Paediatric Research Society

Manchester, 21 and 22 September 1979


Growth in height and osseous maturation in response to human growth hormone therapy. R D G Milner, M A Preece, J M Tanner. Department of Paediatrics, University of Sheffield, and Department of Growth and Development, Institute of Child Health, London.


Physiological properties of dry artificial surfactant. C Morley, B Robertson, B Lachmann, G Grossmann, R Nilsson, A Bangham. Department of Paediatrics, Addenbrooke's Hospital, Cambridge, Department of Pathology, Karolinska Institute, Stockholm, Research Institute for Lung Diseases, Berlin-Buch, and Biophysics Unit, ARC Babraham, Cambridge.

The effect of a dry artificial surfactant (DSA) powder, composed of dipalmitoylphosphatidylcholine and unsaturated phosphatidylglycerol, on the lung mechanics of surfactant-deficient 27-day premature rabbits was compared with the effect of a suspension of crude natural surfactant (NSA) powder obtained by centrifuging mature lung wash fluid. The animals were delivered by caesarean section, kept at 37°C, stroked continuously and tracheostomised in turn. A cannula inner diameter 0.8 mm was tied into the trachea. DSA 1.8 ± 0.54 mg or NSA 50 µl (phospholipid content approximately 8 mg/ml) was instilled into some animals while others were used as controls. Each animal was placed in a separate compartment of a multichamber, whole body constant pressure, plethysmograph at 37°C. They were connected in parallel to a pressure-limited ventilator with a dead space of < 0.05 ml. They were ventilated for one minute at a time, at 35 cmH₂O, with 100% oxygen. Then the pressure was decreased to 22 cmH₂O for one hour. Compliance was measured at 30 and 60 minutes. Results show that DSA has a beneficial effect on lung thorax compliance but is not quite as good as NSA.

<table>
<thead>
<tr>
<th>Compliance (ml/kg per cmH₂O) mean ± SD</th>
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<tbody>
<tr>
<td>30 minutes</td>
</tr>
<tr>
<td>Controls (n=17) 0.082 ± 0.087</td>
</tr>
<tr>
<td>DSA (n=12) 0.269 ± 0.372</td>
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<tr>
<td>NSA (n=9) 0.489 ± 0.346</td>
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<tr>
<td>DSA v. NSA P = 0.05</td>
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<tr>
<td>NSA v. controls P &lt; 0.02</td>
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<tr>
<td>60 minutes</td>
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<tr>
<td>Controls (n=17) 0.075 ± 0.063</td>
</tr>
<tr>
<td>DSA (n=12) 0.27 ± 0.38</td>
</tr>
<tr>
<td>NSA (n=10) 0.30 ± 0.38</td>
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<tr>
<td>DSA v. NSA P = NS</td>
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<tr>
<td>NSA v. controls P &lt; 0.01</td>
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Effects of asphyxia on cerebral blood flow and oxidative metabolism in the newborn lamb. R M Gardiner. Physiological Laboratory, Cambridge.

In this study, the effects of asphyxia on cerebral blood flow and metabolism were investigated in 15 lambs of mean gestational age 145 ± 1 days between 3 and 42 days after birth. The animals were anaesthetised with sodium pentobarbitone, paralysed with gallamine, and maintained on IPPV via a tracheostomy. Cerebral blood flow (CBF) was measured using a hydrogen clearance technique, and cerebral metabolic rate (CMR) quantified by simultaneous determination of arteriocerebral venous concentration differences.

Episodes of asphyxia (n = 13) during which mean PaO₂ fell from 61 ± 1 to 29 ± 1 mmHg, and mean PaCO₂ rose from 34 ± 1 to 56 ± 1 mmHg, were associated with a rise in CBF from 52 ± 3 to 96 ± 5 ml/100 g per minute, a fall in CMR O₂ from 136 ± 11 to 80 ± 6 µmol/100 g per minute, and no change in CMR glucose. The glucose-oxygen index (6 CMR glucose/CMR O₂) increased from 1.2 ± 0.1 to 2.23 ± 0.3 (P < 0.01).

