THE ADMINISTRATION OF VITAMIN C IN A LARGE INSTITUTION AND ITS EFFECT ON GENERAL HEALTH AND RESISTANCE TO INFECTION

BY A. J. GLAZEBROOK, M.R.C.S., L.R.C.P.

AND SCOTT THOMSON, M.D., M.R.C.P.Ed., D.P.H.

*From the Departments of Clinical Medicine and Bacteriology,
University of Edinburgh*

(With 3 Figures in the Text)

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INTRODUCTION

IN any institution, where large numbers of people are supplied with food from central kitchens, the diet usually contains only small amounts of vitamin C. Destruction of this vitamin takes place during overcooking and the reheating of the food while it is awaiting distribution. Fresh fruit and vegetables are rarely supplied.

Crandon, Lund & Dill (1940) concluded that the maximal utilization of vitamin C lies between 30 and 45 mg. daily. Their figures were derived from a study of experimental human scurvy. The 'minimal-optimum' intake of vitamin C for adults has been computed at 25 mg. a day per 10 stones of body weight, and this results in an excretion of 13-15 mg. a day (Abbasy, Harris, Ray & Marrack, 1935; Harris & Abbasy, 1937). The 'minimal-optimum' intake is based on the amount found necessary to prevent a tendency to increased capillary fragility (Gothlin, 1937). Fox (1941) reviewed the results of the experiments of Fox, Dangerfield, Gottlich & Jokl (1940), Crandon *et al.* (1940) and Kellie & Zilva (1939), and concluded that remarkably good health can be maintained on 15 mg. of vitamin C daily, but he remarked on the precarious nature of such meagre supplies.

Certainly large numbers of people live on a diet containing less than the 'minimal-optimum' intake, without apparent ill effect. Investigations by

Orr (1936) and by Crawford & Broadley (1938) indicate that the diet of one-half to three-quarters of the population of Great Britain contains inadequate quantities of vitamin C, the lower figure being obtained by adopting 'minimum' (British Medical Association) standards, and the higher figure by adopting 'minimal-optimum' (League of Nations) standards.

There are, of course, wide variations in the extent to which individuals will tolerate low vitamin C diets. Jennings & Glazebrook (1938) described a man who had taken a scorbutic diet for 40 years before he showed ill effects. On the other hand, children have developed scurvy while receiving generous supplements of vitamin C, such as orange juice, and the condition is cured by giving ascorbic acid parenterally, or in large amounts by mouth (Hess, 1923; Hagmann, 1937; Parsons, 1938).

The requirements of the body for vitamin C vary with several factors. Children require a larger amount per kg. of body weight than do adults (Abbasy *et al.* 1935; Smith, 1938), and it is probable that adolescents also require a greater intake.

The body's requirements are increased if the metabolism is increased (Parsons, 1938). Thus, hard exercise and exposure to cold may precipitate scurvy, and at one time scurvy was considered to be due to damp and exposure. Crandon *et al.* (1940) found an abnormally high level of blood lactate after muscular exercise in their case of experimentally induced human scurvy. The subject was capable of a maximum effort corresponding to that of a man 80 years old. Stewart, Learmonth & Pollock (1941) suggest that ascorbic acid secures a more adequate supply of oxygen to the tissues.

Certain intestinal conditions, by permitting the growth of vitaminolytic bacteria (Kendall & Chinn, 1938), may markedly increase requirements owing to the great destruction of the vitamin and consequent failure of absorption.

Many infective states increase the body's requirements, and this has been shown in tuberculosis by Hasselbach (1936*a, b*), Heise & Martin (1936) and by Abbasy, Harris & Ellman (1937); in rheumatoid arthritis by Abbasy, Harris and Ellman (1937) and by Rinehart, Greenberg & Baker (1936); in osteomyelitis by Abbasy, Harris & Hill (1937); in juvenile rheumatism by Abbasy, Hill & Harris (1936). It has been recorded in other infections by Harde, Rothstein & Ratish (1935).

Abbasy & Harris (1937) found a correlation between the erythrocyte sedimentation rate and the excretion of vitamin C in cases of tuberculosis and rheumatoid arthritis. They concluded that the excretion of vitamin C varied inversely with the severity of the condition, probably because of increased utilization in the body. The Groth-Petersons (1939) found that tuberculous patients require a greater intake of ascorbic acid to maintain a normal serum level than do healthy people.

Rinehart, Greenberg, Olney & Choy (1938) found a low level of ascorbic acid in the blood of cases of rheumatism, not only in the acute phase, but also in convalescence and in very low-grade infections.

This increased destruction of vitamin C in febrile illnesses may be incidental to the disordered metabolism, and serve no useful purpose. It seems clear, however, that there is an increased liability to infection in both man and animals in cases of frank scurvy (Hess, 1920; Hamburger & Goldschmidt, 1922-3; Werkman, Nelson & Fulmer, 1924; Grant, 1926; Schmidt-Weyland & Koltzsch, 1928; Grant, 1930; Bloch, 1931; Mackay, 1934; Robertson, 1934).

