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New simple volumetric sweat electrolyte collection procedure for the diagnosis of fibrocystic disease of the pancreas

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A NEW SIMPLE VOLUMETRIC SWEAT ELECTROLYTE COLLECTION PROCEDURE FOR THE DIAGNOSIS OF FIBROCYSTIC DISEASE OF THE PANCREAS

A STUDY OF SODIUM, CHLORIDE, PHOSPHATE, ALKALINE PHOSPHATASE, AND BLOOD UREA NITROGEN LEVELS IN FIBROCYSTIC DISEASE OF THE PANCREAS USING STANDARD HOSPITAL LABORATORY TECHNIQUES

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I. INTRODUCTION.

Fibrocystic Disease of the Pancreas is an hereditary disease involving the pancreas, the lungs, the liver, the sweat glands, and the salivary glands.

II. SYMPTOMATOLOGY AND PATHOLOGY

a. PANCREATIC. Because of the pancreatic involvement leading to total absence of trypsin, lipase, and amylase, foods are poorly digested and absorbed. The resulting steatorrhea produces not only the loss of much neutral fat, but also much of the liposoluble vitamins: A, D, E, and K. The Islets of Langerhans are not involved in this disease process. The patient typically doesn't gain weight and appears undernourished and underdeveloped. The appetite is very good. The abdomen is distended. Stools increase in number, and are yellow greasy and foul smelling. Pancreatic exocrine function is completely absent in 90% of patients at birth. 10% retain partially or totally intact pancreatic function (1), (4), (8).

b. PULMONARY. The respiratory involvement is the usual immediate cause of death. In di Sant' Agnese's series it accounted for 90% of the causes of death (1). There are repeated respiratory infections involving bronchial obstruction with secondary infections followed by obstructive emphysema. Repeated bouts of this ultimately lead to

respiratory insufficiency. The chest becomes barrel-shaped. Progressive clubbing of fingers and toes develops.

c. HEPATIC. Billary fibrosis with clinical signs of portal hypertension occurred in approximately 2% of di Sant' Agnese's series (1). However, post mortem findings of billiary fibrosis were found in approximately 25% of all cases brought to autopsy. Although this is a small figure percentage-wise, it accounts for one third of the patients with portal hypertension in the pediatric age group.

d. SWEAT ELECTROLYTES (2) (7). Sweat gland findings in Fibrocystic Disease of the Pancreas is an almost constant finding. These children exhibit relatively high sweat sodium and chloride values, which are approximately two to four times the normal range. di Sant' Angese found that sweat chlorides in fibrocystic children ranged from 60-160 meq/L, with a mean value of 106 meq/L. Sweat sodium ranged from 80-190 meq/L with a mean value of 133 meq/L. Controls in his series were as follows: Chlorides 4-60 meq/L, mean 32; sodium 10-80 meq/L, mean 59 (2). The abnormality in sweat electrolytes is confirmed in clinical investigation knowing the poor tolerance these patients have for extreme hot weather, and the sometimes fatal outcome from massive loss of salt. The sweat electrolyte patterns in these patients does not vary with the presence or absence of pancreatic or lung involvement.

e. SALIVARY SECRETIONS. Mixed salivary secretions display an altered electrolyte pattern similar to that found in sweat. However, the values separating the fibrocystic patient from the normal are not sufficiently clear cut to give this test the value of the sweat electrolyte test.

f. MECONIUM ILLEUS. Meconium illeus is present in approximately 10% of all fibrocystic patients at birth. The clinical picture of intestinal obstruction may be complicated by perforation and a meconium peritonitis, either in utero or antenatally.

III. DIAGNOSIS. A combination of pancreatic deficiency, chronic respiratory disease, and a slowly developing child, should arouse suspicion of Fibrocystic Disease of the Pancreas.

a. PANCREATIC INVOLVEMENT. Tryptic activity and duodenal drainage are very useful in diagnosis. They are, however, adequate in only the 90% group who have complete pancreatic exocrine shutdown (3), (4), (8). A duodenal drainage is a very time consuming procedure. Also, many hospital laboratories are not equipped to do enzyme analysis.

b. PULMONARY INVOLVEMENT. Confirmatory pulmonary pathology by x-ray study makes use of a simple hospital routine. The x-ray findings are, however, certainly not diagnostic of Fibrocystic Disease of the Pancreas only.

c. SWEAT GLAND INVOLVEMENT. After di Sant' Agnese's

demonstration of abnormal sweat electrolyte patterns in 1953 (2), (7), a diagnostic tool was made available that was not dependent on abnormal pancreatic activity. Gauze was secured to the patient's back by a covering of moisture proof plastic taped to the patient's back. The gauze was weighed both before and after the sweat collection in a properly tare-weighed flask. A known quantity of water was added to the sweat soaked gauze. Electrolyte determinations were then carried out on this diluted sweat solution. Schwachman's contribution (5), (6), of the zippered plastic bag into which the young patient is placed, with only the head outside the bag, did much to make the sweat test a handier, more rapid instrument in the diagnosis of this disease.