The sensitivity of CBF to alterations in arterial Pco₂ at constant arterial Po₂ was also examined. In the range of Pco₂ 15-95 mmHg there was a linear correlation between CBF and Pco₂ (r = 0.94, P < 0.001) with a slope of 1.95 ml/100 g per minute mmHg Pco₂. During normoxia, an increase in arterial Pco₂ equal to that produced during asphyxia was associated with an equivalent rise in CBF but no significant depression of CMR O₂.
Blood pressure and cerebral blood flow in the healthy neonate. Frances Cowan (introduced by J H Tripp). Neonatal Unit, Department of Physiology, London Hospital Medical College.

Simultaneous measurements were made of the BP (systolic and diastolic) and the cranial blood flow (CBF) in a series of healthy babies using noninvasive and nondisturbing techniques.1 All studies were performed at least 2 hours postprandially and the sleep state was noted. An average of BP readings taken at one-minute intervals during the CBF measurement was calculated and used in the analysis.

The results show that in a group of 12 babies (6 in REM and 6 in NREM sleep) there is a significant correlation between pulse pressure (PP) and CBF, but none between systolic or diastolic pressure and CBF. However, when PP is plotted against CBF in a group of infants all in the same sleep state this apparent relationship is no longer demonstrable. This is true for REM or NREM sleep. PP and CBF readings are lower in NREM than REM sleep but the ratio CBF/PP does not remain the same for a particular child when he changes sleep state.

It therefore seems that the healthy newborn can control his CBF independently of his BP and any apparent relationship between the two is heavily influenced by the sleep state of the child.

References

Cell size and cell number: a reconsideration of organ growth and catch-up potential. J Dobbing, Jean Sands, Charmaine A Gratrix. Department of Child Health, University of Manchester Medical School.

Tissues and organs have been said to pass through three phases of growth and development.1 The first mainly consists of cell multiplication (hyperplasia), the last phase of growth in cell size (hypertrophy), and during the middle phase the cessation of cell multiplication overlaps with the beginning of growth in cell size. Cell number and size in this context were measured indirectly by total organ DNA; and weight or protein content per unit of DNA respectively. It was suggested2 that nutritional growth restriction during the first phase, but not during the last, is followed by a resistance to 'catch-up' on rehabilitation.

We re-examined this premise in the liver, heart, kidney, and gastrocnemius of 392 developing rats, ranging in age from 18 days of gestation to 112 days of postnatal life, and found that the sequence is very different from that which was described. Cell multiplication, instead of ceasing early with an adult number of cells, continues throughout the entire period of growth in organ weight. Growth in mean cell size begins in the early stages of the period, not later, and is complete long before the end of cell multiplication or growth in organ weight.

It is therefore difficult to accept the earlier hypothesis regarding catch-up growth.

References

Enteroendocrine response of coeliac children to gluten challenge. J F T Glasgow, D C Carson, C Shaw, J M Sloan, K D Buchanan. Department of Child Health, Department of Medicine, and Department of Pathology, The Queen's University of Belfast.

11 coeliac children, mean age 6.7 (3.6–11.7) years, who initially had had flat jejunal mucosas at least 2 years before and a good response to gluten withdrawal, were challenged with gluten powder (25 g daily for those >6 years of age, 15 g if <6), Plasma N-terminal glucagon-like immunoreactivity (N-GLI), vasoactive intestinal polypeptide (VIP), insulin and glucose were measured fasting, and after a glucose load (1.75 mg/kg), at 45 and 120 minutes, both before gluten challenge when mucosal histology was normal, and afterwards when it was abnormal as judged by significant deterioration in morphometric indices (P<0.005). Also before and after challenge, counts were made of gut endocrine cells within jejunal biopsies—VIP, gastrin, and gastric inhibitory polypeptide (GIP)—using immunohistochemistry.

After gluten challenge there was a highly significant increase (paired t test) in plasma N-GLI when fasting (P<0.025), and after glucose at 45 (P<0.005), and 120 minutes (P<0.005). The presence of symptoms, which occurred in 6 of the 11, did not significantly influence the size of this increase. Significantly lower after gluten challenge were the one-hour d-xylose, fasting cholesterol, and glucose levels (in each P<0.05), although the 45- and 120-minute values for glucose and all those for insulin and VIP were virtually the same before and after challenge. Per unit area of jejunal mucosa there was a significant increase in VIP staining endocrine cells (P<0.05), but not in gastrin or GIP cells.
Gut hormonal changes (humoral and cellular) are implicated relatively early during relapse in coeliac disease. The high fasting N-GLI values in relapse may have a role in clinical diagnosis and management.


