phils, the theatre staff had $221 \pm 99 \times 10^6/l$ eosinophils and the controls $79 \pm 63 \times 10^6/l$ ($P < 0.001$). When those with any kind of allergic history were excluded, a statistically significant difference remained between the groups. When the leucocyte and differential counts were checked six months later, the leucocyte count was $4900 \pm 780 \times 10^6/l$ in the theatre staff and $4500 \pm 1090 \times 10^6/l$ in the controls. The proportion of eosinophils was 0.04 ± 0.02 in the theatre staff and in the controls 0.02 ± 0.02 ($P < 0.01$), and the absolute eosinophil counts were $206 \pm 119 \times 10^6/l$ and $96 \pm 72 \times 10^6/l$ respectively ($P < 0.05$). Summer holidays of one month in the theatre staff had no effect on the leucocyte and eosinophil counts. However, when the direct chamber method of Randolph⁷ was used, the eosinophil count in the theatre staff was $132 \pm 68 (\times 10^6/l)$ and $94 \pm 67 (\times 10^6/l)$ in the controls ($P > 0.05$).

To verify the previous finding of the increased eosinophil count in the theatre staff of Loimaa Regional Hospital, we studied the operating theatre personnel of Turku University Central Hospital. They included 125 nurses and doctors (117 women and eight men). The controls were 70 nurses from the wards. The proportion of eosinophils, 0.03 ± 0.02 in the theatre staff, was higher than in the controls (0.02 ± 0.02) ($P < 0.05$); but the difference in the absolute numbers of eosinophils ($173 \pm 147 \times 10^6/l$ and $144 \pm 122 \times 10^6/l$, respectively) was not statistically significant.

This study suggests that operating theatre work increases the proportion of eosinophils. The same observation has been made by Werthmann,⁸ but in that study the eosinophil count decreased after six weeks' leave. The clinical significance of this finding remains to be established.

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Whooping cough in Shetland

SIR,—In confining his "experience" to the age group 1-4 years, Dr J D MacGregor (28 April, p 1154) is, like Dr Douglas Jenkinson (19 August 1978, p 577), selecting his data. Their overall attack rates are similar (21% and 19% respectively) but the attack rates in unvaccinated children are very different (27% and 79%). Therefore there must be differences other than vaccine protection between their selected samples. Since Dr MacGregor's sample derives from notifications, it presumably includes data from Shetland already reported to you by Dr R K Ditchburn,¹ which show an overall attack rate of 55% in the age group 1-4 and 48% in all age groups.

The truth is, as Fisher² showed in 1935, that data extracted from less than the whole of

the data are misleading if the data relate to mutually exclusive events. In ascribing significance to the differences between the attack rates in vaccinated and unvaccinated children, Drs Jenkinson and MacGregor both assume that prior probabilities of being infected are equal. Their data provide no evidence of this. If one pays attention to the origin of the 1977-8 outbreak in Shetland, as I was able to do through the kind co-operation of Drs MacGregor, Ditchburn, and others during a brief visit early in 1978, it becomes clear that the outbreak began in October 1977 in Scalloway and Walls in schoolgirls aged 8-16, most of whom had been vaccinated. Thereafter it spread to younger children and to other parts of Shetland. A total of 88 cases were notified between October 1977 and the end of that year and it is a matter of record in Lerwick that 38 (43%) of these had been fully vaccinated. Only 21 of these cases were in the 1-4 age group, but it is by no means certain that all cases in this age group were notified, nor do we know whether there was equality of exposure among them. The occurrence of whooping cough in vaccinated children can legitimately be read, other things being equal, as evidence that protection is incomplete because exposure has obviously occurred; the non-occurrence of whooping cough in vaccinated children indicates protection only when there is proof of exposure and, during the same period, occurrence of whooping cough in unvaccinated children.³

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Useless drugs

SIR,—It was sad to read the report in Minerva's column (7 April, p 961) of out-of-date and useless drugs being sent to Upper Volta.

The Edinburgh Medical Missionary Society has been operating a "Medicines for Overseas" scheme since 1969 and every item is carefully checked before being packed in 45-gallon (203-litre) steel drums. We have been most grateful to doctors, pharmacists, and others who have enabled us to send abroad an ever-increasing supply of drugs and medical supplies to the third world.

Colleagues in the Edinburgh area can hand in supplies to our headquarters at 14 Mayfield Terrace at any time (even weekends), where they will be gratefully received. We would emphasise that liquids and out-of-date drugs should not be passed on to us.

