which were still being investigated at that time. It is difficult to avoid appearing partisan under the pressures of a television interview, but there are two points in Drs Van de Pette and Shirley's letter which deserve further comment.

Hospitals in this region can restock at least three times a week to a level which represents about a week's use, provided blood is available. Drs Van de Pette and Shirley imply that they required two and a half times the amount of O positive blood that they received. In fact between 12 and 18 September Frimley received 17% more than its weekly average use of O positive blood. The confusion arises because during a severe blood shortage hospitals need to ask repeatedly for blood but always get less than they request. The sum total of the requests indicates more the degree of shortage than actual needs.

Secondly, although there was a severe shortage of blood, I am confident that a telephone call to one of our consultants would have had a sympathetic hearing at any time of the day or night. We have strict protocols for recording telephone calls from hospitals and have no record of any call being received on the night of 15 September.

In reply to Professor Cash, Dr E L Harris (19 September, p 722) claims that blood is always available when "clinically necessary." This is untrue unless by "necessary" he means essential to prevent imminent death. Drs Van de Pette and Shirley indicate that surgery was having to be postponed because blood, which was clinically necessary for safe surgery, was not available. This has been fairly common in this region over the past three years and almost certainly occurs from time to time in other parts of London.

Although we have had enormous support from our colleagues in other centres, this support is in the form of blood that is surplus to local requirements because of an unexpected increase in donor turn out or a drop in hospital demands. There seems to be no mechanism for real cooperation between regions, so that a centre with spare donor resources can plan to support another centre.

A serious failing of Professor Cash's article was that it did not distinguish between the national and regional organisation of blood transfusion services. As both Dr H H Gunson (19 September, p 723), who is consultant adviser on blood transfusion to the DHSS, and Dr Harris point out, the regional blood transfusion centres provide a high standard of service to donors and first class quality blood and blood products to their hospitals. In most regions the quantity is also adequate. There is no reason for either donors or hospitals to fear for the quality of service and standard of care provided by their regional centres.

It is the national organisation of the blood transfusion service that is flawed. How is it organised? For many years the consultant adviser chaired regular meetings of regional transfusion directors held to advise him about the needs of the service as a whole. This permitted the uniformity in standards that a national service needs. This relationship ceased with the retirement of Sir William Maycock in 1979. Although the regional directors still meet, with DHSS officers present, their meetings have no official status and they do not advise Dr Gunson. He recently described these meetings, correctly but not encouragingly, as "a club."

Dr Gunson finds Professor Cash's call for a national service to be "premature and unhelpful." I am surprised at this since he knows that at each health service reorganisation, in 1974, 1982, and 1984, the regional directors came to the majority view that a national service should be formed. Pleas to the DHSS have failed twice, and Professor Cash's article will have been helpful if it prevents yet another decision for minimal change.

When the regional directors first suggested a national service in the early 1970s the DHSS response was to set up the central committee on the blood transfusion service. This body met from time to time but I doubt whether it had any real impact on the service. It was replaced in the early 1980s by the advisory committee on the blood transfusion service, which has done much to promote the redevelopment of the blood products laboratory. However, it has no managerial relationship with the meeting of transfusion directors or with the regional transfusion centres and at present it seems to meet only every year and a half.

Dr Gunson and Dr Harris cite testing for human immunodeficiency virus (HIV) infection as an example of the way the service can be made to work nationally. But they know that neither the regional directors as a group nor the DHSS has the power to force a region to fund any particular project. The funding of HIV testing was clearly something which no region could refuse but still each centre had to get the regional rubber stamp before acting. A national service could have simultaneously decided to test and agreed the funding. In this case there were no excessive delays at regional level, but this might not be so for something like the production of plasma for fractionation.

Dr Harris claims that the national objectives for plasma collection are being achieved reasonably well, but this achievement is not uniform. In the first three months of this financial year the service reached 64% of its target, but the achievement in individual centres ranged from 39% to 93%. A good start has been made but full plasma production targets have yet to be reached. Perhaps the apparent "success" of the programme is helped by the new blood products laboratory being considerably behind schedule.

No commercial company could set out to build a major manufacturing unit at a projected cost of £20m, which subsequently escalated to £60m, without ensuring supplies of the raw material it needed for processing. A commercial company leaving the management of such a resource to a committee which met less than once a year, "a club," and 15 subsidiary companies which it had no real power to direct would be judged incompetent and could quickly find itself out of business. There must be a better way to resolve conflicting regional and national interests. Regional health authorities rightly want freedom to decide their own priorities. For instance, should they channel extra funds into the transfusion service or cervical screening? They would be loath to hand over planning of the blood transfusion service to another body and then be recharged its escalating costs. On the other hand, the service needs to work a lot better nationally.

