postoperative endotoxaemia is 32%.[6] Further work should be directed at identifying those who are at risk and assessing their innate immunity in different clinical situations. If antiendotoxin is then given early, rather than after sepsis is established, the results are likely to be superior to those obtained in the trials published so far.

Comparisons can be made with the published trials of steroids in sepsis. For them to be beneficial it was thought necessary to administer steroids in the very early stages. They were deemed ineffective, though confirmatory studies were not performed. Although these two drugs are not comparable, by performing similar studies with antiendotoxins without fully understanding the events leading up to sepsis we run the risk of condemning this potentially useful treatment for the wrong reasons, spending millions in the process.

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Low protein diets in chronic renal insufficiency

SIR,—D Fouque and colleagues report a meta-analysis of the effect of low protein diets on rates of renal death in patients with renal failure of various severities.[1] They conclude that the beneficial effect, if genuine and free of bias, might be due to a reduction in the rate of progression of renal failure induced by diet or to delayed institution of renal replacement therapy consequent on an improvement in symptoms of uraemia. Although low protein diets have long been recognised to alleviate uraemic symptoms, their effects on quality of life and general physical fitness in less severe renal failure have not been adequately addressed in the papers analysed by Fouque and colleagues or elsewhere. These are crucial to the prescription and tolerance of such diets.

We assessed quality of life with the Nottingham health profile and aerobic fitness by low work cycle ergometry in 25 adults with stable renal failure (serum creatinine concentration >350 μmol/l) prescribed 0·6 g protein/kg desirable body weight/day with an energy intake of 125-145 kJ/kg/day for three months. Assessed dietary compliance was good but energy intake remained about two thirds of that prescribed. The mean (SD) baseline respiratory exchange ratio, used as an indicator of fitness, was consistent with weakness, ranging from 0·86 (0·05) at zero watts to 1·02 (0·04) at 60 W. After three months of the low protein diet a consistent improvement in respiratory exchange ratio was evident at all workloads and was significant at 20 W (0·87 (0·03) at three months *v* 0·96 (0·05) at baseline, $p<0·05$), suggesting a beneficial effect on aerobic fitness. The subjects' perceived energy, emotional reaction, and sense of social isolation as determined by the Nottingham health profile also improved significantly.

The results imply that low protein diets improve quality of life and fitness in subjects with renal failure who do not have overt uraemic symptoms. These results will be reported in detail later.

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Establishment of pregnancy after removal of sperm antibodies in vitro

SIR,—Carolyn E Grundy and colleagues report that two pregnancies occurred in three cases after sperm antibodies had been removed in vitro with immunobeads.[1]

Antibodies bind irreversibly to sperm at ejaculation, so any laboratory procedure must either cleave the F_c fragment of the antibody—for example, by use of papain, which requires a pH of 2·2, making sperm non-viable—or prevent the attachment of antibodies at ejaculation. The immunobead procedure that Grundy and colleagues used allows sperm bound to antibodies to be sequestered from those that are free and is not a technique for removing antibodies from the surface of sperm. The technique is therefore unsuitable for cases in which almost all sperm in the ejaculate are bound to antibodies.

We have been using a procedure developed by Chantler *et al*[2] and successfully tested by M Tucker *et al* (meeting of the American Fertility Society, Atlanta, October 1990), which uses carbohydrate and enzyme moieties to competitively inhibit the attachment of sperm to antibodies at ejaculation. Briefly, semen is collected in 10 ml of culture medium buffered with hydroxyethylpiperazine-ethanesulphonic acid (HEPES) containing 0·2M D-galactose and 5000 IU α chymotrypsin and allowed to stand for 30 minutes. Motile sperm are collected by centrifuging the sample on a Percoll gradient, washed once in 0·2M D-galactose, and then washed twice in culture medium buffered with HEPES. The resulting pellet of motile sperm is free of antibodies. In this way we have prevented the attachment of antibodies to sperm in 70% of cases.

We have achieved pregnancies with in vitro fertilisation in two patients, in both of whom two previous attempts at in vitro fertilisation without treatment of semen for antibodies had failed.

