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METABOLISM OF CHLORIDE AND TOTAL FIXED BASE IN PNEUMONIA AND THE RELATION TO SALT AND WATER RETENTION

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Although much has been written regarding an unusual behavior of chloride and certain other ions in pneumonia, the literature fails to supply a clear-cut conception of the sequence of events in the metabolism of acid and base in this disease. Largely because investigations have tended to consider only a few factors at a time it is difficult to evaluate their relationship to other elements in the situation. Several findings have, however, been thoroughly established, and it is the object of this paper to attempt an explanation of them in terms of certain accompanying circumstances. An underlying variable, the effect of which we have particularly studied, is the level of salt and water intake.

Peabody (1) (2), in his papers of 1912 and 1913, summarized the previous literature and reported the observations that most patients with pneumonia have low serum and urinary chlorides, and a high urine ammonia. He reported also a decreased elimination of Na, Ca, and Cl, but a normal or increased excretion of K and Mg, inferring therefrom a retention of the former ions but not of the latter. By analysis of tissues, Peabody went on to show that there is nowhere an accumulation of the "retained" ions, which led him to believe that these must be spread diffusely through the body.

McLean (3) in 1915 confirmed Peabody's findings and noted also that the low serum chloride found in pneumonia returned to normal before the low urinary chloride showed a similar change.

In 1916 Maver and Schwartz (4) observed the presence of pitting edema in some cases of pneumonia and not in others, but felt that their

"elastometer" readings indicated some degree of edema in all cases. These authors also, making 22 determinations on 7 patients, found a diminution in serum chloride which disappeared following the crisis.

Related to the above evidence of water retention is the observation of Lussky and Friedstein (5) that all but one of their 28 cases of primary pneumonia in infants and children lost weight following the crisis. This suggested to them a marked retention of water during the course of the disease.

In 1925 Clausen (6) made the interesting observation that large amounts of organic acid are excreted following the crisis in pneumonia, the maximum excretion corresponding with the period of resolution.

In the same year Haden (7) ventured to draw an analogy between pneumonia and intestinal obstruction on the basis of the low serum chloride and the so-called "toxicity" observed in both conditions. This author suggested the use of large amounts of salt in pneumonia and reported clinical improvement in patients so treated. A further paper by Haden (8) in 1927 demonstrated, (in one patient especially), a marked increase in serum and urinary chloride following the ingestion of sodium chloride, and went on to record additional impressions of clinical improvement with salt therapy.

In 1928 (9) Soule suggested that the accelerated circulation in fevers caused a blood dilution which might tend to lower serum chloride in pneumonia, but went on to say that this theory did not explain the retention of chloride.

Peters (10) in the previous year argued for the presence of a "compensated carbon dioxide acidosis" in pneumonia, and suggested that the bicarbonate, while it remained normal, might in some way force the chloride ion out of the plasma.

With regard to kidney function in pneumonia, McIntosh (11), in 1926 was able to demonstrate a quite normal efficiency.

In 1926 also, Sunderman, Austin, and Camac (12), in an extensive study, reviewed previous findings in pneumonia and reported observations of their own on a large number of factors, such as conductivity, freezing point depression, total electrolytes, and total fixed base of the serum. The gist of their results was that ionic levels in the blood serum tend to be low during the febrile stage and to rise follow-

ing the crisis. In this connection it is worth while to mention a detail noted by Gerstenberger and Burhans, (13), namely that the inorganic phosphate of the serum is reduced in pneumonia and rises following the crisis.

Summarizing the above findings we see that the chloride of the blood serum is usually low in pneumonia and that this phenomenon is accompanied by a low urinary excretion of Cl, Na, and Ca. An extensive retention of these ions is suspected, but no depot can be found in which they have accumulated. Elevation of the blood chloride is accompanied by a rise in chloride excretion, the former appearing to be the primary event. Furthermore, a low blood chloride can be restored to normal by the oral administration of sufficient salt. Another phenomenon observed in pneumonia has been pitting edema in some cases and a marked water retention in others, as evidenced by loss in weight following the crisis. It is by no means established that the edema and water retention are findings accompanying a low serum chloride but such is at least a common impression. A sequence of events, constructed from published findings may therefore be described as follows. During the febrile stage of primary pneumonia, salt is supposed to be retained in the body tissues, even to the point of a "retention sec," although the plasma chloride and base are diminished, and the excretion of these ions is greatly decreased; water is retained along with the retained salt, and weight increases because of edema; salt offered at this time is retained, and if given in sufficient amounts will first raise the blood values to about normal, and then begin to enter the urine. Later, at the crisis, stored salt is released, the blood values rise, large amounts of Na, Cl, and perhaps other ions appear in the urine, and weight drops as a result of the accompanying excretion of body water.

