INCIDENCE AND DURATION OF COLDS

Throughout the experiment the volunteers recorded the number and duration of the colds they experienced. These data are presented in Table 44 (p. 134). At a glance they seemed to indicate that the average number of colds in the deprived and non-deprived groups did not differ markedly, but that they lasted longer in the deprived group. The material was accordingly submitted to a statistician (C. H. Jowett) for analysis, who summarized his investigation as follows:

"The lengths of all colds were subjected to the transformation $y = 20 \log x$. It was considered that this would make the various distributions on which the statistical tests depended more close to 'normal'. The data analysed consisted of the following:

Colds of members of deprived group before dosing.

Colds of members of supplemented group up to and including July 1945.

Assuming for the moment that time of year had no appreciable effect? the following conclusions emerged from the analysis of variance given in Table 18.

TABLE 18

Analysis of variance of transformed lengths of colds

Source of variation	Sum of squares	Degrees of freedom	Mean square	
Difference between groups	431·8	1	431·8	(1)
Differences between individuals within a group ..	1092·1	10	109·2	(2)
Variation of length of cold within an individual ..	1365·8	27	50·6	(3)

The ratio of the mean squares (2)/(3) fell just short of the 5 per cent level of significance, but since it almost attained that level, and moreover for *a priori* reasons, it was considered that differences between individuals did in fact exist; the mean square (1) was accordingly tested against (2), the ratio (l)/(2) being equal to 3-95. This value lies between the 5 per cent level and the 10 per cent level of significance, and hence there is no conclusive evidence of a difference between mean transformed length of colds from supplemented to deprived groups. Such evidence as there is, however, definitely confirms the hypothesis that the absence of vitamin C tended to cause colds to last longer.

The geometric mean length of colds of non-deprived subjects = 3.3 days (4)

The geometric mean length of colds of deprived subjects = 6.4 days (5)

As a further check the seasonal difference in colds was investigated; differences between season lengths were not marked, and the numbers of winter and summer colds did not differ seriously from group to group. It may safely be concluded that the difference between the means (4) and (5) was not a manifestation of the seasonal effect.

In illustration of the seasonal differences, the geometric mean lengths of colds for the 'winter' months and the 'early summer' months are given in Table 19.

TABLE 19

Seasonal incidence and duration of colds

Season	Geometric mean length in group:		No. of colds in group	
	supplemented (days)	deprived (days)	supplemented	deprived
November–February	4·0	7·6	11	8
April–July	3·2	7·2	8	8

Conclusion

The data support the hypothesis that colds of deprived subjects lasted longer, but do not establish it."

In connexion with this result mention should be made of the observation of Glazebrook and Thomson (1942) who studied the incidence and duration of infectious diseases in groups of adolescents living in an institution where the dietary level of vitamin C was very low. The incidence of the common cold and tonsillitis or the average duration of illness due to the common cold was not affected by vitamin C supplements, but the average duration of illness due to tonsillitis was longer in the unsupplemented group.

TABLE 44

Number and duration of colds as recorded by certain of the volunteers in their own notebooks

Name	Vitamin C (mg. daily)	Date	Number of days	Number of colds	Remarks
Bartley ..	70	9. 1.45	2	1	
		11. 3.45	2	1	
		18. 5.45	5	1	
		27. 9.45	4	1	
		11.10.45	1	1	
		13.12.45	6	1	
		Total	20	6	
Garling ..	70	7. 1.45	15	1	
		26. 2.45	5	1	
		7. 5.45	3	1	
		Total	23	3	
Hill ..	70	12.11.44	1	1	
		13. 1.45	6	1	
		29. 6.45	1	1	
		22. 8.45	1	1	
		29.12.45	7	1	
		Total	16	5	
Golding ..	10	5.12.44	14	1	
		28.12.44	13	1	
		23. 2.45	8	1	
		1. 5.45	11	1	
		1. 6.45	1	1	
		23. 6.45	11	1	
		20.10.45	7	1	
		28.11.45	6	1	
		Total	71	8	
Jackson ..	10	11. 1.45	1	1	
		5. 3.45	1	1	
		1.11.45	3	1	
		10.11.45	7	1	
		Total	12	4	
Way ..	10	3. 1.46	4	1	
		Total	4	1	
Woodhouse	10	23.11.44	3	1	
		29.12.44	1	1	
		9. 4.45	1	1	
		2. 6.45	5	1	
		17. 8.45	1	1	
		Total	11	5	

