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Because we receive many more letters than we have room to publish we may shorten those that we do publish to allow readers as wide a selection as possible. In particular, when we receive several letters on the same topic we reserve the right to abridge individual letters. Our usual policy is to reserve our correspondence columns for letters commenting on issues discussed recently (within six weeks) in the BMJ.

Letters critical of a paper may be sent to the authors of the paper so that their reply may appear in the same issue. We may also forward letters that we decide not to publish to the authors of the paper on which they comment.

Letters should not exceed 400 words and should be typed double spaced and signed by all authors, who should include their main degree.

Audit for all

SIR,—I read the Audit Reports (15 June, p 1792) and admired the authors for both their honesty in publishing their results and their determination to improve their practices still further.

The next article, surveying the treatment of primary breast cancer in Great Britain (p 1793), paints a similar picture of suboptimal care and variable organisation. The conclusion, however, that "the time has come to encourage treatment by specialist breast units" is very different.

The leading article by Professor L E Hughes and Mr S P Courtney on the follow up of patients with the same condition (27 April, p 1229) also argues the case for rigorous organised care but again concludes, without any evidence, that this should take place in hospital clinics rather than in general practice. Where such evidence does exist, as, for example, with the measurement of blood glucose and detection of complications in diabetes, the outcomes of care in well organised general practice are comparable with those in hospital clinics, while both are better than disorganised or random care.¹

Our criteria for good quality care should not concentrate solely on technical indices but should include interpersonal factors such as accessibility, continuity, and patient satisfaction. We must remember that the obstetricians who have led the profession by reviewing their performance in terms of maternal and perinatal mortality have also been on the receiving end of the most vociferous criticism from patients for their relative neglect of these other dimensions of quality. Finally, as we have seen in the United States, the economic implications for transferring more patient care to specialist units can be horrendous.

You may feel that all I am doing is making my special case for undertaking the care of patients as the authors to which I refer are making theirs. The conclusion I would prefer to draw, however, is that

all doctors should be involved as part of their normal professional activities in setting criteria for their own work and monitoring the level of performance in achieving them. It is only by this method that we can guarantee good quality care for our patients wherever they receive it.

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1 Dornan C, Fowler G, Mann JI, Markus C. A community study of diabetes in Oxfordshire. *J R Coll Gen Pract* 1983;33:151-5.

Simultaneously acquired hepatitis B and hepatitis D virus infections

SIR,—We would like to refer to a few of the issues raised by Dr Alan G Shattock and colleagues (11 May, p 1377). In contrast to their previous reports,^{1,2} the data reported in this paper suggest a strong association between hepatitis B and hepatitis D virus coinfection and the severity of hepatitis in drug abusers in Dublin. This association has been reported in a group of drug addicts in Milan.³ These observations make unlikely the hypothesis of Dr Shattock about the possible role of ethnic (genetic) factors in the severity of delta coinfection.^{1,2}

We agree with the authors that a high proportion of drug abusers with acute HBsAg positive hepatitis have serological evidence of simultaneously acquired hepatitis D infection and that a significant proportion of these patients have a more severe disease than patients with classical hepatitis B.^{3,4} Nevertheless, we would like to make several points.

The acute (primary) hepatitis B infection might be shown serologically in all the patients by testing the acute sera for IgM anti-HBc. Moreover, the titration of IgM anti-HBc might be used to distinguish individuals simultaneously infected by both agents from carriers of HBsAg (still positive for IgM anti-HBc at a borderline level) superinfected by hepatitis D,⁵ a condition often observed in drug abusers,⁴ whose carrier state is generally of recent onset.

Since anti-δ antibody in patients previously negative for serological delta markers is sometimes detectable only 4-6 weeks after the onset of disease,³ the incidence of hepatitis D infection may be underestimated if serial serum samples are not tested.

Concerning the clinical and biochemical characteristics of the patients with acute hepatitis studied by Dr Shattock and colleagues, it is surprising that most of them had either an asymptomatic disease (29/267) (alanine aminotransferase values less than twice normal) or a mild or moderate illness (223/267) (values <10 times normal). It would be interesting to know if all the first serum samples tested were taken during the acute phase of the disease. Unfortunately there are no indications about the diagnostic criteria since no symptoms were reported and alanine aminotransferase values, in most of the cases studied, were not consistent with clinically acute hepatitis, so the possibility that some of the patients might have been observed after the acute phase of the disease cannot be excluded. Such data are also important for establishing the persistence of hepatitis D antigenaemia.