With somewhat this point of view we began to observe cases of primary pneumonia in infants and at once were struck by the apparent discrepancies between what actually happened and what we supposed would occur. For some time it had been noticed that some patients increased rapidly in weight during the febrile stage of their pneumonia and that others lost weight to an equally striking degree. This contrast was exemplified by the first two cases of primary pneumonia that we placed on metabolism frames for study of their acid-base metabolism.

EXPERIMENTAL

Patient W. H. was studied for the 3 days preceding and the 6 days succeeding his crisis. During the first 3 days he gained nearly 2 pounds in weight, which same amount he lost immediately after the crisis. Determinations of the chloride and total base of the serum showed those values to be normal two days before the crisis, and at that time there were also 104 and 241 cc. N/10 respectively of those ions in the 24 hour urine. Following the crisis there was a sudden large increase of acid and base radicals, chiefly chloride and sodium, in the urine, the maximum values being 1641 cc. N/10 of chloride, and 1791 cc. N/10 of base on the second day after the crisis. Coincidentally, the volume of the urine nearly doubled. This patient therefore, although acting in the expected manner with regard to his weight changes, did not show either a low blood chloride and base, or a low urinary excretion of these ions at the height of his fever.

The second patient, A. S., was studied for 5 days preceding his crisis and 9 days succeeding it. *He lost weight*, to the extent of $3\frac{1}{2}$ pounds, during the first 8 days, (i.e. 5 days *before*, and 3 days *after* the crisis); and although on a nearly zero salt intake this patient excreted 1084 cc. N/10 base, and 442 cc. N/10 chloride in urine and stools, during the $6\frac{1}{2}$ days he was on the metabolism frame. In the blood serum three determinations of base and four of chloride showed steadily decreasing values prior to the crisis and a definitely low chloride as late as 36 hours after the crisis. The urinary values for base and chloride decreased rapidly before the crisis and remained exceedingly small for 4 days thereafter, that is to say for over 2 days after the weight had begun to rise. The patient was put on a full milk diet 48 hours after the crisis, but it was not until 3 days later that base and chloride appeared in the urine in moderately large amounts, amounts nevertheless which did not approach the values achieved by the first patient during his phase of maximum post-critical excretion. In table 1 are given figures which show the extent of loss of base and chloride in the first two periods, (i.e. while on a very low salt intake), and the markedly positive balance of these ions after a salt containing diet was resumed. (It is perhaps noteworthy that base and chloride appear, throughout, to behave very much in

the same way, and it need hardly be mentioned that by far the largest part of the base referred to is sodium.)

From the preceding it is evident that the behavior of the 2nd patient was exactly opposite to that of the first. To be sure his serum and urinary chloride and base dropped to low levels, but contrary to the

TABLE 1
Average base and chloride balances per 24 hours in patient A.S.

	Period I (36 hours), low salt diet	Period II (5 days), low salt diet	Period III (6 days), high salt diet
Fixed base, cc. N/10:			
Intake.....	0	0	1,433
Output in urine.....	130	27	285.5
Output in stools.....	300	61	206.5
Total output.....	<u>430</u>	<u>88</u>	<u>492.0</u>
Balance.....	-430	-88	+941
Chloride, cc. N/10:			
Intake.....	0	0	374
Output in urine.....	152	13	144
Output in stools.....	48	15.5	17
Total output.....	<u>200</u>	<u>28.5</u>	<u>161</u>
Balance.....	-200	-28.5	+213
Water, cc.:			
Intake.....	875	854	1,284
Output (urine and stools).....	<u>509</u>	<u>490</u>	<u>858</u>
Difference.....	+366	+364	+426
Weight, grams:			
Average daily gain or loss.....	+40	-157	+83

conventional idea this patient lost much weight and showed a large negative balance of both base and chloride previous to the crisis. Chart 1 illustrates graphically the contrast between the findings from these two patients. The effort on the part of patient A. S. to restore salt to the body is shown by the early rise of the weight curve through

immediate retention of salt and water, and the late appearance of salt in the urine when placed on a moderately high salt diet.

