

Short Reports

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Screening for Cystic Fibrosis by Testing Meconium for Albumin

The importance of early diagnosis of cystic fibrosis (CF) has been stressed by many authors (e.g. Lawson, Westcombe, and Sagers, 1969; George and Norman, 1971).

Methods involved have been to test either the sweat or saliva of the infant for increased levels of sodium but neither test has proved reliable, easy, or cheap in the neonatal period.

Schutt and Isles (1968) found excessive albumin in the meconium of 9 cases of meconium ileus (due to CF) and wondered if meconium testing for albumin would be a practical screening test.

Wiser and Beier (1964) had previously found that 3 out of 5 newborn sibs of known cases of CF had increased amounts of albumin in their meconium and that all the neonates with raised levels of albumin were subsequently proved to be further cases of CF.

We are in the process of conducting a newborn screening programme to detect the presence of albumin in meconium, and we are writing this preliminary communication because one case of CF has been found in the first year of the trial.

The maternity units involved in the survey have a combined delivery rate of about 5000 babies a year.

Method

The first specimen of meconium is saved in its nappy. A smear is made of this meconium on to a glass microscope slide and thoroughly mixed with a few drops of distilled water with half an orange stick. A Labstix strip (Ames) is then placed so that the edge of each of the test areas is in the resulting mixture; the strip being held horizontally with the test areas perpendicular to the slide. The presence or absence of albumin and blood is noted, traces of either being ignored. Any baby whose meconium shows the presence of both albumin and blood has a further sample of meconium or stool tested at a later date. Any baby whose meconium contains more than a trace of albumin has further specimens of meconium and stool tested and those who are persistently positive have further investigations for CF. The time taken to perform the test is 10 to 15 seconds: it is not necessary to wait for the recommended 30 seconds to look for blood if the test is negative for albumin.

Case Report

A.M. was a forceps delivery at 37 weeks' gestation, his mother being an 18-year-old primigravida. There was no history of consanguinity. His weight was 2.51 kg, length 45 cm, head circumference 32 cm and the Apgar score at 1 minute was 9. A specimen of meconium was obtained at the age of 6 hours and showed albumin +++ to be present. A further specimen was obtained at 22 hours with an identical result. After this his stool changed from meconium to a normal yellow colour, though it was noted to be somewhat bulky, but all subsequent tests confirmed the presence of albumin in amounts from ++ to ++++. Further investigations showed no tryptic activity to be present in the stool, a sweat sodium of 95 mEq/l., and a 5-day faecal fat excretion of 6.9 g per day when being fed on a half-cream milk. A chest x-ray showed no abnormality.

At the age of 3 weeks he has started on pancreatic extracts in each feed and postural drainage with gentle percussion given before feeds. Four days later it was noted that he was beginning to cough and a few medium rales were noted at the right base. A throat swab grew a coagulase positive staphylococcus. Cloxacillin was given in addition to the physiotherapy and pancreatic extracts.

He was able to go home at the age of 4 weeks weighing 2.53 kg, his parents having previously been interviewed on a number of occasions and shown how to carry out the treatment at home. His subsequent progress has been good.

He was last seen at the age of 6 months when he weighed 6.1 kg and his chest was clear to auscultation. His chest x-ray showed no abnormality. He tended to cough with his postural drainage and when he cried. His stools were occasionally greasy and foul smelling.

His treatment consisted of pancreatic powder (Pancrex V 125 mg) with each feed, flucloxacillin suspension 62.5 mg b.d., vitamins A and D 10 drops daily, ferrous sulphate 50 mg daily, vitamin C 50 mg daily, together with regular postural drainage.

Discussion

The trial has now been in progress for 16 months at one hospital and for 13 months at the other, during which time there have been about 6200 births. We have detected one case of cystic fibrosis by screening but there have also been two cases of meconium ileus one of which has survived and been shown to have a high sweat sodium level. We have circulated the paediatricians in the region

about the trial so that we will be notified of any children who are found to have CF who were born in either of the hospitals since the beginning of the trial. In this way we hope to find out how many cases of CF have been missed by the test. As far as we know this is the first attempt at a prospective screening programme for CF using this technique.

The time taken for the test is 10 to 15 seconds and the cost of materials is just under 2p per test. In one of the hospitals the paediatric Senior House Officer does the tests while in the other the midwives and paediatric nursing staff do them.

We hope that this limited trial will stimulate other maternity units to carry out similar surveys so that the efficiency of the method can be more rapidly assessed.

It is of interest that if we had started the trial four weeks earlier we would also have detected a case of intestinal lymphangiectasia which presented at the age of 3 weeks with gross oedema and a protein-losing enteropathy.

Summary

A simple newborn screening programme to detect cystic fibrosis is described in which one case of the disease has been found (in addition to two cases of meconium ileus) in approximately 6200 births. The method involves testing the meconium for the presence of albumin, the cost is just under 2p per test, and each test takes from 10 to 15 seconds to perform.

We would like to thank all those people who are co-operating in this survey, and, in particular Mr. C. Allister for biochemical help.

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Anomalous Sweat Chloride Levels in Cystic Fibrosis During Antibiotic Therapy

It is becoming increasingly common to confirm the diagnosis of cystic fibrosis by using a skin chloride electrode, and estimation of the sodium content of sweat is now often omitted.

The following case report concerns a child with proven cystic fibrosis in whom raised sweat sodium but normal sweat chloride levels were obtained while she was receiving cloxacillin.

Possible explanations for the findings are discussed and attention is drawn to their implications in relation to screening programmes for cystic fibrosis.

Method

Sweat was collected on to sodium chloride free Whatman No. 40 filter paper squares (3.5 cm) after conventional pilocarpine iontophoresis using the EMI sweat unit.* The sweat was eluted with 2.0 ml deionized water. 100 mg of sweat was accepted as the minimum weight for analysis as suggested by Varley (1967). Sodium was estimated by flame photometry and chloride by a modified Schales and Schales technique.

The mean and normal range for sweat electrolytes at this hospital are as follows: *sodium*: mean 21.1 mEq/l., range 5–45 mEq/l. (n = 56); *chloride*: mean 13.6 mEq/l., range 2–40 mEq/l. (n = 55).

Case Report

The infant was delivered by caesarian section after a pregnancy complicated by pre-eclamptic toxæmia, birthweight 2.3 kg. She was the youngest of three sibs, one of whom has diabetes mellitus. On two occasions in the early months of life she was admitted to an isolation hospital with suspected gastroenteritis, and at the age of 10 months presented with a history of recurrent respiratory infections and persistent stridor. Her chest x-ray was normal and a diagnosis of congenital laryngeal stridor was made. The stridor gradually subsided over the next 14 months.

She was referred again at the age of 3 years with rectal prolapse and a history of passing loose, bulky, grey stools. Coeliac disease was suspected and she was admitted for observation. There was no pot belly or muscle wasting and she was discharged after a few days as her stools were thought to be normal. A total faecal fat excretion of 43.2 g over a 5-day period was recorded at this time, but no further action was taken. The rectal prolapse remained troublesome for the next 12 months.

She was next referred at the age of 9 years to the chest clinic with a 3-month history of cough. A chest x-ray then showed increased lung markings and fibrosis in the right upper zone. Breathing exercises were started and antibiotics advised during the winter months. She

*EMI—Electromedical Supplies (Greenham) Ltd.