The situation in the south Thames regions suggests that national solutions may not be easy. Here there needs to be a well coordinated biregional transfusion service but this seems to present insuperable problems for the regions. There is friction over funding, management, overall planning, and coordination. If two adjacent regions cannot solve their problems what hope is there for the rest of the country? But a solution must be found.

It is time for a meaningful change and not just a spring clean. Perhaps what we need is a truly national service encompassing all four countries in the United Kingdom. This at least would allow the two fractionation units, in England and Scotland, to provide mutual support in the event of production problems and answer Professor Cash's criticism of the lack of back up for the new unit at Elstree.

K L L ROGERS

South London Regional Transfusion Centre,
London SW17 0RB

Aluminium and human albumin solutions

SIR,—Dr D Maharaj and colleagues (19 September, p 693) remind us of the presence of aluminium in albumin^{1,3} and other infusion solutions⁴ and the potential clinical consequences of such contamination, particularly in patients with impaired renal function.³

As a consequence of these reports we have undertaken a detailed and extensive investigation to identify sources of metal ion contamination during the manufacture of albumin and other plasma derivatives. We have found several sources of aluminium contamination, including the depth filters used to clarify albumin solutions and the sodium hydroxide solutions used for adjusting the pH or sodium content of the albumin.

The use of depth filtration is essential for the preparation of visually clear albumin solutions.⁵ The quantity of aluminium which can be leached from such filters into the product is reduced by extensive flushing before use. Maximum removal of aluminium can be achieved using a specially defined flush solution containing citric acid at pH 3.0. Sodium hydroxide solutions become contaminated by the leaching of aluminium from the glass containers in which the prepared solutions are stored. This can be avoided by using alternative containers made, for example, from plastic.

Despite these processing changes, some aluminium contamination still occurs during the manufacturing process. Most can be removed by introducing a diafiltration procedure, whereby small molecular weight solutes, including metal ions, pass through an ultrafiltration membrane while large molecular weight materials, such as proteins, are retained in the product solution.

Results from our study suggest that these changes in processing procedures should enable 4.5% albumin solutions to be prepared with an aluminium content of <1.0 µmol/l in contrast to the 18.3 µmol/l reported by Dr Maharaj and his colleagues for the current Scottish National Blood Transfusion Service product. We will shortly introduce these process modifications with the prospect of reducing substantially the level of aluminium and other metal ion contaminants in 4.5% and 20% albumin products.

B CUTHBERTSON
W E MCBAY
A G WELCH
R J PERRY
P R FOSTER

Scottish National Blood Transfusion Service,
Edinburgh, EH17 7QT

- 1 Elliot HL, MacDougall AI, Haase G, Cumming RLC, Gardiner PHE, Fell GS. Plasmapheresis in the treatment of dialysis encephalopathy. *Lancet* 1978;ii:940-1.
- 2 Milliner DS, Shinaberger JH, Shuman P, Coburn JW. Inadvertent aluminium administration during plasma exchange due to aluminium contamination of albumin replacement solutions. *N Engl J Med* 1985;312:165-7.
- 3 Wilhelm M, Sprenger KBG, Vossas U, Ohnesorge FK. Aluminium load in chronic intermittent plasma exchange. *Clinical Toxicology* 1987;25:209-20.
- 4 McElroy JC, D'Arcy PF. Aluminium content of infusion and irrigation fluids. *International Journal of Pharmaceutics* 1986;33:261-3.
- 5 Fiore JV, Olson WP, Holst SL. Depth filtration. In: Curling JM, ed. *Methods of plasma protein fractionation*. London: Academic Press, 1980:239-67.

Liver disease and platelet function in alcoholics

SIR,—Dr M Hillbom and colleagues (5 September, p 581) showed that abnormal platelet function in alcoholics is related to the extent of fatty liver infiltration. We did not show any obvious relation between liver histology and platelet inhibition in a similar study.^{1,2} This discrepancy may be due to differences in selection of patients or technique.

There are, however, additional factors to be considered in interpreting the findings of Dr Hillbom and coworkers.

