which was concerned with different approaches to the medical treatment of duodenal ulcer.

No physician I know believes that medical treatment cures duodenal ulcer disease. Prolonged medical treatment is required for hypertension, epilepsy, diabetes, and myxoedema so why not in principle for duodenal ulcer too? The difference between Dr Wormsley and myself concerns the nature of that treatment.

When should medical treatment be abandoned and surgery be advised? There is little argument about the patient whose symptoms cannot be controlled medically or who has major haemorrhage. But what about the young patient whose symptoms are well controlled without complication? Many such patients do not want surgery and one has to be very confident to advise a young, largely asymptomatic patient to undergo elective surgery on the grounds that it might save his life some decades later.

The mortality from elective gastric surgery is very low but finite, and if the number of operations increases so will the number of perioperative deaths. How many deaths at the age of 30 are acceptable to prevent 100 deaths at the age of 70? The 10% mortality from upper gastrointestinal haemorrhage is largely confined to the elderly, many of whom have other major medical disorders. What would their prognosis otherwise have been and how much has the bleed curtailed life? Only a few elderly patients with bleeding may have a history of peptic ulceration, and a third to a half are likely to have been taking anti-inflammatory drugs.[1,2] They may not have had longstanding ulcers amenable to surgery many years earlier.

The recurrence rate after truncal vagotomy is low but the few patients who develop intractable diarrhoea or dumping are a major problem with little hope of satisfactory medical or surgical treatment, leading to the suggestion that the operation should be abandoned.[3] Nevertheless, it remains the commonest operation for duodenal ulcer in the United Kingdom. Why has proximal gastric vagotomy not been universally adopted? Presumably because it is technically more demanding and frequently carries a higher relapse rate.

It is unreasonable to compare relapse rates after gastric surgery with those during or after medical treatment, when repeating or changing the drug treatment will usually heal the ulcer again. Mr McCloy refers to the substantial relapse rate even on maintenance treatment but omits to mention that such relapses are rarely accompanied by complications.[4] The surgical patient who relapses has to revert to medical treatment or undergo a more radical operation associated with higher morbidity. No mention has been made of the risk of cancer after gastric surgery.[5] This may be small but it has to be considered.

We do not yet know the optimal time to recommend surgery to the patient well controlled on medical treatment but Mr McCloy's letter and the thoughtful article from his colleague[6] are welcome contributions to the debate.

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SIR,—Dr J Paul Miller's and Mr E Brian Faragher's discussion of the relapse of duodenal ulcer after different forms of treatment raises several issues.

The observation that 85% of patients initially treated with cimetidine show at least one relapse within a year compared with 59% of those treated with tripotassium di-citrato bismuthate is important. However, it is not clear in the studies referred to what the true natural relapse rate for duodenal ulcer really is, and attempts to determine this from studies including placebo treatment have failed, because too few patients have been followed up for the ensuing year. Thus relapse after treatment with tripotassium di-citrato bismuthate may represent or be close to the natural relapse rate while that after H_2 receptor antagonists may be higher. As Dr Miller and Mr Faragher point out, a gastrin mediated rebound phenomenon has never been substantiated and indeed there is some evidence that down regulation of the gastrin receptor may occur during treatment with H_2 receptor antagonists.[1]

We have recently suggested an alternative hypothesis for rebound and this may explain the difference in relapse rates, which may be related to up regulation of H_2 receptors on the parietal cell.[2] This was suggested in our study by an increased response to impromidine induced (H_2 agonist) gastric acid secretion after three months' treatment with ranitidine 150 mg at night. These findings are not surprising as there is evidence of up regulation with receptors linked to adenylate cyclase, as the H_2 receptor is on the parietal cell.[3,4] A similar rebound effect of gastric acid secretion after acute ranitidine treatment has been noted by Frislid and colleagues, who used an ingenious meal stimulus, which could be considered to be more physiological.[5] In this study this effect was observed to be present four weeks after the cessation of ranitidine treatment.

Clearly, further studies examining the increased sensitivity of the parietal cell to stimulation, the density of receptor sites after H_2 receptor antagonist therapy, and the duration of these effects are important to understanding the nature and relevance of relapse rates after treatment with receptor antagonists.

