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Epidemiological association with Reye's syndrome. M H Bellman, E M Ross, D R Coid, N S B Rawson. Department of Paediatrics and Community Medicine, Middlesex Hospital Medical School, and Horace Joules Hall, Central Middlesex Hospital, London.

The National Childhood Encephalopathy Study is a 3-year investigation into epidemiological factors associated with acute neurological disorders in children aged from 2 months up to their 3rd birthday. All paediatricians in England, Scotland, and Wales were asked to notify cases admitted to hospital with a defined group of clinical conditions.

Of 48 cases notified as Reye's syndrome, recognised diagnostic criteria were fulfilled in 37. The sex ratio was equal and the mean age at onset was 12 months. 17 (46%) patients died in the acute illness, and of 34 followed up for one year, 11 (30%) were severely handicapped, and 6 (16%) were apparently normal. 23 (62%) children had evidence of an intercurrent infection immediately preceding Reye's syndrome and in 2 a virus was identified.

The mean birthweight for boys was 3236 g, and that for girls 3112 g. Birthweights of matched controls were 3244 g and 3315 g respectively. 15% of the patients had been breast fed for at least 4 weeks compared with 30% of the control subjects.

The diagnosis of Reye's syndrome is often difficult and its aetiology remains unknown. It is a multifaceted manifestation of disorder rather than a distinct disease entity. It affects previously well children and generally has tragic consequences.

Does methotrexate impair its absorption in children with acute lymphoblastic leukaemia? C R Pinkerton, J F T Glasgow, J M Bridges, G Welshman. Department of Child Health and Department of Haematology, Queen's University of Belfast, and Department of Clinical Chemistry, Belfast City Hospital.

Methotrexate (MTX) is an important drug in the maintenance phase of management of acute lymphoblastic leukaemia. It is known however, to affect small gut structure and function1 which may impair drug absorption and perhaps shorten remission. Moreover it has been suggested that certain children absorb MTX poorly2-3 and in a recent study by us of 30 children with acute lymphoblastic leukaemia, 6 were found to reach peak levels lower than 5 x 10^-7 mol/l.

To study the association between therapy and absorption, 4-hour MTX absorption profiles were determined on 6 children on the 1st and 5th days of treatment with MTX. In accordance with a strict protocol, while recumbent in hospital, fasting, and on no other therapy, MTX levels were measured by EMIT immunoassay. Simultaneously a 1-hour D-xylose test was carried out.

Our findings showed no significant differences in the absorption profile between the 1st and 5th days and although D-xylose malabsorption was demonstrable on day 1, it was not significantly greater on day 5.

We conclude that the acute effect of MTX on the gut does not affect MTX absorption.

References

Patients' and parents' understanding of sickle cell anaemia—results of a questionnaire. N Murtaza, A Muller, C E Stroud. Department of Child Health, King's College Hospital, London.

Education is an essential part of the follow-up of any chronic illness. A study was designed to assess understanding of the disease at a children's sickle cell anaemia clinic in south London. 56 subjects (25 patients and 31 parents) answered 51 questions about clinical and genetic aspects of the disease, basic physiology, and their attitudes to sickle cell anaemia.

Answers were graded and statistically analysed. Knowledge of physiology relating to sickle cell anaemia was disappointing, while the level of understanding of the genetic aspects was more
encouraging, with over 70% correct responses. The factor which most influenced understanding was severity of the disease; but age, type of sickle disorder, number of years since diagnosis, and whether or not biology education had been received at school, influenced the replies too. Understanding was not affected by gender.

As a result of this study, measures to improve understanding will be introduced at our clinic. An illustrated booklet is being prepared and we have resolved to simplify our explanations of the disease still further, avoiding the use of unfamiliar words. The effect of these measures will be assessed in a repeat questionnaire.


Visualisation of intracranial structures with diagnosis of haemorrhage by real-time ultrasound has been shown to be a powerful noninvasive method for studying neonatal cerebral pathology. A scan can be performed rapidly in the incubator with little handling, even in the smallest preterm neonate. Information on dilatation of cerebral ventricles and haemorrhage may be obtained.

