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Abnormalities of the complement system in children with liver disease. V. F. Larcher, J. Wyke, A. P. Mowat, and R. Williams. Department of Child Health and Liver Unit, King's College Hospital, London SE5.

Abnormalities of the complement system have been described in adult liver disease (Charlesworth et al., 1977). We studied both classical and alternate pathways of complement in 84 children with liver disease and in 30 control children. Classical pathway components were measured by haemolytic or immuno-diffusion techniques. Alternate pathway activity was measured by determination of yeast opsonisation index (0.1 = mean number of yeasts phagocytosed per normal polymorph in presence of test serum; Soothill and Harvey, 1977). High values of yeast opsonisation (P < 0.001) were found in 10 pre-operative cases of biliary atresia (0.1 = 5.38 ± 0.70 mean ± 2 SD) compared with controls (4.3 ± 1.16 mean ± 2 SD). Defective opsonisation (0.1 = 1.16 ± 1.16 mean ± 2 SD; P < 0.001) and low levels (P < 0.001) of complement factors, 3, 4, 5, B, and D were found in 10 children with fulminant hepatic failure. Normal values were found in 2 survivors and in 4 children with previous hepatic failure. Eight further patients (2 after successful surgery for biliary atresia; 2 untreated chronic active hepatitis; 4 corticosteroid-treated chronic active hepatitis) had defective opsonisation with or without changes in other complement components.

Serum complement abnormalities are common in children with liver disease, but more study is necessary to elucidate their role in pathogenesis of liver disease or its complications.

References

Hepatic collagen synthesis and its modification by colchicine in a rat model of cirrhosis of the liver. M. S. Tanner, D. Jackson, and A. P. Mowat. Department of Child Health, King's College Hospital Medical School, Denmark Hill, London SE5.

An animal model of hepatic cirrhosis, in which rats pretreated with oral phenobarbitone inhale carbon tetrachloride twice weekly, was used to study hepatic collagen synthesis and its modification by colchicine. Hepatic collagen, measured as protein-hydroxyproline, doubled after 4 weeks' exposure, and free proline increased concomitantly. The activity of peptidyl proline hydroxylase (PPH), an enzyme catalysing an early step in collagen synthesis, increased approximately 5-fold, and this higher activity preceded the increase in collagen. PPH activity showed considerable lability, an increase in activity occurring between 24 and 48 hours after each exposure to carbon tetrachloride. Colchicine, 100 µg given daily by orogastric tube, for 6 days a week, partially prevented this collagen deposition. The liver collagen content, in µmol hydroxyproline/g wet liver, for control rats was 1.007±0.109; for rats given 4 weeks' carbon tetrachloride it was 2.086±0.416; for rats given 4 weeks' carbon tetrachloride and colchicine it was 1.309±0.077. PPH activity was similar in the last two groups. Colchicine treatment did not affect growth.

Colchicine, which decreases net collagen deposition both by microtubular inhibition and by stimulating collagenase, may impede the progression of chronic liver disease to cirrhosis.

The Poland anomaly and allied disorders. T. J. David. Bristol Children's Hospital.


Renin and angiotensin in normal, prepubertal girls. O. R. C. Smale, F. Broughton Pipkin, and M. O'Callaghan. Departments of Child Health and Obstetrics and Gynaecology, City Hospital, Nottingham.

Renin and angiotensin II (AII) levels were measured in 30 normal girls, 2 to 11 years old. The older girls
had lower plasma renin concentrations (PRC) which were not significantly different from adult levels. Plasma AII levels however were significantly higher in all children (P<0.001). PRC and AII levels were lower when diastolic blood pressure was greater than 70 mmHg than when it was less than 70 mmHg. This difference was only statistically significant for PRC.

Regression analysis showed that plasma renin activity was inversely related to serum sodium levels and directly proportional to the ratio serum sodium:potassium (P<0.025 for both). PRC was also proportional to serum potassium (P<0.02). Plasma AII was inversely proportional to serum sodium (P<0.025) and related to PRC (P<0.05).

Simultaneously measured renin and AII levels have not, to our knowledge, been previously reported for this age group. The results show that the high levels seen in infancy remain above adult levels during the first few years of life. However, it appears that the stimuli of relative hypotension and hyponatraemia are controlling factors at these ages as well as in adulthood.

