programme on brain death has been followed by a further increase. The nephrologists in our three regions confirmed this general delay, but, as has been pointed out, our survey of deaths under 50 shows that there ought not to be a shortage of kidneys if they were more efficiently harvested, and patients dying from subarachnoid haemorrhage and cerebral tumour are particularly suitable. We agree that many potential donors are unsuitable for various medical reasons and that the number available is further curtailed by the reluctance of some relatives to agree to donation.

Again, there are differences of opinion among surgeons concerning the value of HLA matching, and if a complete match is insisted on this inevitably increases the wait for a graft. Nevertheless, we think that more important is the difficulty that some doctors feel in approaching relatives whose only interest (as is theirs) is in the survival of the potential donor. This sensitivity is understandable and may explain why some units (even those concerned with accidents and emergency) never produce a donor. It must also be remembered that arranging a successful donation consumes a considerable amount of the physician's or surgeon's time. Nurses with experience of nephrology and transplant units may be of great help here because of their valuable persuasive influence.

Another point of interest is that in none of the case notes of the 1168 patients who died from causes other than chronic renal failure was there any mention of a donor card, the approach always being verbal from the physician to the relatives. We appreciate, however, that the donor card may be of much more importance when carried by the victims of road traffic accidents (not included in our survey), though in France changing the law from "opting in" to "opting out" has produced no more kidneys.¹

Deaths from road traffic accidents were, of course, not part of our survey, and the proportion of the total number of kidneys donated which comes from such patients varies from one locality to another.

Other factors which doubtless reduce the number of available

kidneys are, firstly, that there are still many hospitals where the intensive care facilities and staff are scarcely adequate to provide a viable kidney and, secondly, that a high proportion of young patients dying from cerebral tumours are accommodated in hospices and hospitals for the chronic sick. A further important influence is that transplant surgery has become a highly specialised sphere of medicine. As a result surgeons in other specialties are increasingly reluctant to remove donor kidneys, and transplant teams commonly have to cover a wide geographical area.

The problem of harvesting is less in a small population served by one hospital which contains the accident and emergency, neurosurgical, renal, and transplant units, such as is found in the Grampian Area. There it is easier to arrange prompt transplantation for patients for whom such treatment is appropriate.⁵ Compared with the West Midlands and Mersey regions the numbers concerned are, however, small.

We are greatly indebted to the nephrologists and physicians in the three regions for permitting us to study their case notes and to the nephrologists and Sir Douglas Black, PRCP, for their help in compiling this paper.

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(Accepted 30 March 1981)

Lesson of the Week

Isoniazid-induced pellagra

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It is not widely realised that pellagra may develop as a consequence of isoniazid treatment. This assumes special significance in countries that have a large Indian population.

Case report

A 26-year-old Indian woman, who adhered to a vegetarian diet, developed tuberculosis in April 1980 when she was six months pregnant. She was treated with Rimactazid (rifampicin

Patients treated with isoniazid may develop pellagra

300 mg and isoniazid 150 mg) in a dose of two tablets per day. One month after having given birth at term to a normal baby she developed atypical postnatal depression that responded only poorly to treatment with amitriptyline. By November 1980, while continuing to breast-feed her baby, she had become apathetic, lost her appetite, and had tingling and shooting pains in her arms and legs, accompanied by a rash over the extensor aspects of her hands (fig 1), feet, elbows, and knees, and over the lateral malleolus of each ankle. The rash started as a

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sunburn erythema, but subsequently became hyperkeratotic, fissured, and painful. There was associated hyperkeratosis of the palms (fig 2) and soles, follicular plugging over the cheeks and nose, and glossitis.

FIG 1—Rash on dorsae of hands.

FIG 2—Hyperkeratosis of palms.

Assessment of her diet showed an average daily intake of nicotinic acid of only 13 mg, the recommended daily intake during lactation being at least 21 mg.¹ Investigations showed lowered urinary excretion of N-methyl nicotinamide (1.0 mmol/mol creatinine; normal >1.3) and raised urinary excretion of kynurenine (3.9 mmol/mol creatinine; normal <2). The sulphadimidine load test showed that she was a slow acetylator.

After substituting ethambutol for isoniazid and giving her nicotinic acid supplementation her rash and glossitis resolved rapidly and her mood improved.

Comment

Although it is well known that pyridoxine deficiency may develop in patients taking isoniazid, it is much less widely known that a deficiency in nicotinic acid may also occur. Acute pellagra was first described as a complication of treatment with isoniazid (isonicotinic acid hydrazide) in 1952,² and there have

been several reports since. Only two of the data sheets that accompany the five commercially available preparations of isoniazid mention this side effect, however (Rimifon, Roche Products Ltd; Inapasade, Smith Kline and French Laboratories Ltd).

Conversion of tryptophan to nicotinic acid is dependent upon the enzyme kynureninase and its cofactor, pyridoxal phosphate (a derivative of pyridoxine). A complex is formed between isoniazid and pyridoxal phosphate, thereby reducing the synthesis of nicotinic acid.³ In common with chloramphenicol, penicillamine, hydralazine, and alcohol, isoniazid increases the requirement for pyridoxine,⁴ however pyridoxine supplementation alone may not be capable of preventing the onset of pellagra.³

The rate of metabolism of isoniazid varies considerably between fast and slow acetylators with the result that slow acetylators are more likely to develop peripheral neuropathy due to pyridoxine deficiency,⁵ and to suffer from other side effects.⁶ Out of six cases of isoniazid-induced acne (one of whom also developed pellagra), five were slow acetylators.⁷ The prevalence of slow acetylators in different racial populations also varies; 5% of Eskimos,⁸ 48% of Europeans,⁹ and 60% of Indians¹⁰ are slow acetylators.

The most recent national survey showed that Indians accounted for 24% of notified cases of tuberculosis in England and Wales.¹¹ The high prevalence of a vegetarian diet and a slow-acetylator phenotype among Indians means that they are at particular risk of developing pellagra as a complication of isoniazid treatment. As a quarter of all cases of tuberculosis in England and Wales occur in Indians the importance of this easily avoidable complication of antituberculosis treatment cannot be overemphasised. Despite adequate pyridoxine supplementation, isoniazid may unmask pellagra, and we conclude that nicotinic acid supplementation should be considered for all Indian patients receiving isoniazid.

We are grateful to Dr D A Bender and Professor S E Smith for their help in investigating this patient.

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(Accepted 1 May 1981)