protocol with detailed estimates of staff and costs take time. By the time the protocol is considered and accepted by a grant giving body and the research staff are appointed it is quite possible that the situation will have changed. The opportunity to obtain an important baseline may have passed, or staff willing to cooperate may have moved. As long as money for health services research is dealt with in the same way as that for other research this problem will continue. We need more suitable ways of funding this research and a career structure for those involved in it.

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SIR,—Professor G A J Ayliffe (27 February, p 691) mentions that most health districts already have an effective district control of infection system.

The five Birmingham district health authorities, coterminous in boundary with Birmingham City Council and the family practitioner committee, have adopted a corporate approach to control of infection in the city. The computerised systems approach allows the most appropriate people automatically to recognise and carry out their individual functions within a managerial, legal, and professional framework which is the responsibility of the city's only medical officer for environmental health. The framework does not include executive responsibilities.

I suspect that problems have arisen not because of lack of skill or resources but because of a narrow definition of responsibility for control of infection, which the Acheson report accentuates and makes even narrower; it proposes to impose an executive authority, though it is difficult to see how such authority will be exercised—for example, over nurses, consultants, general practitioners, environmental health officers, and administrative and clerical staff.

The components of a control of infection system are becoming increasingly complex. General practitioners, with the help of community paediatricians, are increasingly taking over responsibility for immunisation and child health; environmental health officers have developed skills in various aspects of public health. Diversification is a virtue of necessity. If a metropolitan district like Birmingham finds a single medical officer for environmental health sufficient to draw together the various strands of control of infection into an effective response mechanism the need to employ officers with executive authority in each district becomes highly questionable. For Birmingham this would mean setting up five different offices, which would then have to find the resources to replace local authority activities in this area. The cost would be prohibitive.

Since the government is not afraid of diversity in achieving objectives in the public sector it should insist that individual districts should review their control of infection systems and adopt the best practices available within their existing resources but not embark on a universal adoption of the recommendations made at a time when most district health authorities have already begun to evolve effective systems in the light of the Stanley Royd and Stafford outbreaks.

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Parathyroid hormone and renal transplants

SIR,—Dr Z Varghese and others (6 February, p 393) showed that the pretransplant concentration of C terminal immunoassayable parathyroid hormone was higher in patients who subsequently had

primary non-function of a renal graft than in those whose transplant functioned. They hypothesised that parathyroid hormone may have a nephrotoxic effect on the transplanted kidney. This conclusion is unwarranted.

It is inappropriate to use an assay of C terminal parathyroid hormone in an attempt to represent biologically active parathyroid hormone concentrations in patients with renal impairment.¹ The raised mean C terminal parathyroid hormone concentration in each group reflects poor renal clearance of C terminal fragments. The authors did not show that the two groups had comparable renal function preoperatively. A method using an "intact molecule" of parathyroid hormone is the best indicator of parathyroid activity in renal disease, and this was not attempted.

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¹ Anonymous. Measuring the PTH level [Editorial]. *Lancet* 1988;i:94-5.

SIR,—Dr Z Varghese and others (6 February, p 393) base a hypothesis on an unpaired *t* test significance of <0.01. To make things even worse one of the samples has a skewed distribution. The group that had primary function had a mean immunoassayable parathyroid hormone concentration of 1760 mg/l with a standard error of the mean of 330. As *n* was 26 the standard deviation must have been at least 1650. Negative values of immunoassayable parathyroid hormone concentration have not been reported, so a substantial number of patients with primary function must have had concentrations overlapping those in the primary non-function group. If the sole evidence for the hypothesis rests on the unpaired *t* test I find it difficult to accept, particularly as the effects of anaesthesia and surgery on circulating immunoassayable parathyroid hormone concentrations have been ignored.

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AUTHORS' REPLY—We have no argument about the relative merits of measuring intact parathyroid hormone or N terminal immunoassayable parathyroid hormone fragments to assess parathyroid function in any medical condition. The point of our paper was to suggest the possibility of an interaction between parathyroid hormone and a transplanted kidney resulting in primary non-function.

Previously we have used the antiserum AS211/32 to measure the suppressibility of parathyroid glands when infusing calcium into patients undergoing maintenance dialysis. Because of the shortage of this antiserum we used a C terminal assay. We investigated a group of patients who had no residual renal function and who had been on dialysis for varying times. We have not failed to show that the two groups had comparable renal function preoperatively. Perhaps Dr Gunn is confused on this point.

The clearance rate for C terminal parathyroid hormone should be similar in both groups. Furthermore, there should be a substrate-product relation between the parent compound and its fragments. Parathyroid hormone and its various fragments have this relation in end stage renal failure, but it is preferable to measure the intact or N terminal parathyroid hormone when available.

We find it difficult to accept the various points raised by Dr Shaldon. The assay was carried out on samples collected before renal transplantation and

the effects of surgery and anaesthesia are not applicable. When a non-parametric analysis (Mann-Whitney test) was used to allow for the few high immunoassayable parathyroid hormone concentrations in the primary function group the difference between the two groups was more significant ($p < 0.003$, 95% confidence interval of 443 to 2377). The median for the primary function group was 1012 ng/l compared with 2860 ng/l for the primary non-function group.