In cases of so-called 'latent scurvy' the evidence is equivocal. Hess (1917) first suggested that this condition occurs and is analogous to latent tetany. It is thought that this state is a cause of ill-health and may lower resistance to infection (Harris, 1937; Bourne, 1938; Szent-Gyorgyi, 1938). Vitamin C is said to control outbreaks of pneumonia (Funck, 1931), and a deficiency of it to play a part in the production of both acute juvenile rheumatism and rheumatoid arthritis (Rinehart & Mettier, 1934; Rinehart, 1935). Vogl (1937) claimed to have used it successfully in the prophylaxis of post-operative pneumonia. On the other hand, Fox *et al.* (1940) administered vitamin C over a period of 7 months to adult negroes, previously subsisting on a low intake, and found no difference in illness as compared with controls.

The evidence that vitamin C exerts a beneficial effect in cases of actual illness is not clear. Fresh fruits and their juices, particularly lemons and black currants, have long been common household remedies for simple acute infections. Low levels of vitamin C have been found in many illnesses, so low in some instances that the vitamin has been thought to have some specific aetiological significance. Hopes that saturation with the vitamin would cure such diseases have not been realized. While full tissue saturation is probably unnecessary, it would seem desirable to increase the intake of vitamin C during illness.

Otani (1936) and Ormerod & Unkauf (1937) considered that vitamin C improved cases of whooping cough. Gairdner (1938) in a controlled experiment found that the duration of illness in a group receiving vitamin C was shorter than in controls. The difference in the two groups was not a significant one, and he considered that the alleged benefits of vitamin C in whooping cough were unproven.

Beneficial results have been claimed in diphtheria (Bamberger & Wendt, 1935; Bamberger & Zell, 1936; Dieckhoff & Schuler, 1938; Szirmai, 1940). Zilva (1938) found that vitamin C saturation made no difference to the fate of guinea-pigs injected with diphtheria toxin.

An acceleration of healing, or a general improvement, in cases of tuberculosis treated with vitamin C has been claimed by several workers (Radford, de Savitsch & Sweeney, 1937; Albrecht, 1938; Bakhsh & Rabbani, 1939; Warns, 1938; Birkhaug, 1939). Some of these observations were based on controlled experiments. Hurford (1938), on the other hand, saw no significant change after saturation, except in the blood picture of anaemic cases. Erwin, Wright & Doherty (1940) state quite definitely that vitamin C is of no value in the treatment of tuberculosis. This conclusion was arrived at as a result of

their observations upon a series of chronic, or acute broncho-pneumonic, cases, 'unlikely to improve on any known form of treatment'. With such unpromising material, disappointing results would seem to be inevitable.

There is evidence that it is of value in pneumonia, particularly in hastening convalescence, and the claims made do not appear to have been contradicted (Gander & Niederberger, 1936; Vogl, 1937; Bonnholtzer, 1937; Hochwald, 1937; Gunzel & Kroehnert, 1937; Sennewald, 1938; Szirmai, 1940). Szirmai (1940) noted that while tissue saturation is necessary to obtain maximal benefit in pneumonia, cases of typhoid fever and diphtheria were improved by daily supplements of vitamin C without producing saturation.

ESTIMATIONS OF DEFICIENCY

Of the various methods of estimating a deficiency of vitamin C in the body, that described by Harris, Abbasy & Yudkin (1936) is the most popular. It is recognized that the excretion of vitamin C in the urine is dependent on the reserve in the body as well as on the amount ingested during the previous few days. Accordingly, a test dose (300–600 mg.) of ascorbic acid is given and the amount excreted in the urine during the following 24 hr. is measured. The procedure is repeated for several days until large amounts of ascorbic acid are excreted. It is recognized that although the amount excreted in the urine of normal people depends on the previous amounts in the diet, this amount cannot be used to measure the degree of saturation of the tissues. Abbasy *et al.* (1935) have found that a daily intake of 90 mg. will result in an excretion of 50 mg. in the urine, but an intake of 15 mg. will result in an excretion of 15 mg. Accordingly, it is considered that any deficiency of vitamin C is best measured in terms of saturation of the tissues (Hess & Benjamin, 1934; Johnson & Zilva, 1934; Harris, Ray & Ward, 1933; Harris & Ray, 1935; Pemberton, 1940). Following the same principle, estimations of vitamin C in the blood have been made and an ascorbic acid tolerance curve devised, following an intravenous injection of 1000 mg. (Farmer & Abt, 1935; Mirsky, Swadesh & Soskin, 1935; Wright, Lilienfield & Maclenathen, 1937; Portnoy & Wilkinson, 1938).

In a large training school under our observation there were some 1500 youths aged 15–20 years. For the most part they were drawn from the lower wage-earning classes, and a large proportion came from Scotland and the North Midlands, where economic conditions are probably below the average for the country. It is a reasonable assumption that the previous dietary of the recruits had been somewhat deficient in vitamin C judged by the standards already quoted.

The diet of the institution allowed over 4000 cal. per student per day. The food distribution was badly managed. Electric ovens were used to reheat the food, and to keep it hot whilst awaiting distribution. Often 8 hr. elapsed between the time the food was cooked and its arrival on the dining tables. The minimum time that heat was applied to the food, including the original cooking and the subsequent reheating, was 2 hr.

The daily ration of potatoes was 12 oz. The vitamin C content of potatoes varies, but this quantity in the raw state should contain approximately 50 mg. A full ration of potatoes, as served on the dining tables, after cooking and reheating, was found to contain, on the average, about 4 mg.

The other vegetables suffered an equal loss, with the exception of turnips, portions of which contained up to 6 mg. The milk was pasteurized, and half a pint of it contained about 1.5 mg. The other cooked foods contributed negligible amounts. The total intake of vitamin C varied from about 10 to 15 mg. per student per day.