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Childhood mortality after a high dose of vitamin A

SIR,—In their paper on childhood mortality after a high dose of vitamin A in a high risk population Nils M P Daulaire and colleagues describe one of their objectives as determining whether periodic community wide supplementation of vitamin A could be readily incorporated into an ongoing primary health care programme.[1]

We agree with the conclusion that vitamin A supplementation improves survival in children from a harsh nutritional environment such as in Jumla, Nepal. We question the claim that the supplementation programme was readily integrated into the community health programme as the authors describe only their experience of integration with a large, single intervention research study.

The paper contains some indicators highlighting how different the community health programme is from the basic health service found elsewhere in Nepal.

Firstly, within a defined area (16 subdistricts) all households were visited every two weeks by a local lay health worker from a pneumonia case management programme. In contrast, a random cluster sample household survey in Baglung district found that only 41% of 680 households had been visited by the village health worker. A study of attendance at health posts in the same district showed that a quarter of children aged under 5 from the immediate catchment area were seen in a year and only 11% for the area as a whole.

Secondly, no nutritional services other than vitamin A supplementation were available from any source. The village health worker in the government health service, however, has the responsibility to provide health education and advise on nutrition as well as monitoring the growth of all children aged under 5.

Thirdly, 99% of all life events had been recorded. This is exceptional for any programme in rural Nepal other than an intense research programme.

We suggest that this kind of intervention is unlikely to have the same degree of protective effect elsewhere in Nepal other than in the remote mountain areas with exceptionally high levels of malnutrition. This programme could not be replicated in the present basic health service, especially in the same remote areas. An intervention of this kind should not be considered in the absence of a more comprehensive nutrition education programme in the community.

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Risk of Down's syndrome and amniocentesis rate

SIR,—Charlotte Fleming and David J Goldie highlight the problem of choosing appropriate cut off limits for the risk of Down's syndrome and raise the question of patients' acceptance of such risk and their uptake of offers of amniocentesis.[1] They quote their own experience of using maternal serum α fetoprotein concentration and maternal age in screening women aged over 30: at a cut off risk of 1 in 200 only 39% of women offered amniocentesis took up the offer, while at a cut off of 1 in 300 31% took up the offer.

One of the difficulties in translating these data beyond the confines of their screening programme is that confidence in screening that uses only maternal serum α fetoprotein concentration as the biochemical marker with maternal age is low. Several studies have shown that maternal serum α fetoprotein concentration and maternal age at best can identify only 35% of cases of Down's syndrome for a 5% false positive rate. If a combination of markers that give superior detection rates at the

same false positive rate are used[2-4] the "consumer" confidence in the risk is likely to be enhanced.

We are prospectively evaluating use of the maternal serum marker free β human chorionic gonadotrophin in a screening programme (in conjunction with maternal serum α fetoprotein concentration). Though the study is not complete, preliminary data from screening 6000 pregnancies have shown that of the nine fetuses in this population confirmed cytogenetically to have Down's syndrome, eight were identified by the screening programme—that is, a detection rate of 89%. To achieve this detection rate 330 women whose fetuses did not have the syndrome were identified as having a risk greater than 1 in 300. This is equivalent to a false positive rate of 5·5%. What is even more surprising is that of these 330 women at increased risk, 294 (89%) took up the offer of amniocentesis. This figure remained fairly constant across the bands of risk, with 91·4% uptake for a risk greater than 1 in 100, 90·8% for a risk greater than 1 in 200, and 89% for a risk greater than 1 in 250.

Clearly, rates of uptake of amniocentesis will vary as a result of many factors, of which efficiency of detection and confidence in the screening programme are but two. Clinicians and managers should be clear of the errors in making comparisons and projections from less efficient screening protocols.

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High purity factor VIII concentrates and HIV infection

SIR,—E E Mayne[1] rightly criticises John D Cash's article[2] about high potency factor VIII concentrates. Cash has caused much confusion among financial managers in the NHS, who are establishing contracts for the care of haemophilic patients against a background of direct funding for HIV infection.

