# THE FINGER-PRINT SWEAT TEST

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In the United States and in England the estimates of the incidence of cystic fibrosis of the pancreas amongst children of European descent have varied from 1 : 1,000 to 1 : 10,000 (Lowe *et al.*,[1] Bodian[2]). If we assume a European population in South Africa of 2,500,000 then we expect to find between 250 and 2,500 cases in the country. In fact most paediatricians see only isolated cases. This means either that the incidence in South Africa is lower than overseas or that a large number of cases are being missed. With modern treatment a great deal can be done for these unfortunate children and every effort should be made to detect cases as early as possible before irreparable damage has been done.

I do not think that a case of cystic fibrosis has ever been described in a true Negro, but in Michigan, U.S., it is estimated that the incidence in Coloured patients is less than one-tenth of that amongst Europeans.[3] In South Africa there are far more pressing problems amongst the non-Europeans than cystic fibrosis and it is seldom that the disease is suspected. A widespread survey, however, would be of considerable academic value, particularly if whole families could be screened.

In this article there is no need to review the present knowledge of the disorder, because two excellent monographs and an extensive review have appeared in recent years.[2, 4, 5] It may however be of value to emphasize certain features of the disorder and the methods of diagnosis.

## CLINICAL FEATURES

Cystic fibrosis of the pancreas is a generalized disorder of the eccrine glands characterized by abnormal viscosity of the mucus and an increased concentration of the electrolytes in the sweat. The disorder should be suspected under the following circumstances:

1. When a known case exists in a family all other members should be suspect, particularly infants and children. Sometimes cases are diagnosed in related families, e.g. amongst cousins.

2. Any case diagnosed as coeliac disease in which there is an associated chronic respiratory infection of any type, is a case of cystic fibrosis of the pancreas until proved otherwise. Today cystic fibrosis is probably commoner as a cause of steatorrhoea than idiopathic coeliac disease. All cases of steatorrhoea, therefore, which do not respond to a gluten-free diet should be suspected of suffering from cystic fibrosis and investigated accordingly. A feature of the steatorrhoea in cystic fibrosis of the pancreas is the extraordinarily foul and penetrating odour of the stools; mothers sometimes complain that it 'stinks the house out'.

3. Failure to gain weight associated with a voracious appetite. This paradox of an infant or child who 'eats as much as his father' yet fails to gain weight is fairly common in cystic fibrosis.

4. Chronic, repeated and recurrent respiratory infections, particularly those dating from infancy, are good grounds for suspecting the disease. Chronic dry, useless cough often occurs. Chronic sinusitis, asthmatic bronchitis and hoarseness of the voice are sometimes found. Some cases present as a 'second attack of whooping cough', the misleading feature being the paroxysmal type of cough which may occur.

5. All cases of staphylococcal pneumonia and empyema in infancy should be suspected of the disease.

6. Bronchiectasis, usually generalized and cylindrical occurs in advanced cases.

7. The disease should be suspected in all cases of neonatal obstruction due to abnormally viscid meconium (meconium ileus); 1 in 9 cases of cystic fibrosis present as meconium ileus.

8. Excessive sweating about the head in infancy may occur.

All grades of the disorder may be found. It may present in infancy as intestinal obstruction due to meconium ileus; in infancy as chronic diarrhoea or respiratory infections; or symptoms may not appear until the child is 5 or 6 years of age, when almost any combination of respiratory or alimentary symptoms may occur.

It is rare for these children to survive to adulthood, the majority dying before puberty, though in recent years an increasing number are surviving beyond this age. There is evidence that very mild cases may enter adulthood.[5]

## DIAGNOSIS

The diagnosis can usually be suspected on clinical grounds, but the aid of the laboratory is essential to prove the diagnosis.[5] Until the advent of the sweat test, duodenal intubation and the analysis of the duodenal contents for viscosity and digestive enzymes was the only reasonably reliable test—and it called for special experience in the techniques involved; errors in collection and analysis are easily made. Examination of the stools for trypsin and for fats have not always been reliable. Indirect tests such as the vitamin-A absorption curve, sugar tolerance curve, chylomicron count, iodine excretion test and nitrogen balance tests may assist in the diagnosis but are fraught with error if not performed regularly. The sweat test however gives a high degree of reliability and is the subject of this communication.

### *Disordered Sweat Secretion*

Until recently, as a result of Farber's work,[6] the most acceptable explanation of the aetiology of cystic fibrosis of the pancreas was that the disease was due to a general disorder of the mucus-secreting glands. Farber coined the term 'mucoviscidosis', i.e. 'viscid-mucus disease', and explained that the majority of symptoms were due to the presence of plugs of abnormally tough viscid mucus in the ducts of various organs. In the intestinal tract this resulted in meconium ileus in the newborn, in the pancreatic ducts it caused depression of pancreatic enzyme excretion into the duodenum; in the bronchioles it caused atelectasis, bronchial spasm, emphysema and secondary infection; and occasionally in the biliary tract it resulted in biliary cirrhosis.