IV. PURPOSE OF THIS WORK. The purpose in doing this work was twofold:

a. To develop a simple alternate sweat technique with which sweat sodium and chloride could be determined by any standard hospital laboratory or physician's office laboratory that was equipped to do ordinary serum sodium and chloride determinations on a volumetric basis.

b. Extend sweat determinations to cover the presence or absence of other blood constituents, to see if there were other constant findings in the Fibrocystic patient. For this aspect of the work we chose to investigate alkaline

phosphatase, phosphates, and Sweat Urea Nitrogen. In analyzing sweat in Fibrocystic Disease of the Pancreas we were aware that the sweat glands are the most accessible of the exocrine glands known to be usually involved in this disease process. It was hoped that sweat determinations if broad enough in scope might lead to the use of sweat values more or less as a gland "biopsy", as are urine values in the diagnosis, and prognosis of urinary and generalized disease processes. It was further hoped that studies of sweat malfunctioning in these patients might eventually lead to a better understanding of the etiology of this generalized disease.

V. METHOD.

a. PREPARATION OF THE PATIENT. Thoroughly wash the patient's back with a mild soap and wash cloth. Rinse the back at least five times with clean tap water, making certain that all soap has been removed. Dry the back with an ordinary freshly laundered bath towel.

b. THE AIRTITE WATERPROOF ENVELOPE, OR TENT. (SEE EXHIBITS #1 and #2). A double thickness layer of Saran Wrap is applied to the back and fastened securely with one inch adhesive tape along the lateral, inferior, and superior margins of the back, enclosing as large an area of the back within the tape margins as is possible. The Saran Wrap,

thus applied at the margins is brought to a "raised tent" in the midline. A strip of tape is applied to the joining edges at the "peak", thereby forming an airtite, moisture proof sweat area.

c. THE SWEAT TABLE. (SEE EXHIBITS #3, 4 AND 5). A sweat table was constructed, on which the patient could lie during the course of the test. There is an oblong area cut out of the table top, to permit the Saran Wrap envelope to fit through and be manipulated from the under side of the table. Three varying sized frames, each with a different sized hole were constructed so that varying sized children could be handled on the table, exposing all of the back enclosed in the Saran tent, and yet providing sufficient support to the lateral edges of the patient's back, the head and neck, and the buttocks, to keep the child comfortable during the procedure. Bath towels folded once and placed at the margins of these oblong cut out areas provide sufficient cushioning to prevent irritation while on the sweat table.

With the patient resting on the table a first covering consisting of a cotton sheet or diaper is placed over the patient extending from the neck to the toes. A plastic sheet is then next applied over the cotton covering, and it, too, is tucked in around the neck and extends the length of the table. An electric blanket, with the controls set on

"high" is next applied in the same manner; and then over this a second plastic sheet is tucked high around the patient's neck, and completely covers and seals in all of the layers below. When necessary, adhesive strips may be run across the top of the outermost plastic covering to serve as restraining bands. (SEE EXHIBIT # 6)

d. FLUIDS AD LIB DURING THE TEST. With the patient thus in place, the patient is encouraged to take fluids ad lib. Where possible warm fluids are desirable: Formula, milk, cocoa, lemonade, tea, etc..

e. THE COLLECTOR. We have made use of a number of devices to squeegee the collecting drops of perspiration from the surface of the back within the confines of the Saran tent. A small funnel with the stem inserted through a rubber cork, which in turn is stoppered into a 10 c.c. blood test tube makes for a very handy squeegee-holder handle; and with the funnel and rubber stopper removed, makes for a suitable sample container, with a tight fitting cork to prevent evaporation. A converted plastic stethoscope bell was also made use of as a slightly modified type of squeegee; this was also attached to the test tube in the same manner as the funnel described above. A fifty c.c. wide mouth test tube can also be used as a very satisfactory combined squeegee and sample container if nothing else is available.

The Collector, firmly "corked" into the test tube, is now inserted into the Saran tent from below by cutting a small hole in the midline. The collector and approximately half of the test tube are within the tent. They are thus sealed into the tent by means of a piece of tape about the mid portion of the tube reestablishing the airtite seal within the tent. The lower end of the test tube thus hangs dependently from the mid point of the inverted Saran tent. (SEE EXHIBIT #5). (SEE EXHIBIT # 7)

The actual process of collecting the sweat is accomplished by squeegeeing the enclosed back area every three minutes after the initial beads of sweat appear. Usually within thirty minutes from two to five c.c. of sweat will have been collected in the sample tube. A lamp is usually placed on the floor under the sweat table so that the back may be visualized during the collection procedure.

f. HANDLING THE SAMPLE AT THE CONCLUSION OF THE TEST. The sweat test is complete when 1-5 c.c. of sweat have been collected, depending of course on the number of laboratory procedures planned for any particular sample obtained. We have endeavored to submit sufficient sweat so that the laboratory will not find it necessary to dilute the sample more than three times, if at all. At the completion of the test, the collector and rubber cork are removed from the sample tube and a tight fitting cork is applied. If the sample is

to be held over night, the sample is frozen. In the laboratory the sweat is handled as though it were blood serum.

