

In the third we found a skull, teeth and tibias; they were the colour of old ivory. The Kurds who were with us fell silent and one of them rapidly muttered a prayer for the dead.

"A young girl," said Dr. Mara, replacing the bones with the utmost care for fear they might dissolve into dust.

Awakened by our comings and goings, some of the fellahin interrupted their siesta and joined us. One of them handed Dr. Mara a fragment of pottery beautifully decorated with nude male figures pursuing deer; very like the hunting scenes with which prehistoric man decorated his caves.

Although we knew little of prehistoric times, we remembered the carefully labelled collections in the Gertrude Bell Museum in Baghdad and estimated that the girl had certainly been dead for more than 4,000 years. The hunting scene probably dated from the Sumerian epoch, the dawn of recorded civilization. In any case, the director of antiquities at the Baghdad Museum, when consulted by Dr. Mara, did not contradict our diagnosis.

Since our discovery, however, Iraqi police are keeping watch over the "Necropolis of Dolan," for these old tombs are reputed, here as in other parts of the world, to contain gold and jewels—treasures more tangible and, above all, more negotiable than the evidence of vanished civilizations which archaeologists look for.

### Ovaltine Research Laboratories Fourteenth Annual Report (1954)

THE FAR REACHING importance of nutrition, which was so firmly established during World War II, has received further emphasis in post-war years. It is becoming even more clear that the solution to world food problems depends on the development and application of nutritional research. We have, therefore, been happy to collaborate with many other colleagues in studying these problems, and will endeavour to give a brief outline of our main findings.

#### Vitamin C Requirements of Human Adults.

There was published during 1954, a report on this problem, describing a war-time investigation organised by the Medical Research Council, in which 20 adult volunteers aged 17 to 34, and including one woman, lived on a basal diet stated to be almost free from vitamin C but providing adequate amounts of other vitamins. By giving some of these volunteers supplements of known amounts of synthetic vitamin C, in daily doses ranging from 5 to 70 mg., and observing any signs of deficiency, the conclusion was reached that the minimum daily adult protective dose was, under the given experimental conditions, in the region of 10 milligrams. This is much lower than the corresponding figure of 30 milligrams for the daily adult requirement as estimated by the League of Nations Health Organisation and by the British Medical Association's Committee on Nutrition as accepted by the Ministry of Food. The wide difference between 10 and 30 milligrams emphasises the difficulty in ascertaining the effect of administering extra supplies of vitamins, and the importance of studying more carefully the stages between full requirements and definite deficiency. In an article published in the *Pharmaceutical Journal* some doubt was cast on the reliability of the 10 milligram figure and a slightly higher figure was suggested on the basis of work done in our laboratories.

#### Interrelations Between Vitamins.

Much evidence has been obtained demonstrating interrelations between different vitamins and showing that the requirements of one vitamin may be affected by the intake of other vitamins. This is perhaps seen more clearly in the B vitamins, some of which take part in consecutive enzyme actions, so that a deficiency of one vitamin may hinder the use of all the other vitamins functioning later in the chain of reactions. Our earlier work on the role of B vitamins in germination yielded interesting results particularly with thiamin, nicotinic acid and riboflavin. More recently inter-

relations have been revealed between B<sub>12</sub>, folic and pantothenic acids, and still more recently between B<sub>12</sub> and ascorbic acid. Work on the destruction *in vitro* of hydroxocobalamin by ascorbic acid was described in our previous report. The defective tyrosine metabolism found to be associated with vitamin C deficiency is of interest in view of the defective tyrosine metabolism which we are now studying in vitamin B<sub>12</sub> deficiency.

#### Human Dietary Deficiency of Vitamin B<sub>12</sub>.

A paper on this subject was read to the Third International Congress of Nutrition in Amsterdam in September, 1954. It summarised results obtained in a study, in collaboration with the Laboratory of Human Nutrition and the Radcliffe Infirmary, Oxford, of a group of about 150 volunteers who had been living for a number of years on diets practically free from animal protein and vitamin B<sub>12</sub>. In rather less than half of these signs of dietary deficiency were observed, especially amongst those who had been living on the diet for at least four years. These signs included amenorrhoea and other disturbances of the normal menstrual cycle (in 8 out of 20 women aged 15 to 45), paraesthesia and other signs of nervous disease (20 per cent.) and oral signs especially sore tongues (26 per cent.). In about 7 per cent. there was more severe illness, especially in the central nervous system, and including one or two cases of subacute combined degeneration of the cord. These were associated with low vitamin B<sub>12</sub> levels, and as they were alleviated by administration of this vitamin, were considered to be indicative of human dietary deficiency of vitamin B<sub>12</sub>.

In contrast with the conditions in pernicious anaemia, the red blood cell counts and haemoglobin contents of the blood were not much below normal, even in volunteers with very low serum vitamin B<sub>12</sub> levels. The association of these very low levels with high intakes of folic acid was probably responsible for the onset of the acute nervous conditions, particularly the subacute combined degeneration of the cord, and provided further evidence of the interrelation between these two B vitamins.

As briefly mentioned in our previous report, Professor Donath has been carrying out at the Dutch Institute of Preventive Medicine, Leyden, a similar investigation on about 60 Dutch volunteers also living for some time on a diet providing practically no animal protein or vitamin B<sub>12</sub>. In these Dutch volunteers the signs of deficiency were similar to those in the British volunteers but were much less marked.

The signs of deficiency observed in the nervous systems might have been due to toxic ketoacids derived from tyrosine, in the metabolism of which vitamin B<sub>12</sub> might be implicated because of its relationship to thyroid activity. Tyrosine (about 54 mg. per kg.) was therefore given to some of the volunteers after they had fasted overnight, and samples of their blood and urine were tested for parahydroxyphenylpyruvic acid, a tyrosine derivative, intermediate in the normal breakdown of tyrosine, whose presence in the body could indicate a failure in that breakdown, perhaps due to deficiency of vitamin B<sub>12</sub>. It was found that the initial concentrations of this acid tended to be higher in the volunteers with lower serum B<sub>12</sub> levels, but the data were not sufficient to establish a clear correlation.

Another possible toxic agent is cyanide, which can cause demyelination in the central nervous system. In the liver cyanide is detoxicated by the enzyme rhodanese to thiocyanate, which is excreted in the urine. Vitamin B<sub>12</sub> in the form of hydroxocobalamin can also detoxicate cyanide and serve as a carrier of cyanide and thiocyanate. The urinary thiocyanate which is derived from cyanide may be associated with vitamin B<sub>12</sub> in certain hypothetical systems.

#### Cyanide and Thiocyanate Metabolism and Vitamin B<sub>12</sub>.

Intensive investigations on cyanide and thiocyanate metabolism carried out in our and other laboratories during the last few years have revealed a number of factors affecting

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