Menus for one month

Day and date	Breakfast	Dinner	Tea	Supper
Week ending 4 December 1937				
Sunday, 28 Nov.	Bacon and egg	Tomato soup Roast pork Cabbage Steamed apple pudding and custard sauce	Assorted pastries	Veal loaf Beetroqt
Monday, 29 Nov.	Porridge Smoked fillets	Mulligatawny soup Roast beef Marrowfat peas Suet roll and syrup sauce	Jam, marmalade or syrup	Highland hash Mashed potatoes
Tuesday, 30 Nov.	Bacon and beans	Julienne soup Roast mutton Cabbage Dundee pudding	Doughnuts	Irish stew Doughboys Mashed potatoes
Wednesday, 1 Dec.	Liver and chips	Scotch broth Steak and kidney pie Mashed turnips Prunes and custard	Jam, marmalade or syrup	Fish and crisps
Thursday, 2 Dec.	Bacon and sausage	Pea soup Roast beef Cabbage Sultana roll and custard sauce	Bananas	Bubble and squeak and bacon
Friday, 3 Dec.	Porridge Fried fish	Pea soup Meat pudding Haricot beans Tapioca pudding	Jam, marmalade or syrup	Durham cutlets Marrowfat peas
Saturday, 4 Dec.	Fried sausages	Pot mess Carrots Doughboys Bananas	Tea cakes	Pea soup Cheese
Week ending 11 December 1937				
Sunday, 5 Dec.	Bacon and egg	Tomato soup Roast mutton Cabbage Bananas and custard	Assorted pastries	Preserved meat Beetroot
Monday, 6 Dec.	Porridge Bloaters	Pea soup Roast beef Marrowfat peas Snowdon pudding	Jam, marmalade or syrup	Cottage pie
Tuesday, 7 Dec.	Fried sausages	Pea soup Beef steak pudding Cabbage Tapioca pudding	Jam, marmalade or syrup	Layer pie

*Effect of vitamin C on health*Week ending 11 December 1937 (*continued*)

Day and date	Breakfast	Dinner	Tea	Supper
Wednesday, 8 Dec.	Bacon and liver	Potato soup Ragout of rabbit Marrowfat peas Suet pudding and jam	Assorted pastries	Fish and chips
Thursday, 9 Dec.	Fried or boiled eggs	Pea soup Roast beef Cabbage Apple pudding and custard sauce	Fish paste	Saveloys and pease pudding
Friday, 10 Dec.	Porridge Fried fish	Pea soup Steak and kidney pie Carrots Prunes and custard	Jam, marmalade or syrup	Savoury Mince and haricot beans
Saturday, 11 Dec.	Bacon and sausage	Pott mess Doughboys Butter beans Rice custard	Doughnuts	Salmon Beetroot

Week ending 29 January 1938

Sunday, 23 Jan.	Bacon and egg	Tomato soup Roast pork Cabbage Apple tart and custard	Slab cake	Salmon Beetroot
Monday, 24 Jan.	Fried or boiled eggs	Pea soup Roast beef Marrowfat peas Sultana roll and custard sauce	Jam, marmalade or syrup	Cottage pie
Tuesday, 25 Jan.	Porridge Kippers	Pea soup Steak and kidney pie Cabbage Rice custard	Rock cakes	Fried steak Mashed potatoes
Wednesday, 26 Jan.	Fried sausages	Potato soup Roast beef Turnips Ginger pudding	Jam, marmalade or syrup	Fish and chips
Thursday, 27 Jan.	Bacon and tomatoes	Pea soup Preserved meat Braized onions Durban pudding	Fish paste	Lamb's heart Potatoes
Friday, 28 Jan.	Porridge Fresh fish	Mulligatawny soup Roast mutton Cabbage Prunes and custard	Doughnuts	Bacon and bubble and squeak
Saturday, 29 Jan.	Sausage and egg	Pot mess Doughboys Carrots Bananas	Currant bread	Cheese and sauce

Week ending 18 June 1938

Sunday, 12 June	Bacon and egg	Tomato soup Roast mutton Cabbage Rhubarb tart Custard	Slab cake	Salmon Cucumber
Monday, 13 June	Porridge Kippers	Pea soup Roast beef Marrowfat peas Snowdon pudding and custard sauce	Syrup	Cambridge stew

Week ending 18 June 1938 (*continued*)

Day and Date	Breakfast	Dinner	Tea	Supper
Tuesday, 14 June	Fried eggs	Lancashire hot-pot Doughboys Onions Blanc-mange and prunes	Assorted pastries	Fish and chips
Wednesday, 15 June	Liver and bacon	Pea soup Baked and steamed pies Cabbage Sponge trifle	Bananas	Roast beef Potatoes
Thursday, 16 June	Fried eggs	Stewed rabbits and pork Dumplings Butter beans Macaroni pudding	Lemon curd	Fish and chips
Friday, 17 June	Sausages and gravy	Pea soup Roast mutton Cabbage Durban pudding Custard	Bananas	Lamb's heart Peas
Saturday, 18 June	Porridge Fresh fish	Irish stew Doughboys Haricot beans Rice pudding	Doughnuts	Cheese and pickles

Extra to menu. Tea, sugar, milk, bread, butter and potatoes, cocoa and biscuits: buns at stand easy.