VI. THE METHOD ADAPTABLE TO HOME AND OFFICE DIAGNOSIS. Although the sweat table and collectors described are very useful in a large institution, the testing procedure can be run with relative ease in the home, the physician's office, or in the small town hospital. Two beds are strapped together leaving sufficient space between them equal to the enclosed area of the back. Flat boards placed crosswise between the beds can be used as head supports and buttocks and leg supports. A fifty cc wide mouth test tube with the open end and half the tube length enclosed within the tent will be adequate for the collector.

VII. MATERIAL FOR THIS SERIES. Sixteen sweat determinations were used in the series presented. Many more determinations were made, however the sixteen submitted occurred consecutively after the method was adopted in its present form. The last eleven determinations were performed under conditions such that it is felt that their accuracy is of a higher order than those samples listed as 1-5.

Among the 16 determinations were 5 confirmed fibrocystic disease of the pancreas patients. 5 of the patients were suspected of having the disease; 6 were controls. Patients were selected from the University of Nebraska Hospital, University

of Nebraska Fibrocystic Clinic of Dr. Gordon E. Gibbs, and from the Children's Memorial Hospital, Omaha, Nebraska.

VIII. RESULTS.

a. SODIUM AND CHLORIDE ANALYSIS. As can be seen from the accompanying chart #1, the fibrocystic patient showed consistently high sodium and chloride concentrations in the sweat when compared with the controls and the fibrocystic suspects. Neglecting case #5, which represents one of the confirmed fibrocystic patients, whose laboratory sample inadvertantly concentrated, we find the sodium range in the fibrocystic patients to be 55-220 meq/Liter, with a mean value of 152 meq/Liter. Sweat Chlorides on these same patients ranged from 72-184 meq/Liter, with a mean value of 143 meq/Liter. The combined controls and suspected fibrocystic patients showed a sodium range of 8.2-55 meq/Liter, with a mean value of 29.2. The chloride range was 6-37.6 meq/Liter, with a mean value of 20.2 meq/Liter.

b. SWEAT UREA NITROGEN ANALYSIS. Chart #2 indicates that there was no consistent findings to distinguish the Fibrocystic patients from the controls and suspected Fibrocystic patients. The range was 37 mgm% - 312 mgm%. It will be noted that 8 of the 9 determinations were under 90 mgm%.

c. PHOSPHATE ANALYSIS. Although present in three of the first four determinations, phosphates were consistently

absent thereafter. Values ranged from .48 - 3.00 mgm%.

d. ALKALINE PHOSPHATASE ANALYSIS. Alkaline phosphatase was present in sample number 3 only. It was consistently absent thereafter.

e. EFFECT OF THE TESTING PROCEDURE ON THE PATIENT. Patients experienced no apparent ill effects from the procedure.

IX. SUMMARY. Fibrocystic Disease of the Pancreas is an hereditary disease known to effect the exocrine glands. There is usually some involvement of the pancreas, lungs, sweat glands, salivary glands, and to a lesser extent the liver. Meconium illeus is a frequent finding at birth. In diagnosis, pancreatic enzymes are absent in 90% of the patients. Absence of tryptic activity on undeveloped x-ray film gelatin as a screening test, or the more time consuming duodenal drainage procedure with analysis of pancreatic enzyme content, are both useful tests. X-ray studies revealing pulmonary involvement consisting of obstructive emphysema and/or chronic broncho-pneumonia are confirmatory. The presence of high sweat sodium and chloride values are diagnostic in 99% of cases.

The clinical signs present usually include frequent bulky greasy yellow foul smelling stools in a patient with chronic pulmonary involvement and/or portal hypertension.

Meconium illeus may be present at birth. The patient is usually poorly developed, undernourished and small for his age, in spite of a very good appetite. There is usually a family history of sibling involvement.

The fate of Fibrocystic patients is usually determined by the extent and course of the pulmonary involvement.

With the use of pancreatic enzyme therapy and the prophylactic and therapeutic use of antibiotics, the early diagnosis of this disease can be life saving and life preserving.

The purpose of this work was twofold: 1. Develop a simple accurate volumetric technique for sweat collection and analysis. 2. Investigate possible sweat abnormalities other than the high concentration of sweat sodium and chlorides in Fibrocystic patients.

Sixteen determinations were recorded. Sweat samples obtained were analyzed for sodium, chloride, phosphate, Alkaline Phosphatase, and Sweat Urea Nitrogen. The series included sweat samples, of which 5 were from confirmed Fibrocystic patients, 5 were suspected Fibrocystics, and 6 were controls.

X. CONCLUSIONS. The volumetric collection and subsequent analysis of sweat for sodium, and chloride levels, provides a consistent diagnostic tool in the diagnosis of fibrocystic disease of the pancreas. The results obtained with this technique provide consistent results separating the controls from

those with the disease.

Urea Nitrogen, phosphate, and alkaline phosphatase findings in these same patients were not consistent with or diagnostic of Fibrocystic Disease of the Pancreas.

Children with any combination of symptoms of pancreatic, lung, liver, or sweat gland involvement are entitled to a Fibrocystic work up. The simplest test giving consistent results is the sweat test for sodium and chloride levels.