A systematic method is described for scanning a baby’s head, and a comparison is made between linear array and mechanical sector real-time scanning.

In a retrospective study of 50 infants admitted consecutively to Hammersmith Hospital neonatal unit, intraventricular haemorrhage (IVH) was found in 18 (36%). The infants included 10 (43%) out of 23 of birthweights <1500 g and 3 (27%) out of 11 of birthweights 1501–2000 g. An unexpected feature was the presence of IVH in 5 of the 13 infants above 2000 g birthweight. On sequential daily scans IVH was diagnosed most frequently in the first 2 days of life, and abnormal echoes often persisted for up to 12 days.

Does the pattern of ventilation determine the degree of lung damage after intensive care of the newborn? M J Robinson, C Maayan, F G Eyal, Y Armon, S Godfrey. Department of Paediatrics, Hadassah University Hospital, Mount Scopus, Jerusalem, Israel.

The lung damage associated with mechanical ventilation (IPPV) has been variously ascribed to oxygen toxicity, ventilation damage, or to persistence of the original disease.

Lung function studies were performed on 14 infants 22–67 weeks after undergoing IPPV using the whole body infant plethysmograph, and on 5 infants of comparable size who had received continuous positive nasal pressure (CPNP). The ventilated infants had increased airways resistance (P<0.01) and decreased specific airways conductance (P<0.001) compared with the CPNP-treated group. There was no relationship between peak respiratory pressure and its duration, the level of CPNP and its duration, or the length of time for which more than 60% oxygen had been given. The degree of lung damage was not related to the maximum ventilation frequency used but was related to the duration of rapid frequency ventilation (P<0.025).

This study supports the concept that barotrauma is a major factor in the aetiology of lung disease after neonatal intensive care.

Neural tube defects, the trophoblastic rest hypothesis, and spontaneous abortions. T J David, Caroline M Smith. Booth Hall Children’s Hospital, Manchester.

It has been suggested that residual material from a spontaneous abortion may interact unfavourably with the fetus in an immediately succeeding pregnancy and cause neural tube defects (the trophoblastic rest part of Knox’s fetus-fetus interaction hypothesis). A recent study suggested that there might be a 4-fold increase in congenital malformations in the pregnancy after a spontaneous abortion. It was felt that this supported the rest hypothesis. This increase in malformations applied to non-neural tube defects as well, and was on a scale far higher than had been suggested.

We studied a cohort of women whose final delivery at the Bristol Maternity Hospital was in 1969 and 1970, and there were 2625 informative pregnancies. The rate of malformations was the same whether a pregnancy followed a normal pregnancy or a spontaneous abortion. However, the rate of abortions after a preceding abortion was increased more than 2-fold.

12 of the 30 cases of neural tube defects were first pregnancies, and in 13 of the 18 cases in which there had been a previous pregnancy the previous pregnancy was normal. To fit the trophoblastic rest hypothesis one would have to presuppose an undetected previous spontaneous abortion in these 25 cases.

These results in general do not support the trophoblastic rest hypothesis.
References


A paper by Goldman et al.1 drew attention to the increased respiratory resistance imposed by the use of the Argyle® CPAP nasal cannula which results in increased respiratory work.

We studied Argyle cannulas in our laboratory and found that the resistance to airflow was about twice that of the normal neonatal nasal airways resistance² and that this resistance varied according to the cannula, being increased in some more than 2-fold if the plastic connector was pushed firmly into the soft nasal adaptor.

We compared the resistance of Argyle CPAP nasal cannulas with that of other commonly used devices—such as Portex—endotracheal tubes, and twin nasal CPAP cannulas of varying diameters and lengths, and a nasal adaptor of our own design used for pulmonary function tests in the newborn.

The flow resistance in endotracheal tubes and twin nasal CPAP cannulas is equal to, or higher than, that in Argyle cannulas, but much lower in the Aberdeen nasal adaptor.

The findings have important implications in the choice of method of delivering CPAP to neonates whose reduced pulmonary compliance necessitates increased respiratory effort.

References


*Argyle, Sherwood Co, St Louis, Mo. †Portex, Hythe, Kent.