Which 'small-for-dates' infants are malfourished? O. G. Brooke and Fiona Butters (introduced by R. J. West). Department of Child Health, St George's Hospital, London SW17.

In an attempt to improve diagnostic precision in assessing small-for-dates babies, we measured upper arm muscle and fat area (derived from mid-upper arm circumference and skinfold measurements) in 221 unselected term neonates. Results were expressed per unit upper arm length. Irrespective of birthweight, infants were defined as 'malfourished' if arm muscle and arm fat areas fell more than 1 SD below the mean, or if either area alone fell more than 2 SDs below the mean. By these criteria, 22 infants were malfourished (birthweight range 2100–3570 g). A further 21 infants were small-for-dates by current definition, being <10th centile of weight for gestational age, but not malfourished. We called these 'normal small infants'. There was a predominance of Asians in each group. 14 out of the 22 'malfourished' infants had obstetric complications which could impair fetal growth (hypertension, APH, toxaemia, anaemia). Only one of the 'normal small infants' had any such complications. These differences were highly significant (P<0.001). Skinfold measurements alone gave poor discrimination between 'malfourished' infants with a bad obstetric history and 'normal small infants' without obstetric complications. Birthweight only identifies the grossest forms of intrauterine malnutrition and should no longer be the sole criterion for defining the small-for-dates baby.

Circadian rhythms of melatonin and cyclic-AMP in neonates. A. Evans, N. D. Carter, O. G. Brooke, and J. Smith. Department of Child Health, St George's Hospital Medical School, London SW17 0RE* and the School of Pharmacy, University of Bradford.

Circadian variations in blood and urine levels of cyclic-AMP (Holmes and Hamadah, 1977) and melatonin (Wurtman and Moskowitz, 1977) is well documented, and the melatonin rhythm is maintained in pregnant women (Matthews et al., 1978). We investigated these rhythms in neonates and attempted to assess the influence of maternal circadian activity of melanin on rhythm development in the baby. Blood was taken for serum melatonin estimation from the umbilical cords of 26 normal term infants, and paired samples of cord and maternal blood samples were taken from a further 20 normal infants. Melatonin was measured by radioimmunoassay. Cord blood from another 71 term normal infants was assayed for cyclic-AMP by a competitive protein binding assay.

The results of 26 cord blood melatonin assays (Table 1) show a clear circadian rhythm. The daytime (0800–2000 hours) levels are significantly lower than the night-time (2000–0800 hours) ones (P<0.05). Assay of the paired samples showed no significant correlation between cord and maternal serum melatonin levels. The maternal levels showed no circadian rhythm.

Cord serum cyclic-AMP levels showed a circadian rhythm (Table 2). The morning (0000–1200 hours) levels are significantly greater (P<0.001) than the evening (1200–2400 hours) ones.

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<tr>
<th>Table 1</th>
<th>Melatonin levels of 26 term infants</th>
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<tr>
<td>n</td>
<td>3</td>
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<tr>
<td>Melatonin pg ml⁻¹ (mean ± 1 SD)</td>
<td>61.7±95.5</td>
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<th>Table 2</th>
<th>Cyclic-AMP levels of 54 term normal infants</th>
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<tr>
<td>n</td>
<td>13</td>
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<tr>
<td>C-AMP pmol ml⁻¹ (mean ± 1 SD)</td>
<td>14.3±18.7</td>
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Stools in infancy. Frequency and weight, water, and energy content. N. Lemon and O. G. Brooke. Department of Child Health, St George's Hospital, London SW17.

There is little information on the frequency of defecation in normal infants and toddlers and on their stool weight, water, and energy content. This study was undertaken to provide such data without any attempt being made at energy balance study.

Stools were collected in rayon napkin liners during a period of 3-9 days from 53 healthy infants and toddlers aged 3 days to 2 years, who were either in their own homes or in hospital as social admissions. Those in hospital were given a reasonable period for adjustment before being studied. In a preliminary study a method of stool collection was established. The aim of this was to observe the effect on weight of wet stools exposed to wet napkins. Preweighed samples of wet stools in liners were incubated at room temperature for 2 hours in previously weighed disposable napkins adequately soaked with 0.9% saline solution. The result showed no significant change in stool weight or napkins. Subsequently, freshly passed stools were frozen at —24°C, weighed wet, freeze-dried for estimation of water content and for determination of total daily energy content. Neonates were all bottle fed and older infants were on a mixed diet. Infants with gastrointestinal disorders or other illness were excluded.