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Randomised trial of treatment of hypertension in elderly patients in primary care

SIR,—The study by Drs John Coope and Thomas S Warrender (1 November, p 1145) to determine the benefit of treating hypertension in elderly people in general practice is important because it sought to answer a clinically relevant question using the "natural laboratory" of NHS general practice.[1] Leaving aside the possibility that observer bias towards the treated patients, both in recording blood pressures and in assessing strokes, might explain the results in an unblinded study, there appears to be a statistical mistake. The authors report that "the groups were well balanced apart from a non-significant excess of smokers in the treatment group (28% *v* 21%)." Whether it is an excess in the treatment group (419 patients) or a deficit in the control group (465 patients) is speculation on the data provided. The difference is statistically significant by the usual biomedical standard: for a two tailed test of proportions, $p = 0{\cdot}015$.

But a more intriguing finding is that, while the incidence of fatal strokes was significantly reduced in the treatment group, there was a balancing excess of deaths from cancer, so the total mortality between the two groups was unchanged. The authors suggest that the excess, mainly of bronchial cancers, was "probably a fortuitous cluster." It is indeed unlikely that the higher proportion of smokers in the treatment group would account for this difference. But should the finding be ignored? Epidemiological pelmanism recalls similar "unexpected" findings in other intervention studies—for example, in heart disease, diabetes, and smoking contol.[2-4] It can be argued that the "compensating" increased mortalities are not explicable on biological grounds. Yet could there be facts here that suggest the need for a paradigm shift?[5]

Wilde has suggested, as an explanatory hypothesis, that an individual, group, or society can have a perceived level of risk that is traded against the benefits of the risky behaviour.[6] If the perceived level of risk is lower than the level accepted, other less cautious actions will be taken to balance the risks. Wilde suggests that passive changes in levels of risk will in the long run be unsuccessful: an individual or society must be internally motivated to change the level of risk. The implications for public health strategies would be to emphasise programmes that include self or group motivation and to question programmes that simply "provide" prevention—for example, through opportunistic screening or government intervention. Should we begin to debate these issues?

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Blood cyclosporin concentrations and renal allograft dysfunction

SIR,—The clinical importance of blood cyclosporin concentrations in renal transplant recipients. (Dr D W Holt and others, 25 October, p 1057) is still controversial since many problems beset the search for possible relations between cyclosporin concentrations and clinical events.

The main difficulty is that we still do not know whether trough concentrations of cyclosporin are the best predictor of renal dysfunction or if peak levels are more reliable. Furthermore, cyclosporin concentrations are frequently low in the first days after surgery and rise rapidly when the extravascular deposits are full, so that drug values

measured during this period may be an unreliable marker. For Dr Holt and colleagues to base diagnosis of cyclosporin nephrotoxicity on only the absence of obstruction or histological signs of rejection seems unsatisfactory; some characteristic histological aspects of nephrotoxicity have been described[1] that they did not mention. Moreover, the possibility of viral infections that cause renal dysfunction cannot be excluded, mainly in the first weeks after transplantation.

There is a discrepancy in the study: although its aim was to investigate the relation between the cause of renal graft dysfunction and trends in predose blood cyclosporin concentrations during the week before the episode of renal dysfunction, the authors considered the cyclosporin concentrations in the week before biopsy, and the median time between transplantation and graft biopsy was two weeks, whereas that between transplantation and rejection episodes was five weeks. Moreover, the authors do not report the daily cyclosporin dose given in the week before renal biopsy and any changes during this period. They do say that the cyclosporin dose was reduced whenever blood values were over 666 nmol/l (800 ng/ml), and a reduction might in fact favour rejection, thus explaining the occurrence of rejections in some subjects with high cyclosporin values.

We believe that details of reproducibility of the method not only at 416 nmol/l (500 ng/ml) but also at the lower and upper ends of the standard curve could usefully have been included, as well as data on a control group of patients with neither toxicity nor rejection and their mean cyclosporin levels.

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Prevalence of antibody to poliovirus

SIR,—The findings of Dr Philippa M B White and Mr Jonathan Green (1 November, p 1153) prompt us to report our findings in three separate surveys of poliovirus antibody in children in Northern Ireland.

Sera at a 1/10 or 1/8 dilution were neutralised for one hour at room temperature against 100 tissue culture infecting doses of poliovirus type 1 (Mahoney), type 2 (MEFI), and type 3 (Saukett). The tests were done in duplicate in microtitre plates using Buffalo green monkey kidney cells. The results are shown in the table.

The percentage of children without antibody to poliovirus type 1 and type 3 is higher in Northern Ireland than in England and Wales. This may be due to lower acceptance rates of live attenuated poliovirus vaccine in Northern Ireland, although the trend from 1976 to 1986 is one of improvement in immunity for poliovirus type 1 and type 2. In the neutralisation test the virus strains used and the duration of neutralisation may also affect the detection of poliovirus antibody. However, as in England and Wales, the percentage of children without poliovirus type 3 antibody remains unacceptably high and may require action by vaccine manufacturers as well as education of parents about the value of immunisation.

