(or perhaps none), so long as it is backed up by some manual skill and a will to survive, should entitle the young diabetic to sympathetic consideration for renal support treatment.

Coronary and peripheral arterial disease commonly accompany long-term diabetes and may tip the balance against the decision for renal treatment. Preparatory surgical correction of major arterial obstructions and careful management to protect threatened tissues are feasible and effective in the diabetic. Though large-vessel disease certainly adds to the complexity of management, it should no longer bar consideration of renal supportive measures. The advent of continuous ambulatory peritoneal dialysis has provided an important new therapeutic option, particularly to be welcomed for the nephropathic diabetic, in whom vascular access and anticoagulation for haemodialysis present risks and problems.

In the majority of diabetics dialysis will provide temporary support only, holding the situation until renal transplantation becomes possible. The results of transplantation in the diabetic can be as good as in the non-diabetic¹ but the need is clearly for early evaluation and timely intervention, notable by its lack in the study group's report. Only two of the 19 diabetics described appear to have been under specialist nephrological care for a year or more; for the others the period of survival after referral was only months, weeks, or even days. Many diabetics (in this study an unknown number) are never even submitted for specialist renal care. The onset of persistent clinical proteinuria is a reliable marker of severe nephropathy and a forerunner of a decline in renal function, which it may precede by several years—while this decline may itself take some years to proceed to terminal failure.³ The diabetic with nephropathy, usually seen late in the course of the disease, could and should be seen earlier by the nephrologist if the prospect of a successful outcome is to be improved.

Nephrologists have accorded diabetics in renal failure comparatively low priority in the competition for available and limited resources. If they are to be asked to revise their view and take on more diabetics, they must either receive appropriate additional resources or diabetics will displace other sick people currently considered worthy of treatment. The diabetologist (or physician) must accept a collaborative role in management before and after transplantation and must co-ordinate the variety of specialised therapeutic techniques required to prepare and preserve the patient. All of this will be demanding and expensive and will require a forceful presentation of the case for change, and the provision of additional resources. There is some danger that the conclusions of the study group will be used against the argument for an active attack on diabetic renal failure and to support the view that little more can be done. In respect of diabetes the report should be read as an obsequy to the impotent past rather than as a blueprint for a constructive future.

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¹ Goetz FC, Kjellstrand CM. *Diabetologia* 1979;17:267-81.

² Diabetic Retinopathy Study Research Group. *Am J Ophthalmol* 1976;81:383.

³ Mogensen CE. *Scand J Clin Lab Invest* 1976;36:383-8.

in the United Kingdom. It is hard to see how the authors reach their conclusion that "in no instance . . . was a patient denied dialysis because of a shortage of machines." There are a number of points in addition to those raised in the leading article which cast doubt on the validity of this conclusion.

If one looks at the reasons given in the audited patient chart records for not treating persons with renal failure, phrases such as: "Question of dialysis/transplantation not raised," "Blind and mentally subnormal," "Multiple sclerosis. Wife cardiac invalid" are among those prominently featured. One wonders whether dialysis or transplantation might have been considered in such cases if the number of machines and trained personnel were larger than they presently are in the UK.

Moreover, such statements raise another pertinent issue in considering the allocation of renal therapy. It is not clear that the current reliance on home haemodialysis in many parts of the UK is the optimal mode for treating all persons suffering from renal failure. Many of the persons excluded from treatment were clearly deemed not suitable as a consequence of complicating medical conditions. Many others, however, seem to have been excluded on the grounds that no spouse was available to the patient—a circumstance that would be relevant only for home dialysis situations. The real policy questions facing the British public and medical community are: what level of service should be provided for the treatment of those suffering renal failure, should age be a criterion of relevance in allocating medical resources, and what mode of supply will best meet the needs of persons afflicted with renal insufficiency? The study group's report suggests that many of those who do not now receive dialysis or transplant therapy are not medically suitable for such therapies. The obvious question is whether a different mode of therapy (centre haemodialysis or one of the forms of peritoneal dialysis) would better meet the needs of those deemed unsuitable at present. Many of the persons who now receive treatment for renal failure in the United States would apparently not be treated in the UK—not only as a result of differences in the number of dialysis units available in the two countries but also as a consequence of different modes of supplying renal therapy.¹

