

## Excretion of Sodium-24 and Barium-82 in Cystic Fibrosis<sup>1</sup>

M. Nicolaidou,<sup>2</sup> E. Apostolopoulou, and V. Samara

*Athens, Greece*

Cystic fibrosis, one of the most common chronic diseases in childhood and adolescence, is still of unknown etiology. It is a generalized hereditary disorder of the exocrine glands, with varying involvement of organs or glandular systems, leading to wide variations in the clinical picture (1,2,3,4).

Abnormalities in exocrine secretions include the following. A marked increase occurs in the concentration of electrolytes in the sweat, 98% of C. F. patients, and, to a lesser extent, in the saliva and the tears (5,6,7). Hair and nails proved recently of considerable interest for the high Na and K values (8).

A change takes place in the chemical structure and physicochemical properties of mucous secretions in the duodenum, the bronchial tract, the salivary, and probably the remaining mucus glands (6,9,10,11). Also an increase in the rate of parotid secretion (12, 13) occurs.

Whatever the nature of the widespread dysfunction of the exocrine gland may be, it is generally agreed that it is transmitted as a recessive trait, with an incidence of one per 2,000 live births. Two to five per cent of the population are estimated to be heterozygotes (2,3,4).

The present investigation (14) was undertaken in order to study the excretion of <sup>24</sup>Na and <sup>82</sup>Br in the sweat and in the urine of C. F. patients. The volume of the extracellular fluid was also investigated.

### MATERIALS AND METHODS

Thirteen patients with proven cystic fibrosis were studied at the Pediatric Clinic of Athens University. Fifteen children, belonging to the same age and/or weight group, not suffering from renal disease or adrenal insufficiency, and not receiving steroids, served as controls.

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<sup>2</sup>Pediatric Clinic of Athens U. Medical School, St. Sophie's Children's Hospital, Athens, Greece.

Sweat was collected by pilocarpine iontophoresis (15).  $^{24}\text{Na}$  and  $^{82}\text{Br}$  were prepared at the Nuclear Research Center *Democretos* in Athens, and the samples were measured at the Radioisotope Service of St. Savas Hospital.

After a fasting period of four to six hours a dose of  $20\ \mu\text{C}$  of  $^{24}\text{Na}$  was given orally to the infants and  $25\ \mu\text{C}$  to the older children. Sweat and urine samples were collected five and 22 hours after the ingestion of the radioactive substance, and blood specimens in two cases at five hours, and in all at 22 hours (Tables I, II).

The radioactivity of the samples was measured simultaneously in patients, and their respective controls by a well type scintillation counter EKCO N 664 A, connected with an automatic scaler EKCO N 530 F.

The sweat values for Na and Cl were expressed in mEq/L, and for the radioisotopes in counts per sec per gm of sweat (c/s/gm), and in counts per sec per ml of plasma (c/s/ml). The ratio of sweat to plasma counts was calculated. The radioisotope excretion in urine was expressed as a percentage of the administered dose. The volume of the extracellular fluid was also investigated by  $^{82}\text{Br}$ , 22 hours after the ingestion of the isotope, based on the formula:

$$\text{ECF (L)} = \frac{\text{A-E}}{\text{R}}$$

Where ECF = extracellular fluid volume  
 A = amount of the administered dose (c/s)  
 E = amount of the excreted radioactivity in urine in 22 hours (c/s)  
 R = radioactivity of plasma (c/s/l).

TABLE I  
 SWEAT ELECTROLYTES AND  $^{24}\text{Na}$  EXCRETION IN CYSTIC FIBROSIS  
 PATIENTS AND CONTROLS

	Sweat Electrolytes		$^{24}\text{Na}$ Excretion			
	mEq/L		Sweat		Urine	
	Na	Cl	c/s/gm sweat c/s/ml plasma		% of administered dose	
			5 hrs	22 hrs	5 hrs	22 hrs
Patients N = 8	99.7 (73.5-127)	108.9 (75-136.5)	1.0 0.7-1.3	0.94 0.7-1.6	0.4 0.2-0.6	3.2 0.2-7.9
Controls N = 8	20.2 11-27	22.3 8.6-39	0.3 0.05-0.5	0.2 0.04-0.5	0.9 0.3-1	4.5 0.6-8.7

The extracellular fluid volume was expressed finally as a percentage of the body weight.

