FAMINE OEDEMA.

BY

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FAMINE, war, or hunger oedema is defined by Nixon¹ as a form of dropsy associated with bradycardia, polyuria, and asthenia, occurring in persons subjected to prolonged under-feeding. The "epidemic dropsy" of Bengal may be the same disease, Grieg² having found evidence of its association with faulty nutrition, but the dietetic origin of epidemic dropsy is not accepted by all. Famine oedema has been thought to follow either an actual lack of calories or deficiency in a particular food factor. Clinically oedema has been found at times associated with all the deficiency diseases except rickets. Bloch³ noted its occurrence in some cases of keratomalacia; Falta⁴ recorded the fact that the victims of war oedema sometimes suffered from night-blindness. There is little doubt that both keratomalacia and night-blindness occur in those whose diets are deficient in vitamin A. Bigland⁵ recorded famine oedema as a clinical entity in close association with an epidemic of pellagra, and found that more than half the pellagrins observed suffered from concurrent dropsy. The superadded oedema which makes the difference between a wet and a dry case of beri-beri is very similar in its nature to famine oedema, and wet beri-beri and famine oedema are so closely alike as to have been often confused. The "ship beri-beri" described by Nocht,⁶ in which symptoms of peripheral neuritis rarely occurred, was possibly famine oedema. Similarly, dropsy is sometimes a symptom associated with scurvy, and cases of famine oedema have been recorded with spongy gums and other scorbutic lesions.

In man, vitamin deficiency diseases do not often occur in those whose diets are complete except for the one missing factor. Occasionally a full diet may be lacking in one vitamin only, as, for example, the diets of polar explorers which may be devoid of vitamin C, but otherwise complete, or perhaps the generous rations of an army in the field, which may be deprived of the antineuritic vitamin by sterilization and prolonged cooking in water containing alkalis. But as a general rule vitamin deficiency disease occurs in the very poor, the half-starved, and the victims of war or famine conditions, who can get only the very minimum of the cheapest food necessary to keep body and soul together.

The experimental reproduction of various deficiency diseases (such as keratomalacia, infantile beri-beri, scurvy, and rickets; adult beri-beri cannot be precisely reproduced in the laboratory), which enables the distribution in foodstuffs of the various vitamins to be worked out, has done much to explain the epidemiology of deficiency disease in man. It is not always easy, however, to explain the geographical incidence of deficiency disease in terms of the vitamin hypothesis—to explain why, for example, a wretched diet of milled cereals leads to pellagra in South Carolina, to beri-beri in Java and Newfoundland, to scurvy on the Rand. The diets associated clinically with various deficiency diseases often seem equally deficient in all the known vitamins, in addition to fat, protein, and mineral salts.

It is therefore a feasible hypothesis, since "hunger oedema" has been noted in association with almost all the deficiency diseases, and these in man are usually associated with general mal- or under-nutrition, to regard the oedema as due to a shortage in one of the dietary fundamentals other than vitamins, such as fat, protein, or mineral salts. It has occurred on a regime composed very largely of root vegetables, and the oedema noted in Germany during the war, in infants on a diet almost entirely cereal, was probably a similar condition. The most exhaustive account of the disease is that of Schittenhelm and Schlecht,⁷ who during the war investigated an outbreak in a labour corps attached to the German Army. They came to the conclusion that excessive intake of fluid and protein starvation accounted for the condition.

Harden and Zilva⁸ produced oedema in a monkey fed on a diet deficient in vitamin A. The basic diet consisted

mainly of polished rice with an addition of marmite to supply vitamin B, and was thus far from complete. Bloch attributes the oedema occurring in Danish children during the war to excess of carbohydrates, though a certain proportion of cases showed xerophthalmia (vitamin A deficiency). In other cases of xerophthalmia and keratomalacia, oedema did not occur, and these children had usually been nourished on skim milk, which contains protein in abundance, though little vitamin A or fat.

There is, in fact, little convincing evidence to connect famine oedema with vitamin A deficiency. On the whole, the evidence seems to point to shortage of protein as the most likely cause. Kohman⁹ produced oedema in rats by feeding them on diets containing a high percentage of carrots, and thus low in protein. Butter-fat and wheat germ were given as sources of vitamins A, B, and D, and mineral salts were also supplied. Addition of purified casein to the diet prevented the appearance of oedema. It is probable that Kohman's diets were low in the "(?)anti-pellagra" vitamin (B₂), but oedema does not usually follow deficiency of this factor.