Finally, the study group's report suggests that the British public is being deceived about the realities of the treatment of renal failure. The problem, it is suggested, is one not of insufficient supply but rather of the "unsuitability" of many patients. I would suggest that the public is being deceived, but not in the way the report suggests. It would seem that many of the issues of medical suitability—age, mental status, quality of life, prospects for rehabilitation—require more than medical expertise for their resolution. The hard choices that must be made in deciding where to allocate limited monies for expensive medical therapies would appear to require political, social, and moral choices to be made, which at present are being made solely by the medical profession.²

Surely the correct conclusion to draw from the Clarke-Whitfield audit is that more public involvement is required if questions of individual suitability for medical intervention are to be adequately and fairly resolved.

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¹ Caplan A. *Journal of Health Politics, Policy and Law* (in press).

² Parsons V, Lock P. *Journal of Medical Ethics* 1980;6:173-6.

be substantially fewer suitable patients here than in other developed countries. Patients are not treated because facilities are lacking, whether the shortage be of staff, space, or equipment; and it is likely that if patients are often not referred for treatment it is because these deficiencies are well known to physicians. It is also likely that progressive technical improvements are slowly increasing the number of patients who are suitable for treatment.

Obviously we would like to encourage nephrologists to treat all they think they could benefit, but one has to consider the consequences of an attempt to achieve this goal. It is surely not sensible to suggest that there should be no financial constraints on the expansion of chronic dialysis while the rest of the National Health Service is starved. Diversion of money from other fields to dialysis might not necessarily save more lives. It is equally unrealistic to expect any large increase in funding of the whole National Health Service.

It is for the doctor to advise whether or not a patient would benefit from one of the forms of renal replacement but it is not his responsibility if restrictions imposed by others for political reasons stop him giving treatment. It is also for the profession to give an opinion about the least unfair method of restriction. As a northern physician I would suggest that the dialysis population in each region be increased up to but not above the Western European average, leaving the nephrologist to select the type of patient he could help most. Decisions about the distribution of facilities are not, however, made by clinicians.

Now that the courts are prodded by pressure groups into instructing surgeons to operate on patients incapable of giving consent and against the wishes of their next-of-kin, what is the situation of a physician refusing treatment to a patient actually demanding it? It might be as well to make clear that the responsibility can lie elsewhere.

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Eosinophilia in patients undergoing dialysis

SIR,—We read with interest the recent paper by Dr Jesús Montoliu and others (27 June, p 2098) describing the appearance of peripheral blood eosinophilia among 25% of their patients undergoing haemodialysis (27 June, p 2098), a phenomenon already described by Hoy *et al.*¹

We wish to report further results in that field with four groups of patients: 66 patients with conservatively managed chronic renal failure (creatinine clearances 10-30 ml/min) (group 1), 62 patients on maintenance haemodialysis with single-use hollow-fibre cuprophane dialysers (group 2), 12 patients with end-stage chronic renal failure treated by continuous ambulatory peritoneal dialysis (group 3), and 22 control normal subjects (group 4). We found a raised absolute eosinophil count (that is, $\geq 400/\text{ml}$) in 44.4% of the patients on haemodialysis (group 2) with a mean $\pm$ SEM of $455 \pm 58.5/\text{ml}$; this was not the case in groups 1 and 3, which were not statistically different from the normal group (group 4). Furthermore, we also found high levels of IgE (normal < 100 U/ml) both in 51% of 35 among the 66 patients of group 1 (mean $\pm$ SEM: 287.3 ± 67.4 U/ml) and 33.3% of 56 among the 62 patients of group 2 (211.4 ± 48.5 U/ml) while group 3 showed normal levels that were not different from those of group 4. In patients on haemodialysis the

SIR,—For the most part I find myself in agreement with your leading article (25 July, p 261) criticising the report of the Medical Services Study Group of the Royal College of Physicians (p 283) concerning the adequacy of services for the treatment of renal failure

SIR,—The recent correspondence in your columns (22 August, p 555) makes it very clear that many more patients with end-stage renal failure in this country could benefit from renal replacement than actually receive it. It was always improbable that there would

prevalence and importance of eosinophilia, but not of the IgE levels, were correlated with the duration of the haemodialysis ($p < 0.05$); on the other hand, eosinophilia was strongly correlated with the IgE levels in that group ($p < 0.01$), but not in group 1.