METHODS

For a preliminary survey seventy-seven tests were carried out on otherwise healthy youths by giving them 300 mg. of ascorbic acid, and not one excreted appreciable amounts in his urine. Using the same method on twenty of the administrative staff who had a different dietary, it was found that fifteen excreted a considerable proportion of their test dose. Although it is recognized that other substances in the urine reduce the dye, 2:6-dichlorindophenol, the investigation revealed a difference between the two groups.

Estimations of the resting level of excretion, i.e. the total amount excreted in 24 hr. in the absence of a 'test dose', were also made. The amounts varied between 5.6 and 1.1 mg. with an average of about 2.5 mg. as compared with the normal amount of 13-15 mg.

These preliminary observations, therefore, indicated that the intake of vitamin C was at a very low level. This was to be expected from a consideration of the vitamin C content of the diet, and the probable 'minimal-optimum' requirements of the boys.

Daily excretion levels

Pure ascorbic acid powder was added to the diet of a group of boys numbering 350, whose average age was 16. Initially, 200 mg. per day were given to each boy, 100 mg. being placed in the morning cocoa, and 100 mg. in an evening glass of milk. The mixing was done in bulk in the kitchens before issue. The powder dissolved quickly and easily, and did not alter the appearance or taste of the vehicle.

From time to time samples of milk and cocoa were titrated after issue, in order to ensure that the mixing was properly carried out, and that full doses reached the youths. Figures varying from 78 to 118 mg. per glass were obtained in the case of the milk, and from 58 to 68 mg. per cup in the case of the cocoa. Heating of the cocoa no doubt explained the loss. Together with the amount occurring naturally in the diet, the intake per boy was approximately 200 mg. per day. The daily output of vitamin C was measured in different groups of boys each day, the titration of each sample of urine being carried out immediately after it was passed.

Fig. 1 shows the slow rise in urinary output which occurred. It was not until the 8th day that figures approximating to the resting level of normal adults were obtained, and high figures indicative of saturation point were not noted until the 22nd day. In other words, saturation was not achieved until 22 doses of 200 mg. per day had been given, or a total of some 4000 mg. This figure was probably too high, since it was likely that on occasions the boys under test did not pass all their urine in the Sick Quarters as ordered.

On the 28th day the dosage was reduced to 50 mg. twice a day, and on this dosage excretion continued at a level rather higher than that of a normal adult on optimum intake.

A fresh group of boys was observed, and the initial dosage was increased to 150 mg. twice a day. Figures indicative of saturation were obtained on the 15th day, and subsequently the dose was reduced to 25 mg. twice a day, when an excretion level approximating to the normal adult level was maintained. This is shown in Fig. 2.

A third batch of boys was examined. In this batch all the boys selected were recruits who showed possible clinical evidence of a vitamin C deficiency in the form of a mild gingivo-stomatitis. The ascorbic acid in this case was given in tablet form (Redoxon, Roche Products), in a dosage of 200 mg. once daily. Instead of estimating the vitamin C excretion of individual boys as in the two previous experiments, several were instructed to pass their urine each day and night in the Sick Quarters. The urine specimens were pooled. From the mixed specimens a sample was taken and acidified by the addition of one-ninth the volume of glacial acetic acid. The samples were titrated, and the amount of ascorbic acid per 1500 c.c. of urine recorded and charted (Fig. 3). This chart is very similar in form to Fig. 1. High outputs were observed on the 23rd day; the dose was then reduced to 50 mg. once a day in tablet form.

These charts show that, in order to maintain an optimal excretion level, a daily addition of 50 mg. of ascorbic acid was required.

Fig. 1. Daily output of vitamin C in the urine. Group 1.

Fig. 2. Daily output of vitamin C in the urine. Group 2.

Fig. 3. Daily output of vitamin C in the urine. Group 3.

THE RELATIONSHIP OF VITAMIN C TO RESISTANCE

In the institution, there were some 1500 students whose ages ranged from 15 to 20 years. The establishment was divided into seven groups or divisions for administrative purposes. The youths of one division worked as a unit, and occupied certain tables in the dining hall. To some extent each division occupied particular dormitories, but this separation was not absolute, and there was a fair amount of mixing of divisions in the sleeping quarters. Sleeping and feeding conditions were, of course, the same for all divisions. Careful records had been kept of the incidence of all infections for 1½ years before the observations described here were begun. In the preceding year there had been an epidemic of tonsillitis, which had affected all the divisions uniformly, so that they could not be regarded as separate units within the larger population.

The observations were made by supplying vitamin C in the form of pure ascorbic acid to one or more divisions. This was considered to be the only practical method of carrying out the observations without introducing unnecessary complications. For example, it was not possible to choose boys at random as it would have been impossible to supply them with vitamin C-treated cocoa or milk in the dining room. With the method actually chosen, all that was necessary was to add vitamin C to the supplies of cocoa or milk serving the tables for the appropriate divisions.

Moreover, all of the divisions had a population more or less the same as regards duration of stay in the establishment ('institution age'). Infectious diseases were more common amongst those who had more recently joined the institution. This was known from our previous records of infectious illnesses in the institution (Thomson & Glazebrook, 1942), and in view of these points the method of supplying the vitamin C to a whole division was decided upon.

Many minor infective conditions, such as conjunctivitis, boils, impetigo, etc., were not reviewed, as the number of cases of each disease was small.