Results of three surveys of prevalence of poliovirus antibody in children in Northern Ireland

Year	Age (years)	No tested	Serum dilution	No without antibody to: Type 1	Type 2	Type 3	All 3 types
1976-7	1-5	100	1/10	23	12	33	7
1982	1-5	100	1/10	20	6	20	5
1985-6	2-10	100	1/8	17	2	31	2

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Assessment of non-mydriatic photography in detection of diabetic retinopathy

SIR,—Mr T Barrie and Dr A C MacCuish (15 November, p 1304) have clearly misunderstood our recent study (1 November, p 1140).

Firstly, our aim was to compare the detection rate for diabetic retinopathy of the non-mydriatic camera with those of ophthalmologists and a physician. Far from extolling the results we merely stated the findings for a small group analysed by standard statistical techniques and extrapolated to a larger population with a lower incidence of disease. The incidence of retinopathy may vary between clinics, but suggesting that the incidence is higher than 10% actually improves the calculated detection figures. Furthermore, while we certainly did not suggest that its use should replace clinical skills, we did, however, point out that studies have shown the fallibility of even ophthalmologists in assessing diabetic retinopathy.

Secondly, it is evident that Mr Barrie and Dr MacCuish, writing from a prestigious academic centre, take issue with the idea of the non-mydriatic camera being used in screening for treatable diabetic retinopathy. Inherent in the concept of screening is the ability to deal with large numbers of patients rapidly and cheaply with reasonably good specificity and sensitivity. The fact that peripheral retinal disease will be missed by the 45° non-mydriatic camera taking photographs centred on the macula was predictable and appreciated early.[2] Other possible technical limitations were recently reviewed.[3] But these deficiencies should be viewed in context. In our experience very few cases of diabetic retinopathy are entirely peripheral, and the fact that Mr Barrie and Dr MacCuish take the opportunity to quote a rare case should not be allowed to distract attention from the main argument.

Most diabetic care takes place in non-academic centres. When these facilities were recently reviewed by the British Diabetic Association it was found that 48% of clinics did not have an adequate darkroom for retinal examination and 11% lacked any access to photocoagulation.[4] In addition, the greater pool of potentially blind diabetics is found not in type I but in type II diabetics, prone to maculopathy. These may well not attend a hospital[5] let alone a retinopathy screening clinic and are less likely to be regularly reviewed.[6] In contrast, the much more manageable number of type I diabetics is more likely to be attending hospital and undergoing intensive screening for complications. We do not feel that this problem can be solved solely by urging physicians to practise with an ophthalmoscope.

Thirdly, Mr Barrie and Dr MacCuish claim that the technical failure rate (due to cataracts, small pupils, etc) for non-mydriatic photography is about 10%. This is evidently higher than our figure but is drawn from a larger experience. However, we do not see why this should exclude a role for this method in primary screening. Any technical failures could be noted and the patients recalled for screening by another method.

The place of any camera or other technique in screening for diabetic retinopathy will be earned only after largescale use under field conditions. Such studies with the non-mydriatic camera are under way in several centres.

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SIR,—We would like to add our concern to that of Mr T Barrie and Dr A C MacCuish (15 November, p 1304) at the claims made by Mr Robert Williams and others (1 November, p 1140). The authors claim a predicted negative accuracy of 99·5% in a sample which included only nine cases of proliferative retinopathy. Since diabetics with proliferative retinopathy are likely to develop more profound loss of vision and are more responsive to early treatment, any screening method that is to prove acceptable must show a high sensitivity to detecting proliferative retinopathy. After all, maculopathy by definition affects visual acuity, which will alert the individual or the examiner, and does not result in sudden catastrophic loss of vision, as does its proliferative counterpart. To include in the sample all cases of retinopathy and arrive at a sensitivity of 99·5% is therefore misleading.

Taylor and Dobree reported in a study which included 86 eyes with early proliferative retinopathy that 27% would not have disc vessels.[1] Peripheral retinal new vessels arise more frequently on the temporal side (62·5%) than on the nasal side (37·5%), but the mean distance of origin from the disc was 3·36 and 2·35 disc diameters respectively. With the 45° non-mydriatic camera the nasal vessels will not be photographed at all and the temporal vessels will be either at the edge or outside the field of photography.

Klein *et al*, studying a sample of 99 patients, claimed that 27% of proliferative cases occurred outside the area covered by the photographic field of the 45° non-mydriatic camera.[2] A further dis-