Cystic Fibrosis: Making a Correct and Early Diagnosis

Lynn J. Morris, Armond V. Mascia, MD, and Peter B. Farnsworth, MD
Valhalla, New York

Cystic fibrosis is detected with increasing frequency in older children, adolescents, and even young adults. The quality of life and longevity in patients with cystic fibrosis is more favorable the earlier a diagnosis is made and a therapeutic regimen begun. This report presents and reviews five cases in which the diagnosis of cystic fibrosis was made after the age of six years. Emphasis is placed on the variability of presenting signs and symptoms and the problems that can arise in confirming a suspected diagnosis of cystic fibrosis.

Cystic fibrosis is now recognized with increasing frequency in older children, adolescents, and even young adults which means that many patients escape detection in early childhood. For children with cystic fibrosis, the quality of life and subsequent longevity is proven to be more favorable the earlier a diagnosis is made and available therapy initiated.[1] The purpose of this communication is to discuss the problems that often arise in making an early diagnosis of cystic fibrosis and to emphasize the variability of presenting signs and symptoms of the disease depending on the degree of involvement of the various organs and glandular systems.

Cystic fibrosis is a hereditary disease in which there exists a generalized dysfunction of the exocrine glands. The organs and glandular systems involved include the pancreas, respiratory system, salivary glands, gastrointestinal tract, paranasal sinuses, reproductive tract, and the sweat glands.

In the United States, after the age of one year, in pediatrics, cystic fibrosis is one of the main causes of death from chronic disease, excluding malignancy. In children and adolescents, cystic fibrosis is the etiology of most chronic nontuberculous pulmonary disease, of almost all pancreatic insufficiency, and of some hepatic cirrhosis.[2]

The basic defect in cystic fibrosis is not known, but there is general agreement that it is due to an inborn error of metabolism transmitted as an autosomal recessive trait having variable penetrance and therefore variable extent and severity of clinical manifestations.[2] A conservative and acceptable figure is an incidence of 1 in 2,000 live births for homozygotes for the cystic fibrosis gene in a population of Caucasian descent; that is, approximately five percent of the general population are carriers of the gene. Cystic fibrosis is the most frequent lethal genetic disease among whites.[3] The striking racial distribution of cystic fibrosis, with its prevalence in the Caucasian race, its comparative rarity in Negroes, and its virtual absence in Mongolians, has been documented.[4] Both sexes are affected with approximately equal frequency.

It is now recognized that the abnormality of sweat electrolytes is the most consistent feature, being present in over 95 percent of cases.[5] It was first described by Darling and co-workers in 1953, and determination of sweat electrolytes has become the most reliable single diagnostic test for cystic fibrosis.[6] This has replaced the more difficult, uncomfortable, time-consuming, and less reliable procedures of duodenal fluid aspiration and assay.

From the Division of Pediatrics, and the Pediatric Pulmonary Disease Section, Westchester County Medical Center, New York Medical College, Valhalla, New York. Requests for reprints should be addressed to Dr. Peter B. Farnsworth, Division of Pediatrics, Westchester County Medical Center, Valhalla, NY 10595.

In the Cystic Fibrosis Center of Westchester County Medical Center, a total of 70 patients have been followed from July 1966 through July 1976. Of the 36 male patients followed, the youngest is four months old and the oldest is 30 years of age. Thirty-four female patients have been followed, the youngest female being three years of age and the oldest female, 42 years of age. There have been five deaths among the 70 patients seen. The patients were of varying ages at the time the diagnosis of cystic fibrosis was made (Table 1). The illnesses of twenty-one of the 70 patients followed were diagnosed late, ie, after the age of six years. Five cases are presented to illustrate the extreme variability in the clinical presentation of cystic fibrosis, and to point out the difficulties in differentiating cystic fibrosis from other conditions such as chronic asthma and gluten enteropathy. These cases will also illustrate the problems that can arise in confirming a suspected diagnosis of cystic fibrosis.

Case Reports

Case 1

L.T., an 8 1/2-year-old white female, was admitted for the first time to Westchester County Medical Center in 1972 with a referring diagnosis of liver tumor. The patient had had repeated episodes of bronchitis since the age of five months, requiring several hospitalizations. At three years of age the patient was hospitalized for rectal prolapse. Sweat tests were done at ages three and seven years with both results being "normal." In September 1970, the patient was hospitalized for pneumonia. Five months prior to admission, the patient's mother noted abdominal distention in the patient, though her appetite was good. At that time she was having three to four bowel movements per day which were sometimes greasy and floating in the water. The patient had always been underweight.