The most common infective conditions which occurred were coryza and tonsillitis. The term 'tonsillitis' is used here to be an index of haemolytic streptococcal disease of the nose and throat, and covers all such terms as 'tonsillitis', 'sore throat', 'otitis media', 'pharyngitis' and 'cervical adenitis', as nearly all these cases are of haemolytic streptococcal origin. Throat swabs were taken of large numbers of cases of tonsillitis to determine that the haemolytic streptococcus was the causative organism.

Table 1 shows the number of cases of tonsillitis and common colds recorded in the two groups.

Table 1. *Incidence of tonsillitis and common colds in the two groups*

	Youths on vitamin C (335 youths)	Controls (1100 youths)
Colds	72 = 21.2 %	286 = 26 %
Tonsillitis	29 = 8.5 %	94 = 8.6 %

It is obvious, therefore, that vitamin C had no effect on the incidence either of common cold or tonsillitis.

The experiment was complicated, however, by the admission of 250 recruits into the two groups in the middle of the observations, replacing fully trained youths. This was of special interest, as it was known from previous experience that infections were more common amongst those who had more recently entered the institution. This would be true of any institution where infectious diseases were common. The test group admitted relatively more of the recruits into its population. No recruits were admitted during the 3 months preceding the period of the observations.

The recruits were those of group 6 (Thomson & Glazebrook, 1942), and no observations were made until they had been in the institution for a month. During this period the recruits who entered the test divisions were saturated with vitamin C, and it was during this same period that the recruits experienced much of their heavier incidence of disease. After a month had elapsed a record was kept of sixty youths who entered a test division and ninety who entered a control division. There was still a heavier incidence of infectious diseases amongst them as compared with the others who had been in the institution for some time. The duration of the period over which the recruits were observed was about one-half of the duration of the whole investigation. Table 2 shows that there was a greater incidence of disease amongst the recruits as a whole as compared with the others, but no difference in incidence of disease between the two groups of recruits.

The numbers of cases of tonsillitis and common cold which occurred amongst the 250 recruits were not sufficiently great to alter the incidence rates in the two experimental groups.

Table 2. *Incidence of infection amongst recruits*

	Youths on vitamin C (60 youths)	Controls (90 youths)
Colds	17 = 28.3 %	29 = 32.2 %
Tonsillitis	1	7 = 8 %

The next point examined was to see what effect, if any, the vitamin C had on the duration of the illness.

When a youth fell ill he was admitted to Sick Quarters unless his complaint was very mild. In the latter case he was placed on the out-patients list and excused all duties except attendance at school instruction. Most of the cases of common cold and tonsillitis were admitted to Sick Quarters. In analysing the durations of illnesses, observations were restricted to the cases in the Sick Quarters. The number of days spent there was obviously a more reliable index of the duration of illness, since the patient was under constant medical supervision. Frequently when a youth was discharged from the Sick Quarters he was put on the out-patients list, and this 'convalescent period' was neglected. The admission to and discharge from the hospital was not under our control.

Effect of vitamin C on health

The diet in the Sick Quarters was basically similar to that of the healthy boys. It was modified, of course, to suit the needs of the sick, but was prepared in the central kitchens and suffered an equally drastic loss of its vitamin C. When a student from the experimental division fell ill and was admitted to Sick Quarters, his dosage of ascorbic acid was continued there.

In a period of 6 months the average number of days spent in the sick room per boy due to infective conditions was 2.5 in the vitamin-C treated division, and 4.98 in the control division. In a period of 6 weeks, within the period of 6 months, the corresponding figures among the recruits were 3.2 in the vitamin-C treated group, and 4.0 in the control group.

It would appear that the saturation with vitamin C probably had some effect on duration of illnesses, and accordingly an analysis was made of this.

Days ill with common cold

In the vitamin C classes fifty-nine of the seventy-two cases (81.9%) were treated in the Sick Quarters, and the average period of stay was 6.32 days.

Among the controls 253 cases out of 286 (88.5%) were treated in the Sick Quarters, and the average period of stay was 6.4 days.

There was, therefore, no difference in the two groups either in incidence or duration of illness of common cold, and there was no difference in the proportion of total cases admitted to hospital.

Days ill with tonsillitis

The results are shown in Table 3.

Table 3. *Duration of attack of tonsillitis*

Class	Total no. of cases	No. admitted to hospital	Hospital cases expressed as percentage of total	Average stay in hospital	Standard deviation
Vitamin C class	29	18	62	10.05	6.96 (1)
Controls	94	83	88	16.7	11.86 (2)

An analysis showed that a difference as great or greater than that obtained would be expected once in fifty times in a homogeneous population.

Analysis of the more severe illnesses

It has been shown that youths on vitamin C spent 2.5 days in hospital due to infective conditions as compared with 4.98 in the control group. No conclusions were drawn from this observation, and it has been shown above that some of this difference was due to the duration of illness of tonsillitis in the two groups.

Some of this difference, however, was due to the occurrence of acute rheumatism and pneumonia in the control group with no case of either disease in the vitamin C-treated group.

There were seventeen cases of pneumonia and sixteen cases of acute rheumatism among 1100 controls, and no case of either disease among 335 youths having vitamin C. It would appear that the vitamin C exerted a considerable effect on the prevention of these two diseases. Of the sixteen cases of acute rheumatism, eleven were primary attacks, while five were recurrences.