Results are given in the Table. There was a progressive decrease in stool frequency with age but there were wide variations between individuals. There was also marked variation in daily stool weight but little fluctuation in stool water content. The stool energy concentration tended to fall with increasing age.


Neonatal form of dystrophia myotonica. A report of 5 cases in preterm babies and a review of the literature. R. G. Pearse and C. J. Höweler. Department of Paediatrics and Neurology, Sophia Children's Hospital, and Academic Hospital, Erasmus University, Rotterdam, The Netherlands. To be published in full in the Archives, 1979, 54.


The pathophysiological mechanisms operating in diarrhoeal states are currently under intense study, and this is particularly the case for the mechanisms involved in the adhesion of bacteria to epithelial cells: adhesion to epithelial cells is a prerequisite to intraluminal colonisation and the subsequent sequence of events which induce small intestinal secretion and diarrhoea. We studied adhesion of EC to human BEC using a modification of the method of Ofek et al. (1977).

We established that a strain of EC (026:K60) known to adhere to fetal intestine (McNeish et al., 1975) also adhered to BEC, and that another non-adhesive strain failed to do so. Colonies of EC were isolated from the stools of 13 healthy infants, and 2-6 colonies in 10 of these infants were the nonadhesive organisms (4 of these strains were designated as 'enteropathogenic' on the basis of their agglutinating properties). Agglutinable EC isolated from the stools of 9 children with diarrhoea were studied and 8 were adherent to BEC. Adhesion was partially or completely inhibited by β-mannose, and EC isolated from 2 patients with diarrhoea adhered to their own BEC but not to donor cells.

These results suggest (1) 'enteropathogenicity' of EC is not synonymous with their agglutinating properties, (2) EC binds to specific mannose-like receptor sites, and (3) the BEC system may be a...
simple test to assess whether a bacteria is 'entero-
pathogenic'.

References

Enteropathogens in preschool children and their pets.
R. W. Newton, R. J. Pugh, and I. D. Leighton (introduced by T. Turner). Department of Paediatrics and Bacteriology, Hull Royal Infirmary, Anlaby Road, Hull.

During a 4-month period, 152 consecutive preschool children attending a general outpatient clinic were screened for intestinal parasites and enteropathogenic bacteria. Each child was requested to submit 3 fresh stool specimens and also 3 stool specimens from any animal with which the child had significant contact. Careful record was made of age, social class, type of accommodation, and history of pica in the child. Inquiry was made into the health of any pet.

Of 78 children with no family pets, 34 (44%) failed to submit specimens, while 23% submitted 3 specimens. Only one child of the 44 submitting specimens had a significant culture. 74 children with pets entered the study; 51 (60%) failed to submit specimens while 12 (16%) produced 3 specimens. Among the 23 children submitting specimens 2 were found to have Giardia lamblia, one pathogenic Escherichia coli, and one Salmonella typhimurium. 12 dogs had stools submitted; 2 were infested with G. lamblia, while a third had S. typhimurium. Two children associated with these pets had recurrent diarrhoea, while a third had the same pathogen (S. typhimurium). Other animals including cats, budgerigars, and rabbits failed to produce any positive pathogens.

This study shows the difficulty of patient and pet compliance and confirms that the presence of enteropathogenic bacteria and other parasites is more likely in children in regular contact with family pets, although both the children and pets may well be asymptomatic.

Nebulised salbutamol in the treatment of acute asthma in children. J. B. G. Watson and Olga M. Bannister. Departments of Paediatrics and Physiotherapy, Children's Hospital, Sheffield S10 2TH.

A PGS compressor unit with a Bird’s nebuliser was used to administer nebulised salbutamol or placebo to a group of children with acute asthma in a double-blind trial. The salbutamol group showed a greater rise in peak expiratory flow rate (PEFR) (67 l/min) compared with the placebo group (21 l/min) P < 0.005. A further 57 patients had 190 doses of nebulised salbutamol and the mean rise in PEFR was 55 l/min. When IPPB was used to administer the nebulised solutions, the salbutamol group showed a mean rise in PEFR of 50 l/min compared with 10 l/min in the placebo group. Salbutamol administered by nebulisation offers an effective alternative to parenteral treatment for children with asthma. As a result of nebulised treatment fewer children required parenteral therapy in 1977 compared with 1975.

