but collectively they are significant and hence appropriate investigations should be considered. It is particularly important to consider IMD where more than one case of hydrops occurs in the same family or if there is a history of spontaneous abortion or unexplained deaths in close family members. We would like to describe our protocol for the investigation of fetal and neonatal hydrops for IMD. These investigations are considered when the more common causes of hydrops have been excluded.

From the dead fetus a skin biopsy can be taken for culture. This should be taken as soon as possible. The cultured cells can be assayed for β -galactosidase (GM1 gangliosidosis, Morquio's disease type B, galactosialidosis), β -glucuronidase (Sly's disease), β -glucosidase (Gaucher's disease), α -neuraminidase (mucopolipidosis I), *N*-acetylgalactosamine-6-sulphate sulphatase (Morquio's disease type A), sialic acid (sialic aciduria) and cholesterol esterification (Niemann-Pick C). DNA from the cultured cells can be investigated for the expanded trinucleotide repeat sequence found in myotonic dystrophy.

In cases where hydrops has been diagnosed antenatally amniotic fluid can be tested for I-cell disease and some mucopolysaccharide disorders. Other assays can be undertaken on cultured amniotic fluid cells or chorionic villus tissue (direct or cultured). In the live neonate investigations which can be performed on blood include pyruvate kinase, plasma lysosomal enzymes, plasma carnitine, iron, and ferritin (neonatal haemochromatosis). A skin biopsy may be preferable if a large number of lysosomal enzyme assays are to be assayed. A random urine specimen (10 ml) can be investigated by mucopolysaccharide electrophoresis and oligosaccharide chromatography. Liver tissue may be of value for liver iron quantitation and possibly also for enzyme assays. If liver is to be taken, it should be frozen immediately and stored below -20°C .

While not all these tests will be indicated on every case of hydrops it is important to consider inborn errors of metabolism as a cause of non-immune hydrops and to collect appropriate specimens for investigations where indicated. Hence discussion with a specialist centre for inherited metabolic disorders is important.

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Do maternal β -sympathomimetics influence the development of retinopathy in the premature infant?

EDITOR,—Recent studies suggest that a number of factors other than the injudicious delivery of oxygen contribute to the development of retinopathy in the premature infant.^{1,2} One hundred and fifty infants on our neonatal unit who required oxygen treatment for more than 60 days were reviewed retrospectively in order to determine the range of factors contributing to this pathol-

ogy. All infants requiring oxygen for more than two weeks were examined at two weekly intervals by an ophthalmic surgeon (ES). Fourteen cases of retinopathy greater than stage 3 were identified. These patients were matched for gestation (± 1 week), birth weight (± 50 g), sex, and ethnic group with infants who had oxygen requirements for more than 60 days, but did not have retinopathy. The two sets of cases showed no significant differences in their Apgar scores, requirement for exchange transfusions, or the incidence of clinically significant patent ductus arteriosus.

Mothers of eight of the retinopathy group had received infusions of β -sympathomimetics (seven ritodrine, one salbutamol) to arrest premature labour: only one of the non-retinopathy group had received ritodrine ($p < 0.008$). This observation may be of physiological importance, as animal experiments have suggested that the retinal circulation is strongly influenced by these pharmacological agents acting jointly through the sympathetic nervous system and endothelial factors.³ β -Sympathomimetics are known to induce transient ischaemic changes in the myocardium of the newborn if given over long periods by inducing vasospasm.⁴ Maternal ritodrine has been associated with reduced blood pressure in the newborn.^{5,6} In the premature infant in whom antenatal retinal perfusion is influenced by β -sympathomimetics, there may therefore be a predisposition to damage by other factors, including inappropriate oxygen tensions. This combination of insults to retinal perfusion could lead to the development of ischaemia, and predispose to retinopathy of prematurity. This observation merits review in a larger series of infants. Further, it casts doubt as to the safety of β -sympathomimetics which are widely used in the therapy of premature labour with little evidence to support their efficacy.

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Immunisation and C reactive protein in infants on neonatal intensive care units

EDITOR,—C reactive protein estimation is a well known indirect method of detecting bacterial infection in neonates.¹ Premature infants on our neonatal unit receive their primary course of immunisation for diphtheria, pertussis, tetanus and *Haemophilus*

influenzae b as per the immunisation schedule at two, three, and four months postnatally.²

Plasma C reactive protein estimation is performed as part of a weekly or daily infection surveillance. Serial estimations are continued in infants with an increased concentration (normal < 4 mg/l). We noticed, as an incidental finding, that values increased within 24 hours of immunisation.

During a period of three months (November 1993 to January 1994) 12 babies had C reactive protein estimations before and after immunisation. The median value preimmunisation was < 4 mg/l (range $< 4-7.1$). Postimmunisation the concentrations increased in all of the 12 babies. The median value at 24 hours postimmunisation was 10.3 mg/l (range 8.0-47.1), and at 48 hours the median value was 18 mg/l (range 4.2-48.6). The median duration of increased C reactive protein was two days. During the initial period of the study one of the babies had a full infection screen based on the raised C reactive protein and clinical findings (systemically unwell, postimmunisation).

Plasma C reactive protein is known to increase after immunisation with diphtheria, pertussis, and tetanus vaccines in malnourished children after nutritional recovery.³ To the best of our knowledge it has not been reported in premature infants who have been immunised. It is important to realise that immunisation leads to an increase in the plasma C reactive protein concentrations so that unnecessary investigations may be avoided.

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Diagnosis and management of non-immune hydrops in the newborn

EDITOR,—The article by Stephenson and colleagues concerning the diagnosis and management of non-immune fetal hydrops was both informative and concise; the table of reported associations was particularly thorough.¹ I would like to make a minor point regarding the inclusion of asplenia syndrome among the cardiovascular associations.

Asplenia syndrome (right atrial isomerism) is characterised by complex cardiac defects including primitive atrioventricular septal defects and pulmonary atresia,² both of which are listed in Stephenson's table 1.¹ Nevertheless, it is far more common to see polysplenia syndrome (left atrial isomerism) in association with fetal hydrops.^{3,4} Left atrial isomerism is well associated with complete atrioventricular block, as well as other structural cardiac lesions.³ Complete heart block can occur, rarely, in right atrial isomerism, as in one case in Schmidt's study