The table indicates that 13 patients had "fatty liver" and that another 13 patients had "normal liver." Only 16 patients, however, had biopsy specimens taken (three normal and 13 showing fatty liver). Therefore the definition for 10 of the 13 patients with "normal liver" was not histologically proved but seemed to be based on serum transaminase activities less than four times higher than an unknown normal value. This classification has disadvantages as most patients with fatty liver have serum transaminase activities well below that limit.³ In a study carried out in this department serum aspartate transaminase activities (mean (SD) upper limit of reference range: 25 U/l) were: 28 (6); 31 (14); and 35 (7) U/l in patients with normal liver histology (n=7), mild to moderate fatty change (n=21), and severe fatty change (n=5) respectively (S B Rosalki, personal communication). Clearly, the considerable overlap indicates that histology remains the only acceptable form of classification. The only conclusion entirely based on histology (correlation between bleeding time and fatty infiltration) was of borderline significance and included only three patients with normal histological findings.

Abnormal platelet function in alcoholics tends to correct itself after one to two weeks' abstinence,¹ yet it is unlikely that histological appearances of the liver change considerably during this time. Therefore, a similar degree of fatty infiltration is associated with abnormal or "normal" platelet function, depending on sampling time.

Hillbom *et al* report only platelet aggregation induced by adenosine diphosphate, and others, as well as ourselves, have shown (in vitro and ex vivo studies with patients or volunteers) that this aggregation is fairly insensitive to the effects of ethanol.^{1,4,6}

Non-parametric statistical analysis of the results seems indicated as the standard deviations are often considerable (one actually exceeds the mean). It is also interesting that in primary biliary cirrhosis impaired platelet function was mainly related to thrombocytopenia and not to diminished aggregability.⁷ Others have gone as far as to state that "significant platelet dysfunction is generally not observed in patients with stable chronic liver disease."⁸

D P MIKHAILIDIS
M A BARRADAS
J Y JEREMY
P DANDONA

Metabolic Unit,
Department of Chemical Pathology and Human Metabolism,
Royal Free Hospital and School of Medicine,
London NW3 2QG

- Mikhailidis DP, Jenkins WJ, Barradas MA, Jeremy JY, Dandona P. Platelet function in chronic alcoholism. *Br Med J* 1986;293:715-8.
- Mikhailidis DP, Jenkins WJ, Barradas MA, Jeremy JY, Dandona P. Platelet function in chronic alcoholism. *Br Med J* 1986;293:1307.
- Rosalki SB. Identifying the alcoholic. In: Rosalki SB, ed. *Biochemistry of alcoholism*. Edinburgh: Churchill Livingstone, 1984:65-92.
- Pikaar NA, Wedel M, Van der Beek EJ, *et al*. Effect of moderate alcohol consumption on platelet aggregation, fibrinolysis and blood lipids. *Metabolism* 1987;36:538-43.
- Mikhailidis DP, Jeremy JY, Barradas MA, Green N, Dandona P. Effect of ethanol on vascular prostacyclin (prostaglandin I₂) synthesis, platelet aggregation and platelet thromboxane release. *Br Med J* 1983;287:1495-8.
- Mikhailidis DP, Barradas MA, Epemotu O, Dandona P. Ethanol ingestion inhibits human whole blood platelet impedance aggregation. *Am J Clin Pathol* (in press).
- Mikhailidis DP, Fonseca V, Barradas MA, *et al*. Platelet aggregation and thromboxane A₂ release in primary biliary cirrhosis and effect of D-penicillamine treatment. *Prostaglandins Leukotrienes Med* (in press).
- Stein SF, Harker LA. Kinetic and functional studies of platelets, fibrinogen and plasminogen in patients with hepatic cirrhosis. *J Lab Clin Med* 1982;99:217-30.

Effect of growth hormone on short normal children

SIR,—The study of Drs P C Hindmarsh and C G D Brook (5 September, p 573) provides food for thought but begs a few questions. How do they define "short normal"? Have they included children who were small for gestational age or children of small parents, or children suffering from socioeconomic deprivation? Some further clinical information would provide useful rumination. Further, what are their ultimate objectives (other than a wish to study the effects of bio-synthetic human growth hormone)? What was the cost in £/cm height gain? Could, for example, dietary supplementation have produced a similar 2 cm growth increment?

Which of us, by taking thought, would not wish to add a few centimetres to children's height? But can we afford the clamour, the labour (300 subcutaneous injections a year), and cost of such a campaign if applied to some 3% of the child population, who, by definition are "short normal"?

