simply pass through it as suggested previously. Concerning M. paratuberculosis, however, the conflicting results were reported by Elsaghib et al. They showed significantly increased antibody concentrations in M. paratuberculosis specific protein in Crohn’s disease patients. This difference might result from the antigens used for their experiments. Stainsby et al used antigens that were filtered sonicate preparations of the mycobacterial species, and as they discussed in their article, the study of humoral immunity to M. paratuberculosis in Crohn’s disease should be devoid of the cross reactive nature of mycobacterial antigens. Furthermore, Sanderson et al reported that M. paratuberculosis DNA was identified in 23 (4.3%) ulcerative colitis, and in five of 40 (12.5%) control tissues by PCR. We agree with Sanderson et al that this high percentage of identification of M. paratuberculosis in Crohn’s disease could not be explained by secondary invasion of a previously damaged mucosa. Therefore, some kinds of mycobacteria may be ubiquitously distributed in the human intestine, but M. paratuberculosis might participate in the pathogenesis of Crohn’s disease.

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In conclusion, results from all of the population based studies weigh against the hypothesis that smokers are at an increased risk of H. pylori infection. We would also not expect patient groups may be an inappropriate population in which to study this relation.

WEBB DM, MOLLER H, NEWELL (on behalf of the EUROGAST Study Group)

Reply

EDITOR,—One aim of the EUROGAST study was to identify risk factors for H. pylori seropositivity, using a common protocol to collect blood samples from representative controls from random samples of the general population in a wide range of different countries. Bateson critiques one conclusion from the study: that H. pylori infection, as assessed by serology, is not associated with smoking. He states that serology may be a poor indicator of current H. pylori infection and that the use of different populations, with different prevalence rates, precludes general conclusions concerning risk factors for H. pylori infection. The lack of association between H. pylori and smoking was seen in the whole EUROGAST population1 and not in a subgroup analysis as indicated by Bateson. Furthermore, in none of the 17 individual centres was there a statistically significant association between smoking and H. pylori seropositivity. The estimated odds ratio for smokers v non-smokers was 1·0 or higher in 10 study centres and was lower than 1·0 in 7 centres (data available on request). This conclusion is consistent with the other large, population based studies that have investigated smoking in relation to H. pylori infection assessed by serology,2 by serology and the urea breath test,3 and by serology and histology.4 The last two studies2,3 used measures of current infection in addition to serology. Moreover, there is evidence suggesting that H. pylori infection is most commonly acquired in early childhood,5—that is, before most subjects take up smoking.

Those studies that have investigated the association between H. pylori and smoking in patients undergoing endoscopy have variously reported a positive,6 negative10 or no11 association.

The use of symptomatic patients may, however, lead to a spurious, non-causal relation between H. pylori and smoking because both H. pylori infection and smoking are independently related to gastric disease, especially peptic ulceration. The separate associations between H. pylori and peptic ulceration and between smoking and peptic ulceration do not imply that there is an association between smoking and H. pylori infection. Rather, it is plausible that smoking may increase the risk of disease in an H. pylori infected subject.15 With regard to the use of serology to assess H. pylori infection the evidence suggests that, in the absence of treatment, H. pylori infections will persist for life.14 The conclusion by Meyer et al, cited by Bateson, that spontaneous eradication of H. pylori might occur in healthy subjects is not supported by the EUROGAST data. Indeed, H. pylori infection was not uncommon in healthy subjects,16 and further studies are required to establish the rate at which this infection is lost.


References
1 Avery DZ, Redonsky B, Dollfsg M, Lorai GA, Patz JK, Iacobin M, et al. Campylo-
5 Avery DZ, Redonsky B, Dollfsg M, Lorai GA, Patz JK, Iacobin M, et al. Campylo-


Aldehyde disinfectants and health in endoscopy units

EDITOR,—I read with interest this report and would accept that all workers in the endoscopy unit in an effective and common sense way. I would, however, question the statement that where an employee develops occupational asthma after exposure to glutaraldehyde and continuing exposure cannot be avoided, that the employee must be made aware of the risks of continuing exposure. The implication is that the worker is left with the choice as to whether they can continue being exposed to glutaraldehyde or leave the employment. While an occupational health department has a responsibility to advise on fitness for work. In a case where asthma has been shown to be caused by glutaraldehyde it is not reasonable to leave the decision about continuing exposure with the employee, however well informed. The employer has the responsibility for protecting an employee's health. In these circumstances redeployment and retraining may be the best outcome that an employer can expect. The report drew attention to the need for pre-employment health assessment suggesting enquiry about asthma and other conditions. The authors did not comment on whether subjects who had asthma but were employed in jobs where exposure to glutaraldehyde may occur. This is a difficult issue that seems to have been avoided.

