VITAMIN A AND CAROTENE

ALTHOUGH much had been written and much had been done, nevertheless neither the Medical Research Council in Great Britain nor the National Research Council in the United States of America was in a position to give any definite answer when, at the beginning of the War, their respective Governments asked for information about the amounts of certain nutrients required by the human body.

In the United States, the National Research Council appraised the literature on the subject and formulated tentative dietary allowances. The figures thus set out in 1943 [1] have already been revised twice and will undoubtedly be revised further as more exact knowledge is acquired. In the meantime, however, they have been, and are being, widely misapplied by economists, administrators and others whose understanding of nutrition is, at the best, superficial[2]; they are also frequently misused by people who should know better. It is stated in the preamble to the 1945 revised version that "The term Recommended Allowances rather than Standards was adopted by the Board to avoid any implication of finality"—but they seem to have reckoned without human nature.

The folly of judging the adequacy of supply of a nutrient solely on the basis of its level in the diet is certainly brought out very clearly in a recent report of the Medical Research Council* on "Vitamin A Requirements of Human Adults"; for, with carotene, the degree to which it is absorbed varies to such an extent that, for the few foods tested, "the values for the daily requirement ranged from 4,000 to 12,000 I.U.".

The intention was to give a group of volunteers "a diet virtually devoid of vitamin A and carotene until unmistakable signs of deficiency appeared, and then to determine what dose of vitamin A or carotene was needed to ensure recovery to normal". The report states that "The experiment began in July 1942 and was expected to be complete in six to eight months. In fact it lasted two years and even at the end not all the original expectations had been realised."

Admittedly, vitamin A presents particular difficulties in view of the fact that it is normally obtained partly in the preformed state and partly as a precursor. In the words of the report, "the problem is one in which the human individuals and the different foods offered to them are capable of combining in a pattern so complex that it is difficult to formulate a standard value for the requirement of vitamin A, and almost impossible to deduce accurately from dietary surveys the effective intake of carotene". But I am inclined to think that, if equally detailed studies were made of other nutrients, a good many similar complications might be found to apply.

Perhaps the most unexpected findings in the present instance were "the prolonged delay before the onset of nutritional changes" (eight months of deprivation produced no discernible indication of deficiency), and the fact that some of the abnormalities commonly looked for as signs of vitamin A deficiency (for example, follicular hyperkeratosis) "were either absent or equally present in the deprived and the non-deprived or present in the same subjects both before and after depletion". Defective night-vision, with a raised rod-threshold and prolonged cone-rod transition-time, and a lowering of the plasma level of vitamin A proved to be the first definite signs of deficiency. The Committee is, however, careful to point out that the observations were made on young adults with good liver reserves, receiving a diet adequate in all other respects; where there has been chronic deprivation over a period of many years or where other dietary essentials are also lacking, the clinical picture may well be different.

In an experiment lasting so long and with so many facets under observation, the amount of documentary detail amassed must have made the task of editing the report a particularly onerous one. Some degree of selection and condensation was essential; but the report as published still contains a wealth of detail on the techniques used and the results obtained, and it is stated that all the detailed results of the various special investigations which were undertaken are available for consultation.

The report is divided into three parts: (1) concise account of the experiment; (2) elaboration of special aspects (for example, comparison of Wald's and Craik's adaptometers, effect of consumption of alcohol on capacity for dark adaptation and plasma values for vitamin A, a study of the normal value for the vitamin A and carotenoid content of human blood plasma); and (3) details of the evidence (including particulars and management of the volunteers, and summaries of the reports on the slit-lamp examination of the eye, audiometry, etc.).

Naturally, since dark adaptation and plasma-level of vitamin A proved to be the most useful criteria, most space is devoted to the methods and results concerning them, and anyone contemplating work involving such measurements would be well advised to study the details set out in this report regarding the difficulties that arose and the modifications that were introduced to overcome them and improve the techniques. Rod scotometry is dealt with in detail, in addition to the more usual dark-adaptation measurements.

Good liver reserves of vitamin A are offered as the explanation of the delayed onset of any detectable sign of depletion. Reported values for the general population of Great Britain suggested that it was not unreasonable to expect a total reserve of about 500,000 I.U. If the normal rate of utilization is approximately 1,300 I.U. daily, this reserve would last about 400 days. Support for a figure of this order comes from the fact that none of the volunteers was markedly depleted in less than 400 days, and the smallest therapeutic dose tested (1,300 I.U. of vitamin A daily) proved adequate to restore the capacity for dark adaptation to normal.

It was noted that abnormal values for dark adaptation did not occur unless the plasma-level of vitamin A had fallen below 50 I.U. per 100 ml. Plasma-levels among the general population are reported to be 100–120 I.U. per 100 ml., "but it is not known whether values as high as these are necessary for optimum health". In the test subjects, dark-adaptation values returned to normal when the plasma value returned to about 50, and showed no further improvement when the dose of vitamin A was increased, although plasma-levels did not return to 100 or above until after a period of unrestricted diet coupled with very large doses of vitamin A. The smallest prophylactic dose tested was 2,600 I.U. daily. This maintained normal dark adaptation and

* Vitamin A Requirement of Human Adults; an Experimental Study of Vitamin A Deprivation in Man. A Report of the Vitamin A Sub-committee of the Accessory Food Factors Committee. Medical Research Council Special Report Series, No. 264. Pp. 145. (London: H.M. Stationery Office, 1949.) 3s. net.

a steady plasma-level; probably a smaller dose would have sufficed.

