considerable increase in the excretion of certain unidentified iodoplatinate reacting compounds in the first 6-hour urine. When plasma homocyt(e)ine level was high, cyst(e)ine levels after the load were significantly lower than those when homocyst(e)ine was much reduced following administration of betaine.

The results suggest that when plasma homocyt(e)ine and methionine are raised, the low levels of cyst(e)ine are due to the incorporation of a very significant proportion of dietary cyst(e)ine into homocysteine-cysteine-disulphide and other sulphur compounds (as yet unidentified) which are derived from homocyst(e)ine or methionine.

Temporary tyrosinosis. Douglas Pickering and Brian Bower (*Radcliffe Infirmary Oxford*). A term baby started to vomit at 4 weeks of age and on admission one week later was in hepatocellular failure with haemorrhage from hypoprothrombinaemia. Large amounts of tyrosine in the urine led to the diagnosis of tyrosinosis and treatment with a low phenylalanine, low tyrosine diet for 15 months (though increasing amounts of tyrosine had been introduced towards the end of the period). Initial complications were (1) oedema from hypoalbuminaemia, (2) drowsiness and apathy from hypermethioninaemia after starting the diet, and later (3) failure to gain weight due to a too drastic tyrosine reduction.

The special diet was finally abandoned at the age of 16 months with no complications. When last seen at 3 years 4 months he was normal.

A subsequent sib showed no clinical or biochemical features of tyrosinosis.

Urinary excretion of immunoglobulin E. T. M. Barratt, M. W. Turner, and S. G. O. Johansson (*Department of Immunology, Institute of Child Health, London W.C.1, and The Blood Centre, University Hospital, Uppsala, Sweden*). Immunoglobulin E (IgE) was measured by the radioimmunosorbent technique in sera and urine concentrates of healthy individuals. The urine: plasma ratio of IgE exceeded that of albumin about thirtyfold. As IgE is a considerably larger molecule and would not be expected to cross the glomerular basement as easily as albumin, the data suggest that most urinary IgE does not derive from glomerular filtration but is of local origin within the urinary tract.

If this were so, the urinary excretion of IgE would be independent of the plasma IgE concentration and perhaps also of the alterations in glomerular permeability of the nephrotic syndrome. Urinary IgE excretion rates were therefore measured in individuals with the nephrotic syndrome and in patients with atopic eczema characterized by the very high levels of plasma IgE. The results did not differ from those observed in healthy individuals, and provide further support for the hypothesis that most urinary IgE is locally secreted.

Maintenance of breathing in newborn lamb. P. Johnson, G. S. Dawes, and J. S. Robinson (*introduced by P. M. Dunn*) (*Nuffield Institute for Medical*

Research, Oxford). It has been considered by many that the immersion of the fetus in liquid inhibits respiration. Our experiments show that the fetal lamb with a tracheostomy can establish respiration and that the newborn lamb will maintain respiration when immersed in normal saline but not in water. Likewise in 8 newborn Cheviot lambs under 24 hours of age amniotic fluid, tracheal fluid, and sheep's colostrum do not arrest respiration when introduced into the upper airway, while glucose solutions and cow's milk do. If one of these inhibitory agents remains in the upper airway, then apnoea continues, P_{aO_2} falling to fetal level and P_{aCO_2} rising in excess of 150 mm of mercury the lamb dying in 35–40 minutes.

Cheviot lambs (8) over 48 hours of age and ewes demonstrated exactly the same discrimination between water and saline as described. However they showed 'breakthrough' of respiration after only transient apnoea.

Localization experiments place the site of the receptor at the entrance to the larynx. The use of a variety of chemical solutions suggest the receptor to be a chemoreceptor, possibly a taste receptor. Superior laryngeal nerve section (bilateral) abolished the discrimination between these agents, and apnoea did not occur.

However, of 9 Dorset lambs under 24 hours of age, 8 showed 'breakthrough' breathing with water in the upper airway. These lambs all had a good response to hypoxia. Thus this strain appeared to be more mature in these aspects than young lambs of the Cheviot breed. Nevertheless, two Dorset lambs, one over 48 hours of age having shown a good hypoxic response, remained apnoeic with water in the upper airway. Therefore in 4 Dorset lambs already shown to have a good hypoxic response the carotid bodies were inactivated, removing the response to hypoxia but not affecting the response to water and saline already demonstrated.

We confirm the presence of a chemoreceptor at the entrance to the larynx; at least part of the reflex pathway is contained in the superior laryngeal nerve. There was considerable individual as well as strain variation in the response. The possible role of such a pathophysiological entity in apnoea of the newborn and so-called sudden death in infancy was discussed.

Pulmonary blood flow in newborn. Robert Dinwiddie and George Russell (*Aberdeen*). Previous workers have described the measurement of pulmonary blood flow in newborn infants using nitrous oxide as the indicator gas with a single-breath body plethysmographic technique, and using monochlorodifluoromethane ('Freon-22') with a rebreathing technique; the results obtained have correlated well with estimates of cardiac output made by conventional methods.

Using 3% nitrous oxide as the indicator gas, we have studied effective pulmonary blood flow in healthy newborn infants using a rebreathing technique. The results are similar to those obtained by other techniques (mean effective pulmonary blood flow = 167 ml/kg per min (SD 35.7); 2.80 l/m² per min (SD 0.64)). Recirculation proved to be only a theoretical problem;

in practice it was readily detected by careful analysis of the nitrous oxide disappearance curve.