We soon realized that the key to the difference shown by these two infants lay in the fact that the former received a moderately large amount of NaCl during the course of his illness and retained water,

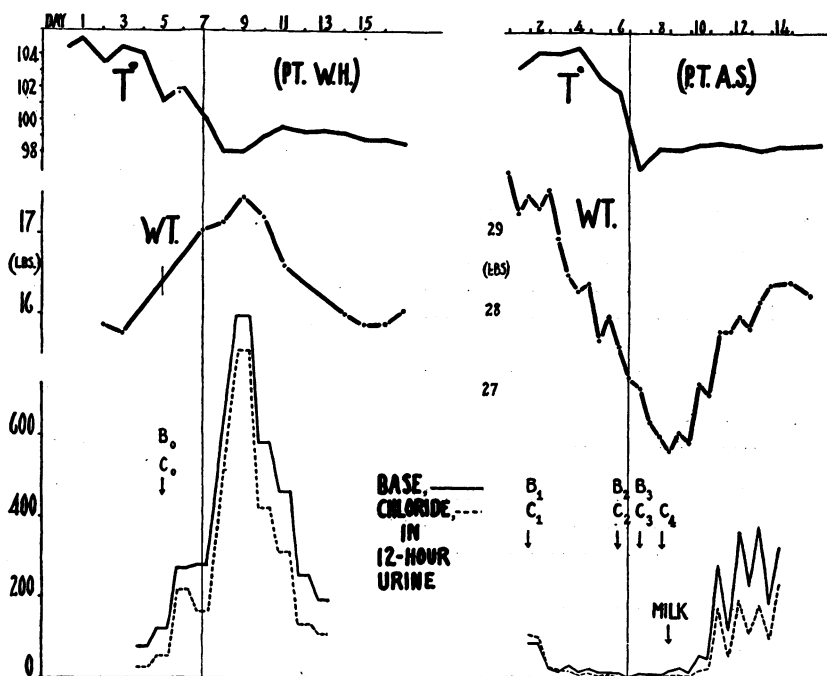


CHART 1. ILLUSTRATING DIFFERENCES IN WEIGHT CURVES AND IN URINARY EXCRETION OF CHLORIDE AND BASE, BETWEEN PATIENT W. H. ON A MODERATELY HIGH SALT INTAKE, AND PATIENT A. S. ON A VERY LOW SALT INTAKE

Crisis occurred at points marked by vertical lines. $B_0 = 153$, $B_1 = 157$, $B_2 = 149$, $B_3 = 137$ cc. N/10 Base in the blood serum; $C_0 = 96$, $C_1 = 96$, $C_2 = 90$, $C_3 = 85$, and $C_4 = 93$ cc. N/10 Chloride in the blood serum.

whereas the latter was given almost no salt and as a result lost weight despite an average daily intake of over 1200 cc. of fluid in the form of orange juice and glucose solution.

This surmise was abundantly confirmed by a survey of the cases of primary pneumonia in the records of the Infants' Hospital. Taking

first a group of infants whose diet had been restricted to orange juice and glucose solution, we found an average salt intake of only 0.7 gram a day or the equivalent in a 20 pound infant of about 6 cc. N/10 NaCl per pound body weight. Like patient A. S. described above, these patients lost much weight previous to the crisis. See chart 2.

In contrast with the above group were other patients which had made gains of 30 to 40 ounces in as short a time as 36 hours. These

