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Discussion

Dr Murphy of Birmingham expressed concern about using phenobarbitone in the presence of a possible metabolic defect in bile salt metabolism. It seemed possible that this might aggravate the situation by stimulating pathways which could, for example, increase production of monohydroxy bile salts. Dr Murphy felt cholestyramine might be the more appropriate agent to use. Dr Javitt stated that they have not carried out any studies on the effect of phenobarbitone on bile acid metabolism and agreed that one had to be aware of such theoretical possibilities, but pointed out that there were some children in whom phenobarbitone did seem to work. He, too, much preferred cholestyramine since its action on bile salts in the bowel is known and also if serum bile salts were altered from its use it would be possible to speculate as to how this has happened. He suggested that both agents might be used in sequence and all possible parameters in bile salt metabolism measured.

Dr Haas of Torquay commented that neonatal cholestasis often carries a good prognosis and the patients get better whatever is done. Dr Javitt agreed that this was so and that evaluation of the effects of treatment was thus difficult. Some children do have persisting symptoms and require treatment.

General discussion on pathology and pathogenesis

Professor Aagenaes of Oslo made a plea that the term 'Neonatal Hepatitis' or 'Neonatal Hepatitis Syndrome' be dropped from the nomenclature of neonatal liver disease since the word 'hepatitis' implies infection which appears to be a rare cause of neonatal obstructive jaundice. He suggested that a more neutral term such as 'Intrahepatic cholestasis' would be a more correct term for this clinical entity.

Dr Danks of Melbourne felt it was very difficult to get an all-embracing terminology. He used the term 'Neonatal Hepatitis' for children in whom liver biopsy showed a degree of cholestasis with liver cell necrosis and some reaction to these two abnormalities in the form of inflammatory cell infiltrate, fibroblastic proliferation and the development of multinucleated cells. This definition would exclude patients with mild disease who did not have a liver biopsy and would include such well defined genetic entities as galactosaemia or hereditary fructose intolerance; conditions which could not be distinguished on histological grounds. He thus found it simplest to use the term 'Neonatal Hepatitis' to cover everything, including those with predominant liver cell necrosis or predominant cholestasis, and

then try to say neonatal hepatitis due to this, or due to that (see definition on page 376 of paper by Cottrall *et al.*, 1974).

Discussion followed on the importance of bile flow in making bile ducts apparent both histologically and at laparotomy. Dr Norman Javitt stated that he thought ducts were often small in children who were not generating bile, reminding the audience that in the adult, if obstruction occurred at the porta hepatis, the distal biliary tree shrunk to a marked degree. Dr Emery agreed with this observation, commenting that infants who died with marked jaundice often had very small ducts. When one tried to get Indian ink to flow back from these ducts into the liver, it was quite impossible until the liver was manipulated. Then the Indian ink would go to isolated lobules. Dr Javitt commented that in the absence of micropuncture techniques for studying bile flow there were still many gaps in our knowledge. It was thought that the transfer of ions into the canaliculus created an osmotic gradient and subsequent water transfer. There was reason to believe that bile salts were the important ions in this regard and that if no bile salts were secreted, no bile flow would be generated. There was some evidence that other ion pumps, particularly sodium and chloride, may be involved, but the evidence was circumstantial.

Mr Nixon of London asked for views on apparent regeneration of bile ducts as seen in the child who on initial biopsy had no bile ducts, but on repeat biopsy when the child was better, ducts were found. Dr Emery suggested that a possible explanation lay in the fact that the biopsies were taken from different parts of the liver and the disease may have been affecting one segment more than the other. Dr Javitt interpreted the observation as meaning that the bile generating systems had improved and bile ducts were now more apparent. Both Mr Nixon and Dr Javitt felt that there was considerable need for a clear definition of the various types of biliary atresia, namely intrahepatic, extrahepatic, combined, and intralobular. In some situations Dr Javitt suggested that the terms 'intrahepatic hypoplasia' or 'aplasia' may be more logical. No clear definitions were forthcoming.