In 1948, during a particularly severe heat wave, 10 children were admitted to the Babies' Hospital in New York with heat exhaustion. Of these cases 5 were known to suffer from cystic fibrosis of the pancreas. In subsequent years 2 further

cases developed heat exhaustion and the series were reported by Kessler and Anderson.[7]

The work was taken up by di Sant'Agnese, Darling and Perera,[8a, 8b, 8c] who measured the sweat electrolytes in 43 known cases of cystic fibrosis and in 50 controls. They found that there was a consistently greater excretion of sodium and chloride in the sweat in cystic fibrosis amounting to 2-4 times that of the controls. An increase in the potassium content was also found but it was not so marked. There was apparently no change in the volume of sweat excreted. The work was subsequently fully confirmed by Shwachman *et al.*[5] and by Webb *et al.*[9] However, the test was cumbersome and required at least half to one hour to collect a suitable sample. Shwachman *et al.*[10] therefore modified the test into a semi-quantitative screening test, the 'finger-print sweat test', which gave 99% reliability in their hands and was subsequently confirmed by MacFarlane *et al.*,[11] who obtained 100% results with it.

*The Shwachman Finger-Print Sweat Test*

The test is performed by *gently* and *lightly* pressing a finger or toe onto the test medium. The medium is made up as follows: 25 g. of pure agar is dissolved in 500 ml. of boiling water. When the mixture is melted 4·2 g. of silver nitrate is added and the mixture stirred. Then 2·5 g. of potassium chromate is stirred in. The hot, red mixture, which should be as clear as a bacteriological blood plate, which it resembles, is poured into Petri dishes and sealed with cellotape. Plastic containers can also be used.

The chloride on the finger bleaches the medium and the degree of bleaching is reported as 1, 2 or 3 plus. A 1+ reaction shows only slight bleaching and indicates a salt concentration of less than 60 mEq./l. A 3+ reaction is a deep white or yellowish-white colour change indicating a concentration of over 250 mEq./l. In between lies the 2+ reaction, which is easily distinguished with a little experience. In Shwachman's preliminary results in 140 known pancreatics, 138 gave a 3+ reaction and 2 a 2+ reaction; none gave a 1+ reaction. Of children with various diseases only 4 out of 103 gave a 3+ reaction. Amongst healthy infants there were no 3+ reactions. Of special interest is the fact that about 15% of parents of patients and about 15% of siblings have a 3+ reaction, a fact which may yet prove to be of great genetic interest.

MacFarlane *et al.*[11] reported the results in 54 cases of cystic fibrosis and 200 controls and obtained no false positives. In doubtful cases the hands were thoroughly washed and the cases retested at 5-minute intervals. All cases of cystic fibrosis became 3+ again within 20 minutes whereas none of the controls became 3+ within 20 minutes.

## AUTHOR'S CASES

In South Africa we do not have the facility of collecting these cases within one large centre as has been done overseas. As a result many cases are missed. In my own practice I have picked up only one proved case in the past 2 years and have seen 2 further cases at the hospital, both unfortunately before the sweat test was available. Several other possible cases I have been able to disprove either by duodenal intubation or by means of the sweat test. I have been doing the finger-print test as a routine for some time, and it may be of interest to report my preliminary results.

*Material and Method*

Up to the time of writing, 230 children have been tested—42 European and 188 Bantu. Of the European children, 36 were tested by routine in my private practice, and 6 were seen at the Beatrix Street Hospital for possible pancreatic disease. All the Bantu children were seen at the non-European out-patient department; they presented with a variety of complaints—kwashiorkor, whooping cough, gastro-enteritis and respiratory disorders predominated. The ages ranged from 3 months to 12 years and the sexes were more or less equally distributed.

In all cases with a 2+ or a 3+ reaction the hands were thoroughly washed and the test was repeated after 20 minutes.

*Results*

Table I shows the results of the preliminary tests. Of the 230 cases, 37 gave a 2+ reaction and 7 a 3+ reaction. After the hands were washed all cases became 1+ except the known case of cystic fibrosis, which became 3+ again within 20 minutes (Table II). A note whether the day was hot or cool was made at the time of testing and the results are recorded in Table III. Our impression is that on very hot days one sees stronger reactions than on cool days, especially amongst Bantu patients, though a much larger series in a wider temperature range will be required to confirm this.