Factors other than the immunoassayable parathyroid hormone concentration influence the incidence of primary non-function, so it is not unexpected that some patients with primary non-function have immunoassayable parathyroid hormone concentrations overlapping those in the primary non-function group. This does not invalidate our observation that patients with primary non-function had much higher immunoassayable parathyroid hormone concentrations.

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False negative colposcopic cervical biopsy

SIR,—We find it surprising that Dr M Jarmulowicz and others (13 February, p 499) were surprised by our high number of false negative results of colposcopically directed cervical biopsies (16 January, p 172). They expressed an interest in our negative biopsy rate.

During the study 1316 women were referred for evaluation of persistent cytological abnormality of the cervix. A biopsy specimen was taken from 1020 patients, in whom the whole of a colposcopically abnormal transformation zone was visualised. In 986 of these each biopsy specimen was considered adequate for histological assessment. Our paper reported the outcome in 132 of these patients in whom initial biopsy did not confirm the presence of disease. Thus our rate of negative biopsies during the study was 13%. Singer *et al*, reporting from the same unit as Dr Jarmulowicz and his colleagues, quoted a negative colposcopic biopsy rate of 23.9% in a group of patients evaluated in 1982.¹ The same unit now quotes a negative biopsy rate of 4.6% (13 February, p 500). Further comment is not possible because they did not give their false negative rate.

Dr Jarmulowicz and colleagues suggest that a possible explanation for our high negative rate could be the pathologist's inability to recognise, or reluctance to report, "minimal change papillomavirus infection." Details of grade of cervical intra-epithelial neoplasia and papillomavirus changes were not given in our short report, but it would be naive to assume that the pathologist who reported these cases, with more than 20 years' experience in gynaecological pathology, ignored or failed to recognise histological evidence of papillomavirus infection. We also find that a high proportion of our cervical biopsy material contains histological features which may reflect the presence of human papillomavirus infection. The evidence implicating koilocytotic atypia as a reliable histological index of papillomavirus infection is strong, although not conclusive.^{2,3} The evidence implicating other "minimal change" histological features such as binucleation, multinucleation, single giant nuclei, and individual cell dyskeratosis is weaker. In our unit these features are reported when present, but we would urge caution in interpreting such features, without koilocytotic atypia, as diagnostic of papillomavirus infection until more conclusive evidence is available to confirm the association.

Finally, the authors report that their practice is to perform a laser cone biopsy when cytological abnormality persists or worsens after a normal colposcopic biopsy. We share their concern that women with abnormal cervical cytology should be rigorously followed up after a negative punch biopsy. As our paper questioned the effectiveness of colposcopically directed punch biopsy in excluding disease, however, we believe that further information on the diagnostic yield of laser cone biopsy in these circumstances would be extremely valuable.

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- 1 Singer A, Walker P, Tay SK, Dyson J. Impact of introduction of colposcopy to a district general hospital. *Br Med J* 1984;289:1049-51.
- 2 Meisels A, Fortin R, Roy M. Condylomatous lesions of the cervix. II. Cytologic, colposcopic and histopathologic study. *Acta Cytol* 1977;21:379-90.
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- 4 Meisels A, Morin C, Casas-Cordero M. Human papillomavirus infection of the uterine cervix. *Int J Gynecol Pathol* 1982;1:75-94.
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Strict product liability arrives

SIR,—Ms Clare Dyer's article (27 February, p 635) on product liability raises many important points for the medical profession at large, but particularly, as she points out, for "doctors who introduce additives into intravenous infusions, which is common practice in operating theatres and intensive care units." It is vitally important that guidelines for such uses are established and accepted by both clinicians and the pharmaceutical industry at an early stage if the interests of anaesthetists and intensivists (and consequently their patients) are not to be compromised.

As supplied some drugs are unsuitable for direct administration to the patient and must be mixed with a diluent before use. Examples would be antibiotics, using a small volume of diluent, and inotropes, using a larger volume. In these cases the manufacturer usually states the diluent and dilution required, and provided these instructions are adhered to it is difficult to envisage any responsibility devolving on to the clinician. Such agents are, however, often diluted differently by individuals or units, who should confirm the suitability of their practice directly with the manufacturer. Other drugs—for example, some muscle relaxants—are supplied ready to use. It may be desirable to administer these by infusion, which can be achieved with the undiluted drug only when a suitable syringe driver is available. As this is not always the case, further dilution may be required. In these instances it would be necessary for the manufacturer to state on the datasheet suitable methods of dilution. Such practice would probably be considered a normal mode of administration rather than the constitution of a new product. The use of a simple diluent such as 0.9% sodium chloride or water for injections, and limiting such mixtures to single drugs, would minimise the likelihood of drug interactions or inactivation *in vitro*.