Clinically, famine oedema seems to respond to a good all-round diet, probably containing all the dietary essentials. The oedema of wet beri-beri clears up rapidly under treatment by diets rich in vitamin B₁ (antineuritic), but such diets are usually rich in other factors also.

The case about to be recorded was observed at St. Anthony Hospital, North Newfoundland. For a variety of reasons, the poorest Newfoundland families in late spring and early summer may be reduced to a diet made up almost entirely of white flour bread, with very scanty additions in the form of molasses, salt meat and salt fish, and little else. At times the additions may run out and the family be reduced to bread and molasses. Such a regime usually produces beri-beri, a common disease in Newfoundland.

Newfoundland beri-beri is identical with the tropical rice-eater's disease, and both wet and dry forms may be observed, the latter being by far the commoner.

CASE.

A. C., 39, female, single, was admitted to St. Anthony Hospital on July 23rd, 1929, complaining of swelling in the abdomen and legs. She stated that she had begun to notice the swelling, which had appeared first in the legs quite suddenly, about three weeks before admission. She complained of considerable general weakness, not specially marked in the arms and legs (as in beri-beri). There was no marked shortness of breath, and vomiting and headache were absent. Constipation was a prominent symptom.

She gave the following dietary history. She and her father, an old man incapable of work, lived alone in circumstances of extreme poverty. For six months before admission they had been able to get only dry bread and molasses to eat, and for years previously their diet had not been far above this level. Sometimes, on Sundays, when neighbours were charitable, they had a little salt meat, and during the sealing season (April) they had three meals of seal meat. Otherwise the patient had subsisted for six months on bread, molasses, and tea. She said she had never been particularly hungry.

Examination showed a cachectic-looking patient, the skin having a peculiar yellow tint. Severe emaciation was evident, where this was not masked by dropsy. The pulse rate was about 80; there was no rise of temperature. The heart was not enlarged, the sounds were clear, and had not the muffling and tick-tack rhythm of the beri-beri heart. The abdomen showed marked ascites, and the legs were generally oedematous. Oedema was also present over the sacrum, and the bases of the lungs were congested. There was no evidence of peripheral neuritis. The right knee-jerk was sluggish, the left normal. No areas of anaesthesia could be discovered. Scorbutic signs were absent. The urine was free from albumin and casts, the output being about 10 oz. per diem.

A blood count showed: red blood cells 2,900,000 per c.mm., white blood cells 4,200; haemoglobin 60 to 70 per cent. The red cells showed no marked alterations in shape or size.

There was a previous history of deficiency disease, the patient having been in hospital in 1914 suffering from typical dry beri-beri, which improved on dietetic treatment.

Treatment.

Taking into account the earlier history of beri-beri, the present dietary history of the patient, and the lack of evidence of renal or heart disease, a diagnosis of hunger oedema was made. Though the colour index was above 1, the case did not suggest pernicious anaemia. The patient was put on a high protein diet, without much vitamin B₁, and an attempt was made to assist diuresis by

magnesium sulphate and digitalis. Tinned meat, fresh salmon, codfish, albumin water, butter, and white bread formed the basis of the diet, and wholemeal bread, wheat germ, cabbages, beans, or peas were not given. These foodstuffs were fed in small amounts at frequent intervals in as palatable a form as possible.

The patient remained on this diet for four days, during which time she got rapidly worse. The ascites increased, and her condition became critical. Paracentesis abdominis was performed and 109 oz. of fluid removed.

At this point she was put on the usual "anti-beri-beri" diet used at St. Anthony Hospital, containing wholemeal bread, fresh meat, milk, eggs, cabbages, potatoes, beans, and peas. In addition, she was given 1 oz. of wheat germ daily.

Following this change her general condition gradually improved. In about three weeks she lost the cachectic look, felt comfortable, and developed a good appetite. The red blood corpuscles rose to 4 million. The oedema, however, did not disappear from the abdomen or legs, and further paracentesis was necessary on three occasions. The urine remained free from albumin.

Seven weeks after admission, since the diagnosis was still in doubt, Dr. Curtis performed a laparotomy. Nothing was found to account for the recurrent ascites. The liver, spleen, and peritoneum were normal.

Nothing further could be done for the patient in the way of dietary treatment. It became necessary to perform paracentesis about every ten days, and when I last saw her in September she was becoming exhausted by the repeated tapplings, but was otherwise in fairly good shape. Some oedema persisted in the calves and over the sacrum.

