

VITAMIN REQUIREMENT OF
HUMAN ADULT

By E. M. Hume Etc.

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**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**

(Compiled by E. M. HUME and H. A. KREBS)

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PREFACE

ONE of the surprises of the early months of war was the revelation of a disconcerting prevalence of scabies among the inhabitants of our larger cities. As a result, towards the end of 1940, the Ministry of Health approved proposals for an experimental study of the natural history and mode of transmission of the disease. The programme had as its central feature a plan for the deliberate introduction of the infestation among a small community of volunteers, upon whom it would be possible to make day-to-day observations over a long period, and for this purpose it was decided to seek the cooperation of conscientious objectors to military service. The scabies investigation, which was initiated and directed by Dr. Kenneth Mellanby, proved a success and the "Sorby Research Institute," as the converted villa in Sheffield where it took place was renamed, became the home of a series of experiments in human biology, which continued, at first under the Ministry of Health and then from the spring of 1942 under the Medical Research Council, for the next five years.

The study described in the present Report was made in response to a request from the Ministry of Food for information on the adult requirement of vitamin A or its precursor, carotene, and was planned and controlled by a team of workers, of which the nucleus was formed by members of the Vitamin A Sub-Committee of the Accessory Food Factors Committee. The investigation was made on volunteer conscientious objectors at the Sorby Research Institute, twenty men and three women, mostly between the ages of 20 and 30, cooperating in it. War conditions made it doubtful how long the inquiry could be continued, and for this and other reasons it was considered necessary to start the volunteers on the experimental diet with no preliminary period of observation. The plan adopted was to give sixteen of them 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 remaining seven volunteers served as positive controls, receiving the same diet as the main group, but with a prophylactic supplement of either vitamin A or carotene from various sources. 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 realized. After eight months of deprivation there was still no discernible change in the volunteers beyond a lowering of the blood carotenoids; this, though useless as a criterion of depletion, was at least evidence to the sceptical that the diet was not being evaded. Gradually there began to appear a drop in the vitamin A level of the plasma and a deterioration in the capacity for dark adaptation, the two changes that proved to be the only reliable criteria of depletion. By these criteria no more than three men could be judged "unmistakably" deficient and hence suitable for therapeutic tests, although several of the volunteers persisted with the diet for more than 18 months and one for over two years. No other unequivocal signs of deficiency were found in any of the sixteen deprived subjects at any time during the whole course of the experiment. Such abnormalities as follicular hyperkeratosis, conjunctival degenerations or undue fatigue—all commonly associated or thought to be associated with

Vitamin A deficiency—were either absent or equally present in the deprived and the non-deprived or present in the same subjects both before and after depletion. Two cases of tuberculosis occurred among the volunteers but it was not possible to determine whether their occurrence during the experimental period was more than a coincidence.

The prolonged delay before the onset of nutritional changes, their sparse incidence and undramatic character aroused in the investigators a feeling of surprise which is in itself a measure of the novelty and value of the results achieved. It is clear that vitamin A deficiency is much less easily or rapidly induced in hitherto well-fed adults than has previously been supposed. This is a conclusion of practical importance, but, it must not be overlooked that the scope of the present investigation was restricted and that its results are not applicable to the needs of children, pregnant or nursing mothers, or the chronically undernourished.

It is the negative conclusions of the experiment and a sense of the complexity inseparable from all such studies on human beings that are the dominant impressions left by a reading of this Report. The positive findings were too scanty to justify a precise estimate of the requirement of vitamin A or carotene, and the tentative recommendations subsequently made by the Sub-Committee allow a generous margin of safety and do not conflict with previous authoritative opinion. Emphasis is laid on the wide differences in the availability of carotene from various sources and the consequent undesirability of fixing any single figure for the carotene requirement.

Much of the interest of this long and elaborate investigation is to be found in the detailed descriptions of experimental technique and apparatus, and of the modifications and improvements introduced as a result of experience. Among the new developments may be mentioned Livingston's method of rod scotometry, which promises to provide a sensitive gauge of impaired night vision.