Child poisoning and child abuse. J R Sibert, J F Murphy. Llandough Hospital, Penarth, South Glamorgan, Wales.

Birth factors that might indicate children to be at risk from nonaccidental injury have been studied before. However, indicators after birth have been difficult to assess. We studied the medical records of 80 children under 5 years on the South Glamorgan Child Abuse Register who had been admitted to hospital for poisoning before the episode of non-accidental injury. We compared these children’s records with the records of 80 control children matched for age and sex from the Cardiff Birth Survey.

10 of the 80 abused children had had poisoning episodes compared with 2 of the controls. This difference was significant (P<0.05).

Although nonaccidental poisoning is recognised as a type of child abuse, we believe these episodes were not deliberate but accidental and indicated family stress. This is further evidence that child poisoning may be an important symptom of family problems.


Spirometry, including FEF₂₅₋₇₅, static lung volumes, maximum expiratory flow volume curves, and single breath nitrogen manoeuvres were performed on these subjects during a period when each was symptomatically well.

FEF₂₅₋₇₅ and the slope of the alveolar plateau, measured from the single breath nitrogen test, were found to be the most sensitive indices of lung function abnormality in early adult life. Of the group that had had mild infrequent wheezing in childhood, half of them were now indistinguishable from the control group and the remainder had only slight abnormalities. Grades with continued wheezing to adult life were readily distinguishable from the control group, and those with persistent wheezing had a greater degree of physiological abnormality than those with episodic wheezing at 21 years of age. More than 80% of the children with active wheezing at 14 still had symptoms in early adult life but spirometric indices showed significant improvement.


In order to assess the incidence of duodenal ulceration in children, and the long-term morbidity with
present management, we have reviewed the case records of all children diagnosed in this hospital as having duodenal ulceration in the years 1968–78. This study included only patients in whom an ulcer crater was found radiologically or endoscopically. 50 patients fulfilled this diagnostic criterion. In a previous series in Glasgow, 35 patients presented over 7 years. An incidence of 5 new patients each year therefore remains unchanged. Acute secondary ulcers were excluded from the study.

As in most reports, males predominated (2:3:1). Half the children had a positive family history. Recurrent abdominal pain was a major presenting symptom in 78%. Only 6 patients presented under 5 years of age. In this group symptoms were vague and there were diagnostic delays.

The majority (86%) of patients were treated with antacids when symptomatic, but 80% of those followed up still had recurrent symptoms at least one year after diagnosis.

Thus chronic duodenal ulceration causes significant long-term childhood morbidity in the west of Scotland, unsatisfactorily controlled by present management.


Four infants with congenital sleep-related central hypoventilation have been described.1 We have studied one more such infant from birth to 9 months. Her neurological status and developmental progress were normal. When awake or in rapid eye movement (REM) sleep she showed mild hypoventilation (150–200 ml/kg per min) but in quiet sleep (QS) hypoventilation was severe (80–90 ml/kg per min) and necessitated ventilator support. Inhalation of 100% oxygen produced no significant change when awake or in REM sleep, but in QS produced a further depression of respiration (to 59 ml/kg per min). Inhalation of 4% CO₂ in air had no effect in REM sleep or when awake. In QS there was a small immediate response but no further increase in respiration after 5 minutes’ breathing CO₂.

These results show profound impairment of the 'metabolic' control of respiration, with absent central chemoreceptor effects (steady-state CO₂ response) and depressed peripheral chemoreceptor effects (hyperoxia and 'immediate' CO₂ responses). They demonstrate the importance of the 'metabolic' control system in QS. In REM sleep or when awake, respiration is maintained relatively independently of metabolic drives.

Our results are similar to those of Shannon1 and support the concept that there are 2 independent control systems for respiration—a 'metabolic' system, acting mainly in QS, and a 'behavioural' system, acting mainly in REM sleep or when awake.

Reference


What are the medium-term benefits of monocomponent insulins? M Webster, P H W Rayner. Children’s Hospital, Birmingham.