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SIR,—In 1977 when on holiday in Iran I was walking through the bazaar in Hamadan, a city in the north west of that country. My eye fell on a large tea chest full of little glass phials. These had brightly coloured labels and some had equally colourful contents. Closer inspection made it clear I had stumbled on a large cache of time-expired parenteral preparations—mostly antibiotics, mostly of

American origin, and all for sale. The stallholder was doing a brisk trade but became very excited when I tried to take a photograph and broke off his sales patter to get rid of me.

I imagined that he had collected this treasure trove from some clinic dustbin; but the variety of preparations and their apparent lack of application in such a country (a few bottles of gentamicin being the most obvious example) made me think that here was a charity "job-lot"—hence my interest in Minerva's note about the time-expired drugs arriving in Upper Volta (7 April, p 961).

Presumably then, this is the end of the line for such drugs—but I would be most interested to know what the purchasers would do with them. Drink them? Wear them on a necklace? The current state of American popularity in Iran makes me wonder whether my unfriendly stallholder is still in business.

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Aetiology of appendicitis

SIR,—May we comment on the letter by Mr F T de Dombal and Dr A H Hedley (24 March, p 820), who strongly criticised the view of Mr D P Burkitt and others that "the geographical distribution of appendicitis indicates that it is a disease associated with modern Western culture" (3 March, p 620)? The latter claim simply that while the disease is common in Western populations it is far less common or even rare in primitive or developing populations—a view with which we agree, knowing of no accurate prevalence data to the contrary.¹

Mr de Dombal and Dr Hedley listed 11 references relevant to the appendicitis experience of less privileged populations, from which they concluded that appendicitis is indeed far from rare. Unfortunately, only six of the references are currently available to us. Their reference to Indonesia² is incongruous, since the authors of the particular paper emphasised that in the city population studied appendicitis rate was "low for a community which has quite easy access to medical care." Actually, the rate is very low, only about double that of Africans living in Soweto, Johannesburg. Their reference to the experience of Africans in Nairobi³ is also inapposite. Of 1351 patients presenting with the principal complaint of abdominal pain, appendicitis was diagnosed in only 16 cases (1.2%). The authors stressed that "the low incidence of conditions comprising the acute surgical abdomen deserves note." In the references to series of patients in Nigeria,⁴ Khartoum,⁵ Basra,⁶ and Dhahran⁷ no information was given on the sizes of the populations from which the series of patients were drawn. The papers mentioned scarcely afford unequivocal evidence that there are little differences in appendicitis rates between Western and non-Western populations.

In Africans in South Africa the disease is certainly very uncommon.¹ As an example of evidence, in 1977, among 90 000 mine workers employed by Goldfields of South Africa Ltd, there were 24 cases of appendicitis—that is, 26 per 100 000.⁸ In contrast, in a Western population of somewhat similar age structure—namely, US naval personnel in the last war—the annual incidence rate was calculated to be approximately 850 per 100 000.⁹

With respect, may we make a plea? Rather than employing entirely inadequate evidence to criticise a hypothesis, would it not be more helpful to present much-needed information on the epidemiology of appendicitis as it currently occurs in Western populations? This would at least provide appropriate comparative information for the

benefit of workers in other parts of the world. In the UK in 1960-5, according to Ashley,¹⁰ evidence suggested that "some 15% of males and 18% of females are subjected to appendicectomy." What are the proportions nowadays? What is the present situation in, say, the Hebrides compared with that in London? In 1942 operation frequency in pre-OCTU student candidates was eight times higher than that in non-student young men.¹¹ Does a like disparity still prevail? Furthermore, in immigrant populations in London such as Caribbeans and Asians, what are the respective frequencies of operations among them? In the USA appendicitis incidence "has decreased 40% in 20 years, perhaps more"¹²; but from what rate to what rate?

We live in a time when the armamentarium for disease detection is far advanced and magnificent. It is therefore ironic that elementary information is almost completely lacking on a disease's precise frequency, the index of which, in a community, is more readily ascertainable than the making of an anthropometric measurement.

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Guar crispbread in the diabetic diet

SIR,—We are naturally interested in the preliminary report by Drs M Cohen and M I R Martin (3 March, p 616) of their study on the addition for three months of either a gel-forming fibre or bran or an unspecified placebo to the diet of obese "maturity-onset" diabetic outpatients, and thoroughly agree with their emphasis on the important need for long-term studies of dietary fibre supplements in diabetics. Hence we have already submitted for publication results on the first small group of diabetics taking a guar-supplemented diet continuously for six months, happily without obvious mineral deficiency.

