VITAMIN "C" NUTRITION

in the

CAPE PENINSULA.

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OBJECT

and

INTRODUCTION

VITAMIN "C" and NUTRITION

A survey of Vitamin "C" Nutrition in Hospital-Class patients of the Groote Schuur Hospital, Cape Town, and of School-children of the Cape Peninsula, both European and non-European.

An investigation into 500 cases with a dissertation on the significance of Vitamin "C" subnutrition and a brief review of the literature.

PREFACE

During the past few years, since the isolation and identification of pure Vitamin C, interest in its importance in relation to health and disease has become almost universal, and the well-nigh overwhelming volume of literature on the subject in all its manifold degrees of interest and wide scope of importance bears imposing witness to the widespread and vast amount of investigation carried out during the last ten years in particular.

There are few countries indeed which have not had their quota of investigation to add to the ever-growing pool of information on Vitamin C and its importance in the economy of man. Surveys of the varying needs of Vitamin C in different countries and localities have enabled us to ascertain with greater degrees of accuracy what the probable standards of an adequate Vitamin C nutrition are. In addition, however, and this is of importance, such investigations have also served to show how these so-called standards may vary from one country to another and also for different races.

Furthermore, in view of the ever-present difficulty in assessing the state of nutrition of any

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particular patient or group of people, chiefly owing to the absence of specific and scientific tests which would be unaffected by subjective factors in examination, it was hoped that by ascertaining the physiological requirements and physiological stores of the essential foodstuffs in good health, that one would be approaching that shadowy ideal of scientific standards for the state of nutrition for any one particular area, race or group, without having recourse to the usual rough and ready clinical assessment which is so subject to individual subjective variation.

For example, having comparatively accurate standards for the normal Haemoglobin content of the blood, we can readily employ this knowledge as one line of investigation, on a scientific basis, into the state of nutrition of a group of patients.

Thus, having similar methods of investigation at our disposal for Vitamin C, it was hoped that we would now have an additional factor to help make an accurate assessment of the nutritional state.

With this idea in view, it was while acting as Clinical Assistant to Professor J. F. Brock of the

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Department of Medicine, University of Cape Town, at the Groote Schuur Hospital, that such a survey of hospital class patients, both European and non-European was embarked upon as the first task of an embryo Department of Clinical Research.

The difficulties attending such a project, not the least of them being lack of financial assistance, are too well-known to be mentioned, but one was buoyed up with the enthusiasm of helping to found a Department of Clinical Research, the ideal of every sound Medical School, and with the knowledge that no such investigation had as yet been carried out in South Africa.

For the first six months of the year 1939, therefore, a routine investigation into the Vitamin C nutrition of hospital class patients was carried out in addition to ones duties as acting Medical Registrar. Towards the end of this period the writer was assisted by a grant from the National Research Council and Board, Johannesburg. Almost coincidentally with this, government interest became stimulated, and under a scheme inaugurated by the Union Department of Health, a Nutritional Survey was planned and the writer invited to

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extend his investigations into the wider fields represented by the children of ages 8 to 16 years in the Cape Peninsula during the subsequent six months.

One was working in unexplored territory as far as Vitamin C nutrition was concerned and in view of the well-known disparity, social, economical and medical, between the European and non-European populations, significant results were expected. How significant and how surprising they were will be shown below.

ACKNOWLEDGMENTS

I am particularly indebted to Professor J. F. Brock who first roused my interest in the subject of Vitamin C. It is he who made most of this work possible by overcoming the initial difficulties, placing unlimited clinical material at my disposal, assuring a constant supply of the large quantities of Vitamin C required, and throughout acting as a guide and source of inspiration. His own work in similar fields of investigation, and resultant experience therefrom, made it possible for him, very generously to assist me in numerous ways.

My thanks are due also to:-

The Cape Hospital Board for the use of three rooms in the Groote Schuur Hospital and a certain amount of equipment and apparatus, the modest beginnings of a Department of Clinical Research.

To Dr. G. C. Linder, of the Department of Pathology and Honorary Biochemist to the Groote Schuur Hospital - for giving me every facility in his laboratory, assistance in the frequent standardisations of my reagents, the loan of apparatus and supplies of crystalline Vitamin C and the dye 2:6 Dichlorophenolindophenol.

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To Professor Wm. Campbell of the Department of Bacteriology, for having solutions of crystalline Vitamin C sterilized and put up in ampoules for intravenous injection.

To Professor J. W. C. Gunn of the Department of Pharmacology and Dean of the Faculty of Medicine who gave me facilities for the construction of apparatus and advice on the writing of this thesis. His interest and encouragement have been of great help.

To Miss Elliott, the Librarian of the Medical Library for her unfailing assistance in obtaining books of reference, various publications and periodicals.

