NEONATOLOGY—THEN AND NOW

Plasma volume changes in the newborn (1958/59)

The fluid shift from the vascular compartment immediately after birth

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Cambridge Maternity Hospital (Arch Dis Child 1958;33:489–98).

Postnatal plasma shift in premature infants

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In 1952, Gairdner and his colleagues drew attention to the fact that there was a consistent rise in the haemoglobin of the newborn immediately after birth. Later they went on to challenge the theory current at the time that this rise was due to transfer of blood from the placenta and the summary of the first of these papers begins:

> 'Immediately after birth there is a rise in concentration of haemoglobin and PCV [packed cell volume] in the majority of infants. The rise may be discernable within a few minutes of birth and is probably completed within an hour or two. It occurs in the absence of any transfer of placental blood'.

The conclusion reached was that these changes were due to a shift of fluid from the intravascular space:

> '. . . . mainly whole plasma and its volume may amount to a large fraction of the circulating plasma at birth, a quarter or more. In addition there is a shift of fluid from the red cells, the volume of red cells contracting after birth by an average of 3%. . . . These results imply that the foetus in utero is hydraemic, i.e. has a large plasma volume'.

The second paper confirms that a similar plasma shift occurs in preterm infants and while:

> 'in this series the magnitude of the postnatal plasma shift bears no relation to the development of respiratory distress. . . .'

> 'It was suggested that the shift might take place particularly from the pulmonary circulation and so contribute to the development of pulmonary oedema and respiratory failure . . . .'

Today. What to do, if anything, about the changes in haemoglobin, packed cell volume, plasma, and whole blood volume in the first day or two of life has exercised the minds of paediatricians for at least 30 years. These early observations have stood the test of time and it is now generally accepted that transfusion of extra blood from the placenta, once actively encouraged, can be harmful. It initially renders the baby hypervolaemic, encourages dilatation of the capillary bed with further transudate, which causes increased oedema and intravascular polycythaemia. It is also accepted that transudation from the pulmonary capillary is a precursor of hyaline membrane formation so retention of plasma within the vascular space would seem a sensible objective. The fact that an early diuresis signals a good prognosis in preterm infants with respiratory distress probably indicates return of this oedema fluid into the intravascular space with the associated improved haemodynamics similar to that seen after haemodilution, the therapeutic equivalent in infants with hyperviscosity.

I have always felt that the advantages of improved oncotic pressure (albeit transient) from infusions of albumin with the consequent reduction of tissue oedema and improved renal output outway any disadvantage there might be in increasing blood volume and so possibly prolonging patency of the ductus arteriosus. The fact that oedema does not correlate well with serum albumin is not the point.[1] Whether the baby benefits from its administration surely is and recent work would encourage the practice of infusion of salt free albumin.[2]

[1] Cartlidge PHT, Rutter N. Serum albumin concentrations and oedema in the newborn. *Arch Dis Child* 1986;61:657–60.
[2] Greenough A, Greenall F, Gamsu HR. Immediate effects of albumin infusion in ill preterm neonates. *Arch Dis Child* 1988;63:307–8.

Douglas Gairdner won a scholarship to Oxford before transferring to medicine at the Middlesex Hospital, London, graduating in 1936. After a fellowship at Bellevue Hospital, New York, he served with the Royal Army Medical Corps in the Middle East. After the war he was appointed assistant to Professor Sir James Spence in Newcastle before moving to Cambridge in 1947. His contributions to paediatric research and literature, which his modesty prevents him from enumerating, are too extensive to detail. His approach is exemplified, however, when he says of neonatal research 'It was a joy for us that the extremely simple technology, which was all we had, was yet capable of yielding worthwhile results' and he praises the dedication of his hard working colleagues. He was one of the many paediatricians of the day who rejoiced in the elevation of babies from being something of second class citizens to fully accepted 'patients' in their own right.

Douglas Gairdner has served all aspects of paediatrics with great distinction and is possibly best known for his 15 years Co-Editorship of the *Archives of Disease in Childhood* and Editorship of the first four editions of *Recent Advances in Paediatrics*. The BPA recognised his many contributions in awarding him the Spence Medal (1976) and electing him to Honorary Membership (1977).

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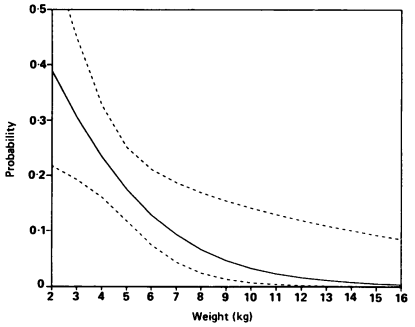
LETTERS TO THE EDITOR

Mechanical ventilation and respiratory syncytial virus infection

SIR,—Drs Lebel *et al* report weight and prematurity as risk indicators for the need for ventilation in bronchiolitis.[1] In their case-control study a viral cause was determined in only 32%; infants with underlying cardiopulmonary abnormalities—who are known to be at increased risk for severe respiratory syncytial virus infections and mortality[2 3]—were excluded. Thus the results from their study may not readily be applied to all infants with bronchiolitis who need hospitalisation.