The accessibility of the sweat glands and the ease of volumetric sweat testing, suggest further and broader pursuit of sweat studies in an effort to uncover the etiology of this generalized disease process.

XI. ACKNOWLEDGEMENTS: To Dr. Gordon E. Gibbs for invaluable guidance and assistance in this work. To Senior Student George Harris for his physical assistance in helping to prepare some of the patients in the series for the sweat test.

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EXHIBI #1

The Airtite Waterproof Envelope(Tent)

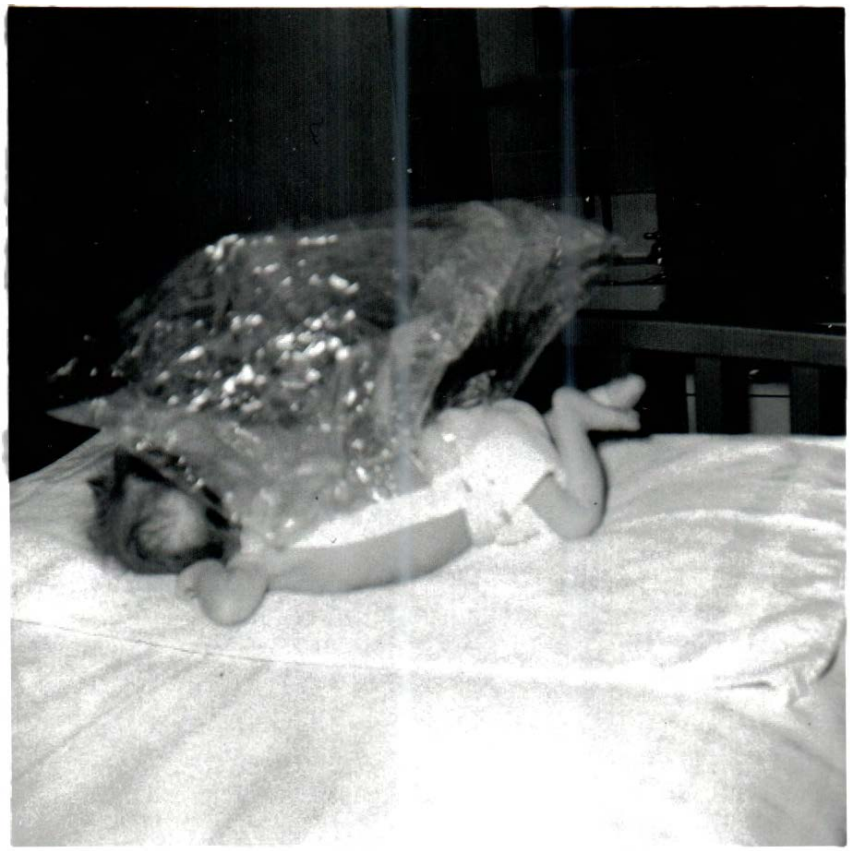
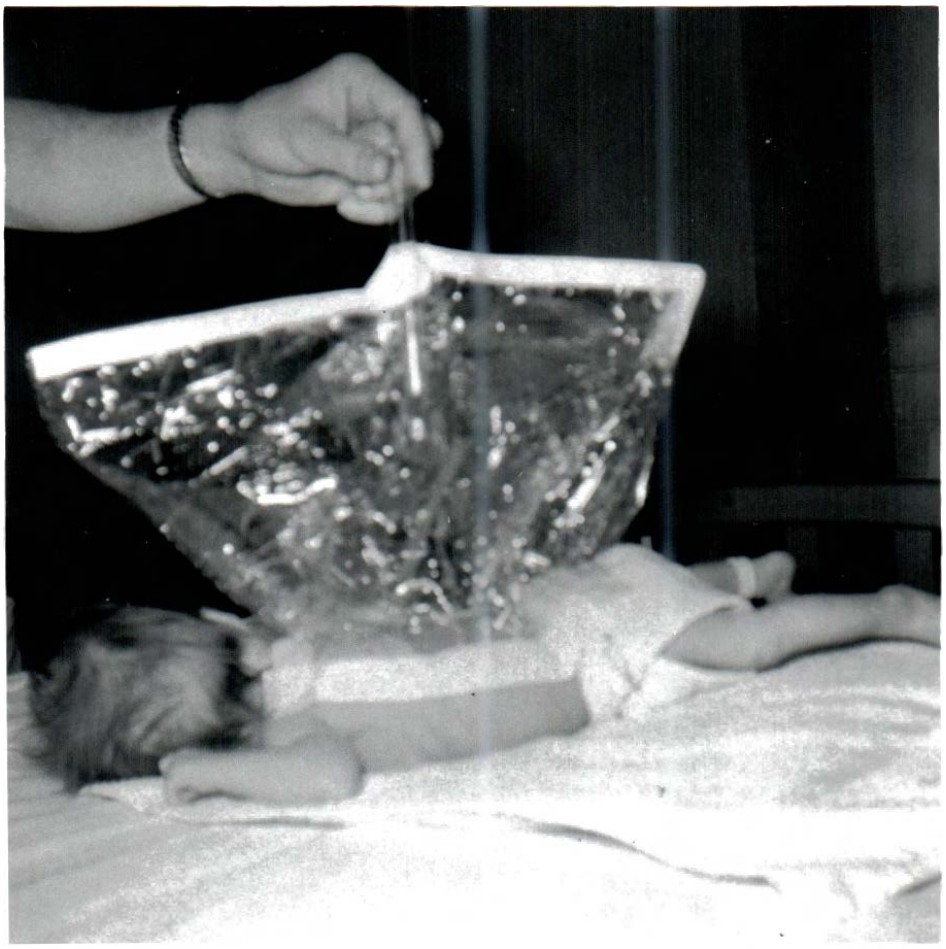