Bronchodilator effects of nebulised chlorpheniramine in childhood asthma. R. C. Groggins, A. D. Milner, and G. M. Stokes. Queen's Medical Centre, Nottingham.

Previous workers have failed to demonstrate a bronchodilator response to antihistamines in childhood asthma, in doses which did not produce side effects. However, a study on adult asthmatic subjects has shown that chlorpheniramine delivered intravenously is an effective bronchodilator (Popa, 1977). We investigated the effect of nebulised chlorpheniramine in a group of 10 asthmatic children aged between 8 and 14 years (mean 11). Response to treatment was measured with a Wright's peak flow meter and FVC and FEV₁ were measured using a Morgan wet spirometer. Measurements were made before and for 2 hours after inhalation of the drug. At the end of 2 hours the children inhaled nebulised salbutamol (5 mg in 2 ml water) and lung function tests repeated after 15 min. Children attended on 3 occasions and received 2, 4, and 8 mg chlorpheniramine successively.

Bronchodilatation was observed, usually within 2 min of the inhalation of chlorpheniramine, and reached a plateau by 45 min. The response to 4 and 8 mg was similar with a greater than 30% improvement in FEV₁ and PEFR response to 2 mg was less dramatic, with improvements of 15–20%. The only side effect was that of coughing, and each patient coughed at least once.

Antihistamines if delivered by appropriate routes and in appropriate doses do produce bronchodilatation in children with asthma.

Reference
Hyposensitisation in house dust mite sensitive childhood asthma. J. O. Warner, J. F. Price, and E. N. Hey. Respiratory Unit, The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH.

Hyposensitisation with Dermatophagoides pteronyssinus tyrosine absorbate in asthmatic children shown to be D. pteronyssinus sensitive by bronchial provocation tests (BPT), was shown to be effective in a double-blind controlled trial. Treated children (27) used less medication while maintaining clinical and lung function improvement compared with controls (24). These children responded to D. pteronyssinus injections alone despite the fact that most reacted to other inhalant antigens on prick skin tests. This confirms that D. pteronyssinus is the predominant antigen responsible for asthma in British children. In most children the benefit occurred despite no change in immediate response on BPT but the late reaction was lost in half the patients and these patients had the greatest symptomatic improvement. This confirms the importance of late reactions in childhood asthma.

Postprandial total serum bile acid concentrations in cystic fibrosis. Bryan J. Starkey and Mary C. Goodchild. Department of Clinical Chemistry, Queen Elizabeth Hospital, Birmingham B15 2TH.

The efficacy of a single 2-hour postprandial total serum bile acid (t.s.b.a.) concentration in the early detection of liver disease in cystic fibrosis (CF) was assessed. 27 CF patients (aged 4–27 years), 21 age-matched controls, and 40 healthy adults (aged 19–52 years) were studied. Venous blood samples were drawn in the morning, 2 hours after ingestion of a weight-related chocolate stimulus. T.s.b.a. concentrations were determined by the method of Mashige et al. (1976) and conventional serum liver function indices by standard methods. T.s.b.a. concentrations expressed as mean ± 1 SD (μmol/l) were: 27.0 ± 26.4 (CF patients), 19.9 ± 5.5 (age-matched controls), and 17.3 ± 4.5 (healthy adults). Most CF patients, therefore, had normal t.s.b.a. concentrations.

Six results in the CF group deserve comment: 2 patients with established liver disease did have abnormally high t.s.b.a. concentrations of 56·0 and 150·0 μmol/l; 3 patients with t.s.b.a. concentrations within the normal range were thought, by other criteria, to have liver disease; one patient, in whom the t.s.b.a. concentration was raised (42·0 μmol/l) had no other finding suggestive of liver involvement.

Thus, a single 2-hour postprandial t.s.b.a. concentration appears not to be particularly informative in CF. Wider investigations of bile acid metabolism, including sequential studies, may be necessary to elucidate the size and distribution of the bile acid pool, at varying ages, in this disease.