The patient was born in 1963 of a full-term, spontaneous delivery. The birthweight was 8 lb 1 1/2 oz, and her growth and development were normal. There were no known familial diseases.

On physical examination, the patient appeared undernourished with a weight of 44 lb (below the third percentile) and a height of 45 in (below the tenth percentile). The patient was slightly cyanotic and jaundiced, and appeared chronically ill but in no acute distress. The patient was afebrile but tachypneic, and had a blood pressure of 90/60 mmHg and a pulse rate of 150/min. Clubbing of the nailbeds was observed. The tonsils were hypertrophied with slight congestion. The thoracic AP diameter was increased and coarse rales were heard throughout the lung fields. The abdomen was protuberant and firm with the liver palpable four centimeters below the right costal margin and the spleen palpable two centimeters below the left costal margin. The skin was dry and scaly with hyperkeratosis. A papular rash was observed over the lower extremities, abdomen, and back, as well as a few scattered small ecchymotic areas. The remainder of the physical examination was unremarkable.

Laboratory data revealed: hematocrit 49.2 percent; prothrombin time 17.3/13.1 sec; partial thromboplastin time 53.0/32.0 sec; total bilirubin 3.8 gm/100 ml; alkaline phosphatase 750 IU; lactic dehydrogenase 245 IU; serum glutamic oxaloacetic transaminase 225 IU; glucose 205 mg/100 ml. Other laboratory findings were within normal limits. Pulmonary function testing demonstrated obstructive lung disease. Chest x-ray films showed increased bronchopulmonary markings at the hilar and perihilar areas.

A diagnosis of cystic fibrosis was made based upon the clinical picture and chest x-ray, and was confirmed by a sweat test of 100 mEq/liter of chloride.

Case 2

M.O., a six-year-old white female, was admitted for the first time to Westchester County Medical Center in 1976 with a referring diagnosis of chronic asthma to be evaluated and for pulmonary function studies. On admission the patient appeared in acute respiratory distress with cyanosis of the lips and nailbeds. The mother of the patient described a two-week history of cough, dyspnea, shortness of breath, and fever in the patient. The respiratory distress necessitated her direct admission into the intensive care unit.

The patient was born in 1970 of a normal, full-term delivery. The birthweight was 9 lb and the neonatal period was unremarkable. At the age of three, because of poor appetite and a history of cystic fibrosis in the family (a sibling had died of

Table 1. Age at Diagnosis and Sex of 70 Patients Followed in the Cystic Fibrosis Center of Westchester County Medical Center from 1966 to 1976

Ages at Diagnosis	Number of Patients	Males	Females
Birth - 1 week	6	5	1
1 week - 1 year	22	14	8
1 - 2 years	6	3	3
2 - 3 years	7	1	6
3 - 4 years	2	1	1
4 - 5 years	4	2	2
5 - 6 years	2	1	1
6 years or older	21	9	12
Total	70	36	34

cystic fibrosis), a sweat test was performed with a result of 50 mEq/liter of chloride and cystic fibrosis was "ruled out" at that time. The patient's condition was diagnosed as bronchial asthma at the age of four years, and since that time she had been receiving desensitization injections. According to the mother, the patient had a history of frequent upper respiratory tract infections.

On physical examination, the patient was observed to be in severe respiratory distress, with substernal and intercostal retractions, cyanotic but conscious and oriented. Her weight was below the third percentile. Vital signs: temperature 102 F; respiratory rate 52/min; pulse rate 152/min; blood pressure 120/70 mmHg. The chest had increased AP diameter and there was reduced air entry and scattered rales bilaterally. The abdomen was slightly protuberant and soft, and the liver was palpable 5 cm below the right costal margin. The remainder of the physical examination was unremarkable.

Laboratory data showed the following values: hematocrit 30.6 percent; calcium 8.2 mEq/liter; alkaline phosphatase 640 IU; serum glutamic oxaloacetic transaminase 137 IU. The following were the values for blood gases: pH 7.44; pCO 34.9 mmHg; pO_2 43.2 mmHg; CO_2 24.2 mEq/liter; oxygen saturation 81.4 percent. Sputum culture revealed Pseudomonas aeruginosa and staphylococcus coagulase positive sensitive to carbenicillin. Chest x-ray revealed patches of infiltration.