The incidence of the diseases in the various divisions of the institution is shown in Table 4.

Table 4. *Incidence of pneumonia and rheumatism in the various divisions of the institution*

	Division	Number of cases	
		Pneumonia	Rheumatism
Vitamin C divisions	A	0	0
	B	0	0
Control divisions	C	5	3
	D	3	5
	E	2	3
	F	4	3
	G	3	2

Thus, the most marked effect of the vitamin C was to reduce the incidence of two severe illnesses.

Analysis shows that a difference as great or greater than this would be expected once in fifty times in a homogeneous population.

DISCUSSION

In a large institution there was a marked difference between the degree of vitamin C saturation of the students and the teaching staff as determined by a simple 'test-dose' method. The students were given a high calorie diet, which was subjected to prolonged heating. This overcooking resulted in a reduction of the total daily vitamin C intake to a level of 10-15 mg. per head. A daily addition of 50 mg. of ascorbic acid per head was required to maintain an optimal excretion level.

Better management of the food distribution and cooking arrangements might have achieved this result. The potato ration alone, allowing for normal cooking losses, should have supplied at least 25 mg. of vitamin C daily.

Some vitamin loss, of course, is unavoidable when food is cooked for communities in central kitchens. Normally, this can easily be countered by the supply of uncooked fresh or canned foods. In this case, for instance, the reduction of the diet from 4000 cal. to the more reasonable level of 3000 cal. per day, would at this time (1938) have probably offset the cost of an orange a day.

The dietary of the teaching staff included the supply of fresh fruit at each of the main meals. It was prepared in separate kitchens and escaped the overcooking. Nevertheless, judging from a single 'test-dose', 25% of the staff

were 'deficient' in vitamin C, in spite of their adequate intake. Harrison, Mourane & Wormall (1938) similarly found that the method indicated a 'deficiency' in 25% of medical students. The single 'test-dose' is not, of course, a reliable measure when applied to individuals.

The surprisingly large amount of 4000 mg. of vitamin C was required to produce tissue saturation of the youths. Attention has been drawn to the possibilities of experimental error, and many of the factors which increase utilization were present.

The subjects were adolescents. Infections were very common in the institution, and there had been a very severe epidemic of tonsillitis during the preceding session. The experiments were carried out during the winter months. Physical training and games occupied much of the day, and it was found that youths at rest in bed required approximately half the quantity of vitamin C, i.e. 2000 mg., to produce full saturation.

A special group of boys exhibited a mild gingivo-stomatitis, considered to be probably a scorbutic manifestation. Their saturation curve, however, was very similar to that of the other groups. The clinical appearance of this gingivo-stomatitis has been described (Roff & Glazebrook, 1939, 1940). It proved resistant to ordinary methods of dental treatment, and responded only to vitamin C saturation. It would appear that, under exactly similar conditions of suboptimal vitamin C intake, a gingivitis occurs in only a proportion of the cases. This, of course, was known to Lind (1772), who wrote: 'In Haslar Hospital the appearances of the disease [scurvy] were various—the gums were not always affected.'

No differences in the incidences of common cold and tonsillitis were found in two groups of boys, one of which received large doses of vitamin C. It was found, however, that the average duration of illness of the cases of tonsillitis in the control group was much longer than in the vitamin C-treated group. No such difference was found in the cases of common cold.

The period of treatment of cases of tonsillitis and common cold in the Sick Quarters was completely outside our control, and no biased attitudes influenced these durations from which we have drawn our conclusions.

In addition, there were seventeen cases of pneumonia and sixteen cases of rheumatic fever in the control group, with no case of either disease in the vitamin C-treated group. These cases were subjected to special investigations by us (X-rays, etc.) to establish certain criteria for the diagnosis. There was, however, in our opinion a relationship between these conditions.

Rheumatic 'pneumonitis' is a condition which is now recognized to occur not infrequently as a complication of rheumatic fever. The post-mortem appearance and pathology of this pneumonitis have been demonstrated by Hadfield (1938).

In the institution a type of low-grade basal lung consolidation or 'pneumonitis' occurred, and appeared to be related both to rheumatism and vitamin C deficiency. It was characterized on the one hand by its tendency

to progress into rheumatism, and on the other hand by its rapid disappearance when treated with ascorbic acid. This pneumonitis, apart from a vague picture of ill health, gave little clinical evidence of its presence, but it probably predisposed towards the development of acute pneumonia.

It is agreed that cases of rheumatic fever almost invariably give a history of upper respiratory tract infection, usually some 2 weeks previously. Such an infection depletes the reserves of vitamin C, more especially in those individuals whose intake is already at a low and precarious level. When the vitamin C reserves have fallen, it may be that the reaction of the body to an infection with the haemolytic streptococcus is altered. This may help to determine the onset of the syndrome of rheumatism in some cases, even although vitamin C has no specific action upon the established disease. In some cases of pneumonia, too, a similar train of events may occur, and there is much evidence that vitamin C does assist recovery.

