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Neonatology—then and now (C H M Walker)

Kernicterus (1957)

Kernicterus not associated with haemolytic disease

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This paper describes the features of 26 cases of kernicterus not associated with haemolytic disease of the newborn, a topic of growing interest at the time. Contrary to the usual experience in which such cases are found mainly in premature babies, all but two (four unknown) were born at full term. Jaundice was noted within 48 hours in more than half and the clinical indications of brain damage included drowsiness and muscular hypertonicity, though only two had fits. There was a high mortality, 15 of the 20 who died doing so within the first week. The discussion begins with a debate as to whether or not kernicterus is caused by bilirubin fixing in injured tissues or invading otherwise normal brain cells. Much is made of the fact that where predisposing factors are concerned the newborn seems able to tolerate profound hypoxia without sequelae and that exchange transfusion seems to provide considerable protection. Thus the conclusions were:

'The argument that premature babies are more prone to kernicterus than full-term infants due to their greater liability to cerebral anoxia and hence brain damage is not really tenable'.

And later 'It is therefore more likely that bilirubin or its products in excessive amounts in the blood are deposited in the brain tissue and cause injury directly.'

The author also considered that the basis of the hyperbilirubinaemia may well have been poorly nourished newborn babies as a result of maternal protein malnutrition with, in some cases, superadded infection.

Today Non-haemolytic jaundice in the newborn is still a serious problem in many parts of the world and the risk of kernicterus is ever present, especially in the preterm infant. While high concentrations of bilirubin can perhaps by themselves injure brain cells there are reports of babies (usually born at full term) with extremely high values who never show clinical evidence of kernicterus. It is now generally accepted that additional factors such as hypoxia, acidosis, hypoglycaemia, and hypothermia are frequent precursors and it is therefore not surprising that kernicterus has been found in preterm babies with bilirubin concentrations as low as 140 $\mu\text{mol/l}$.

Where adequate monitoring and treatment are available the neurological sequelae of kernicterus must now be rare in infants born at full term. It would seem, however, that up to 10% of low birth weight babies may still be found to

have a lesion at necropsy ('silent' or otherwise) with concentrations as low as 140 $\mu\text{mol/l}$. Since the association between bilirubin concentrations and neuropathology is not linear it is difficult to decide which of the several aetiological factors is most responsible, particularly when many of the later findings in the central nervous system of the preterm baby are not of the bilirubin toxicity type.¹

Specific tests for bilirubin encephalography, such as brain stem evoked responses for deafness, are required in carefully controlled long term studies if this uncertainty about kernicterus is to be resolved. Meanwhile the protective effect of exchange transfusion, which I respectively submit to have been erroneously considered to indicate the irrelevance of additional factors, should probably be offered at considerably lower concentrations in preterm babies. Whether it is more effective to give phototherapy prophylactically or to wait until the bilirubin concentration has reached about 150 $\mu\text{mol/l}$ is still uncertain but such treatment has been shown to reduce the need for the more hazardous exchange transfusion.

Reference

¹ de Vries LS, Lary S, Dubowitz LMS. Relationship of serum bilirubin to ototoxicity and deafness in high risk low birth weight infants. *Pediatrics* 1985;**76**:351–4.

Wong Hock Boon, Professor and Foundation Chairman, Department of Paediatrics, National University of Singapore, is one of Asia's foremost paediatricians. The paper chosen above is indicative of his early interest in neonatal jaundice and he has been instrumental in the virtual eradication of mental retardation due to jaundice caused by glucose-6-phosphate dehydrogenase deficiency in Singapore. His other clinical contributions include work on haemoglobinopathies, eosinophilic purpura, infectious mononucleosis, and marrow transplantation.

He has played a principal part in Singapore Ministry of Health Committees (Immunisation, Medical Advisory and Clinical Research) and has, from 1979, been Chief of the World Health Organisation Collaborating Centre for Research and Training in Human Genetics.

His contribution to paediatric writing has been quite exceptional in that he has written numerous books, contributed to many others, and has a most extensive bibliography. He has been editor or a member of the editorial board of more than 10 journals.

It is not surprising that in addition to Gold Medal and Meritorious Service awards he has more recently received the Most Outstanding Paediatrician in Asia (1986), and Inaugural Science and Technology (1987) Awards.