EXHIBIT # 2

The Airtite aterproof Envelope(Tent)



EXHIBI # 3

The Sweat Table

EXHIBIT # 4

The Sw at Table

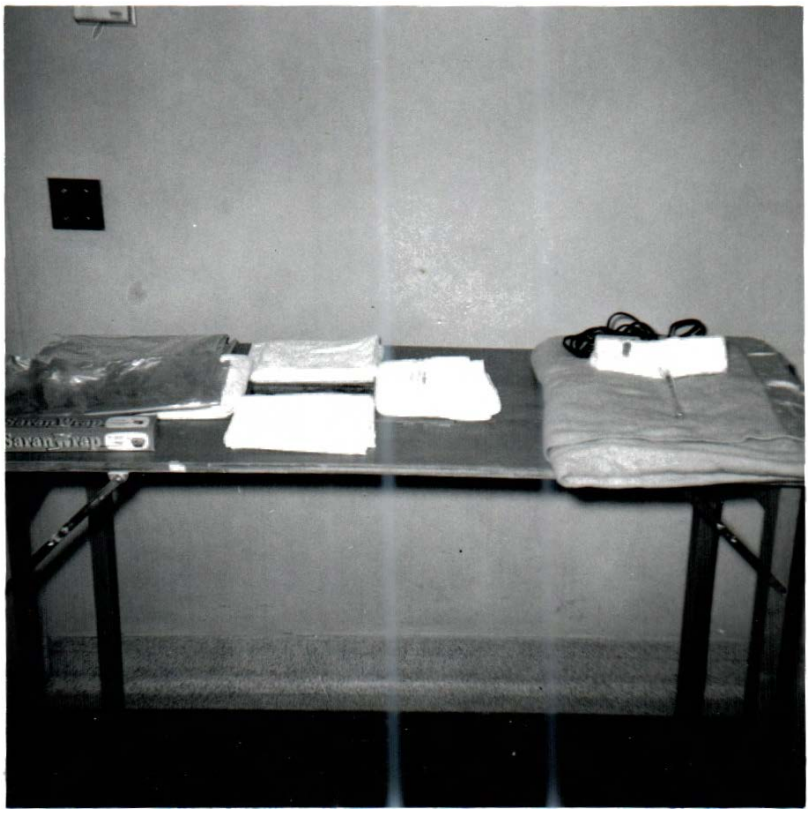


EXHIBIT # 5