We agree with Dr Shattock and colleagues that the detection of HDAg in serum is not uncommon in drug abusers with hepatitis B and D coinfection, since we also have found HDAg by radioimmunoassay in 19.6% (49/250) of the drug abusers with delta infection. Delta antigenaemia is always associated with the presence of hepatitis D RNA in serum and it is detectable until the first or second week after the onset of symptoms (FC, unpublished data). In contrast, and with the same technique, delta antigenaemia is only rarely observed in non-addicts so that this phenomenon could not be explained simply by a lower sensitivity of radioimmunoassay.

Concerning the immune response to hepatitis D infection in drug abusers, we agree with Dr Shattock and colleagues that seroconversion invariably occurs and that total anti- δ persists at low titres for a long period after the acute phase of the disease, regardless of HBsAg clearance.³ This type of immune response (as well as the frequency of serum HDAG detection) is peculiar to hepatitis D infection in drug abusers regardless of the test used (radioimmunoassay or enzyme linked immunosorbent assay) and distinctly differs from that generally observed in non-addicts, who almost always develop only a brief anti- δ response of the IgM class. We have suggested that the peculiar serological pattern of epidemic hepatitis D infection in addicts might depend on more virulent strains obtained through the multiple rapid transfers in an epidemic setting,³ as suggested by experimental transmission in chimpanzees,⁶ or might be explained by an anamnestic immune response due to repeated antigenic stimuli.

As regard the last question put by the authors, about the frequency of the development of chronic liver disease in hepatitis B and D coinfection, our data show that these patients do not seem to be at more risk of developing chronic hepatitis than those with classical hepatitis B.

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Epidemic hypochlorhydria

SIR,—The paper by Mr T Gledhill and others (11 May, p 1383) warrants comments on several important points. As regards the changes noted in the intragastric environment of their four hypochlorhydric subjects, these findings support the now universally held view that a pH ≥ 4 will encourage bacterial overgrowth, especially of nitrate reducing organisms, and increased nitrite concentrations. That they did not observe any increase in *N*-nitroso compound levels, in contrast to reported observations by others,¹⁻³ is not surprising and probably explicable by methodological differences in estimating *N*-nitroso compounds^{2,4} and in gastric juice sampling.^{2,5}

The method they used for determining *N*-nitroso compounds⁴ cannot distinguish them from, for instance, the *S*-nitroso derivatives of cysteine and reduced glutathione,⁶ which can be derived from the action of nitrite in a biological matrix. *S*-Nitrosothiols are recognised as becoming much less stable as the pH is raised from that typical of the normal stomach.⁷ Since they are readily formed, and such compounds would have been included in any determinations of *N*-nitroso compounds by the method adopted, it is not

surprising that lower concentrations were detected at pH values typical of hypochlorhydria.

Furthermore, since most readers of the *BMJ* are not in a position to appreciate the details of the findings reported in fig 6 of their paper it is necessary to bring to light a number of discrepancies. Firstly, the concentrations of *N*-nitroso compounds quoted are about three orders of magnitude smaller than those reported for normal subjects in one of the publications to which they refer.¹¹ Also, no justification is given for the choice of a molecular weight of 460 to provide the relation quoted that 1 mmol *N*-nitroso compound/l ≈ 46 mg/100 ml; this is much greater than the molecular weights of *N*-nitroso compounds derived from most if not all recognised physiological precursors. Another feature which defies obvious explanation is the occasions, quoted in fig 6 of their paper, when the concentrations of the stable *N*-nitroso compounds exceeded those of the total *N*-nitroso compounds—that is, the part is greater than the whole, such as was reported to occur in the controls at 0300 and 0700 onwards.