In our series of eosinophilic subjects, every patient tested remained negative for parasites and ova in the stools, parasitic serology, and circulating immune complexes and in hypersensitivity skin tests; while clinically atopic and splenectomised patients had been previously excluded from the study. There were no significant differences between the patients on haemodialysis who had eosinophilia and those who did not as regards parathyroid hormone levels, number of transfusions or human albumin infusions, hepatitis B serological status, medications, age, sex, or nephropathy.

A comprehensive explanation of these findings awaits further study. Our present hypothesis is that the "uraemic state" could induce an increase in IgE levels, possibly through an impairment in cell-mediated immunity, which could be corrected by continuous ambulatory dialysis but not by haemodialysis. This increase in IgE could lead to the observed eosinophilia in patients having haemodialysis as a response to an allergen or allergens linked to the haemodialysis procedure itself. The conservatively managed chronic renal failure patients, not exposed to the hypothetical allergen or allergens, would not develop eosinophilia despite frequent elevated IgE levels. Finally, our results confirm that reuse of dialysers is not implicated in haemodialysis eosinophilia.

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¹ Hoy WE, Cestero RVM. *Journal of Dialysis* 1979;3:73-87.

Hazards of biliary tract surgery

SIR,—Your statement in the leading article on the hazards of biliary tract surgery (27 June, p 2077) that cell-mediated immunity is suppressed in jaundiced patients is not well supported, we feel, by the paper you cite as evidence. Gianni *et al*¹ added bile acids to cell cultures and in high concentrations found inhibition of lymphocyte transformation to phytohaemagglutinin and pokeweed mitogen. At concentrations frequently found in patients with cholestasis² the inhibition was far less marked, if in fact present at all.

In view of the rather artificial nature of these experiments we decided to look at the cell-mediated responsiveness of lymphocytes of patients with elevated levels of bile acids (table I). We also looked at the effect of serum from patients with raised total bile acids on

TABLE II—Effect of serum from patients with raised concentrations of bile acids on control lymphocytes in culture

Total bile acid concentration	Percentage of lymphocyte population responding to pokeweed mitogen
118.6	94.8
117.3	83.2
100.1	88.9
82.1	89.6
66.9	67.4
62.0	91.2
49.5	90.9
17.5	86.5
12.0	91.4
5.4	95.3
3.7	93.3

control lymphocytes in culture (table II). The assay method used to measure the cell mediated immune responsiveness is that of Gibbs *et al*,³ where the increase in cell size that accompanies transformation is used to determine the population of responding cells. Bile acids—deoxycholic, chenodeoxycholic, ursodeoxycholic, and cholic acid—were assayed by the gas-liquid chromatographic method described by Ross *et al*.⁴ The patients used in this study suffered from chronic liver disease, including cryptogenic cirrhosis, alcoholic liver disease, primary biliary cirrhosis, and chronic active hepatitis. None had known malignancy.

As can be seen from table I, there is no correlation between bile acid concentration and responsiveness to pokeweed mitogen and concanavalin A in the patients studied with mildly and moderately elevated total bile acid levels. Although the patients with elevated bile acid concentrations tend to have a lower population of cells responding to phytohaemagglutinin, all have percentages within the normal range for this laboratory. There was no suppression of control cell responsiveness to phytohaemagglutinin by serum containing elevated levels of bile acids (table II).

Although this is only a small study we feel that it illustrates that the suggestion that elevated bile acids make patients immunosuppressed is unproved.

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¹ Gianni L, Di Padova F, Zuin M, Podda M. *Gastroenterology* 1980;78:231-5.

² Pennington CR, Ross PE, Bouchier IAD. *Gut* 1977;18:903-8.