TABLE 44 *(continued)*

Name	Vitamin C (mg. daily)	Date	Number of days	Number of colds	Remarks
Drake ..	0	8.12.44	2	1	
		27.12.44	16	1	
		Total	18	2	Dosed 3.7.45
Hudson ..	0	7.12.44	16	1	
		21. 3.45	9	1	
		14. 7.45	11	1	
					Dosed 30.7.45
		2.10.45	13	1	
		11.11.45	16	1	
		9. 1.46	9	1	
		Total	74	6	
Robinson	0	31.12.44	2	1	
		26. 6.45	3	1	
					Dosed 27.7.45
		26.10.45	1	1	
		Total	6	3	
Sanderson	0	21. 1.45	24	1	
		27. 4.45	17	1	
		18. 6.45	3	1	
					Dosed 27.7.45
		22. 9.45	7	1	
		Total	51	4	
Tridgell ..	0	13.11.44	8	1	
		28.12.44	4	1	
		15. 1.45	14	1	
		2. 4.45	15	1	
		27. 4.45	3	1	
		2. 5.45	9	1	
		29. 6.45	8	1	
					Dosed 5.8.45
		9. 8.45	1	1	
		22. 9.45	5	1	
		12.10.45	7	1	
		23.11.45	6	1	
		26.12.45	21	1	
		30. 1.46	5	1	
		Total	106	13	
Wodeman	0	23. 3.45	3	1	
					Dosed 25.6.45
		9. 1.46	3	1	
		Total	6	2	

CONTENTS

Colour and monochrome plates will be found at the end of the Report.

VITAMIN C REQUIREMENT OF HUMAN ADULTS

An Experimental Study of Vitamin C Deprivation in Man

INTRODUCTION

THE work described in this Report was undertaken with the object of gaining further knowledge of the vitamin C requirement of human adults. There is no general agreement on even an approximate value for the requirement. The League of Nations Health Organisation (1938) through their Technical Commission on Nutrition estimated the daily requirements of adults at 30 mg., whereas the National Research Council (1948) in the United States recommended an allowance of 75 mg. Some authorities put the daily requirement much below 30 mg. (Rietschel, 1940; Zilva, 1941, 1944), and others suggest quantities even above 75 mg. (Ralli, Friedman and Sherry, 1939; Todhunter and Robbins, 1940; Linghorne, Mclntosh, Tice, Tisdall, McCreary, Drake, Greaves and Johnstone, 1946; Scheunert, 1948-9). The divergences in the estimates arise from the different standards used in assessing the requirement. Most of the high values are based on studies of the saturation of the body with vitamin C, while the lower values are inferred from observations of the prevention and cure of the clinical manifestations of scurvy.

Uncertainty about the requirement was often felt when questions of food policy and the need for dietary supplements were raised during the Second World War. It was, therefore, planned to carry out a trial on volunteers on the same lines as the experiment on vitamin A requirements (Hume and Krebs, 1949). A number of volunteers were to be given a diet deficient in vitamin C but otherwise adequate until signs of scurvy appeared. The minimum amount of vitamin C which would cause the signs of deficiency to disappear was then to be ascertained. Other volunteers were to receive the same basal diet with prophylactic doses of vitamin C given daily from the start of the experiment.

A subsidiary aim of the trial was to study the clinical signs and symptoms of the early stages of vitamin C deficiency and to correlate them with laboratory findings; such a correlation would, for example, provide a practical basis for the interpretation of the concentration of vitamin C in blood in terms of vitamin C intake. It was intended to pay special attention to the question of how far the healing of wounds is affected by the milder degrees of deficiency. Wound healing is known to be retarded in severe scurvy, but whether minor degrees of deficiency interfere with healing and whether administration of large doses of vitamin C after surgical operations, as practised by some surgeons, is warranted must be regarded as uncertain.

Special thanks are due to the volunteers who, in addition to their many other sacrifices, allowed incisions to be made on their legs, and the scars to be removed for examination.

The presentation of the results follows that of the Report on vitamin A requirements published in this Series. The Report is in three Sections. Section I contains a brief account of the main aspects of the trial. Section II elaborates a number of special aspects which might interest a general reader but are not an essential part of the main theme. Section III contains a description of the techniques and some of the full experimental particulars.

The editorial work of Miss E. M. Hume in connexion with the Report is gratefully acknowledged.

As in the Vitamin A report, it has proved impossible to include all the detailed results of the experiment. A list is given below of Tables which have had to be omitted but which were considered to be worth making available. They have been deposited as microfilms at the Library of the National Institute for Medical Research, Mill Hill, London, N.W.7, and at University Libraries in this country, where they can be consulted. Copies in the form either of microfilms or photographic enlargements (size 9 in. × 7 in.) may also be obtained on application to H.M. Stationery Office, P.O. Box 569, London, S.E.I, price 3d. net per frame (microfilms) with a minimum of 10 consecutive frames or Is. Od. net per print (enlargements) excluding postage.

