

disaccharides very rapidly. Within a few minutes much of the disaccharide had been split and no traces could be found after 30 minutes. Since the same process is assumed to take place in the lower gut, children with disaccharidase deficiency cannot be expected to excrete disaccharide alone in their faeces without the corresponding monosaccharides. The lack of a disaccharide in the faeces does not exclude the possibility of disaccharidase deficiency. Acid hydrolysis of faecal samples in cases of suspected sucrase deficiency seems not to be necessary.

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## Effect of gestational length on albumin content of meconium

A raised protein level in the meconium of an infant with cystic fibrosis (CF) was described by Buchanan and Rapoport (1952) in an infant with meconium ileus. This finding was confirmed by Green, Clarke, and Shwachman (1958) who showed that the protein was predominantly albumin. Wisner and Beier (1964) and Green and Shwachman (1968) subsequently showed that the meconium of infants with CF contained high levels of protein even in the absence of meconium ileus. Estimation of the protein content of meconium was suggested as a possible screening procedure for CF by Schutt and Isles (1968) and the results of such surveys have been reported (Cain, Deall, and Noble, 1972; Prosser *et al.*, 1974).

In late 1971 we began to screen the newborn of North Monmouthshire and Breconshire for CF using an immunochemical method for the detection of albumin in meconium (Bull, Gladwin, and Griffiths, 1974). We found that false-positive results (i.e. detection of raised levels of meconium albumin in infants later shown to be clinically healthy and to have normal sweat electrolytes) did occur but the overall rate was low, being approximately 1%. It was our impression that such false-positive results were commoner in premature infants, and the present paper investigates this possibility.

### Materials and methods

During the 3½-year period between January 1972 and June 1975 meconium samples from 6552 infants were tested for the presence of albumin using an immunochemical method previously reported (Bull *et al.*, 1974). In this method a 1/5 dilution of meconium is prepared and a positive result recorded if the meconium albumin level reaches 20 mg/100 ml of this extract. In absolute terms this is equivalent to a level of 4 mg/g dried meconium, as the solid content of meconium averages 24.5% (average of 10 analyses).

During 1973 we began to test all meconium samples which gave positive results for albumin for the additional presence of occult blood using a modification of the method described by Kolmer, Spaulding, and Robinson (1952). In the modified method 2 g powdered guaiac are dissolved in 10 ml absolute alcohol and the solution filtered (this saturated solution is stable for one month). One drop of the solution is added to a smear of meconium on filter paper and followed by one drop of glacial acetic acid and one drop of hydrogen peroxide (20 vol). An intense green or blue colour developing within one minute indicates a positive result. This method will detect blood in a dilution of 1 : 10 000.

Of the 6552 infants screened, 212 were preterm, having gestational ages of <37 weeks.

### Results

Meconium samples from 6552 infants were examined and 70 were found to contain raised albumin levels. 8 infants persistently defaulted for their follow-up appointment despite home visits by the health visitor, and though a further 4 infants have remained clinically well insufficient sweat (<100 mg) has been obtained for satisfactory analysis.

The remaining 58 infants have had negative sweat tests and have remained clinically healthy with no evidence of CF. In 17 of these infants gestational age was <37 weeks, in 35 it was ≥37 weeks, while in the remaining 6 it was in doubt and they were therefore excluded from further analysis.

The Table gives the distribution of raised meconium levels obtained from 52 healthy infants,

TABLE  
*Distribution of raised meconium albumin levels obtained from 52 healthy infants, according to length of gestation*

	Length of gestation (w)	
	<37	≥37
No. of infants screened	212	6334
No. of infants with raised meconium albumin levels		
Occult blood		
+ve	8	5
-ve	3	18
Not tested	6	12
Total	17 (8.0%)	35 (0.55%)
$\chi^2$	145.106 (P < 0.001)	

$$P = 0.001, \chi^2 = 10.827.$$

with no clinical or biochemical evidence of CF, according to the length of gestation.

Seventeen out of the total of 212 preterm infants screened had raised meconium albumin levels (8%), while the corresponding values for term infants were 35 out of 6334 (0.55%). This difference is highly significant ( $\chi^2 = 145.106$ ;  $P < 0.001$ ). The Table shows that 8 out of the 17 positive results obtained in preterm infants (47%) could be accounted for by the presence of occult blood, while only 5 of the 35 positive results in term infants (14%) could be explained on this basis.

In order to exclude the possibility that the increased frequency of raised meconium albumin levels in preterm infants was due solely to the presence of occult blood, a further analysis was performed. 3 out of 212 meconium samples from preterm infants (1.4%) contained raised albumin levels but were negative for occult blood, while the corresponding values for term infants were 18 out of 6334 (0.3%). This still represents a significant difference ( $\chi^2$  with Yates's correction = 5.049;  $P < 0.05$ ).

### Discussion

No cases of CF were found among 70 infants with raised meconium albumin levels detected among 6552 infants screened by the meconium albumin technique during the 3½ years between January 1972 and June 1975, and though it is possible that 1 of the 8 infants who persistently failed to attend for follow-up will prove to have this condition later, there is no evidence from colleagues in neighbouring areas, or from their general practitioners, that this is yet the case. Of the 70

infants with meconium albumin levels in excess of the previously established normal range, 58 had negative sweat tests and were found to be healthy on follow-up, giving a false-positive rate of between 0.89 and 1.06%.

It can be seen from the Table that when gestational age is taken into account the incidence of false-positive results in preterm infants (8%) is significantly greater than that found in term infants (0.55%) and that this difference is due largely but not solely to the increased frequency with which occult blood is found in the meconium of the preterm infants.

The method which we use for the detection of occult blood produces weak positive results at a dilution of 1/2500, and while the frequency with which occult blood is detected will depend upon the sensitivity of the method used (Ford-Jones and Cogswell, 1975) such variations in sensitivity would not account for the increased incidence of positive findings in preterm as compared to term infants. Preterm infants are, however, more likely to be born after complicated deliveries and therefore to swallow maternal blood, and they are also prone to bleeding disorders.

Even when the presence of occult blood is excluded, the meconium of preterm infants is still more likely to contain raised levels of albumin than that of term infants. One possible explanation for this finding is a relative immaturity of the pancreatic enzymes in preterm infants; thus Werner (1948) showed that proteolytic activity (after activation by enterokinase) was detectable in preterm infants weighing 1000 g and subsequently increased by a factor of 10 until the time of birth. Another possible explanation is an increased loss of albumin in preterm infants by transudation into the intestine.

The present findings indicate that screening tests for CF using the meconium albumin technique have a limited application in the case of preterm infants.

### Summary

During a screening programme for the detection of CF using the meconium albumin technique, the overall false-positive rate was found to be approximately 1%. When the gestational age of the infants was taken into account the false-positive rate was found to be significantly higher in preterm (8%) as compared to term infants (0.55%). This was due largely but not solely to the presence of occult blood. Possible explanations for these findings are discussed and attention drawn to the limitation of meconium albumin content as a screening technique for CF in preterm infants.

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