DENIS GILL

Department of Paediatrics,
Royal College of Surgeons in Ireland,
Dublin 2

SIR,—The very careful study by Drs P C Hindmarsh and C D G Brook on the response of normal short children to growth hormone made fascinating reading, although the effects of therapeutically administered growth hormone on normal children might perhaps have been predicted from the rare experiments of nature—gigantism—where supraphysiological amounts of growth hormone are present before puberty.

Of possibly more fundamental interest, however, is the philosophy of using an excess of a systemically active product to increase the height of normal children and the direction that such research might take. While Drs Hindmarsh's and Brook's interest may be confined to the academic investigation of growth hormone's actions in normal children, the interest of the general public, when it learns of their work, will almost certainly extend to demands for treatment on behalf of their short children. The public will already have read a full page article on the authors' work ("Getting High on Hormones"), which seriously confuses the issue of normal and abnormal smallness. Short children undoubtedly suffer socially and scholastically, but shortness is relative and, however great the demand for growth hormone, a third centile will never disappear and the children below it will continue to regard themselves, and be regarded medically, as short.

Because the response to growth hormone does not influence the genes for height the implications for the child of normal small parents whose heights were "normalised" by the use of growth hormone in their own childhood are doubly serious, as they will not only be genetically small but will be subject to an artificial correction factor for parental height. It will be interesting to see data of similarly high quality on the response of the sizable group of short children with reduced growth velocity for ill defined reasons—that is, data on children who are failing to achieve their genetic potential rather than those who may effectively be seeking to exceed it.

TERENCE WILKIN

Professorial Medical Unit,
Southampton General Hospital,
Southampton SO9 4XY

- Doyle C. Getting high on hormones. *Daily Telegraph* 1987 Sept 22:15 (cols 1-5).

AUTHORS' REPLY.—The comments of your correspondents were predictable. We can assure Professor Gill that, as far as possible, we excluded children who were small for gestational age or children who suffered socioeconomic deprivation. We of course included children with small parents. The object of the study was to anticipate questions which parents will ask of their doctors. The profession must be in a position to provide an answer to a parent who asks whether growth hormone will make their child taller. We submit that the science of medicine demands studies of the calibre of ours. We can assure Dr Wilkin that we are pursuing the question of the wider uses of growth hormone in the groups of children he outlines.

CHARLES G D BROOK
PETER HINDMARSH

Department of Medicine,
Middlesex Hospital,
London W1N 8AA

Ruptured abdominal aortic aneurysm presenting as ureteric colic

SIR,—We have been interested by the continuing correspondence relating to the presentation of leaking abdominal aortic aneurysm and, in particular, the confusion between abdominal aortic aneurysm and renal colic (Mr C G Moran and colleagues, 16 May, p 1279; Dr J B Roussak and Mr E R C T Owen, 25 July, p 267; Mr M J Stower and colleagues, 12 September, p 670).

Records available to us in Leeds, including those of the World Organisation of Gastroenterology's acute abdominal pain international survey,¹ show 32 cases in which leaking abdominal aortic aneurysm caused the patients to present to hospital with undiagnosed acute abdominal pain.

The table shows the initial diagnosis made in each of the 32 patients. Our data partly support the comments of others, in that there were three cases in which renal colic was the initial (erroneous) diagnosis. This, however, is not the whole study as only two fifths of patients had correct diagnoses made when first seen. A considerable variety of incorrect diagnoses were made, and in seven cases out of 32 no diagnosis at all was made by the doctor who saw the patient.

Your correspondents have thus performed a valuable service in alerting the clinician to the possibility of leaking aortic aneurysm in patients over the age of 50 with acute abdominal pain. The problem is, however, more widespread than might be imagined. In 2406 cases of acute abdominal pain in patients over the age of 50 the proportion with vascular problems (myocardial infarct, mesenteric occlusion, or leaking aneurysm) was 2%, and among those over 70 it was almost 10%. Furthermore, and no less importantly, a similar proportion had occult cancer.^{1,2}

Initial clinical diagnoses made in 32 patients presenting to hospital with acute undiagnosed abdominal pain (excluding patients presenting with vascular catastrophe)

Initial diagnosis	No (%) patients
Aneurysm	13 (41)
Renal colic	3 (9)
Perforated peptic ulcer	2 (6)
Infarct, obstruction, cancer cholecystitis, pancreatitis, NSAP,* diverticular disease	1 (3) each
No diagnosis made	7 (22)
Total	32 (100)

*NSAP is non-specific (non-surgical) abdominal pain, where symptoms rapidly resolve and no specific cause (particularly no cause warranting surgery) is found.