When carotene was used instead of the preformed vitamin, it was necessary to distinguish carefully between the value of the dose as given and its 'effective value'. The latter was taken as the difference between the amount given and the amount excreted, but it is pointed out that it is not known if this represents the amount actually absorbed; there may be some destruction in the gut. Even with pure carotene in oil, approximately 25 per cent of the dose was excreted; when green leaves or carrots were given, the proportion rose much higher, averaging 75 per cent with sliced or *purée* tinned carrots. When due allowance had been made for these differing levels of availability, it appeared that the minimum protective dose lay between 1,250 and 1,900 I.U., and an effective dose of 1,500 I.U. was adopted as the probable daily requirement in terms of β-carotene.

The fact that the volunteers had to be kept for a year or more on a restricted vitamin-A-free diet before their reserves were sufficiently depleted to make them suitable subjects for therapeutic tests reduced the numbers available and made repetition of the experiments impracticable. In drawing conclusions from the results and, still more, in making recommendations based on them, it is necessary to make some allowance for individual variability among normal adults. The authors point out that "it is difficult to decide whether doubling the [minimum protective] dose would confer the maximum improvement in health or whether the dose should be increased fourfold, eightfold or even more". They have taken their courage in both hands, however, and been content with doubling it, recommending "a round figure of 2,500 I.U. vitamin A daily for a normal human adult". They back their decision with the observation that "the very adequate liver reserves of the subjects of the experiment cannot have been built up in the past on daily intakes much larger than 2,500 I.U. vitamin A or an equivalent mixture of carotene and vitamin A.". They have chosen 3,000 I.U. as the desirable level when the source is carotene, but stress the fact that, in order to ensure this, the diet may well have to supply about 12,000 I.U.

In the War Memorandum of the Medical Research Council on the nutritive value of war-time foods[3], it was suggested that "in calculating the vitamin A potency of *a mixed diet*, the total carotene value should be divided by 3 and added to the value for preformed vitamin A. . . . This correction should not be applied to *individual foods* for which it is to be expected that different correction factors will be found necessary."

The present report recommends dividing by 4 when the source is carrot and by 2·5 when the source is cabbage or spinach, and suggests that, in the absence of data for the availability of carotene in other foods, other root vegetables should be classed with carrots, and other green leaves with cabbage and spinach. The original recommendation (division by 3) has been fairly widely used and has led to much confusion in the assessment of the vitamin A adequacy of different dietaries, for the resultant 'vitamin A potency' has been compared with recommended allowances where no such correction has been applied, and 'deficiencies' reported when, in fact, the deficiency was only in the interpretation.

Dietary survey material is very apt to give rise to these miscegenations of fact and theory—the use of man-value coefficients was another potent source of much misunderstanding. Reports of food consumption studies often omit the only factual data that were collected, that is to say, the amounts of the various *foods* that were eaten. Instead, we are given calculated nutrient values which rarely make any allowance for the effect of the preparation and cooking methods employed, even when they introduce some minor 'correction factor' for availability.

There can be little doubt that the physiological value of a dietary is determined by a large number of different factors, not the least of which is the 'dietary pattern' or way in which the foods are mixed and the intake spaced. We are only beginning to learn about these things, and most of the earlier studies will need to be re-assessed in the light of more recent discoveries. Unfortunately, it is often impossible to do this because of the way in which the data have been presented.

Meantime, in regard to vitamin A, it might be suggested that estimates of *requirements* should always be given in terms of vitamin A *per se*, and that reports of *food consumption* should state the quantities of vitamin A and carotene separately, the estimation of the resultant vitamin A potency being given as an additional figure, together with a description of how it was obtained. Further, is it not time now to drop the 'I.U.' and use 'mgm.' or 'μgm.' instead, as with the other vitamins?

M. W. GRANT

[1] Recommended Dietary Allowances. National Research Council's Reprint and circular series, No. 115. Washington, January 1943. Revised in 1945 and again in 1948.

[2] Wilder, R. M., "Misinterpretation and Misuse of the Recommended Dietary Allowances", *Science*, **101**, 285 (1945).

[3] Nutritive Values of Wartime Foods. Medical Research Council War Memorandum, No. 14. (London: H.M. Stationery Office, 1945.)

NEWS and VIEWS

Education in the University of Leeds

MR. ROGER NOEL ARMFELT has been appointed professor of education and head of the Department of Education from a date early in the session 1949–50, in succession to Prof. W. R. Niblett, who becomes whole-time director of the University of Leeds Institute of Education. Prof. Niblett was appointed professor of education and head of the Department of Education in 1947, and since September 1948 he has also been director of the Institute of Education. His tenure of both the headship of the University Department and the directorship of the Institute was a temporary measure, and Mr. Armfelt's appointment is a realization of plans made when the Institute was established in 1948. Mr. Armfelt was educated at Cranleigh and at King's College, Cambridge. After a period as assistant master at Dulwich College, he was successively an inspector with the Kent Education Committee, assistant secretary with the Buckinghamshire Authority and secretary to the Devon Education Committee. In 1941 he was appointed an assistant controller in the Home Division of the B.B.C., and in 1945 transferred to the secretaryship of the Schools Broadcasting Council. His publications include "County Affairs", "Village Affairs", "Shapton Affairs", and most recently, "Education—New Hopes and Old Habits".