In children with untreated cystic fibrosis (CF) the faecal excretion of bile salts is markedly increased, to a degree similar to that found in children with ileal resection, but the pathogenesis of this abnormality has not been defined. We investigated the effect of dietary and naturally occurring intraluminal compounds on the absorption of taurocholate (TC) in the distal ileum, using the rat as an experimental model.

The absorption of TC was studied by using an in vivo steady state perfusion technique to determine simultaneously the luminal disappearance and biliary appearance of TC, which correlated closely.

1 mmol/l TC absorption was inhibited by 2% albumin (P <0.001) and by 3 mmol/l lysolecithin (P <0.001), the inhibitory effects were additive. Long and medium chain triglycerides (10 and 20 mmol/l) and 3 mmol/l lecithin had no significant effect on the absorption of 0.5 and 1 mmol/l TC.

These data suggest that lysolecithin and unhydrolysed dietary protein have an additive effect in inhibiting the active ileal reabsorption of bile salts and could provide an explanation for the increased faecal excretion of bile salts in CF. Moreover, these results do not support the hypothesis that unhydrolysed triglyceride or lecithin inhibits the ileal re-absorption of bile salts in CF.

Electronic skinfold measurement. G P Wyatt, V Miller, T Brown. Booth Hall Hospital, Blackley, Manchester, and Department of Medical Biophysics, Manchester University.

Skinfold calipers are used extensively in the assessment of body fat in babies and children. They provide information about malnourished children individually in hospital and collectively in the community.

Calipers are not easy to use by the standard technique, but remain one of the few tools of the clinical nutritionist outside the laboratory.

Because it is difficult to read skinfold thickness in burnt children who are receiving large volumes of milk, we examined a normal population of children to measure the decline with time of the skinfold measurement at triceps and subcapular sites.

30 triceps and 29 subcapular sites were measured with electronically adapted Holtain calipers, in the manner described by Tanner and Whitehouse. Because the operator was well practised he was able to identify a point of early contact by visual inspection of the dial.

<table>
<thead>
<tr>
<th>Visual results</th>
<th>% of decline</th>
<th>Time of decline</th>
</tr>
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<tbody>
<tr>
<td>Triceps</td>
<td>7.62 ± 2.38</td>
<td>90% by 5 seconds</td>
</tr>
<tr>
<td>Subcapular</td>
<td>5.9 ± 2.38</td>
<td>96% by 4 seconds</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Electronic results</th>
<th>% of decline</th>
<th>Time for decline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triceps</td>
<td>16.68 ± 8.04</td>
<td>5 seconds</td>
</tr>
<tr>
<td>Subcapular</td>
<td>23.48 ± 12.78</td>
<td>4 seconds</td>
</tr>
</tbody>
</table>

Electronic results showed a greater decline than visual ones because of rapid changes of compression over short periods of time. The % decline was a measure of the compressibility of the skinfold.

A common physical sign in clinical medicine is pitting oedema, achieved by compression of the subcutaneous tissues by the thumb. Electronic skinfold calipers may refine the clinical measurement as well as comment on the compressed skinfold. We measured 18 ellipses of skin with subcutaneous tissue and found a mean water content of 27.28 ± 7.79%. We speculate that if the relatively uncompressed skinfold was measured as well as the compressed skinfold, comment on more than the skinfold fat could be made.


This paper reports the effect of baclofen on gait patterns of 15 hemiplegic children aged 4–15 years. Gait was assessed by polarised light goniometry which enables measurement of hip and knee flexion at different phases of the gait cycle to be made. After initial clinical and goniometric assessment, baclofen 5–10 mg/day was started and increased over 4–6 weeks to a maintenance dose of 1–1.5 mg/kg per day. Assessments were made weekly throughout. Baclofen caused a statistically significant decrease in hip and knee flexion at the ‘toe-off’ phase of the gait cycle in both legs but not at other phases of the cycle. Of 9 children with the greatest improvements in goniometric tracings, 5 showed obvious clinical
improvements, 2 slight improvements; in one there was no change, and in one gait had deteriorated. Of 6 children with slight or no change goniometrically, 4 showed no change clinically, one slight clinical improvement, and one a deterioration clinically. Children with significant shortening of the affected leg did not benefit. Side effects were transient sedation (7 children), difficulty with concentration (1 child), behaviour disturbance (1 child), and nocturnal enuresis (3 children).