We would like to make two main comments concerning their negative finding with guar gum. Firstly, as recently emphasised in correspondence elsewhere,¹ gel-forming fibre is likely to be markedly effective in reducing postprandial blood glucose concentrations only when it is intimately mixed with the carbohydrate portion of the food—for example, guar gum in the bread mix before cooking or extra pectin mixed into marmalade.^{2,3} We are uncertain how the guar gum was added to the diet in their study. Gel-forming fibre must be in the food, not on it, to be fully effective.

Secondly, short-term studies²⁻⁴ of gel-forming fibre have all dealt with the reduction

in postprandial (or postloading) glucose levels. The principal postulated action of guar is to effect a reduced rate of absorption of nutrient from the small bowel without causing malabsorption. Apart from the effect on satiety,⁵ there is no a priori reason to expect from this a weight change or alteration in overnight fasting glucose concentrations. If they occur, they are likely to be secondary consequences of the main action. This is also why we have looked particularly at urinary glucose values, which are so susceptible to alterations in postprandial blood glucose levels.

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Heart rate in diabetes mellitus

SIR,—There is great attraction in simplifying measurements of autonomic function. Dr G Sundkvist and others (7 April, p 924) propose a new test of heart rate variation—the "E:I ratio," which they say "seems to be as accurate as traditional tests for autonomic function and easier to perform." Although they may be right in this claim, the interpretation of the results that they have actually presented must be viewed with some caution.

They have shown clearly that the R-R interval is shortened in their diabetics with sensory neuropathy, and that R-R interval variation is also reduced. They have also shown that the E:I ratio is lower in the same subjects. But what evidence have they that the E:I ratio in these subjects is not just a function of a faster resting heart rate? None of them had any clinical symptoms of autonomic neuropathy, and although diabetics as a group have a faster heart rate than normal subjects its relation to autonomic neuropathy is obscure.

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* * * We sent a copy of this letter to the authors, whose reply is printed below.—Ed, *BMJ*.

SIR,—Dr Ewing has raised the question whether the reason for the observed abnormalities in E:I ratio (1.10 or below) among our diabetics with sensory neuropathy is due to the increase of the resting heart rate. Earlier studies,¹ however, have shown that the heart normally is inhibited by vagal tone, and defective nervous function gives rise to

tachycardia that is easily demonstrated by atropin experiments. The influence of deep breathing on heart rate (beat-to-beat variation) has also been proved to be dependent on normal vagal function.² Thus deficient beat-to-beat variation indicates vagal dysfunction and the same mechanism explains the increased heart rate in such patients. It has also been stated³ that slight impairment in beat-to-beat variation could be the earliest manifestation of neuropathy.

Our study clearly demonstrated that estimation of the E:I ratio was equivalent to the method used in these previous studies.¹⁻³ Therefore our patients probably have vagal neuropathy, which could explain their increased heart rate at rest. In diabetics with abnormal E:I values correlation analysis did not show a significant r value (0.19) between the R-R intervals at rest and E:I ratios. Furthermore, no significant correlation was found in a recent study⁴ between changes in heart rate in response to a single deep breath and mean resting supine heart rate. These results seem to contradict the idea that the increased heart rate gives the abnormal ratio.

In conclusion, our belief is that the abnormal E:I ratios are manifestations of early autonomic neuropathy in the investigated patients. But the final answer to the controversy will, of course, come during the next years when the patients are followed up.

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Heart rate variation in tetraplegic patients

SIR,—Having read the article written by Dr G Sundkvist and others (7 April, p 924) and being very interested in the analyses of heart rate variations as an easy method for the evaluation of autonomic nervous disturbances, we would like to add our experience.

Recently Neubauer and Gundersen¹ have proved that in patients with multiple sclerosis, in whom the autonomic nervous system can be involved, the mean square successive difference (MSSD) and the usual standard deviation (SD) of the R-R successive intervals in the ECG show a reduction comparable to that observed in long-term diabetics with autonomic abnormalities. We are now studying the autonomic disturbances in a group of 15 tetraplegic patients admitted to our intensive care unit because of severe respiratory failure. Ages range from 19 to 45 years, seven patients being women and eight men. The underlying diseases are a traumatic injury of the spinal cord in 12 patients, a cervical tumour in one, Heine-Medine disease in one, and cervical myelopathy in the last. The level of tetraplegia is between C4 and C6. In all these patients, as in 14 members of the medical staff (seven women and seven men) with ages ranging from 19 to 35 years, an ECG was obtained during a period of three minutes with a paper speed of 50 mm per second, measuring the lengths in millimetres of at least 150 consecutive R-R intervals. The statistical analyses of these two groups show an MSSD and SD of 1.36 and 1.77 respectively for the control group and 0.40 and 0.60 for the group of patients. This means a statistically significant difference at the level of $P < 0.00001$ when a comparison of MSSD and SD for both groups is made. We consider the measure-