Studies of Vitamin Deficiency[1]

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BIOCHEMICAL, CLINICAL, neurological, and psychological investigations were conducted on the subjects of this study who were patients in the Elgin State Hospital. The experimental design was such that the effects of diets restricted in their contents of thiamine and riboflavin for three full years could be continuously observed. A special building housed the patients, and very satisfactory facilities were provided for continuous supervision and rigid control of diets. All food was prepared in a diet kitchen adequately staffed with full-time workers. The diets were analyzed frequently, and the service was so arranged that the subjects of separate groups were served separately. Care was taken that the patients were not harmed by the diets or the study. The more important observations are reported here in brief. A full report is contemplated later.

Thirty-six male patients were selected from the State Hospital population. The need for persons who would be in continued residence for a prolonged period of time influenced the selection. The subjects were divided into two main groups: (1) patients whose ages ranged from 58 to 78 years and (2) younger patients who were from 24 to 42 years of age. Each of these groups was divided into three subgroups, designated as Groups A, B, and C, respectively. At the beginning of the project there were three groups of seven old men and three groups of five young men. Each person in the A groups received a daily diet containing approximately 2,200 calories, which was apparently adequate in all the essentials except thiamine, of which approximately 400 μg. were present, and riboflavin, of which the diet contained about 900 μg. Those in the B groups received the same diet except that a daily supplement of yeast extract was given which contained approximately 6 mg. of thiamine and 1.3 mg. of riboflavin. The members of the C groups received the regular hospital diet which they ate *ad lib.*

The clinical effect of this moderate restriction of thiamine and riboflavin on subjects of the A groups was at no time more than minimal. Noticeable, however, in these subjects, young and old, was a gradually increasing self-imposed restriction of activity, a dulling of interest and of ambition, a diminished desire to please, and a lessened tendency to bantering and playfulness. The statement applies to the general behavior of the subjects when left alone. Attempts to measure these changes of behavior by psychological tests were thwarted to a large extent by compensations effected when the subjects were confronted by the conditions of the tests. The skin of several subjects of the younger group became thinner and lost elasticity, these changes imparting an appearance of ageing. The lips showed drying, thinning, and increased wrinkling. A more objective abnormality, noted within nine months from the beginning of the diet and persisting for more than two years, was an unusual elevation in the levels of lactic and pyruvic acids in blood obtained under standardized conditions of exercise and glucose load. Some abnormality in the levels of lactic and pyruvic acids in the blood occurred within the first three months.

At the beginning of the third year of the study the subjects of both B groups, whose diets previously had been supplemented with a yeast extract, were placed on a diet which was more rigidly restricted in content of thiamine and riboflavin than the diets of the subjects of the A groups. This provided 200 μg. of thiamine and 800 μg. of riboflavin. Among the subsequent observations on these subjects were the following:

(1) The levels of lactic and pyruvic acids in the blood were elevated under the standardized condition of exercise and glucose load. The standardized condition referred to consisted of climbing of stairs 60 minutes after ingestion of 1.8 grams of glucose/kg. of body weight. The concentration of lactic and pyruvic acids in the blood was increased more than in the subjects of the A groups, whose intake of thiamine was moderately restricted. This became apparent about three months after the diet of 200 μg. of thiamine was started and was followed shortly by the development of clear-cut clinical evidence of thiamine deficiency.

(2) Effects on the circulation, nervous system, and gastrointestinal tract were acute to subacute in onset. Among the circulatory effects was a nonpitting swelling of the facial skin, especially of the eyelids, which could be observed in subjects who did not develop pitting edema of the lower extremities. Budding of the blood vessels into the cornea with plexus formation in its periphery also was observed in a few subjects. Mental changes were characterized chiefly by loss of inhibitory control and a tendency to interpret distressing somatic changes in a paranoid fashion.

(3) A diagnostic tool which proved useful was an apparatus designed to study vibration sense. This apparatus made it possible to apply various frequencies to the external malleolus and the soft part of the big toe. The amplitude of the vibration was kept constant. The vibration sense in the lower extremities decreased markedly as the nutritional deficiency progressed.