Cystic fibrosis was suspected clinically and confirmed by a sweat test result of 123 mEq/liter of chloride.

Subsequent sweat tests have been performed on her two siblings. A three-year-old male sibling who was asymptomatic had a sweat test chloride value of 128 mEq/liter. An older male sibling of 11 years, who was not gaining weight and who had a productive cough and abdominal pains, also had a positive sweat test.

Case 3

G.W., a 16-year-old white female with Down syndrome, was admitted for the first time to Westchester County Medical Center in 1973 with a diagnosis of cystic fibrosis. The patient had had recurrent episodes of sinobronchial infections and several bouts of pneumonia requiring hospitalization during the preceding three years. The patient had had diarrhea off and on, and loose, greasy, foul-smelling stools.

The patient was born in 1957 and was the first child of her 18-year-old mother. There was no history of drugs, infections, x-rays, or bleeding in the first or second trimesters of pregnancy. The birth weight was 6 lb 11 oz and was a full-term, normal delivery. The patient had had repeated upper respiratory tract infections in the first few years of life. A tonsillectomy and adenoidectomy was performed at age four.

On physical examination, the patient appeared to be in no acute distress. Vital signs were within normal limits. The stature was short and the patient had typical Down features. The nose and throat appeared congested but no exudates were present. Scattered rhonchi were heard in the

lungs. The remainder of the physical examination was unremarkable.

Laboratory data revealed a white blood cell count of 4,000/cu mm and a hematocrit of 55 percent. Sputum culture grew gram positive cocci and a few gram negative bacilli. Chest x-ray showed linear streaking at the left lung base. The patient was almost totally unable to perform any of the pulmonary function studies; however, the results obtained suggested a reduction in volume and expiratory flow.

After two sweat tests resulting in values of greater than 60 mEq/liter of chloride, the illness was diagnosed as cystic fibrosis.

Case 4

C.N., a 16-year-old white female, was admitted for the first time to Westchester County Medical Center in 1969 with suspected cystic fibrosis. Four months prior to admission, the patient began to have episodes of increasing cough with expectoration. There was no hemoptysis at any time. The patient's mother stated that the patient had had a history of coughing and shortness of breath over many years, but that the symptoms seemed to be increasing in the past year or two.

The patient was born in 1952 of a full-term, normal delivery. The birthweight was 6 lb 10 oz and her growth and development were normal. At the age of four, the patient was hospitalized for rectal prolapse. There was no history of diarrhea or loose, bulky, and greasy stools. The patient had no history of allergies.

On physical examination, the patient appeared undernourished with a weight of 92 lb (below the fifth percentile) and a height of 59 in (below the fifth percentile). Vital signs showed the following values: blood pressure 100/60 mmHg; pulse rate 108/min; respiratory rate 36/min; temperature 98.6 F. The lungs were clear and the abdomen was soft with no organomegaly. There was clubbing of the nailbeds but no cyanosis. The remainder of the physical examination was unremarkable.

Laboratory data revealed a white blood cell count of 15,200/cu mm. Stool examintion was 2+ for fat. Sputum culture revealed aeruginosa and staphylococcus coagulase positive. Chest x-ray showed scattered infiltrates in both lung fields, main pulmonary arteries prominent, and honeycombing in both upper lung fields. Pulmonary function studies showed severe obstructive pulmonary disease with a bronchospastic element.

The suspected diagnosis of cystic fibrosis was confirmed by a sweat test result of 100 mEq/liter of chloride.

Case 5

J.G., a six-year-old white female, was admitted for the first time to Westchester County Medical Center in 1973 with a suspected diagnosis of cystic fibrosis. Three weeks prior to admission the patient had developed cough with thick expectoration and pain in the abdomen. The symptoms were accompanied by a low-grade fever. The patient was hospitalized, an initial diagnosis of interstitial pneumonia was made, and the patient was placed on antibiotic treatment. However, the coughing grew progressively worse. A private physician suspected cystic fibrosis and the patient was transferred to Westchester County Medical Center for evaluation and treatment.

The patient was born in 1966 of a full-term, normal delivery with a birthweight of 6 lb 3 oz. At three weeks of age the patient began to have loose bowel movements and was diagnosed as having malabsorption syndrome. The patient was initially placed on a diet of bananas which did not improve her condition. Her grandfather, a physician, placed her on a gluten-free diet which improved her condition. The patient had had a history of frequent rectal prolapse since the age of two years and a chronic cough which had been present since infancy.

