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NUTRITIONAL FACTORS IN GRAVES' DISEASE *

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THAT marked grades of malnutrition may result from thyrotoxicosis has been long known. In 1893 it was that Friedrich Müller [1] noted the paradox of weight loss in the face of increased food intake and concluded therefrom that there must be in this disease an increased rate of katabolism.

Whether or not weight loss or general wasting will occur in Graves' disease depends on whether the appetite increase causes sufficient increase in the ingestion of total calories to offset the increased combustion. Compensatory hyperorexia we may call it. The bank balance, in other words, is determined by the relation of amounts deposited to those withdrawn. In Graves' disease we not infrequently encounter weight losses of as much as 50 pounds or more.

Not only, however, may thyrotoxicosis cause malnutrition, but lately it has come to our attention that malnutrition may cause, or precipitate, thyrotoxicosis.

A few years ago one of us (S. H.) was impressed with the number of patients with toxic goiter who gave histories of having started their thyrotoxic symptoms at the conclusion of a reduction program for obesity. An overweight person would go on a low calory diet and after having lost the desired amount of weight would increase the diet, but find that weight loss continued, perhaps at an accelerated rate. Along with this, nervousness, tremor and other symptoms of thyrotoxicosis would make their appearance. In some of these cases thyroid had been used to augment weight reduction, but in others, mere calory restriction.

Interest having been aroused in this sequence of events, we began to be on the lookout for such cases. They have turned out to be numerous. The total to date is 35. In 14 of these the prethyrotoxic weight loss was occa-

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sioned by reduction cures and in the remainder it was due to a variety of conditions such as restriction of diet in the treatment of ulcer, ulcerative colitis, diabetes and other diseases leading to malnutrition.

It seems to us that this series is too large not to be of significance. Episodes which activate thyrotoxicosis have long been recognized. Psychic traumata, prolonged infections, accidents or physiologic strains, such as puberty, pregnancy or the menopause, fall in this category. Now it seems that acute malnutrition can be added. How it operates, we are not prepared to say, but it is not known how any of the others operate for that matter. It may be associated with changes in blood chemistry or with vitamin or protein deficiency.

In approaching the problem of the inroads which nutritional factors may play in the production of the clinical picture in Graves' disease it will be convenient to distinguish between what we may term general malnutrition due to total negative calory balance and more specific types of malnutrition, or deficiency due to absolute or relative shortage of specific dietary elements. Of general malnutrition, save insofar as it constitutes an indication for treatment, I need say nothing further, it being thoroughly familiar. Certain specific or special types of malnutrition, on the other hand, I believe can be discussed with some profit.

In this group of special forms of malnutrition let us consider first the *musculature*. Myasthenia is a common symptom in toxic goiter. Plummer,[2] Lahey [3] and others have devised diagnostic tests to bring this symptom or sign into evidence. Actual muscle atrophy occurs less commonly, but in certain cases is very striking. Some years ago we [4] reported a case in which there was a picture closely resembling progressive muscular atrophy in an advanced stage. The patient was also found to be suffering from toxic goiter. Cure of the latter by surgery was followed by recovery of the muscles. This is the most marked example of muscle atrophy we have seen in toxic goiter, but very often we encounter lesser grades with atrophy of the temporal, interossei or shoulder girdle muscles. Such atrophy is usually present in a patient who has been severely thyrotoxic over a long period of time and is therefore of prognostic significance. The exophthalmos, in certain types at least, may be a local expression of general muscle weakness. The degenerative changes in the striated recti muscles of the eye and the normal appearance of the smooth muscle of the eye, described by Askanazy,[5] suggest a muscle imbalance which may explain exophthalmos. On the chemical side there is a disturbance in creatinine metabolism with creatinuria and, as shown by Shorr and Richardson [6] a decreased creatine tolerance test.

The skeleton in certain cases shows marked decalcification. This is properly to be classed under specific forms of inanition. Aub and his coworkers [7] in 1929 showed that the thyroid hormone causes a marked increase in the rate of withdrawal of calcium and phosphorus from the skeleton, without, however, in contrast to the parathyroid hormone, any sig-