Conclusions. (1) Polarised light goniometry is a rapid and satisfactory method of assessing change in gait. (2) Although baclofen causes functional improvement in some hemiplegic children its use should be carefully supervised as there can be side effects and gait can deteriorate.

Investigation of a child with narcolepsy. Andrew Evans. St George’s Hospital Medical School, London.

Narcolepsy is a disorder of unknown cause comprising excessive daytime sleep attacks. There is usually nocturnal sleep disturbance, and it may be associated with cataplexy, hypnagogic hallucinations, and sleep paralysis. Early onset REM sleep is a pathognomonic feature of the condition. An 8-year-old girl presented with narcolepsy. She was investigated by polygraphic recording of EEG, EOG, and EMG, and simultaneous hourly blood sampling for 24 hours. The samples were assayed for GH, FSH, TSH, cortisol, cyclic-AMP, melatonin, and 5-methoxytryptophol. The results showed massive GH production with 4 nocturnal peaks greater than 120 mU/l and fasting levels of 109 and 121 mU/l. Pineal function showed an inversion of the usual circadian rhythm. Measurement of urine output showed a very large bladder capacity which may be an adaptive response.


Loperamide (Imodium) is an opiate-like compound which is now widely used in the treatment of diarrhoea. It is known to reduce intestinal motility. Prostaglandins induce small intestinal secretion of fluid and electrolytes and have been implicated in the pathogenesis of certain diarrhoeal states. This study was prompted by the hypothesis that the therapeutic effects of loperamide were related not only to its effect on motility, but also to an effect on small intestinal absorption.

The effect of loperamide on intestinal transport during absorption and during prostaglandin- (PGE) induced secretion has been studied using an in vivo, steady-state perfusion technique in rat jejunum.

Loperamide treatment resulted in increased absorption of fluid (P < 0.05), sodium (P < 0.05), and glucose (P < 0.05) from a glucose electrolyte perfusate. PGE induced secretion of fluid and electrolyte (P < 0.001) and inhibited glucose absorption (P < 0.001). Loperamide treatment reversed this secretion of fluid (P < 0.001) and electrolytes (P < 0.01) to absorption and enhanced glucose absorption.

These results indicate that loperamide is an antisecretory agent, and provide an additional dimension to explain its beneficial effect in diarrhoea.

Cirulating immune complexes in children with fulminant hepatic failure and renal failure. V F Larcher, D Vergani, A P Mowat. Department of Immunology and Child Health, King’s College Hospital, London.

Renal failure of unknown cause is a common and usually fatal complication of fulminant hepatic failure (FHF). Since immune complexes have been found in serum and glomeruli in patients with liver disease, we tested for circulating immune complexes (CIC) in 14 children with FHF, 7 of whom developed renal failure, by Clq binding and Raji cell techniques. Sera from 4 children surviving FHF and 20 age-matched controls were also examined.

Significantly high levels of Clq binding CIC were detected in 10 of 14 children with FHF and one of 4 survivors, compared with controls. For IgG complexes, detected by Raji cell technique, the respective figures were 8 out of 14 and 0 out of 4, and for IgA 2 out of 14 and 0 out of 4, and for IgM 12 out of 14 and one out of 4.

C1q binding CIC were found in all 7 children with renal failure, IgG complexes in 6 out of 7, IgA in one out of 7, and IgM in 7 out of 7.

As complement affects the clearance of CIC we measured functional activity of complement components in these children. All 14 in FHF had significant defects in factors B,D, C3, 4, 5 and total alternative pathway activity, indicating a possible relationship with the high levels of CIC.

CIC in children with FHF are found more commonly in those with renal failure, suggesting a possible role in pathogenesis.