On physical examination, the patient appeared undernourished with a weight of 27 1/2 lb (below the third percentile) and a height of 41 inches (below the third percentile). The patient appeared to be in moderate respiratory distress and showed cyanosis while coughing. Her vital signs showed the following values: blood pressure 90/60 mmHg; pulse rate 110/min; temperature 100 F. The throat appeared slightly congested. There was suprasternal and subcostal retractions and crepitant rales were heard bilaterally. Clubbing and cyanosis of fingers and toes were observed. The remainder of the physical examination was unremarkable.

Table 2. List of the Most Common Symptoms Present at or Before the Time the Diagnosis of Cystic Fibrosis was Made in 70 Patients Followed in the Cystic Fibrosis Center of Westchester County Medical Center from 1966 to 1976 and the Percentage of Patients Manifesting Each Symptom

Symptoms present at or before the time of diagnosis	Percentage of patients
Loose, bulky, foul-smelling stools	50
Cough and/or wheezing	42
Failure to thrive	37
Recurrent URI	23
Pneumonia	19
Bronchitis	17
Rectal prolapse	10
Meconium ileus	8
Voracious appetite	6
Nasal polyps	4
Abdominal pain	3
Cyanosis of lips and nailbeds	3
Salty taste when kissed	3
Atelectasis	2

Laboratory data showed the following values: white blood cell count of 21,900/cu mm with 81 percent polymorphonuclear leukocytes, 1 percent stabs, 14 percent lymphocytes, and 4 percent monocytes. Electrolytes, SMA-12, and urinalysis were within normal limits. Chest x-ray revealed lung markings thickened throughout the lower lung fields with associated infiltration. Sputum culture grew aeruginosa. Pulmonary function studies revealed obstructive pulmonary disease.

Cystic fibrosis was confirmed with a sweat test result of chloride greater than 100 mEq/liter.

Discussion

No known biochemical or structural defect can account for all the pathophysiologic phenomena of cystic fibrosis. Obstruction of exocrine ducts or passageways into which the secretions are discharged occurs in nearly all patients with cystic fibrosis. Inspissation of secretions has been blamed as the cause of the obstructive events. Lack of water, alterations of electrolyte concentrations, and abnormal organic constituents particularly mucous glycoproteins have all been implicated in the pathogenesis of the thickened secretions. It has also been suggested that autonomic control of the secretory process is disturbed in these patients.[7]

The earliest manifestation of cystic fibrosis is meconium ileus which was observed during the neonatal period in approximately eight percent of the 70 patients followed in the Cystic Fibrosis Center (Table 2). After the newborn period, manifestations of pancreatic insufficiency including loose, bulky, foul-smelling stools and failure to thrive occurred in 50 and 37 percent, respectively, of the 70 patients either before or at the time of diagnosis (Table 2).

Patients with cystic fibrosis have morphologi-

cally normal lungs at birth as seen in infants dying of meconium ileus. The earliest pulmonary lesions are dilation and hypertrophy of bronchial glands and goblet cell metaplasia of the bronchiolar epithelium. This is followed by mucous plugging of peripheral airways.[8] The obstruction leads to stagnation of secretions, inflammation, edema, and exudation. A vicious cycle is established with obstruction leading to infection and infection to more obstruction.

The most prominent and constant symptom of pulmonary involvement is cough, which was present in over 40 percent of the 70 patients followed in the Cystic Fibrosis Center at or before the time of diagnosis (Table 2). The cough may be dry and hacking initially, but with progression of the disease becomes productive. Progressive airway obstruction leads to airtrapping with increasing AP diameter of the chest. Digital clubbing is often an early manifestation. The course of the pulmonary disease is highly variable and much influenced by therapy, as confirmed by Doershuk and co-workers.[1] Almost all patients with cystic fibrosis eventually develop chronic pulmonary infection but extrapulmonary infection is rare, except in infants. This implies a defect in local rather than systemic defense mechanisms.[7]

The upper airway is often involved in cystic fibrosis. Chronic pansinusitis has been observed in nearly all 70 patients followed in the Cystic Fibrosis Center. Shwachman and co-workers have reported the occurrence of nasal polyposis in 10 to 15 percent of patients with cystic fibrosis.[9] The presence of nasal polyps may be an important clue to making a diagnosis of cystic fibrosis. Among the 70 patients followed in the Cystic Fibrosis Center here, nasal polyps were present at the time of diagnosis in four percent of the patients (Table 2).

