arrest or respiratory obstruction during "life support." The category of other medical factors includes known or presumptive renal disease, some types of long-term drug therapy, and various constitutional diseases with a nephropathic component. Where the next-of-kin categorically refuse consent or after private discussion withdraw it, we make no attempt to persuade or cajole but let the matter drop. The "miscellaneous" category of exclusion contains instances where the donor's death had such peculiarly painful and distressing overtones that to seek consent from distraught relatives would have seemed inhuman; where the donor's wishes were known in life; where no recipient could be found; and where (an important obstacle in the context of acute surgical practice) theatre time, space, and expertise could not all be stage managed at the optimal moment. Such cases were rare. Donation has never been interdicted by the coroner, but this is always a possibility. As a result of these various exclusions, only 15 (17%) of our potential donors became actual donors.

Our figures suggest that, with the best will in the world on the part of activist donor clinicians, it still cannot be expected that the kidney harvest will readily be doubled. Even if it were, the demands of recipients would not be met. Our data also give rise to speculation about why accident victims provide proportionately so many more donors and so many fewer refusals of consent than tumour and haemorrhage victims. Of the accident victims, 30% became donors, 38% being excluded because of age or cardiorespiratory factors and 8% because of refusal of consent; for the patients with intracranial tumours the corresponding proportions were 6%, 50%, and 25% and for patients with intracranial haemorrhage 7%, 60%, and 16%. Some of the reasons are obvious, others not.

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¹ Osborne DJ, Gruneberg MM. *Injury* 1979;11:3-9.

² Conference of Medical Royal Colleges and their Faculties in the United Kingdom. *Br Med J* 1979;i:332.

Renal impairment and lithium

SIR,—Diane Kimbrell and her colleagues (3 November, p 1145) have joined the argument concerning the possibility of lithium nephrotoxicity with more data on serum creatinine levels. We feel that it should be stated again that serum creatinine concentration is an inaccurate measure of renal function and that creatinine clearance at least should be quoted if at all possible. The inferences about the degree of renal impairment and the cause-effect relationship of renal impairment with lithium assessed by this means are even more tenuous. We would agree with the recent leading article in the *Lancet*¹ that there are grounds for cautious optimism in interpreting results so far obtained on the effects of lithium on the kidney.

The only satisfactory way to determine this issue is to compare a series of patients receiving prophylactic lithium with another group of patients who are matched with the lithium patients at least for age and preferably for diagnosis and also for concomitant administration of other psychotropic drugs. So far

as we know, a study of this type has not been done.

Finally, we would agree with points raised in the final paragraph. The recommended lithium concentrations quoted of 0.6-1.6 mmol/l may well be too high and may well result from earlier studies in which lithium was used as a therapeutic agent. Indeed, in our study of a group of unipolar and bipolar patients we found that successful prophylaxis could well occur at much lower concentrations, although we would point out that there seems to be a cut-off point in that our responders had an average serum lithium level of 0.69 mmol/l whereas the non-responders had an average serum concentration of 0.58 mmol/l, this difference being significant.

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¹ *Lancet* 1979;2:1056-7.

² Poole AJ, James HD, Hughes WC. *J Roy Soc Med* 1978;71:890-4.

Decline of mortality from cardiovascular diseases in North Karelia

SIR,—Dr J T Salonen and his colleagues, in their report (10 November, p 1178) on changes in morbidity and mortality during the community programme to control cardiovascular diseases in North Karelia, stated that mortality from cardiovascular diseases started to fall around 1970 both in the programme area (North Karelia) and in the control area (Kuopio county). We would like to supplement this interesting observation with findings from our recently completed studies on the development of mortality in the counties of Finland in 1961-75.

The decline of mortality from cardiovascular diseases was observed in all counties of Finland. In the western counties the decline began in the late 1960s—that is, about three years earlier than in the eastern counties such as North Karelia and Kuopio (see figure). The

beginning of the decline also was clearly earlier in urban than in rural areas.

The decline of mortality from cardiovascular diseases may be connected with changes in some exogenous or behavioural factors such as changes in dietary or other life habits, although improved treatment of cardiovascular diseases may also be involved. Our results suggest that these changes—whatever they are—have first taken place in the more urban western Finnish counties and somewhat later in more rural eastern counties such as North Karelia and Kuopio.

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Intravenous N-acetylcysteine: still the treatment of choice for paracetamol poisoning

SIR,—In their indignation at the title of our recent paper on the use of intravenous N-acetylcysteine for paracetamol poisoning (3 November, p 1097), Dr J A Vale and his colleagues (1 December, p 1435) have overlooked some important points.

They should know better than to perpetuate the commonly held but erroneous belief that patients with plasma paracetamol concentrations above our treatment line are inevitably "destined for severe hepatotoxicity." In attempts to justify this misconception (which gives a misleadingly optimistic impression of the efficacy of any treatment) they referred¹ inappropriately to studies we carried out years before our first description of a treatment line for paracetamol poisoning.² We stated clearly in our paper that severe liver damage occurred in only 58% of such patients receiving supportive therapy—survival without hepatotoxicity is not necessarily proof of efficacy of treatment. It is for this reason that we emphasised that efficacy is best assessed in patients at high risk (plasma paracetamol concentrations above a line joining semilogarithmic plots of 300 µg/ml at four hours and 45 µg/ml at 15 hours after ingestion), in whom the incidence of severe liver damage was 89% with supportive therapy alone. Only one of our 33 high-risk patients treated with intravenous N-acetylcysteine within 10 hours developed severe liver damage and it occurred in none treated within eight hours, in whom the mean maximum alanine aminotransferase concentration was only 27 IU/l. In contrast, Dr Vale and his colleagues reported severe liver damage in no less than six similarly poisoned patients given oral methionine within 10 hours—but, inexplicably, they failed to mention the total number in this group. How then can they seriously suggest that oral methionine is as effective as intravenous N-acetylcysteine? We should also point out that one of their patients developed acute renal failure despite oral methionine given within 10 hours. We have never encountered this complication with any specific intravenous therapy started within this time.

We also find it difficult to accept the apparent low incidence of vomiting before treatment (16%) in the patients described by Dr Vale and his colleagues, since in a recent prospective survey of patients requiring treatment we found that vomiting occurred before admission in 62% and in a further 15% subsequently. We wonder if this discrepancy reflects the difference between the indirect

Age-standardised mortality from cardiovascular diseases per 10 000 among males aged 35-64 in two eastern and two western counties of Finland and in the whole country in 1961-75 (three year moving averages).