The use of highly purified (monocomponent MC) insulins has now become routine treatment for newly diagnosed juvenile diabetes. This has markedly reduced the incidence of injection lipatrophy. The long-term benefits of MC therapy cannot yet be assessed. The possible benefit of MC insulins in terms of dosage required and the length of the remission phase was retrospectively examined.

Two groups of patients were studied. Group 1 received only MC insulin (22 children followed for one year, including 17 followed for two years). Group 2 received only standard insulins (24 children followed for two years). The severity of metabolic disturbances was similar in both groups. Insulin dosages were expressed according to U/kg body weight. No significant difference was found in the initial stabilisation dose (group 1 0·83 ± 0·36, group 2 0·88 ± 0·34) or in the lowest dose achieved (group 1 0·54 ± 0·27, group 2 0·50 ± 0·27). At one year group 1 children were receiving 13·5% insulin less than group 2 (0·77 ± 0·32; 0·89 ± 0·27), and at two years 20% less (0·81 ± 0·26: 1·01 ± 0·36). These differences were not statistically significant.

The length of time during which the insulin dosage continued to fall after initial stabilisation and the time taken to show an increase of +20% over the initial dose was not statistically different in the two groups.

These results suggest that while a slightly lower insulin dosage may be required, monocomponent insulins do not affect the duration of the remission phase in juvenile onset diabetes.


Hypertriglyceridaemia is common in children with glycogen storage disease (GSD). Their ability to clear
circulating triglyceride was therefore, investigated by estimating the activity of 2 triglyceride hydrolases, lipoprotein lipase (LPL), and hepatic lipase (HPL) in postheparin plasma (PHP). 10 children with GSD had a mean LPL activity (±1 SD) of 0.6 ± 0.4 \( \mu \text{mol fatty acid released per ml/hour} \) which was significantly reduced compared with that of normal adults (2.2 ± 1.0, \( P<0.002 \)) and with children with familial hypercholesterolaemia (3.4 ± 1.4, \( P<0.001 \)). The HPL activity in GSD of 2.4 ± 1.8 was also reduced compared with normal adults (12.1 ± 3.1, \( P<0.001 \)) and children with familial hypercholesterolaemia (8.8 ± 3.4, \( P<0.001 \)).

Evidence for a circulating inhibitor of triglyceride hydrolase activity in GSD plasma was suggested, for (1) preheparin and PHP GSD samples inhibited the hydrolase activity of normal PHP, (2) serial dilutions of PHP GSD PHP gave increasing hydrolase activity, (3) normal hydrolase activity was obtained from GSD PHP after purification of the enzymes by affinity chromatography.

Preliminary studies suggest the raised nonesterified fatty acid concentration in GSD, particularly nonesterified fatty acid not bound to plasma albumin, is implicated in the hypertriglyceridaemia of GSD.

Liver volume estimation in children. G W Rylance, M D Cowan, T A Moreland. Department of Child Health, Department of Radiology, and Department of Pharmacology and Therapeutics, University of Dundee, Ninewells Hospital and Medical School, Dundee, Scotland.

Paediatricians frequently have difficulty in deciding whether a child's liver is enlarged or of normal size. The usual method of estimating the projection of the liver below the costal margin may not be representative of liver volumes, and other methods use x-ray or radioisotopes.

We have estimated the liver volume of 14 normal healthy children aged between 5 months and 14 years by an ultrasound scanning technique. Serial scans were recorded at 1-cm intervals between the limits of visualisation of liver outline.

Liver volume per unit weight correlated significantly with age (\( r = 0.79 \); \( P<0.02 \). The relative liver volume in the first year of life was approximately twice that at 14 years. Liver volume per unit surface area and per unit length showed no significant correlation with age.

Values for children with diseases leading to liver enlargement will be compared with the normal values and the possible use of the technique will be outlined.


Experimental zinc deficiency in animals during pregnancy, led to a significant increase in fetal malformations, retarded fetal growth, and reduced postnatal survival of the offspring. In humans low maternal serum zinc has been implicated in the aetiology of preterm birth, growth retardation, and fetal malformation.

