Correspondence

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Rickets in neonatal hepatitis

Sir,

In their recent paper in the Archives Kobayashi et al. (1974) provided further evidence that rickets is a common complication of neonatal hepatitis (Yu, Walker-Smith, and Burnard, 1971). The bone disease in these patients shows certain characteristics which separates them from the infants with rickets and biliary atresia. It is of practical significance to recognize these characteristics and consider them in the management of these patients.

The scant attention that rickets receives in articles dealing with neonatal hepatitis and the paucity of published cases are in sharp contrast with the observed high rate of these two diseases occurring together (Yu et al., 1971; Bastis-Maounis, Matsaniotis, and Maounis, 1973; Kobayashi et al., 1974). Several factors may account for this discrepancy.

1. The milder cases are likely to be overlooked altogether because of a tendency for spontaneous recovery.
2. There is a time-lag between the occurrence of the clinically active phase of hepatitis and that of the rickets. This might be partly explained by the fact that a certain amount of skeletal growth has to occur under abnormal biochemical conditions before rickets becomes clinically and radiologically detectable. Maternal supplies should secure normal bone growth initially, as the half-life of 25-hydroxy vitamin D was shown (in adults) to be 3 weeks (Bayard et al., 1972).
3. Early biochemical diagnosis is difficult: in the presence of liver disease, unless tissue-specific isoenzymes are determined, the interpretation of raised alkaline phosphatase becomes uncertain. Screening amino acid chromatograms would present a similar problem.
4. With recovery from the hepatitis spontaneous healing of the rickets appears to be common, around 6 months of age, though this is seldom observed because once rickets is diagnosed treatment is usually given.

An impaired conversion of vitamin D to 25-hydroxy vitamin D might be responsible for the development of rickets in neonatal hepatitis to a greater extent than an impaired absorption of vitamin D and bone building materials. The suggestion has been made that ‘pre-term delivery may also have contributed to the development of rickets’ in 2 infants with neonatal jaundice (Thomas and Glasgow, 1974). As all these substances are stored in the body, the occurrence of manifest bone disease might very well depend on the size of the infant’s stores. In the few reports where gestational age at delivery is given, actually all the infants with neonatal jaundice and rickets were premature, in contrast with the full maturity of the infants with the combination of rickets and biliary atresia (Yu et al., 1971; Thomas and Glasgow, 1974).

Prematurity as the primary or main cause of rickets has been reported (Boissiere et al., 1964; Lewin et al., 1971). The mechanism has not been investigated with up-to-date techniques. Thus, there is no reliable information available on the vitamin D stores, or on the ability to activate vitamin D in the liver of premature infants, compared with fully mature infants. Considering the small fat tissue and muscle mass of premature infants, the sites of storage for vitamin D, and the ‘immaturity’ of hepatic enzymes, one could reasonably expect that these factors would play a role in the development of rickets in these infants. It does seem, however, that even in premature, some additional insult, such as is represented by neonatal hepatitis, is necessary for the frequent development of clinically significant rickets.

Treatment of infants with neonatal hepatitis, using 2000 IU vitamin D daily has been recommended (Yu et al., 1971). A prematurely born infant was admitted to our hospital at the age of 5½ months suffering from rickets and cytomegalovirus hepatitis. Administration of 100 IU vitamin D orally for 2 weeks produced significant hypercalcaemia. This observation and the natural history of the disease, with a tendency for spontaneous recovery, suggests that optimal management of such patients has to be based on more specific information than such a general recommendation. Studies are needed using such methods as the estimation of urinary hydroxyproline excretion, the measuring of parathyroid hormone and 25-hydroxy vitamin D concentrations, for the early diagnosis of rickets, for follow-up and selection of patients who need treatment, for determining the appropriate dose for the individual patient, and for clarification of the specific pathological mechanism in these patients.

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REFERENCES