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To the various Honorary Physicians and Honorary Surgeons who allowed me to examine their cases.

To the Housemen who saw to the maintenance of a steady supply of clinical material for investigation.

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HISTORY

of

SCURVY.

BRIEF HISTORICAL SURVEY

o f

VITAMIN C DEFICIENCY

For centuries scurvy was of common occurrence not only among sea-farers, explorers and soldiers but also among large sections of the communities of Northern Europe.

Probably one of the earliest and distinct accounts of clear-cut scurvy dates from the 13th Century in the time of the Crusades, that of de Joinville being the result of personal observation, but some writers would have us believe that even Hippocrates makes reference to this deficiency disease. However, other Greek, Roman and Arabian writers show no acquaintance with scurvy, and when we reflect that fruit and vegetables grew abundantly in their countries one can understand how the disease must have been either non-existent, or of so infrequent an occurrence as not to arouse interest, recognition and consequently description.

It is interesting to note today that as far back as 1498, when Vasco da Gama first sailed round the Cape of Good Hope, the scene of the present investigation, he lost on that historic occasion no less than 100 men out of a crew of 160 as a result of the disease scurvy, the consequence of ignorance as to its true cause.

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A further illustration of the havoc which the disease wrought is recorded by the experience of one man, Admiral Sir Richard Hawkins, who stated in 1593 that within his own knowledge 10,000 seamen had died from scurvy.

In spite of this long history of scurvy many centuries passed before it became common knowledge that scurvy occurred after deprivation for long periods of fresh foods, and that it could be prevented and miraculously cured when fresh vegetables and fruits were made available.

Thus the earliest account of a deliberate cure of frank scurvy that I could find is recorded in the account of Jacques Cartiers' second voyage to Newfoundland in 1535, at the time when long sea voyages were becoming more common and scurvy becoming a scourge of the deep seas - "the calamity of sailors". Thus, voyaging in the St. Lawrence River 100 out of 103 of his men became stricken severely with scurvy and twenty-six of them died. Later, ashore, one of the sailors learned from the Red Indians that a decoction made from the needles of spruce trees would cure the disease. Such a

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preparation was forthwith prepared and the results were miraculous, the scurvy disappearing with amazing swiftness. The remarks of a contemporary observer on the effects of this barbarous medication are noteworthy for he declared that if "all the doctors of Montpellier and Louvain had been there with all the drugs of Alexandria, they would not have done so much in a year as that tree did in six days". It is interesting to note that very recently investigation has shown an infusion of pine needles to contain significant quantities of Vitamin C.

Just under 200 years later we have another account of scurvy and its treatment, this time not on the high seas but in the heart of Western Europe, and here again it is illustrated that scurvy was the first disease the aetiology of which was associated with a definite mode of nutrition.

Thus Kramer, an Austrian army physician was faced with a severe epidemic of scurvy in a field army in Hungary in 1720. In answer to his appeals he found that a hurried shipment of dried anti-scorbutic herbs failed to curb the disease and thousands died. His following inscription is of interest when one compares it with present day standards and records.

"Scurvy is a terrible disease for which there

is no known cure. Medication does not help, neither does surgery. Be careful of bleeding; shun mercury as a poison. The gums may be massaged, the stiff joints may be rubbed with fat - but all in vain. If one could only have available a supply of green vegetables, or a sufficient amount of the vital anti-scorbutic juices; or if one could have at hand oranges, limes or lemons, or their preserved pulp or juice so that a lemonade could be made out of them; or administered as such in three or four ounce doses - then one could be in a position to cure this dreadful disease, without other help".

Apparently from his seeming contradiction of "no known cure" and "one could be in a position to cure" he quite failed to realise, along with many others, that the fresh fruit and vegetables contained a specific ingredient for the cure of scurvy.

A few years later in 1734, Bachstrom in his "Observationes circa scorbutum; eiusque indolem, causas, signa et curam" wrote as follows, thus marking the beginning of a more scientific character in observations on scurvy, a departure carried forward brilliantly by Lind in 1747. Bachstrom wrote as follows:-

"From want of proper attention to the history

of scurvy, its causes have been generally, though wrongfully, supposed to be cold in northern climates, sea air, the use of salt-meats etc., whereas this evil is solely owing to a total abstinence from fresh vegetable food and greens; which is alone the true primary cause of the disease. And where persons, either through neglect or necessity, do refrain for a considerable time from eating the fresh fruits of the earth, and greens, no age, no climate or soil are exempted from its attack. Other secondary causes may likewise concur, but recent vegetables are found alone effectual to preserve the body from this malady, and most speedily to cure it, even in a few days, when the case is not rendered desperate by the patients being dropsical or consumptive".