As plasma zinc represents less than 1% of total body zinc and its concentration is directly related to the serum albumin, the zinc content of the leucocyte was studied, as this may more accurately reflect changes in tissue zinc concentration. Blood was drawn from mothers before and during labour, and from the clamped umbilical cord after delivery. Leucocytes were separated using the method of dextran sedimentation and the zinc content measured by atomic absorption spectrometry. Zinc content of the leucocyte is expressed as ng/mg dry weight.

Results showed (1) a significant correlation
between muscle and leucocyte zinc content in non-pregnant subjects \( (r = 0.8, P < 0.005, n = 29) \). (2) Maternal leucocytes were zinc-deficient at term compared with nonpregnant controls \( (control \bar{x} 71.6 \pm 11.2, \text{term pregnant } \bar{x} 59.1 \pm 22.2, t = 3.95, P < 0.005) \). (3) Maternal and fetal leucocyte zinc content were directly related \( (r = 0.61, P < 0.05) \). (4) Mothers who gave birth to small-for-gestational-age infants were found to have lower leucocyte zinc levels than the mothers of normally grown infants \( (SGA \bar{x} 51.0 \pm 9.0, AGA \bar{x} 63.1 \pm 10.6, P < 0.05) \). It is suggested that mothers of small-for-gestational-age infants may be zinc deficient.

References


Severe asthma in pre-school children is particularly difficult to manage, as most children cannot use inhalers effectively. We have compared the effectiveness of cromoglycate nebuliser solution, choline theophyllinate, and placebo in a double-blind, three-period crossover trial. 16 patients, 11 boys and 5 girls, between the ages of 1 year 9 months and 4 years 5 months took part.

In the preceding year each child had had between one and five asthma attacks requiring admission to hospital and all but one had received treatment with systemic steroids. These patients took cromoglycate nebuliser solution \( (20 \text{mg 4 times a day}) \), choline theophyllinate \( (6 \text{mg/kg 4 times a day}) \), and placebo in turn, each for a period of 8 weeks. Salbutamol \( (2-5 \text{mg 3- to 4-times hourly}) \) by nebuliser was used as necessary. No significant differences between treatments were seen in bronchodilator usage or in clinical assessment results.

Diary card symptom scores were analysed by two methods.

Theophylline and cromoglycate treatments were both more effective than placebo in relation to cough, night disturbance, and daytime activity. Neither drug was superior to the other.

The use of a mouthwash to detect oral colonisation with Candida albicans in children with acute lymphoblastic leukaemia. O B Eden, T A Gentle, M C Mott. Department of Child Health, Royal Hospital for Sick Children, and Department of Microbiology, Royal Infirmary, Bristol.

Mouthwash investigations on 35 children with acute lymphoblastic leukaemia showed a 43% incidence of oral colonisation (not candidiasis) with Candida albicans. A few patients were found to be continual carriers and a necropsy finding of systemic candidiasis was recorded in one of them. A second series in which salivary immunity was examined in 39 patients showed that 33% were colonised compared with an expected 10% in normal children. The age and sex distribution did not follow the normal children's pattern and colonisation did not correlate with anti-leukaemia therapy. Within each study the colony count/ml was remarkably constant in serial positive samples on individual patients and from the one series to the next for that patient. In each subject granulocyte and lymphocyte counts and total salivary IgA did not enable prediction of colonisation. The presence of salivary IgA anti-C. albicans antibody was at a lower incidence \( (25\%) \) in those consistently colonised compared with those showing occasional colonisation \( (62\%) \). The antibody titre was also lower in the former group. Mouth swabs frequently fail to identify colonisation if there is no overt candidiasis. The use of a noninvasive mouthwash culture procedure to detect children at risk of systemic candidiasis is recommended.

Tooth germs as a record of metabolic disturbance in pregnancy and infancy. R W Newton, R S Levine, E P Turner, A D Barson, J Dobbing. Department of Paediatric Neurology, and University Department of Oral Medicine, and University Department of Child Health, Manchester.

Purine nucleoside phosphorylase deficiency with a fatal lymphoproliferative disorder. A R Watson, D I K Evans, H B Marsden, V Miller, P Rogers. Booth Hall Children's Hospital, Manchester, and MRC Biochemical Genetics Unit, The Galton Laboratory, University College, London.