The Sweat Ta le

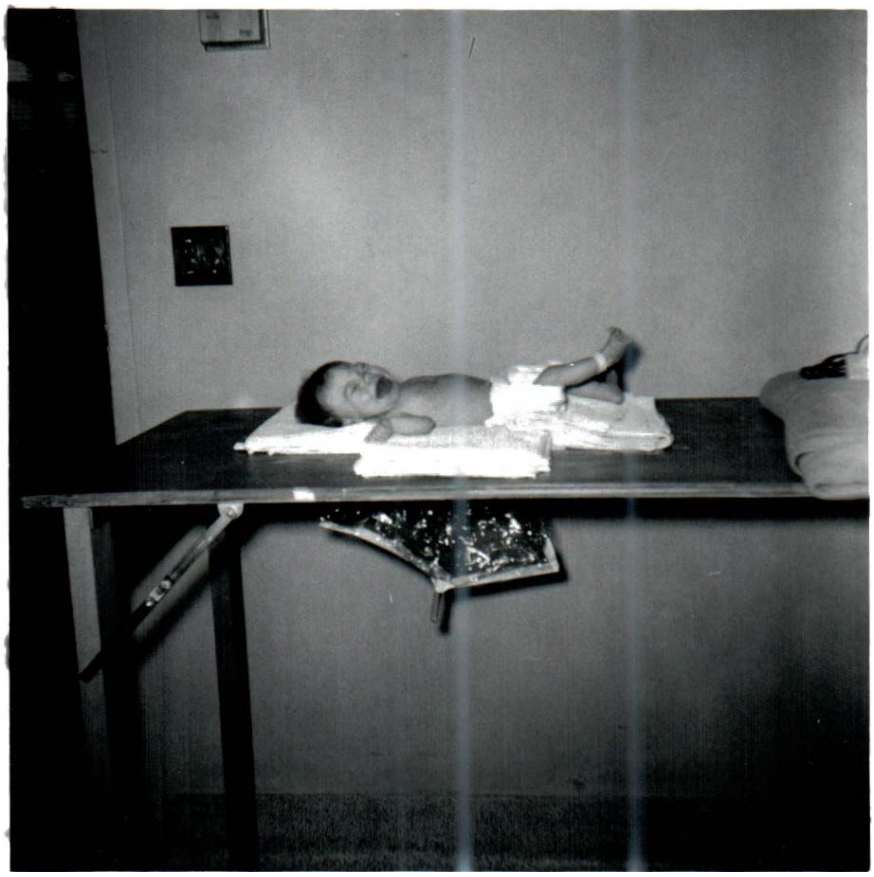


EXHIBIT # 6

The Sweat Table

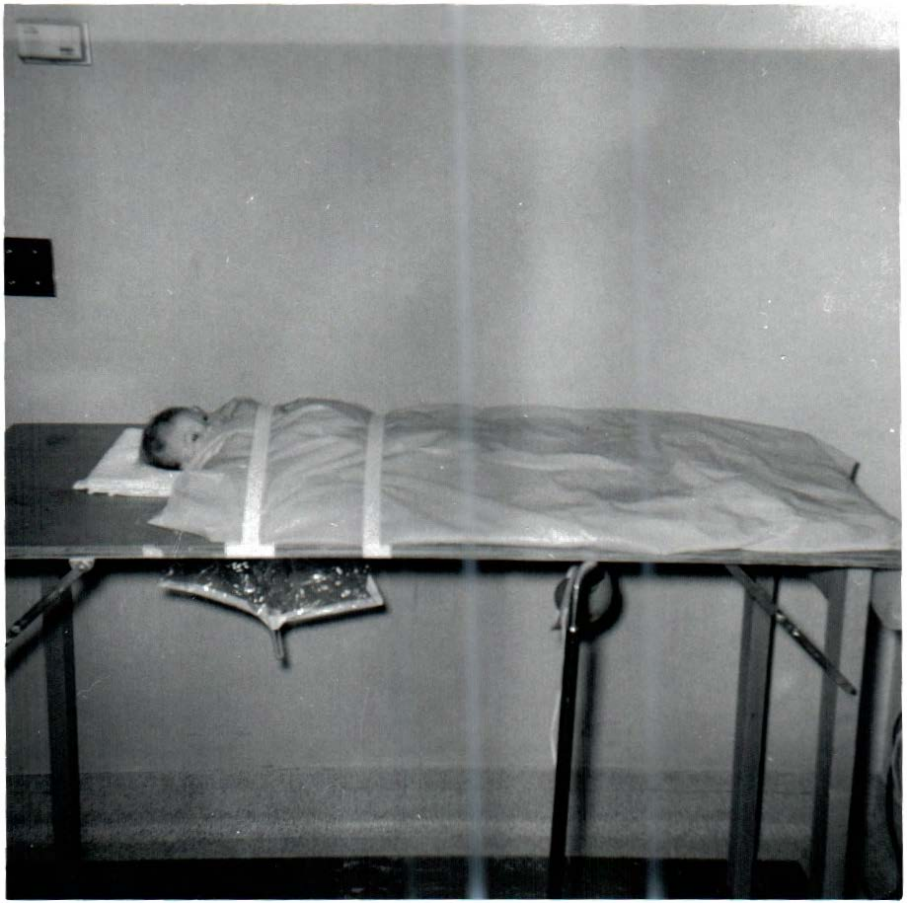
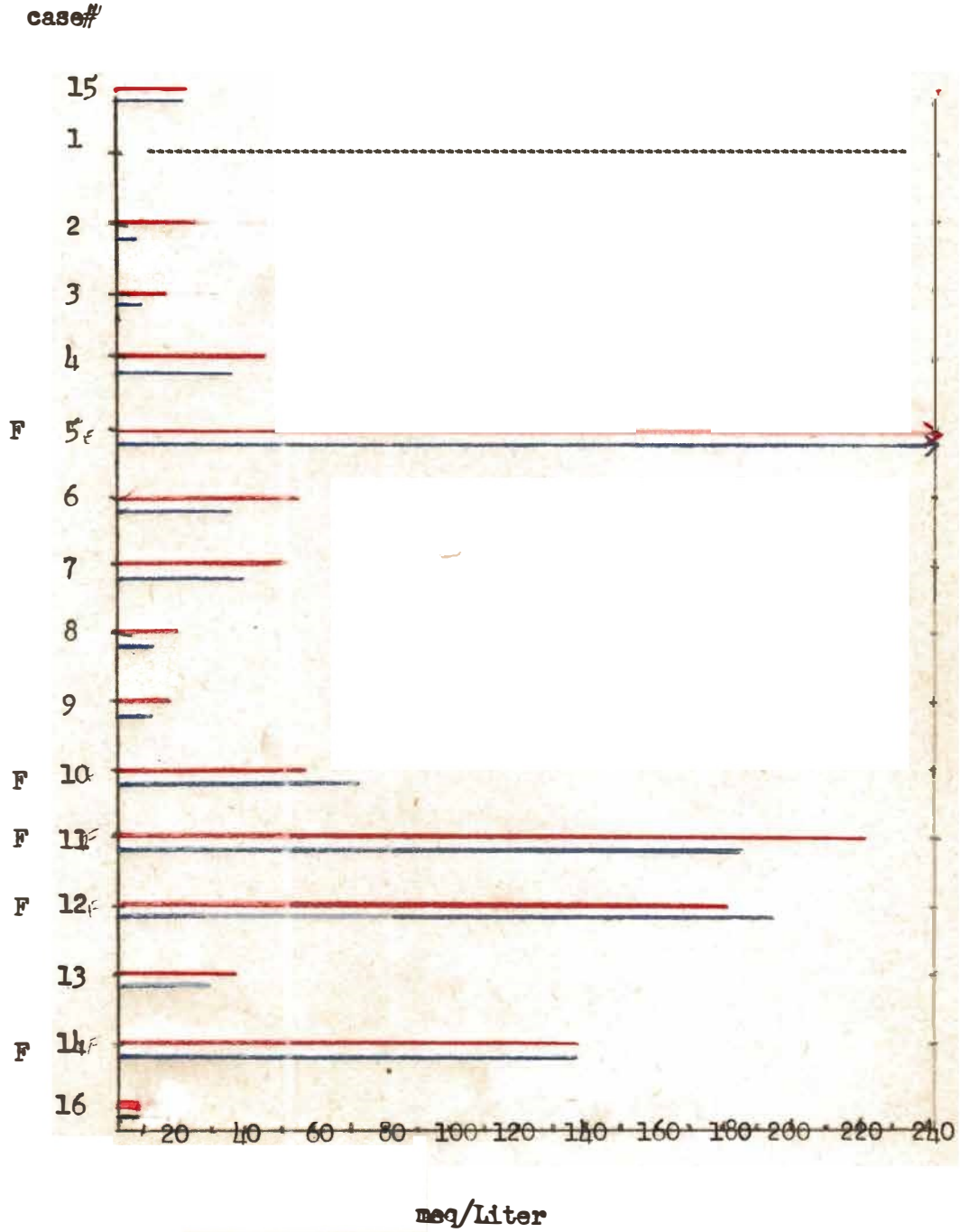


