to provide permanent protection for the population living in the area.—I am, etc.,

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Alpha-fetoprotein and Rh Alloimmunization

SIR—An increase in alpha-fetoprotein (AFP) has been reported in amniotic fluid from fetuses with fetal distress, including fetal distress of Rh alloimmune origin.^{1,2}

We have assayed by radioimmunoassay³ specimens of amniotic fluid from a number of Rh alloimmune pregnant women and report the results of the assay of: (1) 72 specimens from 46 women with 27-42-week-old normal or subnormal fetuses and (2) 27 specimens from 12 women with 27-38-week-old fetuses with severe haemolytic anaemia which, 3-14 days after amniocentesis, either died or required intrauterine blood transfusion or were born with levels of haemoglobin below 10 g/100 ml. Results of AFP determinations are shown in the figure.

Amniotic AFP determination at various gestational ages in cases of severe Rh alloimmunization (X) and normal controls and/or mild cases (●). Means represented by horizontal bars (—).

There was an overall tendency to higher levels in the groups of fetuses with severe alloimmune anaemia, at least until the 36th week of gestation before which most of our specimens were taken.

From a practical point of view, we think that because of wide individual variations and consequent overlapping with controls, AFP determinations on amniotic fluid from Rh alloimmune pregnant women provides less information than bilirubin determination.

We also think that recent observations by Whyley *et al.*⁴ of significant AFP increase in the amniotic fluid of pregnant women whose fetuses did not survive may be explained by the AFP rise which takes place shortly before fetal death.—We are, etc.,

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Renal Amyloidosis in Chronic Granulomatous Disease

SIR—The association of chronic granulomatous disease and amyloidosis has not been previously documented. We report the development of renal amyloidosis in a boy with long-standing chronic granulomatous disease.

The patient had had recurrent bacterial infections, particularly with *Staphylococcus aureus* and *Salmonella typhimurium*, from the age of 8 months. The diagnosis of chronic granulomatous disease, the subject of a previous report,¹ was made at the age of 10 years on the basis of a nitroblue-tetrazolium test and cutaneous granulomas.

He presented at the age of 16 years with a pure nephrotic syndrome (oedema, serum albumin 2 g/100 ml, serum cholesterol 260 mg/100 ml, proteinuria 2 g/24 hr) without microscopic haematuria or hypertension. In contrast to his previous hypergammaglobulinaemia, low levels of serum immunoglobulins (IgG 146 mg/100 ml) with elevated urinary levels (IgG 450 mg/l.) were observed. Long-standing *S. typhimurium* septicaemia responded to rifampicin. Oedema was controlled by diuretics and a low-sodium diet. Renal biopsy revealed renal amyloidosis, predominantly glomerular but also involving interstitial, peritubular, and vascular structures.

Recent studies indicate that amyloidosis is largely composed of fragments of kappa light chains.² In patients with chronic suppuration amyloidosis has been attributed to prolonged antigenic stimulation producing excessive immunoglobulin synthesis with deposition of immunoglobulin fragments as amyloid material.³

Continuing antigenic stimulation is the most likely mechanism of amyloid production in this patient. Immune function is normal in chronic granulomatous disease⁴ and Gram-negative endotoxin has been shown experimentally to stimulate amyloid formation.⁵ Alternatively, abnormal immunoglobulin catabolism may be involved, as in hypogammaglobulinaemia or agammaglobulinaemia,⁶ or dysfunction of the reticuloendothelial system.⁷

In vitro amyloid can be phagocytosed by leucocytes⁸ and the reticuloendothelial system⁹ and this is probably the mechanism of the regression of amyloid deposits reported in liver and kidney.¹⁰ Defective catabolism of immunoglobulins and amyloid substance might also occur in chronic granulomatous disease, in which phagocytic degradative activity is known to be defective, in both leucocytes¹¹ and the reticuloendothelial system,¹² particularly in respect of bacterial phagocytosis.—We are, etc.,

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Haemodialysis and Forced Diuresis for Tricyclic Antidepressant Poisoning

SIR—The encouraging experience of Drs. H. W. Asbach and H. W. Schüler (18 May, p. 386) in using haemodialysis for the treatment of two young children with severe imipramine poisoning has stimulated us to report a recent dramatic clinical success we have had in an adult who took a massive overdose of tricyclic antidepressants.

A 50-year-old woman with a long history of depression ingested a large quantity (precise number of tablets not known) of imipramine and amitriptyline, possibly with a few tablets of opi-pramol, trifluoperazine, haloperidol and thiothixene. About six hours later she was admitted to hospital deeply comatose, areflexic, and hypothermic, with a sinus tachycardia and a systolic blood pressure of 80-90 mm Hg. An electrocardiograph showed an intraventricular conduction defect. The patient was intubated and given gastric lavage. She was treated with continuous gastric aspiration, body warming, intermittent positive pressure respiration, and a noradrenaline infusion. Forced diuresis was commenced through the central venous pressure line.

Nine hours after admission the patient had shown no signs of clinical improvement and it was decided to commence haemodialysis. An arterio-venous shunt was placed in her leg and dialysis started using two hollow fibre kidneys in parallel (dialysate flow rate 500 ml/min; arterial flow rate 150 ml/min) and a standard dialysate solution. Dialysis was continued for six hours. Within four hours of commencing dialysis the vital signs improved significantly and there was a definite improvement in the level of consciousness. This improvement was maintained over the next 48 hours and the patient made a full recovery.

Chemical analyses of the gastric lavage showed the presence of a large amount of imipramine and amitriptyline and a very small quantity of a phenothiazine. Plasma imipramine levels were determined by a modification of the method of Grove and Halliwell.¹ No attempt was made to distinguish between imipramine and its fluorescent metabolites and results are reported as imipramine. Samples were taken soon after admission and during the period of haemodialysis. The plasma imipramine level fell from 6.3 µmol/l. to 1.7 µmol/l. within 14 hours. These results are shown in the figure. According to Niyogi,² 1.7 µmol/l. is the upper limit of the therapeutic range for plasma imipramine.

During the period of forced diuresis the urine volume was 23,370 ml, and contained 151.5 µmol (43 mg) of imipramine. No imipramine was detected in the dialysate when it was analysed by the same method as used for plasma. A 20-fold