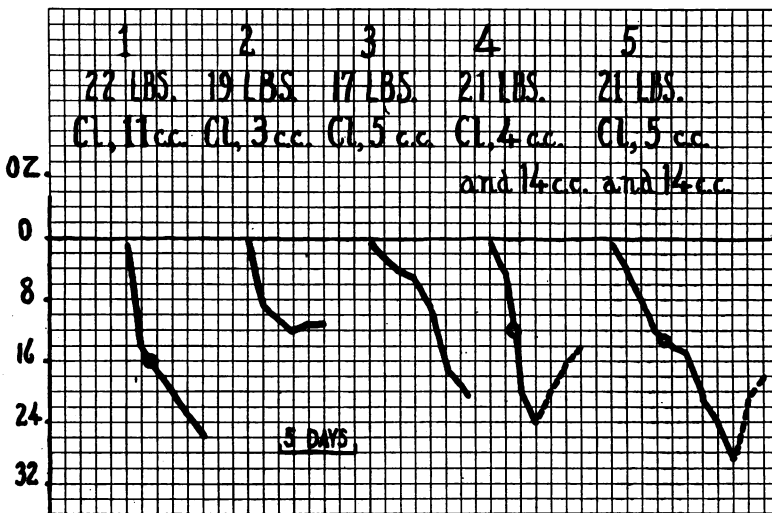


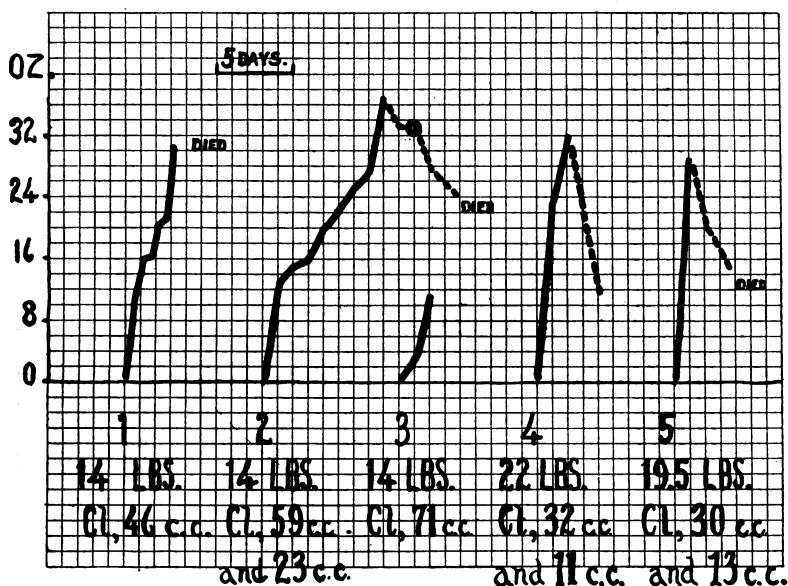
CHART 2. ILLUSTRATING EXTENT OF WEIGHT LOSS OBSERVED IN PATIENTS ON LOW INTAKES OF SALT, EXPRESSED AS CHLORIDE

Dotted line represents weight curve following increase of salt intake. Circle represents crisis.

were all found to have received large amounts of salt in their diets, usually in the form of a mixture of normal saline solution (0.9 per cent), and orange juice. Some of these infants took 6 grams of salt a day, or from 50 to 75 cc. N/10 NaCl per pound body weight, in other words about ten times the amount obtained by the group on a low salt intake. See chart 3.

In addition to the primary differences in the weight curves of infants on low and infants on high salt intakes, charts 2 and 3 illustrate

in certain patients the effect of changing from one diet to another. In chart 2 may be noted two infants, (no. 4 and no. 5), who lost weight while on salt intakes of 4 and 5 cc. N/10 respectively per pound body weight, but who gained rapidly as soon as the intake was increased to 14 cc. The reverse effect is seen in chart 3. Patients no. 2, no. 4, and no. 5 gained in weight when getting 59, 32, and 30 cc. N/10 NaCl



CHAR1 3. ILLUSTRATING EXTENT OF GAINS IN WEIGHT OBSERVED IN PATIENTS ON HIGH INTAKES OF SALT, EXPRESSED AS CHLORIDE

Dotted line represents weight curve following decrease in salt intake. Circle represents crisis.

per pound body weight, and then lost when the salt was reduced to 23, 11, and 3 cc. respectively.

From these findings it seems clear that the patients represented by chart 2 could not retain water until they were also provided with a certain level of salt intake. Like A. S. they lost weight, and like him no doubt they also had a negative base and chloride balance at the time. A negative balance indeed is strongly suggested in these patients by the fact that their weight loss continued beyond the crisis

until after their salt intakes were increased, indicating that in them there had been no appreciable storage of salt that could be released at the crisis as a sort of endogenous supply. In other words it appears that the hypothesis of chloride retention in pneumonia is incorrect when applied to the group of patients on low chloride diets that show low blood and urine values of base and chloride and are losing weight. Extensive retention of Na and Cl, however *does* occur on a high salt diet but in this event there will be found a normal or high level of base and chloride in the serum, with considerable amounts of these ions entering the urine, chemical findings again, which are contrary to current theories.

