Effect of gentamicin on renal function (creatinine clearance) in six oliguric patients (left-hand column) and 23 patients with stable renal function (right-hand column).

associated with transplant rejection. The authors give no indication as to the renal pathology in four patients whose function deteriorated to such an extent that they required graft nephrectomy or dialysis but implied that gentamicin was the causative agent.

We suggest that there is a wide gap between the electron microscopic changes and urinary enzyme alterations induced by gentamicin and renal failure which progresses to graft nephrectomy or dialysis. The implication that gentamicin is involved in the process of total graft failure without the renal biopsy exclusion of transplant rejection is a serious one which we feel these authors have not supported with concrete evidence.

Our experience with gentamicin, guided by frequent monitoring of blood levels, has been quite different. Twenty-nine transplant patients have been treated with gentamicin, six being initially oliguric and 23 having stable renal function at different levels. The figure shows that renal function remained very low in only one oliguric patient and that in only two of the other 23 patients was there a fall in creatinine clearance during gentamicin therapy. In all three patients renal biopsy showed that the deterioration was due to severe rejection.

Taking our own results into account, we conclude that gentamicin is not a nephrotoxic drug in renal transplant patients, provided it is prescribed using a suitable nomogram and with frequent monitoring of blood levels.

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1 Wellwood, J M, et al, *British Medical Journal*, 1973, 2 261.

Heparin and acute renal failure

SIR,—The study by Dr E A Ribes and others (27 September, p 745) is of value in emphasising the hazards of full-dose heparin anticoagulation, particularly in high-risk patients, and in pointing out that obvious disseminated intravascular coagulation (DIC) carries a poor prognosis. I feel that certain comments would be of help to the general reader.

(1) The loading dose of heparin used in this study was exceptionally large.

(2) Even those who are heparin enthusiasts would be careful with obstetric, traumatic, and certain types of surgical patient. If a patient dies of a complication one cannot tell whether in that case the heparin would have been of benefit.

(3) The authors used the criteria of Colman¹ for DIC—namely, platelet count $\leq 150 \times 10^9/l$ ($\leq 150,000/mm^3$) prothrombin time ≥ 15 s, and fibrinogen ≤ 1.6 g/l (≤ 160 mg/100 ml). It is necessary to point out that these criteria select only the florid cases of DIC. Using the radiofibrinogen catabolism study I find that the catabolic rate can be increased to twice normal before coagulation criteria start to be abnormal. Indeed, the radiofibrinogen study shows that some DIC is a concomitant of almost all types of acute renal failure² and that severe DIC is commonly the result of septicæmia³ or endotoxinaemia.⁴

(4) If indeed endotoxinaemia was the principle explanation for the very high mortality in this series, then it is probably quite valid to claim that heparin only prevents cortical necrosis. In animal experiments heparin has to be in the circulation before the endotoxin for there to be any benefit. What we do not yet have are adequate endotoxin neutralising agents.⁴

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Multiple factors in the hyperlipidaemia of hypervitaminosis D

SIR,—The interesting report of an inverse correlation between serum triglyceride and calcium levels in subjects over 60 by Dr Marianne Schroll and others (26 July, p 226) does not negate the epidemiological correlation of moderate hypervitaminosis D with increased serum cholesterol reported by one of us (12 April, p 87). Clinical studies of the hyperlipaemic effects of vitamin D in healthy adults¹ are in accord with the hyperlipaemia seen in infantile hypercalcaemia,² associated with hyperreactivity to vitamin D,³ and with hypervitaminosis D in rodents.^{4,5}

Hypocalcaemia can be caused not only by vitamin D deficiency but also by magnesium deficiency. A syndrome of hypomagnesaemia-hypocalcaemia that is unresponsive to administration of either vitamin D or calcium until the magnesium deficit is repaired has been reported in neonatal infants and in adults with chronic magnesium loss or malabsorption.⁶ Magnesium deficiency has been associated with hyperlipaemia,⁶ and vitamin D excess causes magnesium loss.⁷ It is possible that magnesium deficit may have contributed to the hypertriglyceridaemia of the hypocalcaemic patients reported by Dr Schroll and her colleagues.

The lower serum lipids in patients with higher serum calcium levels suggests that they may have been on diets rich in calcium. Calcium has been shown to interfere with fat absorption, thereby lowering blood cholesterol.¹ However, in a study⁸ of dietary and serum minerals and lipids in hard- and

soft-water cities in Great Britain and the United States serum cholesterol and triglycerides were found to be higher in residents of both cities (London and Omaha) with hard water, despite the lower rates of ischaemic heart disease (IHD) there, than they were in the cities with soft water (Glasgow and Winston-Salem). In neither London nor Glasgow was the serum calcium high (2.14 and 2.18 mmol/l (8.57 and 8.70 mg/100 ml)). In both American cities the serum calcium was higher—particularly in the hard-water city (2.59 and 2.40 mmol/l (10.37 and 9.59 mg/100 ml)). Residents of both hard-water cities had higher serum magnesium levels than those of their paired soft-water cities. The difference was significant in Great Britain. (London/Glasgow, 1.25/1.07 mmol/l (2.50/2.14 mEq/l); Omaha/Winston-Salem 1.05/1.0 mmol/l (2.10/2.01 mEq/l.)) Whether the generally higher intake of calcium and vitamin D in milk in the United States than in Great Britain a contributory factor should be explored.

The possibility that magnesium deficiency might contribute both to the hyperlipaemia and the cardiovascular lesions of infantile hypercalcaemia and that deficiencies of vitamins A, B₆, and E might also participate was suggested in 1960.⁹ Reviewed elsewhere¹⁰ is further evidence that susceptibility to vitamin D excess may be intensified by deficiencies of other vitamins and of magnesium.

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"Sectorisation" in psychiatric hospitals

SIR,—I cannot allow to pass without comment Dr D A Spencer's letter (4 October, p 39) in which he questions the practicability and clinical propriety of the principles involved in sectorisation. Leaving aside the sinister connotation which he senses in implied bureaucratic and dictatorial clinical direction (increasingly I wonder whether imputation of this nature is not a means of rationalising absence of desirable initiative on the part of clinicians who should be prompting change), it seems to me totally logical and to the benefit of patients that the large psychiatric hospital should be organisationally dismembered, allowing relatively discrete communities in what is so often a catchment area with extraordinary