Our technique has advantages. It is technically fairly simple, the apparatus required is likely to be widely available in departments of anaesthesia and respiratory medicine, and in the concentrations used nitrous oxide is less toxic than 'Freon'.

Serial lactic acid measurements in respiratory distress syndrome. J. P. Beca (*introduced by J. W. Scopes*) (*Hammersmith Hospital, London*). Blood lactic acid was measured 4-hourly in 21 newborn infants with respiratory distress syndrome (RDS). 13 survived and 8 died. In general lactic acid levels were higher in babies who died than in survivors, but there were inconsistencies which were uninterpretable if a single estimation was made in a given baby. Analysis of serial determinations done in each baby showed that all patients whose highest lactic acid was always below 35 mg/100 ml survived, and babies with high values but decreasing curves also had a good outcome. Only those who had increasing lactic acid curves, even if initially normal, died.

In most cases a high or normal P_{aO_2} was associated with normal or decreasing lactic acid; but babies with P_{aO_2} below 60 mmHg had often also normal or decreasing lactic acid.

If one intends to use lactic acid levels for prognostication of outcome in RDS, serial determinations are needed and single measurements are of limited value. Furthermore these data support the concept that there may be a wide range of hypoxaemia without oxygen deficit in body tissues and that it is therefore impossible to define a 'lower acceptable P_{aO_2} ' enough to achieve adequate tissue oxygenation.

Adrenal response to tetracosactrin in newborn infants. Hugh Price, Theresa Cowley, and E. H. D. Cameron (*Welsh National School of Medicine and Tenor Institute for Cancer Research*). Current belief holds that the fetal pituitary-adrenal axis is intimately involved in the initiation of labour, and indeed recent studies have shown that antenatal corticosteroid therapy may diminish the incidence of respiratory distress syndrome in prematurely born infants. Our studies were undertaken to provide basic data on the human newborn adrenal response to tetracosactrin (β^{1-24} corticotrophin, Ciba) stimulation.

Four types of study were performed.

(a) Standard 30-minute tetracosactrin tests on 50 infants admitted to a neonatal special care baby unit.

(b) Tetracosactrin tests in 12 normal infants; 6 on day 1 and 6 on day 5 after birth, cortisol and glucose levels being measured at 0, 30, 60, 120, and 180 minutes after intramuscular injections.

(c) Deposynacthen (tetracosactrin zinc complex, Ciba) responses were measured serially to give dose response curves.

(d) Cortisol plasma clearance rates were calculated on 6 newborn infants after intramuscular injection of

cortisol. All infants in groups (c) and (d) had been admitted to the special care baby unit.

Plasma cortisol was measured by 'micro'—Mattingly (50 μ l—venous plasma/assay) or by competitive protein-binding methods (10 μ l peripheral plasma/assay). Correlation curves for these two methods were presented.

The results showed that the newborn infant adrenal responds well to stimulation by tetracosactrin in terms of plasma cortisol concentration, but that the time of maximum response is somewhat delayed compared with that of the adult. No significant difference was observed in the response to tetracosactrin at day 1 and day 5. With Deposynacthen, the peak response time was variable but again was later than that reported for adults which may reflect either a slower absorption of the depot in the infant or a slower adrenal response to stimulation. With all infants receiving Deposynacthen, the maximum cortisol concentration exceeded 100 μ g/100 ml plasma. In general, basal levels were not reached until 3 to 5 days after administration of the depot.

Effect of glucose on plasma glucagon, insulin, and growth hormone levels in exchange transfusions. R. D. G. Milner, M. Fekete, R. Assan, and J. S. Hodge (*Departments of Child Health and Chemical Pathology, University of Manchester, and Hotel Dieu, Paris*)

Insulin excretion in cystic fibrosis. M. C. Goodchild and G. A. Brown (*introduced by P. H. W. Rayner*) (*Institute of Child Health, Francis Road, Birmingham B16 8ET*). Reduced tolerance to oral glucose with insulinopenia has been shown in 42% of cystic fibrosis (CF) subjects investigated by Handwerker *et al.* (1969). Abnormal results have also been reported after intravenous glucose loads. Histological investigation of pancreatic islet tissue has shown it to be substantially normal and reduced tolerance may therefore be a primary feature of cystic fibrosis and not secondary to the fibrotic process.

Significant positive correlation has been demonstrated between plasma insulin levels and urinary insulin excretion. To assess overall insulin secretion in cystic fibrosis therefore, 24-hour urinary insulin excretions were measured on 28 CF children using a double antibody radioimmunoassay. Excretion was also measured in the parents of the CF children. Results were assessed by comparison with results of similar investigations in non-CF families. Mean insulin excretion in the CF children was 257 μ U/kg body weight per 24 hours, and was lower than the control children's mean of 323 μ U/kg body weight per 24 hours. Mean insulin excretion in the parents of the CF children was 158 μ U/kg body weight per 24 hours, and in the control adults 215 μ U/kg body weight per 24 hours. The difference between the means of the CF parents and the control adults was significant ($P < 0.01$).

The tendency to lower insulin excretion in CF children was not unexpected in view of the results of plasma