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 is discovered in the same family or community. It is a history of spontaneous abortion or unexplained deaths in close family members. We would like to describe our protocol for the investigation of foetal and neonatal hydrops for IMD. Investigations are considered when the more common causes of hydrops have been excluded.

From the dead fetus a skin biopsy can be taken for this should be undertaken 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 (musculopathy I), N-acetylgalactosamine-6-sulphate phosphatase (Morquio’s disease type A), sialic acid (sialic aciduria) and cholesterol esterification (Niemann-Pick C). DNA from the cultured cells can be investigated for an 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 or other family members for trisomy 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 can be investigated for mucopolysaccharidosis 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 informally the infants 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 pathology. 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 infusions.4 Malignant hypotensive syndrome, which has been associated with blood pressure in the newborn,5 6 is a complication of foetal life in which renal ischaemia and predispose to retinopathy.6 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 diptheria, 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 prior to immunisation was 0.6 mg/l (range 0.4–1.1), and at 24 hours the median value was 18 mg/l (range 1.4–48.6). 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 towards nutritional recovery.1 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 interesting. However, a closer look at the commented letters revealed that a number 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 stenosis, and is usually listed as a group which are listed in Stephenson’s table 1. Nevertheless, it is far more common to see polysplenia syndrome (left atrial isomerism) associated with fetal hydrops.2 3 Left atrial isomerism is well known to involve the 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.
(v 17 cases with left atrial isomerism).2 It is thought that the fetal bradycardia and/or structural cardiac lesions contribute to low cardiac output and consequent hydrops, with a dismal prognosis.3-5 After browsing the literature, I remain perplexed that right atrial isomerism is detected so infrequently in utero, given the typical severity of its lesions. However, the current data from fetal echocardiography centres indicate that left atrial isomerism accounts for many more cases of fetal hydrops than right atrial isomerism. Apparently, it is the combination of heart block with structural cardiac defects which puts the fetus at high risk for hydrops, as the prognosis is much better for heart block without structural abnormalities.3 4

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Cerebral autoregulation of preterm neonates – a non-linear control system?

EDITOR.—We read with interest the detailed paper of Zernikow et al on cerebral autoregulation of preterm neonates.1 However we would caution against the use of the term autoregulation. This term implies maintaining a constant cerebral perfusion in the face of a changing cerebral perfusion pressure.2 The slow wave cycles we, and others, have described in the cerebral blood flow velocity values occur independently of blood pressure and are indices of velocity and not flow.3 They undoubtedly reflect some underlying physiological control but it would be incorrect to describe this as autoregulation.

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Professor Jorch and coauthors comment:

We use the term 'autoregulation' in a more general meaning to describe the autonomous regulation of cerebral haemodynamics. It addresses the complexity of regulation, is not limited to the mean arterial blood pressure—cerebral blood flow autoregulation relationship, and the regulatory result is not necessarily the constancy of cerebral blood flow.1 If this was not clear from our paper, we thank Dr Anthony and Professor Levene for their comment.