Early diagnosis of cystic fibrosis requires a high degree of awareness on the part of the physician. Symptoms arousing concern include one or several of the following: failure to thrive, voracious appetite, abdominal pain, foul, bulky, and fatty stools, persistent runny nose, and wheezing and cough.[10] Incorrect or incomplete diagnosis such as celiac disease, allergic reactions, asthma, or bronchitis have resulted in treatment which fails to relieve the symptoms and prolongs the time until the correct diagnosis is made and the proper management instituted. This point is well illustrated by Case 2. This patient was diagnosed as suffering from bronchial asthma at age four and was treated with desensitization injections. Two years later this patient was admitted to Westchester County Medical Center in acute respiratory distress with cyanosis of the lips and nailbeds. The correct diagnosis of cystic fibrosis was made, the patient placed on an appropriate therapeutic regimen, and her condition stabilized.

At least two of the following four diagnostic criteria are required to confirm a diagnosis of cystic fibrosis: (1) a positive sweat test (sweat chloride greater than 60 mEq/liter, (2) presence of chronic obstructive lung disease, (3) exocrine pancreatic insufficiency, and (4) family history of cystic fibrosis. The diagnosis of cystic fibrosis is rarely made in the absence of a positive sweat test.[7]

The question arises as to the reliability of the sweat test. Gibson reports that there have been patients who miss early treatment because of a falsely negative sweat test.[11] In Case 1, two sweat tests were performed at ages three and seven years and both results were "normal." In Case 2, a sweat test result of 50 mEq/liter of chloride, considered by many to be a borderline result, was used as a basis for ruling out cystic fibrosis at that time despite a family history of the disease. Unlike progressive changes that may occur in the lungs, liver, and pancreas, the defect in the sweat glands is an inherited and not an acquired one, as it may be detected as early as one day of age.[12] This abnormality in sweat electrolytes is present throughout life and is unrelated to the severity of the underlying disease.

Many factors can influence the result of the sweat test such as increasing age, the condition of the patient, salt intake, and the method of sweat induction and collection.[13] The physician should be familiar with the reliability of the laboratory performing the sweat test. It is recommended that sweat testing be performed only at locations where the test is done frequently and where very careful control of the technique is maintained. The most reliable and safe technique to date is the pilocarpine iontophoresis method of sweat collection of Gibson and Cooke, coupled with chemical analysis of ionic composition.[14] Values of sweat chloride of 70 mEq/liter or greater are considered indicative of cystic fibrosis. A borderline result of 50 to 70 mEq/liter of chloride should be followed up by a repeat examination by the same method

along with flame photometry to determine the sodium concentration. Large discrepancies of greater than 30 mEq/liter between sodium and chloride also call for a repeat examination of the sweat electrolyte concentrations.

Table 2 presents symptoms which were present at or before the time of diagnosis of cystic fibrosis in the 70 patients followed in the Cystic Fibrosis Center. All of these symptoms are indications for sweat testing. Other symptoms indicative of a sweat test include hemoptysis, mucoid pseudomonas infection, malabsorption, childhood cirrhosis, hypoprothrombinemia beyond the newborn period, hyponatremia, and heat prostration.[7] A common clinical finding seen in Cases 1 and 4 is rectal prolapse, observed at ages three and four, respectively. This may be the presenting sign of cystic fibrosis and is an indication for a sweat test. Rectal prolapse was present at or before the time of diagnosis in ten percent of the 70 patients followed in the Cystic Fibrosis Center (Table 2). Kulczcki and Shwachman have reported an incidence of rectal prolapse in up to 20 percent of patients with cystic fibrosis, and its occurrence appears to be related to pancreatic enzyme deficiency, bulky stools, poor nutrition, and/or perineal muscle tone.[15]

Recognition of the hereditary predisposition towards cystic fibrosis and a consequent careful evaluation of the family may lead to detection of the disease in other members.[16] In Case 2, the detection of cystic fibrosis in that patient led to the correct diagnosis in a symptomatic sibling and in another asymptomatic sibling. The presence or knowledge of cystic fibrosis in the family should alert the physician to have a sweat test performed on every sibling irrespective of age. In the Cystic Fibrosis Center, half of the patients diagnosed before the age of one year had a family history of the disease. Of the 21 patients followed who were diagnosed at six years of age or older, nine had a known family history of cystic fibrosis.

