that the earliest clues to interpretation of MIP (and indeed vague upper abdominal pain: ? pancreatic) are gleaned by direct assessment of the induction/antioxidant axis using non-invasive methods.¹³ This

is better than relying on more remote consequences of induction – for example, increased synthesis and secretory rates of digestive hydrolases – or the resultant activation of crinophagic mechanisms¹⁴ and those that inhibit lipid peroxidation – for example, apolactoferrin.¹⁵

J M BRAGANZA AND D W K ACHESON

Manchester Royal Infirmary,
Oxford Road,
Manchester M13 9WL.

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Liver and obesity

SIR,—Following the paper by Braillon *et al.*,¹ we would like to confirm that also in our experience obesity *per se* does not play a major role in the development of liver disease. We have, in fact, recently reviewed the frequency of abnormal liver function tests (serum GPT > 25 mU/ml and/or γ -globulines > 2 g/dl) in 313 obese patients consecutively hospitalised from June 1981 to December 1984 in our medical unit. Fifty five (23 men with Body Mass Index – BMI = $W(Kg)/H(m)^2$ – of 40.8 ± 9.8 (DS) and 32 women with BMI of 39.8 ± 9.0) with mean age of 46.6 ± 15.1 years corresponding to 17.5% of the patients were affected by one or both haematochemical abnormalities while the remaining 258 (85 men with BMI of 38.6 ± 8.9 and 173 women with BMI of 44.3 ± 9.4) with mean age of 48.1 ± 12.3 years did not show any biochemical abnormality indicative of liver pathology. Among the two groups no difference was detected for the frequency of the following: diabetes 29% in the first group vs 36% of the second group, use of hepatotoxic drugs 24% vs 28.6%, alcoholism 13% vs 12%, hypertriglyceridemia 33% vs 45.3%, hypercholesterolemia 9% vs 14%, hyperphagia (with a diet mainly rich in CH and fat) 51% vs 60%, right heart cardiac failure 0% vs 1.2%. On the other hand, B hepatitis virus contact, evaluated by measuring serum B hepatitis antigen and autoantibodies, was much more frequent, 46.3% vs 17.4% ($p > 0.0001$) in the first group. Cholelithiasis was also slightly more frequent (25%) in the first group than in the second group (15%) ($p > 0.06$).

In conclusion these observations in a group of obese individuals, with hypertransaminasemia and/or hypergammaglobulinemia, in South Italy show that liver abnormalities are independent of obesity by itself and are mainly caused by contact with B hepatitis virus (endemic in our region). Alcoholism is the main cause of liver pathology in obese patients living in regions where alcohol consumption is very high (2–5).

F CONTALDO, M MANCINI, L A REED *et al*
Departments of Medicine and
Metabolic Diseases, and
Department of Gastroenterology,
University of Naples,
Naples, Italy.

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Statistical tests for 2×2 tables

SIR,—The letter from Boyd and Marks¹ in the June issue of *Gut* is correct in saying that the 2×2 table

	Healed	Unhealed
TDB	10	2
Cimetidine	5	8

gives a χ^2 value with Yates' correction of 3.53 leading to $p=0.06$ rather than $p<0.02$ as claimed in the Lam *et al*² paper.

The references they give in their discussion, however, of which tests to use on which occasions, all date from before the main impact of the present computer revolution. As long as there is a suitable computer (and program) available there is now little reason to use anything but the exact test for 2×2 tables. There is a difficulty, however, in agreeing on what is the correct version of this to use for a two-tailed test. It is a pity that even eminent statisticians seem to disagree here. Those who have a taste for such things may be referred to a recent paper by Yates³ and the published discussion with it. (This paper celebrated the 50th anniversary of Yates' earlier paper on the subject.)

My own view is that there is nothing to be said in favour of doubling the observed one-tail probability, which is what Boyd and Marks¹ are doing. Instead I believe the best rule to be to include in the second tail all terms such that the sum of their probabilities does not exceed the probability in the observed tail. In the case under discussion there are 11 possible tables (with the observed marginal totals) corresponding to probabilities of 0.00009, 0.00262, 0.02599, 0.11549, 0.25986, 0.31183, 0.20211, 0.06930, 0.01181, 0.00087 and 0.00002 respectively. The observed tail consists of the first three terms with a sum of 0.0287; the second tail consists of the last three terms, because to take the last four would give a sum exceeding the observed one. This gives a probability of 0.0127, and a total two-tail probability of $0.0287+0.0127=0.0414$ which is significant at the conventional 0.05 level.

Most statisticians nowadays would agree that the fact that the probability is round about 1 in 20, in this instance, is what matters, however, rather than