The volunteers were free to abandon this experiment whenever they chose. That they preferred to persevere month after month with the insipid monotony of their diet and the disagreeable routine of clinical and laboratory examinations is no small tribute to their tenacity and public spirit.

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16th November 1948.

CONTENTS

	Page
INTRODUCTION	7
Organization of the Research Team	9
Acknowledgments	10
I.—CONCISE ACCOUNT OF THE EXPERIMENT	11
A.—General Plan	11
B.—Effects of the Vitamin A Deficient Diet	12
<i>Criteria of deficiency</i>	13
C.—Therapeutic Tests with Vitamin A and Carotene	24
<i>Vitamin A</i>	24
<i>Carotene</i>	26
<i>Summary of the effects of dosing</i>	28
D.—Prophylactic Tests with Vitamin A and Carotene	29
<i>Vitamin A</i>	29
<i>Carotene</i>	31
E.—Requirement of Vitamin A and Carotene	39
<i>Requirement in terms of vitamin A</i>	40
<i>Requirement in terms of β-carotene</i>	41
<i>Requirement of carotene in relation to its availability from different sources</i>	42
<i>Effect of tocopherol or other stabilizers on the carotene requirement</i>	43
<i>Amount of β-carotene equivalent to vitamin A</i>	43
<i>Discussion of the literature</i>	44
II.—ELABORATION OF SPECIAL ASPECTS	46
F.—Measurements with the Adaptometer of Craik	46
<i>Final rod threshold</i>	46
<i>Cone-rod transition time</i>	46
G.—Comparison of Wald's and Craik's Adaptometers	46
H.—Time Required for Maximum Dark Adaptation	47
I.—" Seasonal " Changes in the Final Rod Threshold	50
J.—Rod Scotometry	54
<i>Procedure</i>	54
<i>Effects of the deficient diet</i>	56
<i>Effects of dosing</i>	57
<i>Conclusion</i>	58
K.—Effect of Consumption of Alcohol on Capacity for Dark Adaptation and Plasma Values for Vitamin A	58
L.—An Examination of the Vitamin A Reserves in the Liver of a Sample of the Population of Great Britain, Made by T. Moore with the Assistance of A. C. Cooper	62
M.—A Study of the Normal Value for the Vitamin A and Carotenoid Content of Human Blood Plasma, Made by T. Moore and Z. A. Leitner	65
N.—Is Carotene Synthesized in the Human Gut?	71

	<i>Page</i>
III.—DETAILS OF THE EVIDENCE	74
O.—Particulars and Management of the Volunteers	74
P.—Diet	77
<i>Composition of the basal diet</i>	77
<i>Adequacy of the diet</i>	81
<i>Vitamin A potency of the basal diet</i>	84
<i>Supplements of vitamin A and carotene</i>	86
Q.—Methods Used for the Estimation of Vitamin A, Total	
Carotenoids and Carotene	90
<i>Blood plasma</i>	90
<i>Faeces</i>	97
<i>Foodstuffs</i>	99
R.—Measurement of the Capacity for Dark Adaptation ..	100
<i>Meaning and characteristics of the dark adaptation curve</i>	100
<i>Adaptometer of Wald</i>	102
<i>Adaptometer of Craik</i>	110
<i>Technique of rod scotometry</i>	114
S.—Particulars of Medical Examinations	120
<i>Enlargement and hyperkeratosis of the hair follicles</i> ..	120
<i>Summary of the report by W. J. Wellwood Ferguson on</i> <i>the slit-lamp examination of the eye</i>	123
<i>Summary of the report by J. L. Burn on audiometry</i> <i>measurements</i>	124
<i>Summary of the report by D. Russell Davis on the</i> <i>psychological state of the volunteers</i>	124
T.—Statistical Report on the Values for the Contents of Vitamin A and Total Carotenoids in the Blood Plasma, by J. O. Irwin	127
U.—Monthly Average Bodyweight for Each Volunteer (<i>Table</i>)	136
GENERAL SUMMARY	138
REFERENCES	143

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