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EXPERIMENTAL SODIUM CHLORIDE DEFICIENCY IN MAN

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Editor's Note: This classic first description of diet-induced salt deficiency deserves to be read in its entirety. In his elegant study, McCance found that loss of water was fully compensated, and the clear-cut experimental conditions emphasize the effects of salt loss without water loss.

Dehydration plays an important part in the pathology of a number of diseases. The loss of water may take place through the kidney (as it does in diabetic coma), the gut (as in pyloric stenosis, paralytic ileus, acute diarrhoea, and vomiting or cholera), the lungs and skin (as in hot dry atmospheres) or occasionally through other channels. This loss of water has been known for a very long time to be associated with loss of salt, but a study of the literature reveals considerable confusion of thought as to the relationship of one to the other. This is particularly well illustrated by the discussions of some of the experimental work on Addison's disease. Much experimental work has been done on the lower animals to elucidate the pathology of the intestinal obstructions; diabetic coma has been studied to some extent, and in the last 5 years Addison's disease has been produced and controlled experimentally in numerous rats, cats, and dogs. In every case, however, the salt or water deficiency is but a part of the picture. From the acute and dangerous nature of the human diseases and the complications they introduce it is particularly difficult to study the effects of severe water or salt deficiency in patients. Some work has been carried out on diabetic coma, which, however, presents water and salt loss in its most complicated form. No papers of any value have been found on severe uncomplicated salt deficiency. It was therefore decided to make a direct experimental attack on the question and normal human adults were selected as the most suitable subjects. The deficiency was produced by a salt free diet combined with sweating. . . .

Symptoms and Signs

As the deficiency developed all three subjects lost weight (see later). Their cheeks fell in and they began to look ill. People who had no idea that they were being used as experimental animals commented on their appearance. Their sense of flavour and taste

was affected. E. interpreted this aberration or lack of sensation as thirst. She complained of it constantly and drank freely but without obtaining any relief. R.A. recognized the feeling as distinct from thirst. His mouth was not unduly dry but food was tasteless, even highly flavoured food, and this was the more noticeable because such foods were eagerly sought to make the meals more appetizing. Chewing fried onions, for example, evoked only a sensation of greasy sweetness which was extremely nauseating. The distaste, however, was not confined to meals and was a feature of every waking hour. "Even cigarettes don't taste." R.B.N. was not so much troubled by this symptom but felt it from time to time. He noted once that he was "Thirsty all morning—drank a lot but water seems to make little difference" and on another day reported that he had a "funny feeling in the mouth."

On the whole all slept well but R.A.M. and R.B.N. were apt to be roused by attacks of nocturnal diuresis, and both were troubled by nightmares. Both were probably in a fairly exhausted state by the end of the deprivation period, and R.A.M. went to sleep in the laboratory about an hour and a half after his first meal containing salt. R.B.N. and R.A.M. both found it very difficult to get through their prescribed rations. R.A.M. was "never hungry" but preferred the bread to anything else, while R.B.N. found it almost uneatable towards the end. "It's the bread that gets me down." Nausea accompanied almost every meal but neither subject had indigestion after meals or any constipation. R.A.M. suffered considerable abdominal discomfort during and after the hot air baths on several days, but food tended to relieve it and this was certainly not the cause of the nausea.

Both the male subjects suffered considerably from cramps, but E. escaped, probably because her deficiency was relatively slight. These muscular cramps were not of the very severe localized type which are said to affect stokers and miners, but were widespread, frequent, not very painful, and generally controllable. Any muscle in the body was liable to go into spasmodic contractions, especially if some little effort was demanded of it. "Coughed a little over something, cramps round chest, mild." R.B.N. experienced occasional cramps in the muscles lining the floor of the mouth but the extremities were most affected, and it was possible sometimes by suitable movement of the toes to alternate the spasms for hours on end between the extensor and flexor muscles. Perhaps the most characteristic of all were the manual cramps. R.A.M. experienced "constant mild cramps of the fingers and thumb when using forceps at the balance," and R.B.N. found that he "cramped quickly when working, telephoning, or using pipettes."