A third metabolic study, (included as case no. 1 in chart 3), may be mentioned briefly here as a patient that received, under our observation, a relatively large amount of salt in his diet, (i.e. 46 cc. N/10 NaCl per pound body weight), and furnished us with some significant post-mortem data. Details of the acid-base metabolism and of tissue analyses will form the subject of a succeeding paper, but it is of interest to note here the principal findings, namely, normal serum chloride and base, high urinary chloride and base, rapidly increasing weight with pitting edema, a positive balance of Na and Cl ions, great retention of water and salt in the form of edema fluid, and a marked "retention sec," in the body tissues in general. As the patient was a Mongolian idiot with a congenital lesion of the heart, death was perhaps due to that condition. The grave potential dangers, nevertheless, of high salt therapy are suggested by the intense edema that developed in this infant, a finding that was also recorded in the autopsy reports on patients no. 3 and no. 5 of chart 3. Although not conclusive evidence against salt therapy it is at least suggestive that among 19 cases of primary pneumonia in infants on whom we could get adequate data, the three deaths that occurred were confined to the small group of five cases that received large amounts of salt in their diet, and as noted above, developed extensive edema of their tissues.

There is little evidence to suggest that edema in these patients might have been due to disease of heart or kidneys, either functional or organic. Indeed, marked efficiency of these organs in the patient mentioned above is indicated by the fact that the concentrating power of the kidneys was high throughout the illness. Parallel with the

increasing elimination of salt, both the concentration and the actual amounts of chloride and fixed base in the urine mounted steeply without showing signs of having approached a maximum prior to death.

Why the tissues of the body are so markedly at the mercy of the salt intake in pneumonia, despite normally functioning kidneys is not clear. A hint of a specific effect referable to the pneumococcus is offered by the fact that intense general edema sometimes develops in the presence of a pneumococcus abscess, only to vanish when the abscess is drained. On the other hand it is possible that other febrile diseases do manifest in lesser degree the same sort of phenomena, described above, that in pneumonia are rendered especially striking because of the contrasts this disease furnishes in its abrupt onset and its termination by crisis.

DISCUSSION

The data given in this paper deal principally with the relation in pneumonia of salt intake to salt and water retention, and appear to show that the latter depends largely on the former.

Leiter (14) has already pointed out that any study of salt metabolism must take into consideration the salt intake for several days previous to the study. This generalization we believe applies to primary pneumonias, and the reason so many cases described in the literature have a low blood chloride when first seen may well be that these patients correspond with our infants on low salt intakes by virtue of having refused or neglected to take salt-containing foods during the prodromal stage of the illness, previous to admission to the hospital. Findings in this type of case have come to be regarded as characteristic of the disease only because the majority of pneumonia patients desire water and fruit juices (or are offered nothing else), and so become established on a nearly salt-free diet.

The opposite situation of high salt intake reveals in pneumonia an obligatory retention of salt and water which is most striking. In extreme cases the edema becomes so great as to be possibly dangerous. It is also conceivable that the incidence of effusions into serous cavities is greater in patients on high than in patients on low salt diets. Consequently it has become our practice to observe caution with salt in pneumonia, giving enough however to keep the patient from losing

weight, namely, about 15 cc. N/10 NaCl per pound body weight, per 24 hours. This quantity is supplied by a solution made up of 1 part saline (0.9 per cent), 2 parts orange juice, and three parts 10 per cent glucose, provided the patient takes 2 ounces of the mixture per pound body weight in 24 hours; thus far cases of pneumonia so treated have maintained nearly stationary weights, and have not developed edema.

CONCLUSIONS

1. In infants with primary pneumonia we find a negative base and chloride balance if the intake of these ions is low, and a markedly positive balance if the intake is high.

A. In the former situation one observes low values for total base and chloride in the serum, rapidly diminishing values for these ions in the urine, rapid loss of weight, and later a gain in weight only after the salt intake has been adequately increased.

B. In the latter situation the serum values are at least normal, the base and chloride of the urine are normal or high, weight rises rapidly before the crisis, (often with visible edema), and after the crisis there is usually a sharp loss in weight accompanied by an outpouring of chloride and base in the urine.

2. An extensive and perhaps a dangerous degree of edema is often seen to develop in patients who receive large quantities of salt during the early stages of their pneumonia. These patients, despite normal heart and kidneys, appear to be forced to retain in their tissues amounts of salt which a normal individual would excrete without difficulty.

3. In an attempt to maintain an even weight in patients with pneumonia, we have administered 15 cc. N/10 salt solution per pound body weight per twenty-four hours, with satisfactory results.

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