## RESULTS

From the comparative study of sweat electrolyte values and the isotopes, it can be seen that both concentrations of Na and Cl, and the excretion of  $^{24}\text{Na}$  in the sweat were invariably increased in the C.F. patients (Table I).

The mean ratio of sweat to plasma counts was found to be 0.25 in the controls and 0.97 in the patients (Fig. 1).

Excretion in urine of  $^{24}\text{Na}$  is somewhat lower in C.F. patients both at five and 22 hours. However, only the difference between the means at five hours have been found to be statistically significant.<sup>1</sup>

In another series of experiments  $^{82}\text{Br}$  was used for the followup of Cl metabolism (Table II). The excretion of  $^{82}\text{Br}$  in the sweat was also increased.

Urinary excretion of  $^{82}\text{Br}$  was slightly decreased in C.F. patients, but the difference statistically is insignificant.

The mean ratio of sweat to plasma counts in C.F. patients, almost equal to 1, was four times higher than that of controls (Fig. 1).

We should additionally report two patients with sweat electrolytes in the upper normal limits, Na = 52 and Cl = 57 mEq/L, or low abnormal, Na = 74

TABLE II  
SWEAT ELECTROLYTES,  $^{82}\text{Br}$  EXCRETION AND EXTRACELLULAR FLUID VOLUME  
IN CYSTIC FIBROSIS PATIENTS AND CONTROLS

	Sweat Electrolytes		$^{82}\text{Br}$ Excretion				E C F
	mEq/L		Sweat		Urine		Volume
	Na	Cl	c/s/gr sweat c/s/ml plasma		% of administered dose		% B.W.
Patients N = 5	102.8 80.2-118	108 75-136	0.94 0.78-1.1	0.97 0.7-1.2	—	3.7 1-6.6	31 26-35
Controls N = 7	19.9 11.4-41	18.7 9.6-30	5 hrs	22 hrs	5 hrs	22 hrs	31.7 25-35.5
			0.08 0.01-0.14	0.2 0.7-1.2	—	5.14 3.7-61	

<sup>1</sup>In the statistical analysis of the above mentioned values the "t" test of significance was used ( $P < 0.01$ ).

and Cl = 82 mEq/L, where the diagnosis of cystic fibrosis was excluded by the consequent clinical picture and the radioisotope study, ratio: 0.18 to 0.31. The volume of the ECF determined by  $^{82}\text{Br}$  was found to be normal.

Since the urinary radioisotope excretion was not greatly reduced, the main finding is the increased  $^{24}\text{Na}$  and  $^{82}\text{Br}$  excretion in the sweat.

Our data show that this increase was about 500%. It was observed in every case, with both substances used.

DISCUSSION

The high concentration of Na and Cl in the sweat is generally accepted as the index for the diagnosis of cystic fibrosis (2,3,4,5,7,13,16).

In the present study an attempt was made to correlate the excretion of  $^{24}\text{Na}$  and  $^{82}\text{Br}$  in the sweat, to the excretion of these substances in the urine. In spite of an increased excretion of both  $^{24}\text{Na}$  and  $^{82}\text{Br}$  in the sweat, the elimination of these substances in the urine was essentially normal.