On the other hand, the Consumer Protection Act probably means that there is no longer any place for the ad hoc mixture of drugs in one container. Uncertainty about the resulting

pharmacological constitution, physicochemical characteristics, and stability of such mixtures will almost certainly result in their being considered new products and the clinician a producer. While this practice is unnecessary in many instances, it is widespread among anaesthetists—for example, in the use of atropine and neostigmine for reversing muscle relaxation. Some such mixtures are becoming commercially available, although they have the possible disadvantage that dosage ratios are fixed.

More generally, the widespread use of generic prescribing and dispensing, whether in hospital or general practice, inevitably makes it more difficult to keep a record of the source and batch number of a particular drug used in any patient. Anaesthetists are generally exacting in their records, yet these consist mostly of approved names, not trade names; indeed it is difficult to see how any of the proposed additional information could be recorded in practice, unless by the use of some automated system such as a barcode reader.

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Dietary management of gastroenteritis

SIR,—We are surprised that the leading article by Dr B A Wharton and others on the dietary management of gastroenteritis (13 February, p 450) dismisses the use of a low lactose special formula without mentioning the use of a milk based low lactose formula, which has been shown to speed recovery from gastroenteritis.¹ We have not seen such a dramatic reduction in lactose intolerance after gastroenteritis as the author of an editorial in the *Lancet*.²

Until three months ago our policy on the management of gastroenteritis in bottle fed infants was similar to that recommended by Dr Wharton and colleagues. We then changed our management to give 5% dextrose feeds for 12 hours followed by a full strength low lactose milk based formula (HN25, Milupa Ltd, Denham, Middlesex). This is continued for 10-14 days and then normal formula feeds are reintroduced.

In the three months since the new policy was introduced we have treated 37 infants with mild gastroenteritis not requiring intravenous therapy. The formula was well tolerated without vomiting in all but one infant. Diarrhoea ceased within 12 hours and only one infant relapsed when the special formula was stopped by the general practitioner and normal formula feeds reintroduced after only four days.

During the same period one year ago 67 infants were treated for mild gastroenteritis. In 14 infants diarrhoea returned immediately feeds were reintroduced and these were given soya based lactose free formulas. A further four infants relapsed after discharge home and required readmission to hospital. There was no difference in the average length of hospital stay of the two groups.

Our preliminary conclusion is that the use of a low lactose milk based special formula is beneficial in the treatment of mild gastroenteritis and reduces the risk of relapse of diarrhoea.

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- 2 Anonymous. What has happened to carbohydrate intolerance following gastroenteritis? [Editorial.] *Lancet* 1987;i:23-4.

Refusing to treat the indigent

SIR,—Minerva's suggestion that a patient in the USA would be asked about his hospital insurance before being given tissue plasminogen activator for acute myocardial infarction is a misunderstanding of the quotation. Usually statistical data—name, address, phone number, next of kin, social security number, insurance carrier, etc.—are asked for before treatment. In an emergency such as an acute myocardial infarction, however, the need for treatment pre-empts such information gathering.

The hospital cost of treatment with tissue plasminogen activator for acute myocardial infarction is \$2300, not the \$10 000 to \$15 000 quoted, and it is already available in an overwhelming majority of local United States hospitals.

To withhold medical care in an emergency on the grounds of inability to pay is unacceptable in American medicine. To do so would be to invite multi-million dollar malpractice suits, with the expectation of large punitive damages, and it would bring down the wrath of the local peer review organisation. The doctors concerned could be banned from treating any patient paid for by federal funds—over 40% of hospital patients—and could be reported to the state health department, which might cancel the doctor's licences to practise. Federally mandated peer review organisations examine the records of every patient who dies in hospital, along with those of all patients injured in hospital accidents, including those affected by allergic reactions to drugs and bedsores, patients readmitted within 30 days of discharge, those who make an unscheduled return for surgery, etc, along with a random sample of other patients. Sanctions are applied if the care is substandard. If a pattern of refusal to care for indigent patients were discovered the matter would be referred to the state health department, which would then impose sanctions ranging from a fine to removal of the hospital's operating certificate and closure of the hospital.

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Genetic counselling

SIR,—The two personal view articles by Professor Michael Drummond and the pseudonymous Louise Knight (20 February, p 566 and p 567) are a graphic illustration of the problems of obtaining informed consent for procedures in which the outcomes have not only low probabilities but a wide range of utilities. Your correspondents report one 38 year old woman who was not offered amniocentesis for Down's syndrome and was later worried that she might have accepted it if it had been. Another woman aged 35 was offered amniocentesis in an apparently neutral way and accepted it. She later concluded that this was the wrong decision for her since she probably values the accidental abortion of a normal child as much worse than the birth of a child with Down's syndrome. The situation was complicated in the second case because the woman became aware of a further possible risk from amniocentesis which preyed on her mind. Both women went on to deliver normal healthy babies yet were dissatisfied with the care they received. What can the obstetrician do?

Genetic counsellors do not usually know the patient's utilities before describing the possible outcomes and probabilities of a course of action. Without detailed counselling patients will often make wrong decisions because of faulty information. Counselling, however, may influence patients to make decisions not in accord with their