Certainly, protracted mild deficiencies of vitamin C produce bone and cartilage changes, the histological and skiagraphical appearances of which have been accurately described (Park, Guild, Jackson & Bond, 1935; Wolbach & Howe, 1926). Ham & Elliott (1936) showed that the epiphyseal changes occurred when the vitamin C intake was sufficient to prevent scurvy although less than the basic requirements. These changes are marked during the period of growth. Under similar circumstances Mouriquand & Edel (1940) have demonstrated osteophytic formation. Rinehart & Mettier (1933, 1934) produced lesions simulating rheumatism in the myocardium of guinea-pigs fed on a scorbutic diet. Wolbach (1936) showed the presence of vitamin C to be essential for the formation of collagen. Swelling of the collagen is the earliest pathological change in rheumatism.

The calcium and vitamin B content of the dietary of the institution could perhaps be criticized, but the only *outstanding* deficiency, according to modern standards, was in vitamin C. As far as this one factor was concerned, the boys were almost certainly worse off, subsisting on the institution diet, than they would have been at home.

SUMMARY

1. The vitamin C in the dietary of an institution was largely destroyed by the methods of cooking and distribution.

2. Some 50 mg. of ascorbic acid per head per day were required to be added to the diet to produce an optimum excretion level.

3. Large doses of ascorbic acid were given to a group of adolescents in the institution over a period of several months. A record was kept of the incidences of infectious diseases in this treated group and in the remainder (controls). The following conclusions were reached:

- (a) The incidences of common cold and tonsillitis were the same in the two groups.

(b) The average duration of illness due to the common cold was the same in the two groups.

(c) The duration of illness of tonsillitis was longer in the control group than in the test group.

(d) Cases of rheumatic fever and pneumonia occurred in the control group but no case of either disease occurred in the test group.

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REFERENCES

- ABBASY, M. A. & HARRIS, L. J. (1937). *Lancet*, **2**, 1429.
 ABBASY, M. A., HARRIS, L. J. & ELLMAN, P. (1937). *Lancet*, **2**, 181.
 ABBASY, M. A., HARRIS, L. J. & HILL, N. J. (1937). *Lancet*, **2**, 177.
 ABBASY, M. A., HARRIS, L. J., RAY, S. N. & MARRACK, J. R. (1935). *Lancet*, **2**, 1399.
 ABBASY, M. A., HILL, N. J. & HARRIS, L. J. (1936). *Lancet*, **2**, 1413.
 ALBRECHT, E. (1938). *Med. Klin.* **34**, 972.
 BAKHSH, I. & RABBANI, M. (1939). *Indian med. Gaz.* **74**, 274.
 BAMBERGER, P. & WENDT, L. (1935). *Klin. Wschr.* **14**, 846.
 BAMBERGER, P. & ZELL, W. (1936). *Z. Kinderheilk.* **58**, 307.
 BIRKHAUG, K. E. (1939). *Acta tuberc. scand.* **13**, 45.
 BLOCH, C. E. (1931). *Amer. J. Dis. Child.* **42**, 263.
 BONNHOLTZER, E. (1937). *Dtsch. med. Wschr.* **26**, 1001.
 BOURNE, G. (1938). *Brit. med. J.* **1**, 560.
 CRANDON, J. H., LUND, C. C. & DILL, D. B. (1940). *New Engl. J. Med.* **223**, 353.
 CRAWFORD, W. & BROADLEY, H. (1938). *The Peoples Food*. London: Heinemann.
 DIECKHOFF, J. & SCHULER, K. (1938). *Klin. Wschr.* **17**, 936.
 ERWIN, G. S., WRIGHT, R. & DOHERTY, C. J. (1940). *Brit. med. J.* **1**, 688.
 FARMER, C. J. & ABT, A. F. (1935). *Proc. Soc. exp. Biol., N.Y.*, **32**, 1625.
 FOX, F. W. (1941). *Brit. med. J.* **1**, 311.
 FOX, F. W., DANGERFIELD, L. F., GOTTLICH, S. F. & JOKL, E. (1940). *Brit. med. J.* **2**, 143.
 FUNCK, C. (1931). *The Vitamins*. London.
 GAIRDNER, D. (1938). *Brit. med. J.* **2**, 742.
 GANDER, J. & NEIDERBERGER, W. (1936). *Munch. med. Wschr.* **83**, 1386.
 GOTHLIN, G. F. (1937). *Lancet*, **2**, 703.
 GRANT, A. H. (1926). *J. infect. Dis.* **39**, 502.
 — (1930). *Amer. Rev. Tuberc.* **21**, 115.
 GROTE-PETERSON, I. B. & GROTH-PETERSON, E. (1939). *Nordisk. Med.* **2**, 1565.
 GUNZEL, W. & KROEHNERT, G. (1937). *Fortschr. Therap.* **13**, 460.
 HADFIELD, G. (1938). Communication to Pathological Society of Great Britain and Ireland.
 HAGMANN, E. A. (1937). *J. Pediat.* **11**, 480.
 HAM, A. W. & ELLIOTT, H. C. (1936). *Amer. J. Anat.* **58**, 127.
 HAMBURGER, R. & GOLDSCHMIDT, L. (1922-3). *Jb. Kinderheilk.* **100**, 210.
 HARDE, E., ROTHSTEIN, I. A. & RATISH, H. D. (1935). *Proc. soc. exp. Biol., N.Y.*, **32**, 1088.
 HARRIS, L. J. (1937). *Brit. med. J.* **1**, 774.
 HARRIS, L. J. & ABBASY, M. A. (1937). *Lancet*, **2**, 1429.