In Case 3, a known Down syndrome was diagnosed as having cystic fibrosis at the late age of 16 years. The patient had many of the classic features of the disease including several episodes of pneumonia as well as loose, foul-smelling, greasy stools. The association of cystic fibrosis and Down syndrome was documented for the first time in three cases presented by Milunsky in 1968.[17] Milunsky points out the shared features of cystic fibrosis and Down syndrome which include: increased sodium content of parotid saliva, abnormal morphology of nailbed capillaries, autonomic dysfunction, increased frequency of diabetes mellitus, and intestinal atresia. Genetic linkage of cystic fibrosis to Down syndrome cannot be supported at this time.[7]

It is not unusual for patients with steatorrhea to have their illness misdiagnosed as gluten enteropathy rather than cystic fibrosis. Case 5 is a patient whose symptoms were initially diagnosed as malabsorption syndrome and whose problem of loose bowel movements was alleviated by a gluten-free diet. However, the patient had had a chronic cough since infancy, a symptom not explained by gluten enteropathy. No sweat test was performed until the patient reached age six years, and at that time was having increasing respiratory symptoms. Confirmed cases of both cystic fibrosis and celiac disease found together have been reported, and it has even been suggested that cystic fibrosis may predispose to the development of celiac disease.[18-20]

Cystic fibrosis may present with symptoms of wheezing and cough which are suggestive of chronic asthma. The sickness of Case 2 was misdiagnosed as chronic asthma despite her history of poor appetite, frequent upper respiratory tract infections, and a family history of cystic fibrosis. A sweat test should be included in the evaluation of every white individual with chronic moderate to severe asthma.

Local biliary cirrhosis occurs in four to six percent of patients with cystic fibrosis.[21] In Case 1 the primary findings were those of liver dysfunction which prompted referral resulting in the correct diagnosis of cystic fibrosis.

Sputum cultures performed in Cases 2, 4, and 5 revealed aeruginosa which presently is the most common pathogen isolated from cystic fibrosis patients.[22] Any patient with a mucoid pseudomonas infection of the respiratory tract should have a sweat test.

Abdominal pain, at times severe and varying in location, may be seen in patients with cystic fibrosis, as in Cases 4 and 5. Abdominal cramps and flatulence may be a result of maldigestion in patients with pancreatic insufficiency who prefer a normal diet. Acute pancreatitis may be the presenting complaint in a young adult with cystic fibrosis.[23]

The increasing longevity of patients with cystic fibrosis is accompanied by an increasing incidence of complications not directly related to malabsorption or pulmonary disease. Among these complications is an increased incidence of diabetes mellitus. Case 4, diagnosed as having cystic fibrosis at age 16, was subsequently discovered to have diabetes mellitus one year later. It has been found that diabetes complicates cystic fibrosis but does not necessarily shorten survival. When diabetes in persons with cystic fibrosis is fully developed, it is indistinguishable from labile juvenile diabetes except for the infrequent occurrence of ketosis.[24]

There is an estimated national total of 15,000 to 20,000 cystic fibrosis patients. An additional 800 to 1,000 new cases are diagnosed annually in the United States.[7] The earlier the diagnosis and treatment, the better the prognosis.[25] At present, there is no known method to identify the heterozygote carrier of the trait or to make an antenatal diagnosis of cystic fibrosis. Sweat testing is unrealistic for screening of the normal population because of the high cost and relative unreliability of the test during the immediate newborn period.[7] It has been found that the albumin content of meconium is raised not only in infants with meconium ileus but also in cystic fibrosis without this complication.[26] Results of mass screening for cystic fibrosis with the Boehringer Mannehim test strip for albumin in meconium have been reported. This test was suggested as feasible for screening because it detected 60 cases of cystic fibrosis in 69,000 infants screened.[27] The future validity of this test remains uncertain. It is presently being studied by the Cystic Fibrosis Foundation.[7]

Cystic fibrosis may mimic many conditions, but if there exists the slightest suspicion, the sweat test should be performed. The physician must discard the false concept that the patient looks too well to have cystic fibrosis, and must recognize the great variation in severity of the disease and in the degree of organ involvement.[28]

Acknowledgement

Supported in part by grants from the Cystic Fibrosis Research Foundation and the Westchester Heart Association.