EXHIBIT # 7

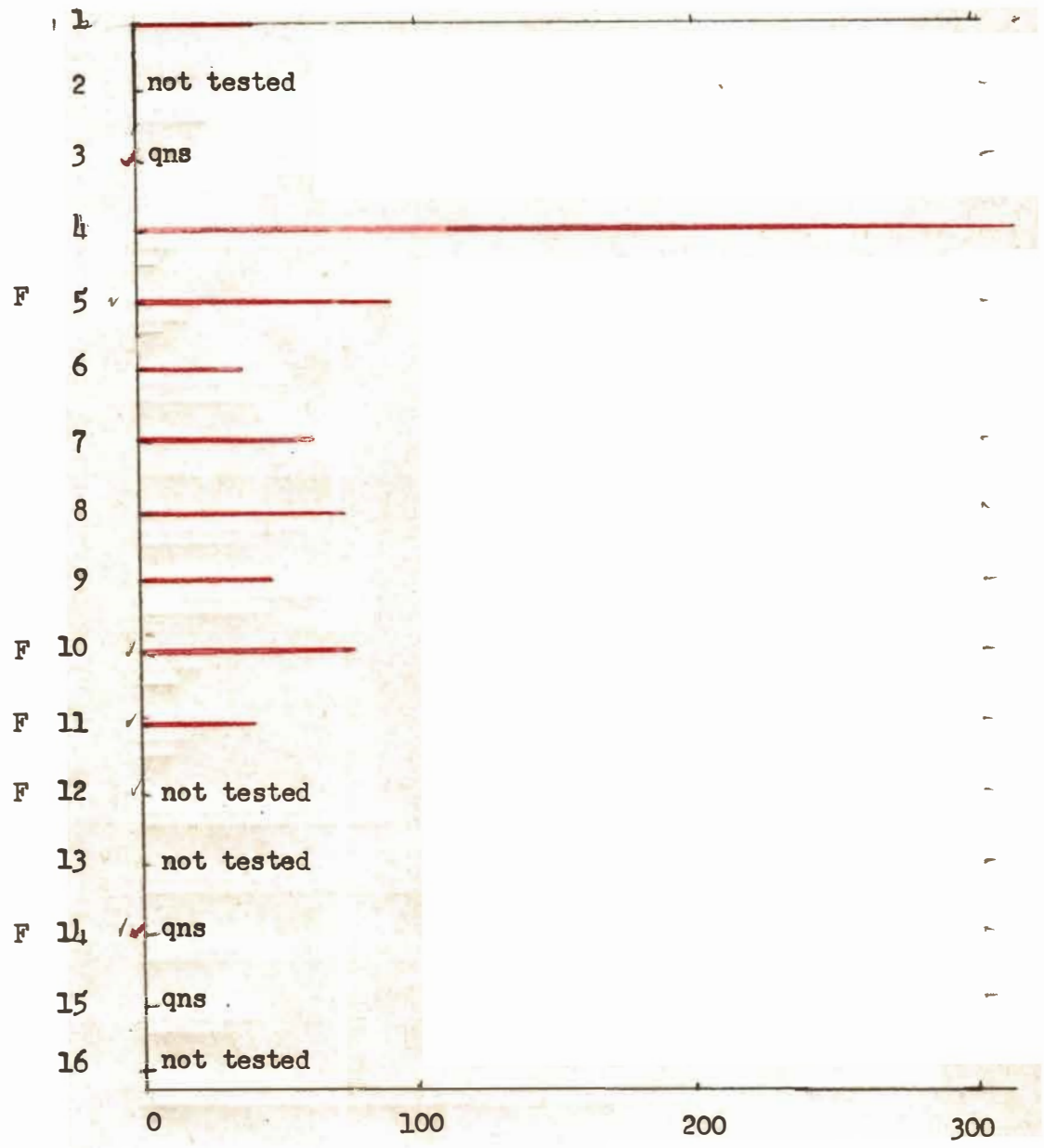
The Collector

CHART # 1



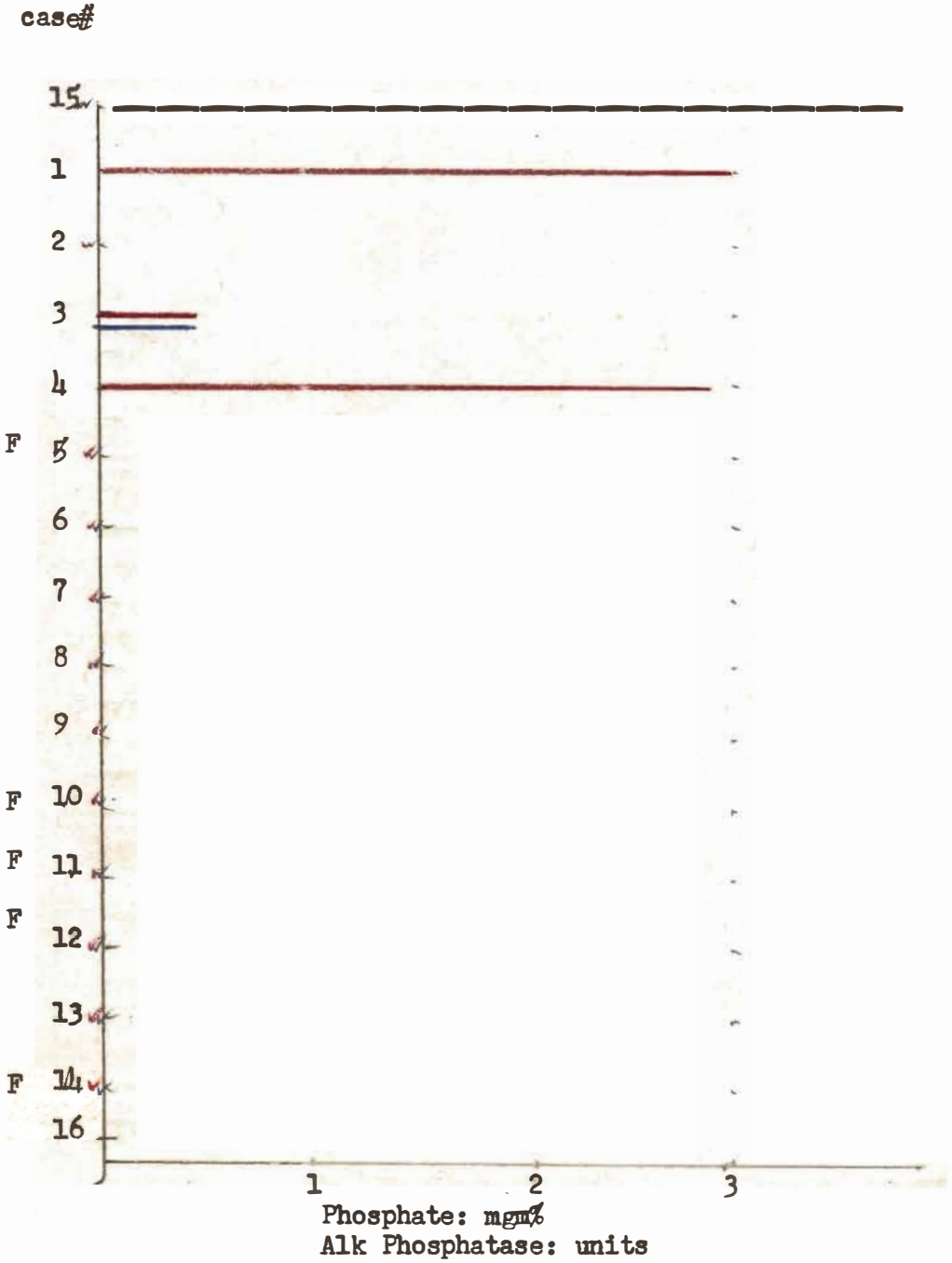
F: Confirmed cases of Fibrocystic Disease.

CHART #2



F: Confirmed cases of Fibrocystic Disease.

CHART # 3



F: Confirmed cases of Fibrocystic Disease.

Phosphate ————

Alkaline Phosphatase ————