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Reply

EDITOR.—Dr Stevens makes two main points in his letter. Firstly—what is the management of a member of the endoscopy staff who develops glutaraldehyde related asthma? secondly—what is the recommendation of the working party regarding employment of people with pre-existing asthma who will be required to work with glutaraldehyde?

We would like to point out that it was not within the remit of the working party to produce a manual detailing all health and safety policies might be implemented. It was assumed that individual hospitals will take steps to comply with COSHH regulations.

With regard to the first point, Dr Stevens has interpreted the report as leaving it up to the subject to decide whether he or she should continue to work with glutaraldehyde. We feel this is an extreme interpretation of what has been said. The report states quite clearly that the report's experts believe exposure to glutaraldehyde should be avoided, but recognises that there may be circumstances when this is not possible or desirable. We have to assume that the development of occupational asthma in a member of staff working in an endoscopy unit will inevitably involve the local occupational health department, which will make an appropriate risk assessment and also inform the hospital management. This would take away the decision from the subject and give the responsibility to management.

It is reasonable to assume that any such decision will not be made in a vacuum. If the diagnosis of occupational asthma resulting from glutaraldehyde exposure is definite and exposure to glutaraldehyde will probably continue, the employee should be removed from that working environment. If exposure can be reduced, however, and it is the considered opinion of the medical team that continuing to work in the environment is not a significant risk to the employee, and there is no suitable alternative workplace such that the subject wishes to continue working in that environment, the subject should be made aware of the pros and cons of doing so, we believe this is a suitable plan of action. The final decision would have to rest, however, with the manager of that department.

With respect to the issue of employing people with pre-existing asthma in jobs where exposure to glutaraldehyde may occur, we believe it would have been inappropriate for the working party to report that had this been the case, consistent with its stated intention to formulate recommendations rather than instructions. Once again a risk assessment would have to be carried out to take account of the degree of exposure and the likelihood of exposure to glutaraldehyde. The final judgement about fitness to work is the responsibility of an occupational physician and we did not think it was the role of the working party to preempt this.

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Correlation of PCNA with bromodeoxyuridine

EDITOR.—We noted with interest the paper by Weigert et al (Gut 1993; 34: 1587-92) on proliferation cell nuclear antigen (PCNA) and its correlation with bromodeoxyuridine (BrdU) and we like to express our reservations about their conclusions. The most important one in their decision to only count the 'strongly stained nuclei' in the PCNA assay. This necessarily makes the assay highly subjective because of the difficulty of maintaining an identical standard for every nucleus that is assessed. The assay could only become reproducible in large numbers if either all stained nuclei were counted as positive, or if some form of semi-automated sophisticated image analysis system that could differentiate stained nuclei on the basis of intensity and colour of their staining was used.

While a significant correlation between the two methods assessed has been shown, analysis has been performed on only 17 values. The correlation coefficient of 0·6 and Figure 1 shows the rather vague interrelation between PCNA and BrdU in this context. This is more important than the non-significant difference seen between the mean proliferation indices for two reasons. Firstly, there is ongoing debate about which fraction of the replicating population of cells PCNA measures—that is, the growth fraction, as in Ki67 labelling, or the S phase fraction as in tritiated thymidine or BrdU labelling. It may be dependent on the form of tissue fixation. 1-3 This study cannot identify which proliferating component has been labelled with a particular assay. Secondly, if there was a strong numerical relation between the two measured values for a given sample, then some form of paired t-test could then be used to give appro-priate p-value. No evidence is given that this sort of test has been performed in this study.

We do not feel that this paper does show a close relation between the PCNA and BrdU assays. We believe it is necessary to assess a greater number of biopsy specimens taken from a much greater number of subjects; to score all PCNA stained nuclei; and place more emphasis on the correlation between the two assays rather than the actual numerical values measured.

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Reply

EDITOR.—We appreciate the critical evaluation of this paper by Drs Wilson and Schofield. We agree with most of their comments, some of which have already been considered in the discussion of our article.

In an attempt at trying to mimic an S phase marker using only strongly stained nuclei in the PCNA assay, the evaluation procedure certainly has to be highly standardised and the best way is by use of image analysis. If this standardisation cannot be achieved there may be a case to include all labelled cells in the PCNA analysis. The inclusion of all labelled cells in the PCNA assay, however, does not result in a significant correlation between the two markers in our study. We could possibly show such a correlation with a greater number of subjects, as suggested by Wilson and Schofield, and we agree that this correlation is