The introduction of acid to the duodenum, in health, results in a brisk rise in plasma secretin levels. This endogenous secretin stimulates pancreatic secretion of water and bicarbonate, which neutralises the duodenal acid and inhibits further secretin release. As most children with CF have pancreatic exocrine insufficiency, we studied the pattern of secretin release in this condition. Nine children with CF were studied, all of whom were considered to have pancreatic exocrine insufficiency. Two different acidic drinks were given—0·2 M citric acid and 20% glucose, and pure lemon juice. Plasma secretin was measured before and after the drinks by radioimmunoassay. In only one case was there basal hypersecretinaemia (i.e. >60 pg/ml). The children who received the citric acid and glucose mixture showed a mean basal and mean peak plasma secretin of 37 and 120 pg/ml respectively. The values in the children who took citric acid alone were 34 and 48 pg/ml respectively. Thus both groups showed a positive response which was significantly greater in the citric acid and glucose group (P < 0·05). These preliminary studies provide some new information of the regulation of pancreatic secretion in disease.


Patients with cystic fibrosis have a high prevalence of positive skin prick tests to common inhaled antigens, but the importance of bronchial allergy in the disease is uncertain. We have investigated the response to antigen inhalation and exercise, and symptoms of respiratory allergy in a group of children with CF. 10 of 15 CF children with positive skin tests gave an immediate bronchial response to the antigen inhaled, 5 of them also gave a late (4–8 hour) response; however only one gave a history of asthma. In 6 patients tested with Aspergillus fumigatus the
bronchial response varied, 2 were negative, one gave an immediate response, and 3 gave a dual (immediate and late) response. None of the children showed the characteristic pattern of response to exercise seen in asthmatic patients, an initial rise in peak flow rate (PFR) followed by a fall of greater than 14% below the resting level. Two patients showed an abnormal rise in PFR during exercise, a pattern previously described in CF.

The results suggest that bronchial allergy, immediate and late, does not completely explain susceptibility to asthma, and that other factors including perhaps the type of bronchial reactivity shown by bronchoconstriction after exercise may be required.

Growth patterns in children with malignant disease. N. K. Griffin and Jane Wadsworth. The Hospital for Sick Children, Great Ormond Street, London WC1N 3JH, and St Bartholomew's Hospital, West Smithfield, London EC1A 7BE.

Short stature has been described as a complication of malignant disease in childhood. We studied 71 children with leukaemia and 24 with extracranial solid tumours and compared their growth with normal children for age and sex. Variables studied included diagnosis, radiotherapy field and dose, duration of chemotherapy, and the patient's age and sex. Children with leukaemia grew at a reduced rate in the year after presentation, and had a mean height after one year that was 0.41 SDs below their value at presentation (P < 0.001). This effect was related to cranial and craniospinal irradiation, and was particularly pronounced after craniospinal irradiation. After one year from presentation growth rate was normal in all groups of patients, with no evidence of 'catch-up growth'. Failure of normal growth in the first year of treatment was observed in 59 of 65 patients who had received cranial or craniospinal irradiation.

It is concluded that prophylactic central system irradiation in leukaemic children causes a transient reduction in growth rate, but that the effect on eventual height attained is likely to be small.

Investigation using psychological tests in children with recurrent abdominal pain of nonorganic cause. R. H. Davies, St David's Hospital, Bangor, and E. Knassel, Department of Psychology, University College of North Wales, Bangor.

Twenty children with recurrent abdominal pain of nonorganic cause were compared with 20 children with appendicitis. They were subjected to Eysenck personality inventories, social maturity scales, the family relations test, the Rep test, and the self as implied pole test. Results showed the subjects were not different from the controls in the Eysenck extraversion/introversion or neuroticism tests. The subjects scored normally on the social maturity scales. In the family relations test they scored significantly lower than the controls in applying attributes and statements to themselves. In the Rep test they differed from controls in thinking themselves messy not tidy, failures not successes, but not unduly nervous. They scored significantly higher than the controls in the self as implied pole test. So the 'little bellyachers' were not neurotic, introverted, or socially immature, but although relatively confident they felt themselves untidy and failures; they dissociated attributes from themselves, and felt themselves poles apart from others.