Mr Gledhill and colleagues conclude that both the nitrate reducing bacterial counts and the intragastric nitrite concentrations, resulting from their action in reducing available nitrate, could be risk factors in gastric carcinogenesis. Yet on the basis of the responses of just four subjects with hypochlorhydria they dismiss the possible involvement of *N*-nitroso compounds, most of which are recognised to be carcinogenically active at very low concentrations in a wide range of different animal species, including mammals.⁸ This conclusion would hardly be justified even if the method of estimation adopted by them had been the most specific available. Nitrite can form many types of compounds other than *N*-nitrosamines and *N*-nitrosamides during its reactions in a biological matrix, including predominantly *C*-nitrosophenols and nitrophenols and *S*-nitrosothiols, which of themselves are probably of little or no importance in terms of carcinogenesis, not to mention nitrate itself, the responses of which would not have been excluded in the procedure used.

In postulating bacterial contamination as the most likely cause of the active superficial gastritis which resulted in hypochlorhydria Mr Gledhill and colleagues make no mention of pyloric campylobacter (*C. pyloridis*). That this organism was probably the most likely cause of the syndrome described by them is supported by recently published data from Marshall *et al.*⁹ A previously healthy volunteer rendered temporarily achlorhydric with cimetidine took pyloric campylobacter by mouth and developed a mild illness lasting 14 days, and histologically proved gastritis was observed 10 days after ingestion of the bacteria; this had largely resolved by the 14th day. Furthermore, a retrospective examination of biopsy specimens taken from subjects studied by Ramsey *et al.*¹⁰ who developed epidemic gastritis with hypochlorhydria, quoted by Mr Gledhill and colleagues, has shown pyloric campylobacter.² A similar case from Holland¹¹ has also been found to be associated with pyloric campylobacter on subsequent histological re-examination.⁹ It is noteworthy that in Gledhill's subjects superficial gastritis was most marked in the antrum and that clusters of polymorphs were prominent within glands. In a series of 150 patients studied histologically we observed pyloric campylobacter often in close proximity to polymorphs in the superficial glands of patients with antral gastritis.¹²

It would be of great interest to know if a review of the histological material from the subjects of Mr Gledhill and others would also yield *C. pyloridis* and whether the two subjects who developed chronic gastritis will eventually develop peptic ulcers. If so, then this would lend further support for Marshall's hypothesis that ingestion of *C. pyloridis* in susceptible individuals who subsequently developed chronic gastritis might make them more vulnerable to peptic ulceration.

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SIR—We read the paper by Mr T Gledhill and his colleagues on epidemic hypochlorhydria with considerable interest. One possible cause may be the recently described gastric organism referred to as *Campylobacter pyloridis* or gastric campylobacter like organism. This organism was shown in biopsy specimens of most patients with chronic gastritis by Warren and Marshall in 1983, using the Warthin Starry silver stain.^{1,2} Campylobacter like organisms are microaerophilic and acid intolerant and are found deep beneath the mucus layer, particularly in association with the active form of chronic gastritis, where polymorphonuclear cells are involved in the inflammation as well as chronic inflammatory cells.^{1,3}

Whether these organisms have a pathogenic role or are merely commensal is unclear. Marshall *et al* have, however, described the development of vague symptoms, gastritis, and gastric colonisation after the deliberate ingestion of live campylobacter like organisms by a volunteer known to have no such organisms and normal gastric histology before the experiment.⁴ The normal mode of spread of gastric campylobacter like organisms is unknown, but they would seem to be a possible cause for the illness in the volunteers of Mr Gledhill and colleagues, which would not have been detected by the investigations performed. Gastric campylobacter like organisms are best identified using a silver stain on biopsy material and can be reliably cultured only from gastric biopsy specimens.³ The detection of campylobacter like organisms in the volunteers' biopsy specimens would certainly be of interest, although in the absence of a gastric histological examination before their illness pre-existing colonisation by the organisms could not be excluded.

If serum were still available, a possible method of determining whether gastric campylobacter like organisms were implicated would be to look for circulating IgG and IgA antibodies both before and after the experiment. Using an enzyme linked immunosorbent assay we have shown raised IgG and IgA anticampylobacter like organism antibody titres in colonised patients.⁵ We have also shown IgA and IgM anticampylobacter like organism antibodies in the gastric juice of patients with the organisms. If they are implicated in the