into the extracellular fluid when they are destroyed. The principal site of katabolism of extracellular lysozyme is the kidney: it enters the glomerular filtrate, and is re-absorbed and catabolized by the proximal tubule.

The fractional excretion of lysozyme (clearance of lysozyme/clearance of creatinine, C_L/C_C) was measured in healthy adults:

$C_L/C_C = 1.05 \pm 0.96 \times 10^{-3}$ (mean $\pm$ SD, $n = 16$). C_L/C_C showed a positive correlation with the rate of urine flow, but no correlation with albumin excretion was observed.

In healthy full-term newborns, C_L/C_C was not significantly increased:

$C_L/C_C = 1.44 \pm 1.02 \times 10^{-3}$ ($n = 8$).

This aspect of proximal tubular function is therefore normal in the neonate.

C_L/C_C was normal in the nephrotic syndrome in children:

$C_L/C_C = 0.76 \pm 0.68 \times 10^{-3}$ ($n = 12$).

These data indicate that the presence of high concentration of albumin in proximal tubular fluid does not interfere with lysozyme reabsorption, and support the hypothesis that small and large proteins do not compete for the same transport system.

In 4 children with the Fanconi syndrome due to cystinosis, the excretion of lysozyme was much increased, confirming proximal tubular dysfunction:

$C_L/C_C = 56 \pm 10^{-3}$ (mean; range = $20-84 \times 10^{-3}$)

The possibility of local production of lysozyme was examined in children with pyuria. In such children with structurally normal kidneys and normal blood ureas the urine lysozyme/creatinine concentration ratio did not differ from that of the normal adults.

The excretion of lysozyme therefore offers a simple test of proximal tubular function, and, in contrast to techniques of assessment of amino acid excretion, provides easily obtained quantitative data to which statistical techniques can be applied to assess the natural history and response to therapy of tubular disorders.

Use of Rat Fetus in Experimental Teratology.

C. L. Berry (*Institute of Child Health, Guilford Street W.C.1*). Abnormalities of cell growth, differentiation, or morphogenetic movements during organogenesis represent the principal cause of major malformations in man. In teratological experiments it is difficult to observe organogenesis directly in mammals. The rat fetus may be grown in organ culture throughout the period of organogenesis, and this experimental model is of considerable value. It enables the possible effects of maternal metabolism on teratogens to be excluded, and the ability to initiate the direct absorption of antibody without the possibility of maternal cross-reaction is useful. The relations of growth and differentiation in this system, and the effects of trypan blue, methotrexate, and specific antisera have been studied.

Porosity of Placenta in Mouse to Maternal Cells. R. D. Barnes (*Department of Haematology, Institute of Child Health, London*). There have been

occasional reports of maternal cells in the cord blood of newborn infants; however, it is commonly accepted that this is perhaps an infrequent occurrence. In theories concerning the immunological significance of the foeto-maternal barrier the placenta has been considered to protect the fetus (an allograft) against maternal rejection.

Using an ovum transplantation model it has now been shown that a substantial number of nucleated cells from the mother are present in the young mice. Fertilized ova from normal CFW mice have now been successfully uterine-nurtured to term in the uterus of pregnant CBA/T6T6 mice, having cells with a characteristic chromosomal marker. Surprisingly, CFW mice derived in this way have up to 30% of maternal cells with the chromosomal marker—in fact these animals are chimeras. In these animals there is no evidence for the rejection of this 'graft' and no apparent evidence of any graft-versus-host reaction. The morphological nature of these foreign maternally derived cells is as yet unknown, but it seems likely that they represent nucleated blood cells. If these cells include maternal lymphocytes then their apparent immunological inactivity as a graft towards a genetically foreign host needs explanation. Chimerism here has been demonstrated in uterine-nurtured animals, and conceivably the surgical procedure of ovum transplantation itself might be held responsible. Preliminary data, however, suggest that chimerism in mice is a natural phenomenon since normally derived mice have maternal cells.

The significance of these observations might well influence theories of genetic transmission and development of immune tolerance. In addition, maternally derived cells may play a part in the development of both autoimmune disease and neoplasm, and these cells could conceivably be utilized in an active immunotherapy programme of neoplasms.

Blood Viscosity in Newborn Infant and Diagnosis and Treatment of Hyperviscous States. T. Mackintosh (*Royal Infirmary, Dundee*). Viscosity is the factor that determines how a fluid will behave when it flows. The viscosity of blood is not fixed but varies with the rate of shear, gradually increasing as shear rate decreases.

The normal range of blood viscosity was determined by studying 110 full-term, singleton, normal infants weighing over 2600 g., using a Wells-Brookfield synchroelectric microviscometer model L.V.T. (shear rate range 1.16 to 232 sec^{-1}), with a special attachment for small blood samples. This confirmed that blood was a non-Newtonian fluid, with a viscosity varying from 5.47 c.p.s. at a shear rate of 232 sec^{-1} to 33.6 c.p.s. at 1.16 sec^{-1} . A close correlation exists between blood viscosity and the venous PCV, but there is no relation to birthweight or time from birth.

Further studies showed that respiratory distress (20 infants) and prematurity (21) were not usually associated with increased viscosity, but the mean for 12 dysmature infants is only just within the normal range.