The extracellular fluid volume as determined by  $^{82}\text{Br}$  showed no difference between the studied groups. The extracellular fluid volume values, determined

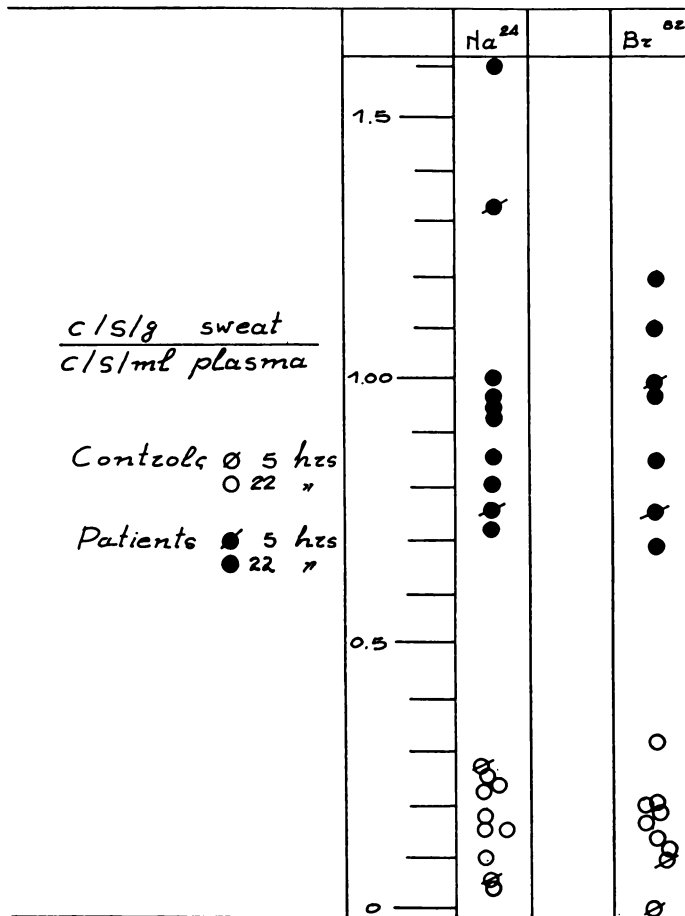


Fig. 1.

#### EXCRETION OF $^{24}\text{Na}$ AND $^{82}\text{Br}$ IN CYSTIC FIBROSIS

by isotopic techniques, range from 26% for adults, to 43% for infants (17,18,19,20, 21). In our studies, the average value was found 31% for both groups. No hypothesis could be advanced; therefore, a depletion of extracellular fluid volume occurs in C.F. patients due to excessive salt loss. Obviously, this is compensated by adequate salt intake. Our findings with  $^{24}\text{Na}$  and  $^{82}\text{Br}$  provide evidence that electrolyte transport and excretion by the sweat glands is extremely rapid.

Sweat production is an energy consuming process. The hypothesis has been advanced by Vink (22) to find that in C.F. patients the metabolism of the sweat gland is disturbed. Several suggestions have been made about the nature of this abnormality. These include enzyme dysfunction, or impairment of membrane permeability. However, no convincing evidence has been presented so far, and the site of the defect requires further investigation.

The determination of the ratio of sweat to plasma counts of  $^{24}\text{Na}$  and  $^{82}\text{Br}$  appears to be a sensitive method, which may prove to be helpful in the diagnosis of cases suggestive of cystic fibrosis.

#### SUMMARY

For the study of Cl and Na metabolism in C.F. patients,  $^{24}\text{Na}$  and  $^{82}\text{Br}$  was utilized in 13 patients and 15 controls. The ratio of the sweat to plasma counts of the isotope is approximately one in C.F. patients. Whereas, in controls it is 0.25. By this technique, two patients with a probable diagnosis of cystic fibrosis, which was made on both clinical and chemical grounds, were excluded from the C.F. group, and this impression was confirmed by their follow up and the subsequent clinical picture.

An attempt was made to correlate the excretion of  $^{24}\text{Na}$  and  $^{82}\text{Br}$  in the sweat with their excretion in the urine. In spite of an increased excretion of both isotopes in the sweat, their urinary elimination was essentially normal. No change was found in the extracellular fluid volume as determined by  $^{82}\text{Br}$  in C.F. patients.

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