Physical symptoms predominated in the case of R.A.M. but all experienced them in some degree. A mild breathlessness at first and sense of fatigue gave place later to general exhaustion and distress on the least exertion. The effort of dressing, breakfasting, and getting into and out of a car was so great that R.B.N. "lay exhausted on a couch in the common room on arriving." R.A.M. found that going up two flights of stairs to the laboratory was a serious undertaking, causing a sense of breathlessness and a most unpleasant feeling of constriction across the sternum which compelled him to stop and rest. Throughout the experiment he used to go for a measured walk of about a mile after breakfast. Towards the end of the deficient period the breathlessness and sense of constriction forced him to sit down and rest two or three times at a hill, for which he would ordinarily not have slackened pace. Little acts of the daily routine produced a localized sense of fatigue; his "arm got tired shaving" and finally his "jaw got tired eating toast."

Mentally R.A.M. felt normal but R.B.N. felt "slow in the head" and showed it in his behaviour. He would remain in a chair for periods of 30–60 minutes "content to sit and do nothing." He never slept on these occasions and was always willing to talk, but spoke slowly and rarely initiated conversation. For several days he experienced at frequent intervals sensations of "*déjà vu*." He became apathetic and his mental processes ap-

peared to be dulled. R.B.N. longed for salt and often went to sleep thinking about it. R.A.M. felt no specific craving for salt and had difficulty in convincing himself that taking salt would at once make him feel all right again.

In both subjects the resting pulse rate remained normal, but the volume became very small. The pulse during exercise was not investigated. The blood pressure was taken on numerous occasions in the case of R.B.N. and rather less frequently in the case of R.A.M. Both subjects had normal blood pressures and maintained them within narrow limits throughout the experiment. No fall of systolic or diastolic pressure accompanied the salt deficiency and actually the lowest figure in each subject was obtained under normal conditions.

The eye tension of all three subjects was investigated when they were normal and at the height of the deficiency. The results indicate no consistent change. Temperatures were taken in the mouth before and during the hot air baths. They were always within normal limits before entering the bath.

Recovery was quite dramatic. Half an hour after eating 15 gm of NaCl with bread, butter, and an egg E.'s sense of flavour and taste had returned, although no fluid had been taken. This she spoke of as a quenching of her thirst. Genuine and almost unbearable thirst supervened later and was only satisfied by copious draughts of water. R.A.M. found his sense of flavour returned before he had finished his first salt meal. About an hour later he felt hot all over, he experienced a deep-seated pricking and tingling in his extremities and was conscious of bounding pulsation. In a few hours he was much more comfortable in mounting the stairs, and by evening was "no longer aware of his legs as he moved about the room." His carriage and movements were observed to be more normal. He felt more "himself," and on the next day although not yet normal, he experienced an "exhilarating sense of well-being" from morning till night.

R.B.N. ate his first meal containing salt in the evening and made no comment on the return of flavour and taste, but this is not surprising because this symptom had never worried R.B.N. very much. He did, however, feel as though "his heart was beating all over him" and his vaso-motor reactions were no doubt very similar to those of R.A.M. During the night he had some colic and diarrhoea, and was still breathless and very easily tired the next day. After 48 hours he "jumped off the bus while it was going, and ran up the stairs"—simple pleasures, but keenly enough appreciated to make him record that he had "had a grand day." . . .

Summary

Forced loss of sodium and chlorine was produced by a very low NaCl intake and sweating. At least 25 to 30% of the body's extracellular ions were removed in this way. The fluid intake was not limited.

Such deprivation led to aberrations of flavour, cramps, weakness, lassitude, and severe cardio-respiratory distress on exertion.

The nitrogen balance became negative and the blood urea rose.

When subjected to such treatment the human body compromised between (*a*) maintenance of its total osmotic pressure at the expense of anhydraemia a reduction of blood volume, rise of haemoglobin, proteins and colloidal osmotic pressure in the serum, and (*b*) maintenance of its plasma and extracellular fluid volumes at the expense of a reduction in the concentrations of sodium and chloride in the serum, with a fall in its total osmotic pressure. Some evidence was obtained that (*b*) was followed by a fall in the total and colloidal O.P. of the cells.