³ Gibbs JH, Brown RA, Robertson AJ, Potts RC, Beck J. *J Immunol Meth* 1979;25:147-58.

⁴ Ross PE, Pennington CR, Bouchier IAD. *Analytical Biochemistry* 1977;80:458-65.

Child-resistant containers: are we kidding ourselves?

SIR,—I was interested to read the report (25 July, p 271) by Dr A D Grieg and colleagues of the child who bit the bottom of a polystyrene bottle and was poisoned by eating the contents. They are clearly right in drawing attention to the apparent flimsiness of the container, and if it can be shown that this cause of poisoning occurs with increasing frequency in the future as the use of child-resistant containers becomes still more widespread the British Standards Institution would be well advised to review the existing standard (BS 1679 part 4).

At the present moment, however, I do not think that it is a common problem: as a member of the BSI committee concerned with the testing of child-resistant containers I cannot recollect any child getting into a container in this way while participating in the test protocol (which specifically allows children to use their teeth if they want to), and neither have I heard of any case similar to that reported by Dr Grieg and his colleagues. Nevertheless, a watch must be maintained; and if any doctor comes across a similar instance I would be very grateful if he could let me know.

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Pertussis vaccine

SIR,—The recent letter by my former colleagues Drs A H Griffith and D S Freestone (20 June, p 2051) raises many important points about pertussis vaccines which I feel merit further comment, especially their observation that "there are significant clinical, biological, immunological and toxicological differences between the pertussis components of various triple (DTP) vaccines used in the United Kingdom during the last 25 years."

The possibility of the existence of such differences was pointed out in the aftermath of an earlier pertussis survey in the United Kingdom,¹ but little investigation outside the statutory requirements seems to have been undertaken anywhere since then. If the statement is true it must surely call in question the value of the statutory requirements: it should be remembered that all pertussis vaccines in Europe and North America meet the relevant statutory requirements before release yet the debate about reactivity goes on.

Research on pertussis is currently aimed at isolating the mouse-protective antigen in the hope that it will give the protection needed from a pertussis vaccine without any of the current reactivity. A realistic estimate suggests, however, that such a preparation will not be generally available for several years. In the meantime we still have to live with the whole-cell vaccine.

The only statutory test concerned with the toxicity of pertussis vaccines is the mouse-toxicity or mouse-weight-gain test.² As its name implies, it indicates the degree to which a particular lot of pertussis vaccine when injected into mice affects their weight gain. It may be useful in controlling the lot-to-lot reproducibility of single strains of *Bordetella pertussis*, but to assume that it can detect the qualitative differences already mentioned—"clinical, biological, immunological, and toxicological"—is hardly acceptable. Nor is it any longer necessarily regarded as an indicator of any unique toxicity of pertussis vaccine in that in North America it is now carried out on cholera and typhoid vaccines.³

Is it not time, perhaps, to consider the use of reference or standard strains for pertussis vaccine production? This would be no new departure. One has only to think of strain 35A3, Inaba serotype, and strain 41, Ogawa serotype, used in cholera vaccine production; strain TY2 for typhoid vaccine; strain 19 for brucella abortus vaccine; strain 34F2 (Sterne) strain for anthrax vaccine; the PW8 (Park Williams) strain for diphtheria toxin; and the Mueller strain for tetanus toxin. Currently, in pertussis work one strain, 18323 or the Kendrick strain, is used throughout the world to challenge immunised mice in the potency testing of vaccines. There is no foreseeable shortage of candidate strains for vaccine production since most manufacturers tend to use their own strains. This would then suggest that there are probably 50-100 strains in regular use throughout

TABLE I—Cell-mediated response of lymphocytes of patients with raised concentrations of bile acids

Total bile acid concentration	Percentage of lymphocyte population responding		
	Phytohaemagglutinin	Pokeweed mitogen	Concanavalin A
118.6	73.3	23.2	64.4
117.3	70.4	3.15	47.0
100.1	59.0	47.3	54.9
82.1	81.1	42.0	69.6
66.9	81.6	61.4	61.6
49.5	72.3	25.5	78.0
5.4	84.1	22.2	33.2
3.7	89.3	15.5	34.3