(4) Psychologically, the patients on the more deficient diets (200 μg. of thiamine/day) manifested exaggera-

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tions of their psychotic complaints and showed distinct changes in attitudes toward their environment.

(5) Marked individual differences in response to the diets were observed in both old and young groups, not only in time of onset of symptoms but also in the degree of resulting abnormality. The subjects who gave evidence of vitamin deficiency early manifested abnormalities which were greater in degree than those observed in others who were affected more slowly. Especially was this true with respect to the cardiovascular system. In general, the older persons were affected earlier and more severely than were the younger.

Recovery when yeast extract providing 6 mg. of supplementary thiamine was added to the diet was dramatic, especially in the subjective fields of appetite, general feeling tone, pain, and paresthesia. The levels of lactic and pyruvic acids after the standardized conditions of exercise and glucose rapidly returned to their predeficiency levels. Likewise, patellar reflexes which had been lost commenced to return soon after the yeast extract was added to the diet. On the other hand, return of the Achilles tendon reflex was very slow.

Technical Papers

Distribution of Sodium and Water in Muscle Following Severe Cold Injury[1]

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In a recent investigation of experimental cold injury (frostbite) it became evident that the physiological and chemical changes occurring in the injured regions after thawing resembled those found after severe injury produced by other means. The similarity in the natural history of the pathological processes in burns and frostbite has already been noted by Harkins (*5*). Our complete data, to be published later, demonstrate further points of similarity. We wish here to report the distribution of sodium and water in normal muscle and in muscle removed from rabbits' legs subjected to severe cold injury.

Six rabbits were anesthetized with dial, the hair removed from one hind limb as far as the lower end of the femur, and the leg immersed for 3 minutes in a water-alcohol-ethylene glycol mixture cooled to −55° C. Blood samples from the marginal ear vein and muscle samples from the tibialis anticus of the normal and injured leg were taken 166 to 255 minutes after injury. Determinations of water and sodium by the method of Butler and Tuthill (*1*), as modified by Consolazio and Dill (*2*), were made on samples of plasma and muscle.

The results of the analyses and derived values obtained by the method of Harrison, Darrow, and Yannet (*6*) are presented in Table 1. Since the experiments involved comparisons between muscles in the same animal and since only brief intervals were allowed to elapse between injury and sampling, it was considered to be unnecessary to determine and correct for fat content of the muscle.

TABLE 1

CHANGES IN WATER AND SODIUM IN TIBIALIS ANTICUS MUSCLES AND PLASMA OF RABBITS AFTER IMMERSION-FREEZING

Animal Nos.	31	64	66	67	75	80
Plasma						
$[Na]_e$ m. eq./l. plasma ultrafiltrate	138.1		145.8		141.9	
Control Muscle						
Total H_2O*	313.5	321.2	318.0	315.0	328.5	360.0
Total Na†	7.56	7.32	6.76	7.44	8.26	8.58
Extracellular H_2O	54.7		46.4		53.2	
Frostbitten Muscle						
Total H_2O	328.5	399.0	440.0	507.0	500.0	530.0
Total Na	9.84	24.65	34.63	40.05	53.90	68.40
Extracellular H_2O	71.2		237.4		380.0	
Gain of water (%)	4.8	24.4	38.4	61.0	52.4	47.2
Gain of sodium (%)	30.2	237.0	412.3	438.0	553.0	697.2

* H_2O expressed in grams/100 grams dry tissue.
† Na expressed in m. eq./100 grams dry tissue.

The data show that the gain of water by muscle following severe injury by cold ranged from 5 to 60 per cent, while the increase in sodium was proportionately much larger: 30 per cent in the case of the smallest increase and 237–697 per cent in the remaining five animals studied. Such large disproportion between the gain of water and that of sodium could occur only if large quantities of sodium penetrated the intracellular phase or in some other way became excluded from free equilibrium with the remainder of the sodium in the extracellular phase.

A fall in the level of serum sodium in man (*8*) and animals (*7*) after severe burns led Lowdon, *et al.* (*7*) to suggest that sodium was being lost into the injured tissues. Sodium in venous blood was found to be lower than in arterial blood, but tissue analyses were

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