Breast feeding has been implicated as a major factor
in protection of infants against respiratory syncytial (RS) virus bronchiolitis. The mechanism of protection however, remains obscure. In this study we examined the immunological reactivity of humoral and cellular components in colostrum and milk collected throughout lactation from healthy primipara.

All mothers tested secreted virus neutralising inhibitors in colostrum correlating with high levels of specific antiviral IgA. Only 4 of 16 mothers continued to secrete antibody in their milk during the period that their infants were most vulnerable to RS virus infection, 2 to 6 months postpartum. Low titres of virus neutralising inhibitors were detected in milk samples from all mothers, probably representing a nonimmunoglobulin inhibitor.

Lymphocyte transformation assays were performed on cells collected from colostrum, on cord blood, and maternal blood. Of 17 colostral samples which produced a significant proliferative response to PHA only 5 reacted significantly to RS virus antigen. Specific RS virus reactivity in colostral lymphocytes did not correlate with reactivity in maternal or cord blood lymphocytes.

Thus, although there was evidence that most mothers had experienced RS virus, in less than one-third was substantial immune reactivity detected in colostrum and milk.

Comparison of the radioallergosorbent test with skin and provocation tests and the clinical history in asthmatic children. R C McWilliam, T H MacDonald. Department of Child Health, Royal Hospital for Sick Children, and Stobhill Hospital, Glasgow.

A comparison of the radioallergosorbent test (RAST), skin test, nasal provocation test, and the allergen exposure history was made in 39 asthmatic children using a panel of 8 allergens: house dust mite, cat fur, dog dander, Aspergillus fumi-gatus, Cladosporium herbarum, Mucor racemosus, grass pollen, Betula verrucosa. Skin tests were performed by the scratch technique using undiluted extracts, and nasal provocation tests were performed using one drop of undiluted extract on the septal mucosa of one nostril (the other nostril acting as a control). The history was recorded.

The overall agreements obtained were: RAST/skin test 80%; RAST/nasal test 74%; RAST/history 81%; skin test/nasal test 82%; skin test/history 81%; nasal test/history 81%.

It is concluded that the RAST is as reliable as a test for allergen identification as are skin testing and nasal provocation testing.


Finnish type congenital nephrotic syndrome is associated with certain morphological characteristics (large placenta, low birthweight, small low bridged nose, widely open anterior and posterior fontanelle, increased separation of skull sutures, calcaneovalgus deformities). There are other histological types of congenital nephrotic syndrome, the most common being diffuse mesangial sclerosis. During the last 4 years we have seen 6 cases of congenital nephrotic syndrome all of which showed the characteristic morphological features, irrespective of histological type. In addition other articular deformities were commonly present affecting predominantly the upper and lower limbs.

The morphological features are not, therefore, confined to the Finnish type of congenital nephrotic syndrome but are a consequence of being nephrotic in utero. These characteristic features should enable an early diagnosis to be made if the presence of oedema, proteinuria, and hypoalbuminuria are sought.

Controlled trial of cromoglycate and slow-release aminophylline in perennial asthma in childhood. A T Edmunds, F Carswell, Pat Robinson, A O Hughes. Bristol Royal Hospital for Sick Children.

In a randomised double-blind crossover trial 30 children with perennial asthma received slow-release aminophylline (Phyllocontin), cromoglycate (Intal), and placebo for periods of one month each. Before the trial began the therapeutic dose of slow-release aminophylline was individually adjusted and each patient was taught how to use a spinhaler. Control of asthma was assessed by comparing daily records of symptom scores, morning and evening peak expiratory flow (PEF), and use of salbutamol for treatment of intermittent symptoms.

During treatment both with slow-release aminophylline and cromoglycates, symptom scores were lower, use of salbutamol was less, and PEF was significantly greater than during the placebo month. Severe attacks requiring treatment with prednisolone at home or admission to hospital were also significantly fewer during active treatment. Symptom scores were significantly lower during the cromoglycates period than during the slow-release aminophylline period, but no difference between the two treatments was shown by the other measurements. There were few side effects with either treatment and 80% of patients preferred taking slow-release aminophylline.

Both drugs provided effective prophylaxis for perennial asthma in children.
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