1960

Thiocynate excretion in sweat in cystic fibrosis

Roger Herrick Hutchings
University of Nebraska Medical Center

THIOCYANATE EXCRETION IN SWEAT IN CYSTIC FIBROSIS

Roger Herrick Hutchings

Submitted in Partial Fulfillment for the Degree of Doctor of Medicine

College of Medicine, University of Nebraska

March, 1960

Omaha, Nebraska

TABLE OF CONTENTS

THIOCYANATE EXCRETION IN SWEAT IN CYSTIC FIBROSIS

Cystic fibrosis is a disease which affects many or all of the exocrine glands of the body,[2] including the pancreas, eccrine sweat glands, salivary glands, and the mucus glands of the respiratory tree. Most of the cases found are in infants and children. Kessler and Andersen in 1951 first reported the susceptability to hot weather of persons with cystic fibrosis.[10] In 1953 di Sant'Agnese, et al, reported that the sweat of fibrocystic's contains two to four times as much sodium and chloride as that of normals, but the volume of sweat is within the range of normal.[4] It has been suggested that the excessive excretion of chloride ion is due to failure of reabsorption of chloride in the sweat tubule, and that the rate of sweating is not unusual in cystic fibrosis.[2] Salt loss during hot weather is believed to account for the finding noted above. Thus for several years determination of sweat chloride, as described by Gibbs[6] and others,[1, 11, 13] has been used as a reliable diagnostic test for cystic fibrosis.

The exocrine gland abnormality has not yet been determined. It has been suggested that there is a defect in an unidentified enzyme system concerned with energy required

for retention of electrolytes by the sweat glands.[9] These authors calculate that a sodium concentration of 100 meq/L as seen in cystic fibrosis requires a minimum expenditure of energy by the sweat gland. A recent report indicates that there is a vitamin E deficiency in cystic fibrosis and other diseases, and as vitamin E has a role in various respiratory enzyme systems, this may furnish a clue to the pathogenesis of the disease. However, the vitamin E deficiency is more likely secondary to the steatorhea resulting from pancreatic exocrine deficiency. Other studies have been conducted in an attempt to delineate the exact enzyme deficiency.[7]

The present studies were undertaken to further characterize the sweat abnormalities in this disease. It was of interest to us to determine if anions other than chloride are excreted in excessive quantities. Little data concerning this is available, but it has been shown that iodide is handled similarly to chloride by fibrocystic sweat glands.[7] The anion chosen for these studies was thiocyanate, which is quickly absorbed from the gastrointestinal tract and distributed throughout the extracellular fluid.[5] This ion has been shown to behave similarly to halogens in the body.

METHOD

Two groups of subjects were utilized. One group consisted of patients shown to have cystic fibrosis by clinical and laboratory methods. Other patients were selected as a control group. These patients had various diseases, but were in generally good health and good nutrition, had not received steroids or salicylates, and did not have known renal or adrenal disease. All tests were conducted during the summer or early fall, and all patients were on a general diet.

The subjects were all given 10 ml./square meter body surface of elixer of 4% sodium thiocyanate orally, a dosage calculated to give a 6-7 mg% blood level of thiocyanate within 2-4 hours after ingestion. Two to four hours later these patients were sweated for a 20-30 minute period, using the method advocated by Gibbs.[6] Immediately after sweating, 5 cc. of venous blood was drawn, allowed to clot, and the serum removed. Both sweat and serum were carefully sealed and frozen until the determinations were made. In seven patients, samples of serum were obtained before thiocyanate was given, and serum blanks were determined. However, these samples did not give a significant color

reaction for thiocyanate, so this procedure was omitted for the other subjects.

Thiocyanate was determined using a micro modification of a well known method.[14] The general procedure was as follows, and was the same for sweat and serum: To a trichloracetic acid centrifugate of sweat or serum in a cuvette, a 10% solution of ferric nitrate was added. The color was allowed to develop in the dark for 15 minutes, and then optical density readings were taken, using a reagent blank, at 460 mmicra with a Beckman model DU spectophotometer. A standard curve was obtained in a similar manner using standard thiocyanate solutions, and from this curve the concentration of thiocyanate in the samples was obtained. A sweat/serum ratio was then determined.

RESULTS

Figure 1 lists the results obtained in eight control subjects and seven fibrocystics. In the control group sweat/serum ratios for thiocyanate ranged from 4.7 to 19.9 with a mean of 11.0 and standard deviation of 5.6. The diagnosis in these cases is listed. In the fibrocystic group the sweat/serum ratio was almost uniformly higher, with only one value falling within the control group range. The mean value was 37.7 and due partly to two very high values; the standard deviation was 22.9. Sweat chloride levels are given for the fibrocystic patients. The normal range for sweat chloride is 10-35 meq/L while the levels seen in fibrocystics are 50-110 meq/L.[12]

Statistical analysis reveals that these results are significant in excess of the 1% level, as the relative deviate of the standard error of the means is 3.4.

