importance in patients with discoid lupus erythematous. Unfortunately it is neither pathognomonic nor specific for lupus erythematous, but, if perfected, it may become a useful test of other disorders in which hypersensitivity plays a part.

Heredity in Club Foot

Uncomplicated club foot appears at first sight to be purely an effect of intrauterine posture and pressure. Against this, however, is the difficulty with which some patients are treated and their tendency to relapse. A study of twins in Germany first showed clearly that genetic factors must play a part, for of identical twins with club foot both were found to be much more often affected (33%) than among fraternal twins (3%). In addition, the fact that in many pairs of identical twins only one was affected showed that genetic factors were only part of the aetiology.

Until recently no good family studies have been available, only series based on questionnaires or routine inquiry in the hospital outpatient department. Now, however, Ruth Wynne-Davies has made a thorough family study from the Orthopaedic Hospital at Exeter, which serves most of the county of Devon apart from Plymouth. The series covers patients who attended the hospital over a period of 20 years in the case of talipes equinovarus and 15 years in the case of other forms of club foot.

There was a substantial familial concentration for talipes equinovarus. About 2% (12 out of 560) of first-degree relatives (parents and sibs) were similarly affected, compared with the population incidence of 0.12%. This is about a 20-fold increase. It is of interest that the relatives of the rarer female index patients were more often affected than the relatives of the male patients. Second-degree relatives (aunts and uncles) had a proportion affected of about six times, and third-degree relatives (first cousins) about twice the incidence in the general population.

Other forms of talipes on rather smaller series showed a similar concentration among relatives. In addition the family findings suggested an association of talipes equinovarus with metatarsus varus, postural equinovarus, and calcaneo-valgus. Talipes calcaneo-valgus showed the usual association with congenital dislocation of the hip, and, like the latter condition, occurred especially often in first-born babies. Unfortunately Wynne-Davies had no information on the proportion of breech births in any of the groups. Both talipes equinovarus and calcaneo-valgus, but not metatarsus varus, showed an association with generalized joint laxity, and the two former conditions were also associated with inguinal hernia.

Family patterns of the type shown by club foot are best interpreted in terms of a genetic predisposition, governed by a multiplicity of genes, interacting with intrauterine environmental factors. Nothing is yet known of the nature of the genetic or the environmental factors. But the fact that the proportion of parents affected is similar to that of sibs indicates that the intrauterine environmental factors, presumably postural, are not such that they tend to persist from one pregnancy to the next. Although data on the proportion of breech-born babies are missing from the Exeter inquiry, the association with congenital dislocation of the hip suggests that the posture associated with breech malposition is important in causing talipes calcaneo-valgus, though perhaps not equinovarus.

Genetic counselling of parents may be based on the empirical finding that the risk of normal parents who have had one child with talipes equinovarus having a second affected child in the next pregnancy is about 1 in 50. The risk of an affected parent having an affected child is about the same. If there is already more than one affected person in the family the risk is increased.

Thrombosis in the Newborn

Though newborn babies do not often suffer from thrombosis, the fact that they do occasionally has recently become of importance for two reasons. First, the recognition that unilateral renal-vein thrombosis can be treated successfully has given a special urgency to the diagnosis of it. Secondly, the increasing use of intravenous therapy for premature babies with the respiratory distress syndrome or neonatal hypoglycaemia has posed the question whether it makes intravascular thromboses more common than they used to be. Some workers feel that the use of the umbilical vessels is particularly hazardous, while others believe that the risk is offset by the speed at which dehydration and consequent haemoconcentration can be reduced.

Thromboses of the dural sinus and cerebral veins may occur in older infants in association with dehydration or sepsis, but in the newborn they tend to be a consequence of birth trauma. Adrenal haemorrhage with or without thrombosis may follow distress at birth, but renal-vein thrombosis is commoner. It may occur in combination with an infection, especially in cases of gastro-enteritis with additional dehydration. The infant becomes acutely ill, cries constantly, refuses to feed, and shows a fever. There may be haematuria, oliguria, and a rising blood urea in association with a renal mass. In accordance with the extent of the process the infant may die within a few hours or may develop a nephrotic syndrome, with massive proteinuria and increasing oedema.

M. E. Avery and colleagues drew attention to the fact that renal-vein thrombosis is commoner in babies of diabetic mothers than in general. A. Takeuchi and K. Benirschke confirmed this when they reviewed the necropsy records of 16 babies who died of renal-vein thrombosis in Boston. Of these 16 six were stillborn and eight died before the third day. In one baby a mass in one flank was palpated shortly after delivery, but despite nephrectomy he died at 12 days. The thrombotic process probably began before birth in all but one of these infants; five of the mothers had diabetes and there was evidence suggestive of prediabetes in a further seven. The authors of this report suggest that the hyperglycaemia causes polyuria, with a consequent haemoconcentration and slowing of renal blood flow. Perhaps a similar mechanism accounts for the occlusion of large vessels of the chorionic plate sometimes found in babies of diabetic mothers.