References

1. Doershuk CF, Matthews LW, Tucker AS, et al: Evaluation of a prophylactic and therapeutic program for patients with cystic fibrosis. Pediatrics 36:675, 1965
2. di Sant'Agnese PA, Talamo R: Medical Progress. Pathogenesis and pathophysiology of cystic fibrosis of the pancreas. N Engl J Med 277:1287, 1344, 1399, 1967
3. Steinberg AG, Brown DC: On the incidence of cystic fibrosis of the pancreas. Am J Hum Genet 12:416, 1960
4. di Sant'Agnese PA, Vidaurreta AM: Cystic fibrosis of pancreas. JAMA 172:2065, 1960
5. Anderson CM, Freeman J: Sweat test: Results in normal persons of different ages compared with fibrocystic disease of the pancreas. Arch Dis Child 35:581, 1960
6. Darling RD, di Sant'Agnese PA, Perera A, et al: Electrolyte abnormalities of the sweat in fibrocystic disease of the pancreas. Am J Med Sci 225:67, 1953
7. Wood RE, Boat TF, Doershuk CF: State of the art: Cystic fibrosis. Am Rev Respir Dis 113:833, 1976
8. Esterly JR, Oppenheimer EH: Observations of cystic fibrosis of the pancreas: Part 3: Pulmonary lesions. Johns Hopkins Med J 122:94, 1968
9. Shwachman H, Kulczycki LL, Mueller HL, et al: Nasal polyposis in patients with cystic fibrosis. Pediatrics 30:389, 1962
10. McCollum AT, Gibson LE: Family adaptation to the child with cystic fibrosis. J Pediatr 77:571, 1970
11. Gibson LE: Reliability of sweat tests in the diagnosis of cystic fibrosis (letter). J Pediatr 81:193, 1972
12. Elian E, Shwachman H, Hendren H: Intestinal obstruction of the newborn infant. N Engl J Med 264:13, 1961
13. Shwachman H, Antonowicz I: The sweat test in cystic fibrosis. Ann NY Acad Sci 93:600, 1962
14. Gibson LE, Cooke RE: Test for concentration of electrolytes in sweat in cystic fibrosis of the pancreas utilizing pilocarpine by iontophoresis. Pediatrics 23:545, 1959
15. Kulczycki LL, Shwachman H: Studies in cystic fibrosis of the pancreas: Occurrence of rectal prolapse. N Engl J Med 259:409, 1958
16. Tomashefski JF, Christoforidis AJ, Abdullah AK: Cystic fibrosis in young adults: An overlooked diagnosis with emphasis on pulmonary function and radiological patterns. Chest 57:28, 1970
17. Milunsky A: Cystic fibrosis and Down's syndrome. Pediatrics 42:501, 1968
18. Hide DW, Burman D: An infant with both cystic fibrosis and coeliac disease. Arch Dis Child 44:533, 1969
19. Goodchild MC, Nelson R, Anderson C: Cystic fibrosis and coeliac disease: Co-existence in two children. Arch Dis Child 48:684, 1973
20. Taylor B, Sokol G: Cystic fibrosis and coeliac disease: Report of two cases. Arch Dis Child 48:692, 1973
21. Shwachman H: Gastrointestinal manifestations of cystic fibrosis. Pediatr Clin North Am 22:799, 1975
22. Mearns MB, Hunt GH, Rushworth R: Bacterial flora of respiratory tract in patients with cystic fibrosis. Arch Dis Child 47:902, 1972
23. Shwachman H, Lebenthal E, Khaw KT: Recurrent acute pancreatitis in patients with cystic fibrosis with normal pancreatic enzymes. Pediatrics 55:86, 1975
24. Rosan R, Shwachman H, Kulczycki L: Diabetes mellitus and cystic fibrosis of the pancreas. Am J Dis Child 104:625, 1962
25. George L, Norman AP: Life tables for cystic fibrosis. Arch Dis Child 46:139, 1971
26. Green MA, Shwachman H: Presumptive tests for cystic fibrosis based on serum protein in meconium. Pediatrics 41:989, 1968
27. Stephan U, Busch EW, Kollberg H, et al: Cystic fibrosis detection by means of a test-strip. Pediatrics 55:35, 1975
28. Shwachman H: Commentary: The sweat test. Pediatrics 30:167, 1962