THIOCYANATE SWEAT/SERUM RATIO

CONTROL			FIBROCYSTIC		
					Sweat Chloride meq/L
J. B.	5.1	Intake obesity	B. B.	68.4)	133
D. B.	4.7	Colonic polyps	B. B.	31.9)	
J. C.	9.2	Cerebral palsy	P. B.	23.2	116
A. C.	11.8	Achalasia	B. G.	72.0*	121
D. C.	19.9	Recto-urethral fistula	M. A.	46.4	113
C. A.	8.6	Bronchitis	R. B.	21.8	195
B. M.	18.5	Bronchitis	L. B.	24.1	110
J. Z.	10.5	Normal	D. L.	17.7	68
			B. G.	33.6*	120
Mean	11.0		Mean	37.7	
Std. Dev.	5.6		Std. Dev.	22.9	

Fig. 1. Sweat/Serum x 100.

*---Same patient with tests performed three years apart.

)
)---Same patient with tests performed several days apart.

DISCUSSION

According to this evidence and other data already mentioned, it is evident that the abnormality in the excretion of sweat in fibrocystic disease includes an excessive excretion of certain anions, both endogenous and exogenous. This abnormality includes excess excretion of certain cations as well, particularly sodium, and one might speculate that many other anions and cations are similarly handled.

Of the cations studied, however, there is none in which the abnormality corresponds to that of sodium as closely as the abnormality of thiocyanate and iodine corresponds to that of chloride. The potassium levels in sweat in cystic fibrosis average only about 50% higher than normal[4], and calcium levels are only slightly elevated[8], whereas sodium values are 2.5 times normal.[4] On the other hand, values for chloride,[4] iodide,[7] and thiocyanate average 4, 4, and 3.5 times normal, respectively. The significance of this observation is not yet definite. However, with further elucidation of the transport systems involved for these ions, the defect may become clear.

It is thought that the abnormality of sodium, chloride,

iodide and thiocyanate is due to a failure of reabsorbtion of excreted ions, rather than excretion in excessive concentration. The mechanism for this malfunction is not known, but may involve an energy producing enzyme system, and is probably common to the defect in the various exocrine glands involved in this disease.

SUMMARY AND CONCLUSION

Utilizing a well-known method, samples of sweat obtained from a group of subjects with cystic fibrosis and from a group of controls were analyzed for thiocyanate ions after the subjects had received an elixer of thiocyanate by mouth. Serum thiocyanate concentrations were also determined allowing a sweat/serum ratio to be determined for each subject. The results of these experiments are presented and their significance is discussed. Other pertinent information in the literature concerning the pathophysiology of cystic fibrosis is presented and discussed.

The evidence presented in this paper indicates that thiocyanate ion is excreted in higher concentration in the sweat of subjects with cystic fibrosis than it is in normal persons.

BIBLIOGRAPHY

1. Barbero, G. J., Kim, I. C., and McGavran, J., A Simplified Technique for the Sweat Test in the Diagnosis of Cystic Fibrosis of the Pancreas, Ped., 18, 189, 1956.

2. Barbero, G. J., Sibinga, M. S., The Electrolyte Abnormality in Cystic Fibrosis of the Pancreas, Ped. Clin., N. A., 6, 221, 1959.

3. Blanc, W. A., Reid, J. D., Andersen, D. H., Avitaminosis E in Cystic Fibrosis of the Pancreas, 22, 494, 1958.

4. di Sant 'Agnese, P. A., Darling, R. C., Perera, G. A., and Shea, E., Abnormal Electrolyte Composition of Sweat in Cystic Fibrosis of the Pancreas, Ped., 12, 549, 1953.

5. Fellers, F. X., and others, Change in Thiocyanate and Sodium Spaces During Growth, Ped., 3, 622, 1942.

6. Gibbs, G. E., Sweat Tests for Diagnosis of Cystic Fibrosis, G. Rev. Ped., 18, 188, 1958.

7. Gibbs, G. E., and others, Cystic Fibrosis, Postgraduate Medicine, 22, 515, 1957.

8. Gibbs, G. E., personal communication.

9. Gochberg, S. H., and Cooke, R. E., Physiology of the Sweat Gland in Cystic Fibrosis of the Pancreas, Ped., 18, 701, 1956.

10. Kessler, W. R., and Andersen, D. H., Heat Prostration in Fibrocystic Disease of the Pancreas and Other Conditions, Ped., 8, 648, 1951.

11. Mauer, A. M., and West, C. D., A Simple Method for the Collection and Analysis of Sweat for Chloride, AMA J. Dis. Child., 92, 160, 1956.

12. Nelson, W., ed., Textbook of Pediatrics, Saunders, Philadelphia, 1959, 195.

BIBLIOGRAPHY

13. Shwachman, H., and Gahm, N., Studies in Cystic Fibrosis of the Pancreas; A Simple Test for Detection of Excessive Chloride on the Skin, New Eng. J. Med., 255, 999, 1956.

14. Visscher, M. B., ed., Methods in Medical Research, Year Book Publishers, Inc., Chicago, 4, 48, 1951.