The choice of the clotting factor concentrates used for replacement treatment in patients with haemophilia is one of the main considerations in their clinical management. It is of particular concern for patients with HIV infection because of the potential detrimental impact of alloantigenic proteins on the immune system. Although one previous study showed no decisive benefit,[3] there is now convincing evidence that high purity concentrates slow immunological deterioration in haemophilic patients infected with HIV.[4] Twenty asymptomatic HIV positive haemophilic patients were assigned randomly to receive a high purity product or to continue treatment with an intermediate purity product. After 96 weeks the CD4+ lymphocyte count had fallen significantly in those who had continued to receive the intermediate product but had not fallen in those receiving the high purity product; the difference in mean CD4+ counts between the two groups at the end of the study was $0·25 \times 10^9$/l. We have monitored a cohort of 111 HIV positive haemophilic patients for 11 years[5] and have shown that the differences in the rate of progression to AIDS are largely explained by differences in the rate of fall of the CD4+ count[6]; the median slope of the CD4+ count for this large group was $-0·08 \times 10^9$/l a year. Thus a difference in CD4+ count of $0·25 \times 10^9$/l represents a three year decline in an average haemophilic patient infected with HIV.

The only complication of treatment with high purity factor VIII concentrate so far has been the greater than expected prevalence of inhibitor formation, particularly in children.[7] New inhibitor formation has not been described in haemophilic patients with HIV infection: in fact, the level of inhibitor often falls in these patients.[8]

Are we justified in withholding high purity factor VIII concentrate from haemophilic patients with HIV infection? The cost of using this concentrate, which is more expensive, should be part of the overall cost of the care and treatment of HIV infection in haemophilic patients. High purity factor VIII is comparable to antiviral treatment for these patients: it is not a cure, but it does seem to delay the progression of HIV disease. In conventional medicine we would test this strategy by a larger controlled trial, but haemophilic patients with HIV infection do not live long enough to wait for the results of another study. The continuing tragedy of AIDS in haemophilic patients is a reminder of the inadequacy of delayed decision making. It will be another tragedy if we cannot afford to implement technological advances that offer optimum management of this devastating disease.

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Could an outbreak of poliomyelitis occur in the UK?

SIR,—A V Spedding and E Gradwell report a case of fatal acute poliomyelitis diagnosed at postmortem examination.[1] Though we agree with the need for examination of the spinal cord in these cases, it is important not to overlook virological investigation to search for both polioviruses and other enteroviruses that may cause poliomyelitis-like syndromes.[2] The World Health Organisation recommends that two faecal samples collected 48 hours apart, or colonic contents at postmortem examination, should be cultured for virus.[3] Neither was done in this case.

S O Cameron and colleagues express concern about the possibility of a wild poliovirus type 3 strain causing an outbreak in the United Kingdom.[4] It is difficult to assess the risk of such an outbreak in the United Kingdom and it is certainly not possible on the basis of their small, selected serological study. The most recent survey of antibodies to poliovirus, done on 995 serum samples collected in England and Wales in 1984-6, showed an overall prevalence of antibody to poliovirus type 3 of 83%.[5] Since then, however, uptake of vaccine has improved, reaching 93% by November last year.[6] Only one outbreak due to poliovirus type 3 has been reported in a well vaccinated population (in Finland[7]), and this was against a prevalence of antibody to type 3 virus in children of 60% and use of subpotent inactivated poliovaccine rather than live attenuated vaccine, as in the United Kingdom.

In England and Wales the control of poliovirus infection is monitored at two levels. Vaccine coverage is assessed quarterly through the COVER programme.[8] Information on suspected cases of poliomyelitis is obtained from four sources: notifications, laboratory reports, death certificates, and (since last year) reports to the British Paediatric Surveillance Unit. Twenty one cases of paralytic poliomyelitis were identified from 1985 to 1991, of which 13 were associated with vaccine and five were imported. The source of infection was not identified in three cases, but no wild poliovirus of indigenous origin was isolated during this period. The two deaths attributed to poliovirus infection since 1985 were both deaths of young infants with severe congenital immune deficiency who had received oral poliovaccine.

We agree with the need to consider poliomyelitis in all cases of flaccid paralysis including the Guillain-Barré syndrome. They should be investigated virologically, and cases of suspected poliomyelitis should be reported to the Communicable Disease Surveillance Centre or the Communicable Disease (Scotland) Unit at an early stage.

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Setting a strategy for health

SIR,—In discussing setting a strategy for health Alwyn Smyth rightly emphasises the social model as an alternative to the economic view of rationing.[1]

Health economists seek to maximise the health benefit per unit cost, usually on the basis of quality adjusted life years.[2] In the NHS this would inevitably result in selected low priority services being withdrawn, as has been proposed in Oregon. The social model of resource allocation, whereby everyone is deemed worthy of treatment and resources are limited across the board, has a lot more going for it. This approximates to the current