L. Jørgensen and colleagues reported the case of an infant delivered by caesarean section in whom a mass was felt at birth and in whom a successful nephrectomy was performed. An interesting case is described by A.-J. Bret and colleagues. Some 19 days before delivery a woman had a placental
haemorrhage which necessitated transfusion, and the baby, delivered by caesarean section, lived only 17 hours. At necropsy there were old organized thrombi in the renal vein which probably occurred at the time of the maternal haemorrhage.

Further confirmation of the role of maternal diabetes in the causation of neonatal thromboses comes from E. H. Oppenheimer and J. R. Esterly. They analysed the records of 4,000 infants who died under the age of 2 weeks in Baltimore between 1933 and 1964. Thromboses were found in 45 cases, 15.8% occurring in babies whose mothers had diabetes, while the overall incidence was only 1.1%. The majority of infants of non-diabetic mothers had only terminal thrombi, and there was often an association with sepsis or recent surgical operation. In contrast, the babies of diabetic mothers had organized thrombi, which had been present for some days. In this group there was a clearer correlation with hydramnios and toxemia than with sepsis. These workers point out that the total volume of body water is lower than average in infants of diabetic mothers and that further water is lost with the metabolism of glycogen stores. This is an added reason for rehydrating these infants with intravenous fluids.

The umbilical vein is a tempting route by which to introduce fluids. Injection into it is certainly more reliable and causes less disturbance to a sick premature infant than into scalp veins. On the other hand, the fear of sepsis and portal-vein thrombosis necessitates caution. It is probably wise to introduce the catheter so that its tip lies below the renal veins but above the ductus venous. J. P. M. Tizard and F. A. Oski and colleagues drew attention to the occurrence of portal-vein thrombosis in infants who had previously had an exchange transfusion, but E. N. Thompson and Sheila Sherlock, in a recent study of the aetiology of portal-vein thrombosis, were unable to find any causal relationship with this treatment.

Since the umbilical route is likely to be preferred for the treatment of small premature infants, a paper by J. M. Scott discussing the pathological findings in 92 babies with the respiratory distress syndrome is particularly important. Of 200 babies treated with intravenous bicarbonate and laevulose 92 died, and in six it seemed likely that the use of the umbilical vein might have been the cause of death. Three of these babies had umbilical-vein phlebitis and pyaemia, two had thrombosis and liver necrosis, while the last had a large pulmonary embolus. It is important to note that all these disorders occurred when the catheter had been in position for more than 47 hours. Yet it was by means of this therapy that J. H. Hutchison and colleagues were able to report a reduction in mortality from 66% to 46% in babies with respiratory distress syndrome.

Lactulose may be preferable to glucose in averting umbilical-vein thrombosis, since glucose often has a pH of 5 or lower. Although on occasions the umbilical vein may be the best route for giving intravenous therapy in the newborn, it would seem to be contraindicated for babies of diabetic mothers until their initial rehydration has been accomplished.

An Odd Leukaemia-like Disease

Some conditions can produce changes in the peripheral blood that closely resemble leukaemia. These "leukaemoid" blood pictures usually resemble that seen in chronic myeloid leukaemia. The patient is anaemic, and the white-cell count is raised to 40,000 per c.mm., occasionally as high as 100,000 per c.mm. The differential white-cell count shows a preponderance of polymorphonuclears with some early granulocytes and even a few myeloblasts; some normoblasts are always found.

Such leukaemoid blood pictures may be associated with infections, including tuberculosis, some malignant diseases, and the somewhat vague group of "myeloproliferative diseases" that are not leukaemias, the commonest example of this group being myelofibrosis. In children high white-cell counts and even leukaemoid pictures are more frequent than in adults and usually accompany infections. But D. L. Randall and his colleagues in the Denver Children's Hospital have drawn attention to a myeloproliferative non-leukaemic condition that produced both clinical and blood changes strongly suggesting a true myeloid leukaemia.

This odd disease occurred in nine related children; seven were first cousins and two were the offspring of an apparently unaffected first cousin. The onset was between the ages of 5 months and 4 years. The clinical picture was one of increasing lethargy, pallor, and retardation of growth; the abdomen was swollen by a grossly enlarged spleen and some enlargement of the liver. The blood showed anaemia and a leukaemoid picture, with early granulocytes and some blasts present, though in some patients a predominant lymphocytosis was found. The bone-marrow, which was examined in eight of the nine patients, showed a general hyperplasia including megakaryocytes, presenting a very different picture from the predominance of one particular line or cell-type seen in leukaemia. In three children the disease ran an acute course terminating in early death. In six the condition remains chronic; two have apparently recovered and the other four are unchanged or slightly improved. Treatment seems to make no difference.

Randall and his colleagues simply call this very unusual condition a familial myeloproliferative disease. It is possible that other cases will now be discovered. The existence of such a syndrome underlines the advice, often given, not to make a diagnosis of leukaemia in children unless the evidence is absolutely clear. The most important diagnostic point is that the bone-marrow should show an overwhelming preponderance of one cell type or series. Most leukaemias in childhood are of the acute variety, and the marrow shows replacement of the usual mixture of granulocytes, erythroblasts, lymphocytes, and megakaryocytes by masses of primitive cells or by proliferation of small lymphocytes. Without such evidence the existence of a leukaemoid state should be suspected, and in particular cytotoxic treatment should not be given.