It is difficult to be completely certain that the patient's condition was due to faulty diet. The very low dietary level, which is actually below that which usually leads to severe beri-beri, and the absence of other causes to account for the oedema, makes it probable that we were dealing with a nutritional condition. Except for the fact that the dropsy did not clear up on a good diet, the case was identical with famine oedema, which certainly occurs in Newfoundland, though rarely. Appleton¹⁰ noted four cases on the Straits of Belle Isle in 1920, and an oedema occur-

ring in ill-nourished children, not due to nephritis, and usually responding to a good diet, is recognized at St. Anthony Hospital.

The mechanism of the production of oedema in cases of famine dropsy is unknown. Some alteration in the permeability of the capillaries is presumably present, though histological evidence of local damage has not so far been obtained. The following are among the theories that have been formulated: an extreme deficiency of calcium in the blood leading to altered permeability of the vessel walls; a "nephritis without albuminuria"; damage to the endothelial linings of the vessel walls by the products of excessive endogenous protein metabolism.

It seems possible that this was a case of famine oedema in which the capillary walls were permanently damaged and unable to recover, though the patient's general condition improved under dietary treatment. It must be remarked that wheat flour carries a fair amount of protein (10 per cent.). The high protein diet without much anti-neuritic vitamin did not produce improvement in the oedema or the general condition, but was tried only for a few days.

Whatever the diagnosis, it seemed worth while recording an obscure dropsical condition which followed a long period on an extremely faulty diet. It is peculiar that a patient who had practically lived on dry bread for six months or longer should develop this condition rather than one of the better-known deficiency diseases.

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BLOOD CHANGES FOLLOWING INJECTION OF SANOCRY SIN IN PULMONARY TUBERCULOSIS.

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PRELIMINARY REPORT.

WHEN sanocrysin was first introduced for the treatment of pulmonary tuberculosis it was believed to be capable of destroying the tubercle bacilli *in vivo*, and the reaction which frequently followed its administration was attributed to the endotoxins set free. An antitoxic serum was prepared for the purpose of counteracting this reaction and was given before each injection. This, however, was soon found to be of doubtful value and fell into disuse. It is now realized that sanocrysin acts on the tissues rather than on the bacilli, but how exactly it combats the disease is not clear. The opinion has been expressed that it acts by speeding up curative processes that go on slowly in its absence.¹

In view of the prognostic importance attached to the variations in the white blood cells in pulmonary tuberculosis it was thought that some light might be thrown on the mode of action of sanocrysin in this disease by a study of leucocytic changes that follow its injection. A neutrophilia in phthisical patients is a bad sign, while an increase in lymphocytes is a good omen, especially in early cases. Much work has been done on the significance of the monocytic response and of the monocyte-lymphocyte ratio in tuberculosis. Some increase in monocytes is common, Cunningham and Tompkins² having found it in 85 per cent. of cases. It is generally stated that a diminution of monocytes and an increase of lymphocytes

is a sign of improvement, and that a rise in monocytes denotes progress of the infection.³ It is interesting to note that a monocytosis to the extent of 15.5 per cent. was found by Pittaluga and Garcia⁴ in infants receiving B.C.G. vaccine.

This preliminary report deals with observations made on four patients suffering from extensive chronic bilateral disease. All were febrile when resting. In No. 1 the first dose (0.5 gram) gave rise to some improvement, but the second (0.1 gram) produced a bad effect and the treatment had to be stopped. No. 2 received only one injection, which made his condition worse. The effects of two doses (0.05 gram and 0.1 gram) were observed in No. 3. There was slight but definite benefit, especially after the second injection. No. 4 improved steadily from the start; after 4 doses (0.1, 0.25, 0.35, and 0.5 gram) the fever disappeared, the weight increased, and the sputum became scanty and free from tubercle bacilli. Injections were given at intervals of four to seven days, and there were no complications except a rise of temperature on two occasions. Control experiments with 0.1 gram to 0.15 gram were made on two individuals who were free from any evidence of active tuberculosis. Blood counts were done each morning at the same hour while the subjects were fasting. On "injection" days two counts were made, one just before and one two hours after administration of the drug. This interval was chosen because it had been noticed that when reactions occurred they were most marked two to three hours after the injections. In the differential counts at least 300 cells were noted.

The daily counts showed that in both tuberculous and non-tuberculous individuals the changes in the red cells and total white cells were irregular, but there was often a steady fall for two to four days after the injections. Abrupt rises were seen on some occasions, notably in patient No. 3, who suffered from severe night sweats. They were probably caused by concentration of the blood. An increase in the monocytes took place after every injection. This was generally observed on the following day and lasted one to three days. In the non-tuberculous

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