- HARRIS, L. J., ABBASY, M. A. & YUDKIN, J. (1936). *Lancet*, **1**, 1488.
- HARRIS, L. J. & RAY, S. N. (1935). *Lancet*, **1**, 71.
- HARRIS, L. J., RAY, S. N. & WARD, A. (1933). *Biochem. J.* **27**, 2011.
- HARRISON, R. J., MOURANE, A. E. & WORMALL, A. (1938). *St Bart's Hosp. J.* August, p. 224.
- HASSELBACH, F. (1936a). *Dtsch. med. Wschr.* **62**, 924.
- (1936b). *Z. Tuberc.* **75**, 336.
- HEISE, F. H. & MARTIN, G. J. (1936). *Proc. soc. exp. Biol., N.Y.*, **34**, 642.
- HESS, A. F. (1917). *J. Amer. med. Ass.* **68**, 235.
- (1920). *Scurvy, Past and Present*. London and Philadelphia.
- (1923). *System of Pediatrics*. Philadelphia.
- HESS, A. F. & BENJAMIN, H. R. (1934). *Proc. Soc. exp. Biol., N.Y.*, **31**, 855.
- HOCHWALD, A. (1937). *Dtsch. med. Wschr.* **63**, 182.
- HURFORD, J. V. (1938). *Lancet*, **1**, 498.
- JENNINGS, G. H. & GLAZEBROOK, A. J. (1938). *Brit. med. J.* **2**, 784.
- JOHNSON, S. W. & ZILVA, S. S. (1934). *Biochem. J.* **28**, 1393.
- KELLIE, A. E. & ZILVA, S. S. (1939). *Biochem. J.* **33**, 153.
- KENDALL, A. I. & CHINN, H. (1938). *J. infect. Dis.* **62**, 330.
- LIND, W. (1772). *Scurvy in Hampshire*. London.
- MACKAY, H. M. M. (1934). *Lancet*, **2**, 1462.
- MIRSKY, I. A., SWADESH, S. & SOSKIN, S. (1935). *Proc. Soc. exp. Biol., N.Y.*, **32**, 1130.
- MOURIQUAND, G. & EDEL, V. (1940). *Bull. Acad. med. Paris*, **123**, 8.
- ORMEROD, M. J. & UNKAUF, B. (1937). *Canad. med. Ass. J.* **37**, 134.
- ORR, J. (1936). *Food, Health and Income*. London.
- OTANI, T. (1936). *Klin. Wschr.* **51**, 1884.
- PARK, E. A., GUILD, H. G., JACKSON, D. & BOND, M. (1935). *Arch. Dis. Child.* **10**, 265.
- PARSONS, L. G. (1938). *Lancet*, **1**, 65.
- PEMBERTON, J. (1940). *Brit. med. J.* **2**, 217.
- PORTNOY, B. & WILKINSON, J. F. (1938). *Brit. med. J.* **1**, 554.
- RADFORD, M., DE SAVITSCH, E. C. & SWEENEY, H. C. (1937). *Amer. Rev. Tuberc.* **35**, 784.
- RINEHART, J. F. (1935). *Ann. intern. Med.* **9**, 586.
- RINEHART, J. F., GREENBERG, L. D. & BAKER, F. (1936). *Proc. soc. exp. Biol., N.Y.*, **35**, 347.
- RINEHART, J. F., GREENBERG, L. D., OLNEY, M. B. & CHOY, F. (1938). *Arch. intern. Med.* **61**, 552.
- RINEHART, J. F. & METTIER, S. R. (1933). *Amer. J. Path. (Proc.)*, **9**, 952.
- (1934). *Amer. J. Path. (Proc.)*, **10**, 61.
- ROBERTSON, E. C. (1934). *Medicine*, **13**, 123.
- ROFF, F. S. & GLAZEBROOK, A. J. (1939). *J. Roy. nav. med. Serv.* **25**, 340.
- (1940). *Brit. dent. J.* **68**, 135.
- SCHMIDT-WEYLAND, P. & KOLTZSCH, W. (1928). *Z. Hyg. InfektKr.* **108**, 199.
- SENNEWALD, K. (1938). *Forschr. Therap.* **14**, 139.
- SMITH, S. L. (1938). *J. Amer. med. Ass.* **111**, 1753.
- STEWART, C. P., LEARMONTH, J. R. & POLLOCK, J. A. (1941). *Lancet*, **1**, 818.
- SZENT-GYORGYI, A. (1938). *Pr. méd.* **46**, 995.
- SZIRMAI, F. (1940). *Dtsch. Arch. Klin. Med.* **185**, 434.
- THOMSON, S. & GLAZEBROOK, A. J. (1942). *J. Hyg., Camb.*, **41**, 570.
- VOGL, A. (1937). *Munch. med. Wschr.* **84**, 1569.
- WARNES, E. H. J. (1938). *Ned. Tij. Geneeskunde*, **82**, 393.
- WERKMAN, C. H., NELSON, V. E. & FULMER, E. I. (1924). *J. Infect. Dis.* **34**, 447.
- WOLBACH, S. B. (1936). *J. Amer. med. Ass.* **108**, 7.
- WOLBACH, S. B. & HOWE, P. R. (1926). *Arch. path. lab. Med.* **1**, 1.
- WRIGHT, I. S., LILLENFIELD, A. & MACLENATHEN, E. (1937). *Arch. intern. Med.* **60**, 264.
- ZILVA, S. S. (1938). *Lancet*, **1**, 1411.