Table A Haematological data
B Monthly average of body weights
C Average body temperatures
D Resting pulse rates
E Pulse rates in exercise tolerance tests
F Final rod thresholds
G Cone-rod transition times
H Rod scotometry.

A preliminary report of the trial has been published in *The Lancet* (Vitamin C Sub-Committee: Medical Research Council, 1948).

Certain conventions have been adopted for the presentation of the results. In connexion with analytical determinations, "Cambridge" refers to analyses carried out by L. W. Mapson with technical assistance by A. Ward, Dunn Nutritional Laboratory, University of Cambridge and Medical Research Council. "Oxford" refers to analyses carried out by J. R. P. O'Brien and G. Higgins, Department of Biochemistry, The Radcliffe Infirmary, University of Oxford. "Sheffield" refers to analyses carried out at the Sorby Research Institute and under the direction of H. A. Krebs, Department of Biochemistry, University of Sheffield.

The Subcommittee much regrets the decease of Sir Leonard Parsons while the Report was being prepared.

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Roche Products, Ltd., Welwyn Garden City, for the supply of vitamin C, other vitamin preparations and dummy tablets.

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I. CONCISE ACCOUNT OF THE EXPERIMENT

A. General Plan

THE experiment began in October 1944 and lasted until February 1946. Nineteen men and one woman, aged 21 to 34, volunteered; particulars concerning them and their management are given on page 56. They lived a normal life without strenuous physical work.

DIET

The basal diet was designed to be as low as possible in vitamin C but complete in every other respect. It was sufficiently varied to be reasonably acceptable. It included milk aerated at 70°C. after addition of 1 part per million of copper sulphate, and a number of items such as dehydrated meat, potatoes and carrots selected because they could be purchased in bulk. The dehydrated vegetables were cooked in a special way to remove vitamin C. Plum jam, containing negligible amounts of vitamin C, was given to meet any possible criticism that factors included under the term, vitamin P, were omitted. A representative daily intake for a volunteer was: protein 104 g., fat 130 g., carbohydrate 340 g., Calories 2900, calcium 1.2 g., iron 17.8 mg., vitamin A (exclusive of carotene) 4,800 I.U., vitamin D 900 I.U., vitamin B1 1.1 mg., riboflavin 2 mg., and nicotinamide 13 mg. From chemical analyses it was calculated that on the average each individual obtained not more than 1 mg. of vitamin C daily from the diet (see page 66).

Full details of the composition of the diet, of the treatment of special foods, and various samples of the individual food intakes are found in Section III pages 56–67.

GROUPS OF VOLUNTEERS

To obtain base-line data the experiment began with a preliminary period, in most cases of 6 weeks, of a complete diet including about 70 mg. vitamin C daily. At the end of the period all the volunteers were given the basal deficient diet and divided into three groups (Table 1), ten having no supplements, seven having 10 mg. vitamin C daily, and three having 70 mg. vitamin C daily.

TABLE 1

Initial grouping of the 20 *volunteers according to the supplements of vitamin C given*

Volunteers receiving daily vitamin C supplement of:		
70 mg.	10 mg.	0
Hartley	Golding	Drake
Garling	Jackson	Hudson
Hill	Parry	Milburn
	Proctor	Robinson
	Way	Sanderson
	Whinfield	Tridgell
	Woodhouse	Williams, D.
		Williams, H.
		Wodeman
		Another

The volunteers did not know to which group they belonged, nor did the physicians responsible for the clinical investigations. All the volunteers were given each day 7 supplementary tablets of identical taste and appearance, some containing vitamin C, others being dummies (p. 67).

The group receiving a supplement of 70 mg. was intended to serve as a positive control and the group receiving 10 mg. was to be used for a prophylactic test. The dose of 10 mg. was chosen for the latter because it seemed to be near the minimum dose capable of preventing clinical scurvy (Zilva, 1944). The original scheme of dosing had to be somewhat modified later in the experiment when it was realized that even early stages of vitamin C deficiency might be more dangerous to life than had been thought at the start (p. 10). The need for such emergency modifications was responsible for some seemingly erratic variations in the size of the supplements given to some of the volunteers. Full details of the vitamin C supplements given to each volunteer throughout the experiment are shown in Table 30, p. 58.

INVESTIGATIONS

The investigations made on the volunteers at regular intervals included general clinical examinations, chemical analyses of blood and urine, haematological examinations, tests of capillary strength, capillaroscopy, radiography, electrocardiography, dark-adaptation tests, audiometry, studies of fatigue and studies of experimental wounds. Details of the investigations, their frequency and the investigators are shown in Table 2.

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A Report by the Vitamin C Subcommittee
of the Accessory Food Factors Committee

and

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compiled by

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