We would like to present the preliminary results of a prospective study (1987–9) of children admitted with a respiratory syncytial virus infection to the Sophia Children's Hospital, The Netherlands. In all patients the infection was proved by direct immunofluorescent assay. Nineteen patients needed mechanical ventilation and 82 were admitted to the general ward.

Weight and age (corrected for prematurity) on admission were significantly related with mechanical ventilation (by χ^2, $p<0{\cdot}05$). No relation between mechanical ventilation and risk factors for severe respiratory syncytial virus infections (prematurity, congenital heart disease, bronchopulmonary dysplasia, or immunodeficiency states) was found. Nine (47%) of the ventilated patients and 36 (43%) of the non-ventilated patients belonged to the risk group. In a stepwise logistic regression analysis (while controlling for the covariates: age, prematurity, and risk factors for severe respiratory syncytial virus infection) only weight appeared to be significantly related to the need for mechanical ventilation (coefficient $-0{\cdot}36682$ (SE 0·1685), $p=0{\cdot}01$), while none of the other variables did. Prematurity and age were not independent risk indicators for mechanical ventilation in this study. In contrast to Lebel *et al*, who report odds ratios as 'relative risk', from the data of our prospective study we are able to estimate the absolute risk of mechanical ventilation related to the weight on admission (figure). A low weight is related to an increased risk for mechanical ventilation. For infants less than 5000 g, a relative risk for mechanical ventilation of 4·3 (95% confidence interval 1·3 to 13·9) was estimated.



Probability of need for mechanical ventilation. Dotted lines show 90% confidence interval based on logistic model.

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1 Lebel MH, Gauthier M, Lacroix J, Rousseau E, Buithieu M. Respiratory failure and mechanical ventilation in severe bronchiolitis. *Arch Dis Child* 1989;**64**:1431–7.
2 Brunell PA, Daum RS, Scott Giebink G, *et al*. Committee on infectious diseases 1986–1987. Ribavirin therapy of respiratory syncytial virus. *Pediatrics* 1987;**79**:475–8.
3 MacDonald NE, Breese Hall C, Suffin SC, Alexson C, Harris PJ, Manning JA. Respiratory syncytial viral infection in infants.

Helicobacter pylori and protein losing enteropathy

SIR,—We have demonstrated a high prevalence of anti-*Helicobacter pylori* (formerly *Campylobacter pylori*) antibodies in children under the age of 3 years in The Gambia, West Africa.[1] Using a serological test validated by histology and microbiology, 41/77 (53%) of children with chronic diarrhoea were shown to have significantly high anti-*H pylori* IgG antibody titres, and indeed, the prevalence of *H pylori* antibodies in healthy asymptomatic children of the same age was also high at 26%.

It was against the background of these findings that we were interested in the description, in 1987, by Hill and colleagues, of transient protein losing enteropathy in association with acute infection with *H pylori*.[2] This observation might be due to chance but could have important consequences in the nutritional rehabilitation of infants with chronic diarrhoea and severe protein energy malnutrition.

Therefore we undertook a study to establish whether or not *H pylori* infection was associated with protein losing enteropathy in Gambian children with chronic diarrhoea.

Fifty three subjects (25 boys, 28 girls; mean age 19 months) were studied and all had chronic diarrhoea (more than three loose stools per day for more than two weeks) and severe protein energy malnutrition (32 marasmus, 21 marasmic-kwashiorkor).

After admission, three consecutive fresh stool samples were collected for virological, parasitological, and bacteriological investigation. Specific anti-*H pylori* IgG antibody was measured by enzyme linked immunoabsorbent assay (ELISA) in all subjects. Gastroscopy and antral mucosal biopsy were performed in 20/53 children.

Protein losing enteropathy was estimated by random faecal α_1-antitrypsin measurement. Whole single stools were collected ensuring that both the liquid and solid phase were obtained. These were frozen and lyophilised and α_1-antitrypsin measured by a single radial immunodiffusion method. Random faecal α_1-antitrypsin measurement (normal mean (SD) value in healthy Gambian children=1·54 (0·23) mg/g stool) has been shown to be a reproducible screening test for excessive enteric protein loss and has been validated against ^{51}chromium labelled albumin excretion in the stool.[3]

Fifty six percent of this group of children had significantly raised anti-*H pylori* antibody titres and in 11/20 gastroscoped this was associated with recovery of the organism and histological gastritis. *Strongyloides stercoralis*, and *Giardia lamblia* were found in 11 and 38% of the patients respectively. Hypoalbuminaemia occurring in children with *S stercoralis* was found to be associated ($r=0{\cdot}952$, $p<0{\cdot}001$) with increased faecal α_1-antitrypsin excretion (mean (SEM)=2·47 (0·9) mg/g stool) whereas there was no difference between levels of faecal α_1-antitrypsin found in children with (1·57 (0·2) mg/g stool) or without (1·62 (0·3) mg/g stool) evidence of *H pylori* infection.

Therefore, in this study we failed to show that chronic infection with *H pylori* is associated with protein losing enteropathy.

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1 Sullivan PB, Thomas JE, Wight DGD, *et al*. Helicobacter pylori in Gambian children with