

Influence of Induced Variations in Electrolyte and Water Exchanges with Pitressin in Bronchial Asthma.*

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During the course of studies on the influence of various therapeutic procedures on the mineral and water exchanges in children suffering from bronchial asthma, it was observed that artificial fever was usually followed by remission of symptoms when the sodium chloride content of the diet was extremely low, but not when the intake of this salt was unrestricted. This observation suggested the desirability of examining more critically the relationship between the electrolyte and water balance in the mechanism of asthmatic attacks.

Starling and Verney¹ and McQuarrie, Manchester and Husted² have shown that pitressin, the antidiuretic principle of the pituitary gland causes, not only a retention of body water, but a coincident absolute increase in the output of sodium and chloride in the normal subject. Therefore, when the sodium chloride intake is very low and the water intake is relatively high during a period of sustained pituitary antidiuresis, body water is retained without coincident storage of sodium chloride. Since this procedure offers a unique opportunity to dissociate the effects of water and salt in the asthmatic patient, the following experiments were undertaken.

Six children, selected on the basis of severity and intractability of their asthmatic attacks, were placed under constant environmental conditions in the hospital, in charge of specially instructed nurses. The patients were given 4 evenly spaced daily feedings of a weighed formula having reasonably adequate basal dietary constituents, but an extremely low sodium content. Calculated daily intake of sodium was 120 to 700 mg. Distilled water was given at equally spaced intervals, 400 cc per day during control periods and 1200 cc to 2000 cc per day during pitressin sessions. Urine was collected in 24-hour specimens, measured and preserved for future chemical analysis. The subjects were weighed daily on a metabolism balance

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¹ Starling, E. H., and Verney, E. B., *Proc. Royal Soc. Biol.*, 1925, **97**, 321.

² McQuarrie, Irvine, Manchester, R. C., and Husted, Clara, *Am. J. Dis. Child.*, 1932, **43**, 1519.

under uniform conditions. Hourly observations of the patients' condition were made and all asthmatic attacks were tabulated.

An initial control period accustomed the children to the regimen and established the frequency and severity of the asthmatic attacks. Then, while the low salt and high water intakes were maintained, pitressin was administered by hypodermic injection in doses of 0.3 to 0.5 cc every 3 hours which had been found by McQuarrie and Peeler³ to be sufficient to sustain antidiuresis over a considerable period of time. After 24 to 36 hours, during which the weight increased due to retained water 2 to 5% of the initial body weight,

TABLE I.
Influence of Pitressin on Attacks of Bronchial Asthma.

Case	Exp. No.	Intake mg per day		Amt of asthma during various periods*			
		Na	K	Control	Pitressin	Diuresis	Subsequent
I. H.B.	1	120	360	4	1	1	3
	2	120	360	4	1	1	2
	3	120	360	4	2	2	0
	4	120	360	1	0	0	0
II. M.M.	5	120	360	1	0	0	0
	6	200	600	3	0	0	0
	7	200	2100	3	0	0	0
	8	200	2100	3	1	0	0
	9	200	2100	2	1	0	0
	10	500	1500	3	1	0	0
	11	500	1500	1	0	0	0
	12	200	600	4	2	0	0
III. R.K.	13	500	1500	2	0	0	0
	14	200	600	3	0	0	0
	15	200	600	2	3†	4†	1
IV. R.F.	16	700	2000	4	2	1	1
	17	700	2000	3	3	2	1
V. B.C.	18	120	360	4	2	0	0
	19	120	360	2	1	0	0
VI. R.V.	20	200	600	4	1	0	0

*Amount of asthma was determined by hourly observations day and night and number of doses of epinephrine required to give the patients some comfort. The following code was adopted:

- 0—No asthmatic wheezing observed and no epinephrine used.
- 1—Wheezing present for at least 1 hr per day requiring 1 dose of epinephrine.
- 2—Wheezing lasted 3 hr per day requiring usually 3 doses of epinephrine.
- 3—Wheezing present about half the time or at least 12 hr per day, requiring around 5 doses of epinephrine per day.
- 4—Continuous wheezing existed requiring 8 or more doses of epinephrine per day.

†Vomiting, cramps, and diarrhea were present during these periods and the asthma was temporarily aggravated.

³ McQuarrie, Irvine, and Peeler, D. B., *J. Clin. Investigation*, 1931, **10**, 915.

the pitressin and extra water were stopped. This resulted after 6 hours in a copious diuresis, the patients usually reaching a new weight level below the initial figure.

A total of 20 observations or studies were made on the 6 subjects. During the water retention phase of each period of observation a reduction in the number and severity of asthmatic attacks occurred in 18 instances, 7 of which showed complete cessation of symptoms. In one case the symptoms remained unchanged and in another child who developed diarrhea a slight increase in symptoms occurred. During and after the diuretic phase improvement in symptoms continued in 19 instances with complete remissions developing 14 times. In the case which had diarrhea the asthma continued to be slightly aggravated during diuresis but improved during the subsequent period. In 6 instances symptoms recurred spontaneously after the end of the period of observation, while the remainder had remissions until upset by some extraneous factor. In one case 4 g of sodium chloride were administered after 10 days, which were free of asthma, all other factors remaining constant, and the asthmatic symptoms reappeared promptly. The results of the experiments are summarized in Table I.

From the foregoing it would appear that bronchial asthma can be ameliorated even in the presence of excessive hydration if there is an associated depletion of sodium chloride. This preliminary group of observations suggests that the sodium ion may exercise an adverse influence on the asthmatic patient, independent of its usual relation to hydration.

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Studies on Enzymatic Formation and Destruction of Uric Acid in Mammalian Blood.

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The colorimetric estimation of uric acid by a phosphotungstic acid reagent is made more specific by the use of uricase. The uricase preparation used consists of ox-kidney which has been acetone-dehydrated, benzene-defatted, air-dried, and finely ground. In the studies described here we used the direct colorimetric method¹ that

¹ Koch, F. C., *Practical Methods in Biochemistry*, 2nd edition, Wm. Wood, Baltimore (1937), 130, 284.