16 infants had signs attributable wholly or in part to

hyperviscosity. The signs were (1) 'cerebral'—jitteriness, stiffness, fits, lethargy, and hypotonia; (2) plethora and cyanosis; (3) respiratory distress.

Active treatment was undertaken in 8 infants: increased oral fluids in 2 produced no improvement, but the remaining 6 had a plasma exchange (20–30 ml./kg.) with resultant marked reduction in blood viscosity and clinical improvement in 5.

Hyperviscosity of the blood may cause abnormal signs in infants with respiratory distress, 'cerebral' irritation, and in the parabolic syndrome. These signs together with a venous PCV greater than 75 may be an indication for a plasma exchange.

Perforation of Bowel in Newborn as Complication of Exchange Transfusion. R. Orme (*Royal Devon and Exeter Hospital, Exeter*). (Introduced by J. Scopes). Spontaneous perforation of the bowel without evidence of intestinal obstruction occurred in 6 infants who had exchange transfusions for Rhesus incompatibility. The clinical signs followed a distinct pattern which may misleadingly suggest portal vein thrombosis in the early stages. The pathological findings resembled those found in acute necrotizing enterocolitis in adults, which is known to be associated with arterial hypotension. It is suggested that the cause in these infants may also be due to periods of hypotension during the exchange transfusions. Hypoxia and infection may also be important, though the infection when it occurs is superimposed upon the necrosis of the bowel.

Human Breast Milk Jaundice; Estimation of Steroids in Milk. J. A. B. Darling and R. A. Harkness. (*Department of Paediatric Biochemistry, Royal Hospital for Sick Children, and Department of Clinical Chemistry, University of Edinburgh*). About 1% of newborn breast-fed infants develop jaundice, which starts during the first week of life and may be severe. The jaundice, which is due to defective conjugation of bilirubin, can be related to the infants' intake of breast milk, and factors inhibiting conjugation have been shown in milk, serum, and urine. Many steroids have been shown to inhibit the glucuronyl transferases *in vitro*. After the isolation of 5 β -pregnane-3 α , 20 β -diol from human milk, it seemed reasonable to assume that breast milk jaundice was due to steroids transmitted in the milk. However, the evidence supporting this assumption was largely indirect. There have been no quantitative studies of the steroids in human milk, probably due to the analytical difficulties.

In the present investigation, a method has been developed for the group analysis of 17- and 20-oxogenic steroids in milk. Group analysis has been used since many steroids are capable of inhibiting conjugation mechanisms. The method consists of the following steps—saponification, gentle mechanical extraction, CrO₃ oxidation, Girard separation, thin-layer chromatography, and, finally, gas-chromatography. Preparative gas-chromatography has been used to provide evidence of specificity. The quantities of steroids in cows' and in human milk are small. The mean concentration

($\pm$ SD) of 5 α -androstane-3, 17-dione in the final fractions from 48 samples of cows' milk was equivalent to 0.52 ± 0.46 μ g./100 ml. milk. Similar small quantities of steroids with a predominantly 5 α -structure were found in human milk. There was no large difference in the quantities present in the milk from mothers with jaundiced babies. However, it has so far only been possible to study a small number of such cases.

The results obtained so far are consistent with previous work on other problems, mainly in animals, and suggest that the metabolism of steroids by the breast is an important factor affecting the steroids present in milk. Breast milk jaundice may therefore be a complex problem.

Assessment of Gestational Age in Newborn: A Practical Scoring System. L. Dubowitz (*Department of Child Health, University of Sheffield*). (Introduced by V. Dubowitz). At the Aberdeen meeting of the Paediatric Research Society we reported on the variability and subjective nature of many of the traditional neurological criteria used in assessing gestational age (*Arch. Dis. Childh.* (1969), **44**, 135).

We have now tried to quantitate 10 neurological criteria which we have found to be most objective and reproducible. Each criterion has been scored, the grades range from 0–2 to 0–5, depending upon the number of substages one could readily define and recognize. In each case 0 is the grading consistent with the earliest gestation.

The scoring system has been applied in 400 newborn infants of varying gestational age. We have also assessed in these infants 11 superficial or skin criteria, along the lines and scoring system of Farr *et al.* (*Develop. Med. Child Neurol.* (1966), **8**, 507).

After clinical assessment of the infants all the mothers were personally questioned with regard to the date of the last menstrual period and regularity of the menstrual cycle. Contrary to the confidence of the obstetrical notes, we found that in only 150 out of 400 were the data from the mother reliable enough for further analysis.

In these 150 infants we have analysed statistically the correlation between the gestational age and the total score of neurological signs, the total score of the superficial signs, and the grand total score. All three scores showed a correlation coefficient in the region of 0.9. We also analysed separately observations done within 24 hours of birth and those done after 24 hours—the earlier observations, if anything, gave a better correlation. The highest correlation coefficient (0.97) was that of total score within 24 hours and gestational age.

We have found this scoring system to be a practical one. It can be done in about 10 minutes and has been readily reproducible by resident staff and nurses.

Further Studies of Motor Nerve Conduction Velocity in Newborn Infants. A. Moosa (*Department of Child Health, University of Sheffield*). (Introduced by V. Dubowitz). Recent studies have shown that motor nerve conduction velocity of the ulnar and posterior