TABLE I. RESULTS OF PRELIMINARY FINGER-PRINT READINGS IN 230 PATIENTS

| | + | ++ | +++ | *Total* |
|---|---|---|---|---|
| European .. .. | 31 | 8 | 3 | 42 |
| Bantu .. .. | 155 | 29 | 4 | 188 |
| Total .. .. | 186 | 37 | 7 | 230 |

TABLE II. RESULTS OF FINGER-PRINT READINGS 20 MINUTES AFTER WASHING OF HANDS

| | + | ++ | +++ | *Total* |
|---|---|---|---|---|
| European .. .. | 41 | 0 | 1* | 42 |
| Bantu .. .. | 188 | 0 | 0 | 188 |

* Known case of cystic fibrosis of the pancreas.

TABLE III. EFFECT OF TEMPERATURE ON THE RESULTS OF THE FINGER-PRINT TEST

| | *Cool Day* | | | | *Hot Day* | | | |
|---|---|---|---|---|---|---|---|---|
| | + | ++ | +++ | *Total* | + | ++ | +++ | *Total* |
| Eur. No. | 25 | 5 | 2 | 32 | 6 | 3 | 1 | 10 |
| % | 78 | 15·6 | 6·4 | 100 | 60 | 30 | 10 | 100 |
| Bantu No. | 97 | 10 | 0 | 107 | 58 | 19 | 4 | 81 |
| % | 90·6 | 9·4 | 0 | 100 | 71·6 | 23·4 | 5 | 100 |

It is of interest that of 17 children with kwashiorkor only 2 gave a 2+ reaction and both were complicated by pneumonia—the rest were 1+ and often no visible change on the test plate was made by their finger-prints. Of 11 infants with gastro-enteritis none gave more than a 1+ reaction Most of the cases who gave a 2+ or a 3+ reaction on preliminary testing had respiratory infections, though a few cases were apparently normal.

## DISCUSSION

Although the reasons for the increased electrolyte concentration in the sweat in cystic fibrosis of the pancreas are not

known, its occurrence has provided us with one of the most specific diagnostic tests known in medicine. It seems clear from the literature that the Shwachman finger-print test for chlorides, which was originally designed as a screening test, may prove to be an even more valuable diagnostic procedure than the original sweat test, which is cumbersome and requires skilled laboratory assistance in its performance. From my own small experience with the test I am convinced that it may safely replace duodenal intubation as a diagnostic procedure, particularly in areas where intubation is seldom done.

So long as the test medium is freshly made and checked against suitable controls, no difficulties should arise in its use, once one has gained a little experience in interpreting the results. I find that a good control is to apply one's own fingers one after the other onto the same spot, thus getting increasing bleaching on that spot. If one finger produces a slight change in the medium, then applying a second finger produces a 2+ reaction and a third finger a 3+ reaction. By this means one easily gains experience in reading the results.

In infancy, sweating is normally at a minimum and it is uncertain at what age it becomes sufficient to test. MacFarlane *et al.*[11] found a 3+ reaction as early as 4 weeks of age in an infant known to have cystic fibrosis of the pancreas. Normally infants do not produce even a 1+ impression until at least 3 months of age. Shwachman thought that the test was satisfactory after the age of 3 months.

Owing to the uncertainty at what age the finger-print chloride test becomes positive, an additional screening procedure is useful. The stool trypsin test, also developed by Shwachman,[12] may be used in the first year of life. Three negative stool trypsin examinations in the 1 : 5 or 1 : 10 dilution should be considered sufficient evidence for the tentative diagnosis of cystic fibrosis. The test can be confirmed after the age of 3 months (perhaps sooner) by the finger-print test, thus giving one a double check.

In our short series no false positive reactions were obtained in European or Bantu children. As was expected, cases of gastro-enteritis, most of which were severe, did not produce more than a 1+ reaction, probably because of the excessive loss of electrolytes in the stool. Whether electrolyte retention occurs in the oedematous tissues in cases of kwashiorkor, resulting in a compensatory 'shutting off' of electrolyte in the sweat, is to be further investigated in a larger series. The large number of 3+ reactions occurring in the preliminary tests on children with fever suggests an increased electrolyte excretion in these cases, but after washing the hands no more than a 1+ reaction occurs 20 minutes later. The test is obviously of no great significance in these cases and merely emphasizes the need to repeat the test after washing.

SUMMARY

1. Preliminary experience of the Shwachman finger-print test for chlorides in the sweat in routine practice is described in 230 children aged from 3 months to 12 years. No false positives were obtained.

2. The value of the test as a routine screening test and as a specific diagnostic test for cystic fibrosis of the pancreas is discussed.

3. It is suggested that during the first year of life the best results will be obtained by combining the Shwachman finger-print test with the examination of 3 consecutive stool specimens for trypsin.

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