Correspondence

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Breast Milk Bilirubin Conjugation Inhibitors in Neonatal Hyperbilirubinaemia

SIR,

We were interested to read the observations of Cole and Hargreaves (1972) on Conjugation Inhibitors and Early Neonatal Hyperbilirubinaemia. We, also, were unable to find a correlation between the serum bilirubin concentration in breastfed, 6-day-old infants and conjugation inhibitors in the mother’s milk (Arthur, Bevan, and Holton, 1966). However, it would be wrong to conclude that breast feeding is not a factor determining early neonatal bilirubin levels. Our studies and those of Stiehm and Ryan (1965) have suggested that breastfed infants tend to have higher serum bilirubins and an increased incidence of clinical jaundice. It may be that conjugation inhibitors play no part in this, or it is possible that milk inhibitor levels, measured with an adult rat liver slice system, are not altogether relevant to the situation in the human newborn infant’s liver.

The validity of in vitro measurements of bilirubin conjugation inhibitors is also in question because of the increased activity of the milk samples on storage. We found that this occurred to a significant extent in only a few milks, but we have elucidated the mechanism of this effect (Bevan and Holton, 1972). The enhanced inhibitory activity in stored milk correlated with an increased concentration of free fatty acids. On fractionation of the milk, using thin-layer chromatographic techniques, the inhibition was found in the free fatty acid zone. We have shown pure free fatty acids to be potent inhibitors of bilirubin conjugation in rat liver slices, probably by affecting glucuronol transferase.

Prolonged jaundice in infants, caused by breast feeding, was originally described by Arias et al. (1964). It was concluded that this was due to the presence of pregnane-3α, 20β-diol in the milk, and this interfered with bilirubin metabolism in the infant’s liver. Other workers (Ramos, Silverberg, and Stern, 1966) have failed to find pregnane-3α, 20β-diol in what they believed to be inhibitory milk, and theoretical objections to this steroid being the cause of prolonged neonatal jaundice have been put forward (Adlard and Lathe, 1970; Hargreaves and Piper, 1971). The possible role of free fatty acids in this condition has to be considered. It would be anticipated that the mature infant could handle some dietary excess of fatty acids, administered in either the free or esterified form, but it is possible that, during the first few weeks of life, these could accumulate and inhibit bilirubin conjugation in the liver.

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References


Cystic Fibrosis Care—Further Considerations

SIR,

In describing the prevention of pulmonary complications in cystic fibrosis patients at Queen Elizabeth Hospital for Children, instituted by Dr. Winifred F. Young and carried on so capably by Dr. McEwn (Mearns, 1972), Dr. Mearns states that we have claimed an improved lifespan in our series of patients (Warwick and Monson, 1967) due to the introduction of mist tent therapy. Dr. Lawson, in his annotation (Lawson, 1972), questions the need for mist tent therapy.

In 1967 we reported improved pulmonary function with mist therapy using several groups of cystic fibrosis patients as their own controls. We still feel that...
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this is an effective form of therapy and employ it from the time of initial diagnosis. However, despite Dr. Mearns’ statement, we did not claim mist tent therapy to be the important factor in improved life expectancy (Matthews, Doershuk, and Spector, 1967).

We find it disturbing that not only physiologists but apparently also clinicians (Mearns, 1972; Lawson, 1972) have allowed their personal viewpoint to cloud their interpretation of what we have written, in that they have emphasized only the use or nonuse of mist tents in cystic fibrosis care. Our theme has been and continues to be one of early diagnosis, prompt and comprehensive care, and, whenever possible, prophylactic (maintenance of normal hygiene) care (Matthews et al., 1964; Doershuk et al., 1965; Doershuk and Matthews, 1968). Centres using such an approach have enjoyed success just as we and others have reported (Mearns, 1972; Shwachman, Redmond, and Khaw, 1970).

Since our centre has been active from 1957, the same period covered by Dr. Mearns’ second group of patients, we reviewed our series of patients for comparison. From 1957 until 1964, 60 patients were referred with cystic fibrosis under 1 year of age including those with meconium ileus. One died of nonpulmonary complications after meconium ileus surgery and one did not survive the initial infection. After 5 years of follow-up of the 58 survivors, there were two deaths at 3 and 5 years of age. The latter also had meconium ileus at birth. Thus, for patients surviving their initial episode, there was a 3·4% mortality (2/58), and if the meconium ileus patients are separated, there is only a 1·8% mortality (1/56). These mortality results and those of Dr. Mearns are comparable, the major differences in treatment being continuous antibiotic therapy in the first year without mist tent therapy vs. discontinuous antibiotic therapy with mist tent therapy during the first year. Complete comparison is difficult because it is not clear to us whether Dr. Mearns’ group included patients with meconium ileus or patients who died during an initial hospitalization before admission to the clinic.* It now becomes increasingly important that future reports begin to document not only mortality but also the quality of life of survivors by reporting the physical or chest x-ray status (Shwachman and Kulczycki, 1958) or by another method.

The central issue seems to us to be not how little one can do in treating a progressive, life-threatening disease; but rather, how effective a programme one can develop and maintain for the long-term home management of these patients. In our opinion, each measure recommended for long-term management works best in conjunction with the other measures. However, the continued presence of a concerned and interested physician, routine and regular outpatient visits, and respiratory cultures cannot be replaced in any way and must be repeatedly emphasized.

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REFERENCES


*Dr. Mearns informs us that she excluded from her discussion the babies who died after surgery from their surgical complications. These babies died during the first month; the majority dying in the first week after operation. Other babies with meconium ileus were included.—Editors.