Lind in 1747 published the results of his celebrated experiment carried out on board the scurvy stricken "Salisbury". He used 12 patients as similar as he could find them, and it is interesting to note how in the light of present day knowledge his experiment was exceedingly well controlled. Thus, he wrote:-

"Two of these were ordered each a quart of cyder a day. Two others took 25 drops of elixir vitriol,

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three times a day, upon an empty stomach, using a gargle strongly acidulated with it for their mouths. Two others took two spoonfuls of vinegar three times a day upon an empty stomach; having their gruels and their other foods well acidulated with it, as also the gargle for their mouths. Two of the worst patients with the tendons under the ham rigid (a symptom none of the rest had) were put under a course of sea-water. Of this they drank half a pint every day, and sometimes more or less, as it operated by way of gentle physic. Two others had each two oranges and one lemon given them every day. These they ate with greediness, at different times, upon an empty stomach. They continued but six days under this course, having consumed the quantity that could be spared. The two remaining patients took the bigness of a nutmeg three times a day of an electary recommended by a hospital-surgeon, made of garlic, mustard-seed, rad. raphan, balsam of Peru, and gum myrrh; using for a common drink, barley water well acidulated with tamarinds, by a decoction of which, with the addition of cremor-tartar, they were greatly purged three or four times during the course. The consequence was, that the most sudden and visible good effects were perceived from

the use of the oranges and lemons, one of those who had taken them being at the end of six days fit for duty..... The other was the best recovered of any in his condition, and being now deemed pretty well, was appointed nurse to the rest of the sick.

Some persons cannot be brought to believe that a disease so fatal and dreadful can be prevented or cured by such easy means. They would have more faith in some elaborate composition dignified by the title of an antiscorbutic elixir or the like ..... Facts are sufficient to convince the unprejudiced ..... It is no easy matter to root out old prejudices or overturn opinions which have acquired an establishment by time, custom and great authorities". It is worthy of note that in agreement with the findings on Jacques Cartiers' journey 200 years earlier, the same period of time, that is, six days elapsed before a cure was pronounced.

Similar conclusions were reached by physicians in other countries and their advice was relied upon by many expeditions. Thus, Captain Cook in his famous circumnavigation of the world, 1772-5, made his men eat fresh food "both of the animal or vegetable kind" whenever possible and so remained free from scurvy.

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His experiences were recorded and presented to the Royal Society upon which a special prize medal was struck for him.

From this period onward the ships of the East India Company carried stores of oranges or lemons, but as recorded above, over two centuries elapsed before similar measures to combat scurvy were adopted by the British Navy.

More recently, scurvy is still met with today in isolated regions and during famines and droughts. Outbreaks occurred in belligerent countries during the World War on all fronts.

Since then only isolated, sporadic cases are met with as a rule, usually occurring among lonely elderly men in poor circumstances, who having to fend for themselves, subsist mainly on a diet of carbohydrates, preserves and tea and so come to suffer from what Meulengracht so aptly termed "Bachelor's Scurvy". In this country, most of the cases seen come from the native and coloured populations usually as a result of prolonged drought and deprivation, but often enough as a result of ignorance of the antiscorbutic properties of fresh foods as well.

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Thus far, in tracing the story of Vitamin C deficiency throughout the ages we have been concerned wholly with the manifestations of marked or severe Vitamin C deficiency, that is, the disease known as scurvy.

It is not unexpected, therefore, that at some stage or other endeavours would be directed toward a recognition of the earlier symptoms of the disorder. Of recent years, therefore, we have come to concern ourselves less with these comparatively infrequent and isolated cases of manifest scurvy which are usually easily recognised and dealt with, and have directed our attention to the undoubtedly numerous cases of ill-defined Vitamin C deficiency. Before discussing this group of hypovitaminosis and to enable us the better to appreciate what such a state may entail, a word must be said about the Physiology and Pathology of Vitamin C nutrition.

HISTORY

of

VITAMIN C

V I T A M I N C

ITS NATURE AND CHEMISTRY

History of its Isolation and Identification.

VITAMIN "C" -
History of its Isolation and Identification

About seven years ago Vitamin C was an elusive quarry defying attempts at isolation and so of identification. In contrast, today it can be purchased at a reasonable price in ampoules, tablets, or crystalline form. This relatively swift change has been brought about as the result of ten years of tedious and laborious investigation and makes Vitamin C the first Vitamin to be isolated in crystalline form.

The earlier steps, gropings in the dark, must first be briefly indicated before passing on to the more recent work of enquiry. The early knowledge of Vitamin C is intimately linked with our understanding of scurvy, the classical disease for which it is the specific preventive and cure.

However, it was but two centuries ago that the value of fresh fruit and vegetables as anti-scorbutic therapeutic agents became established knowledge. Bachstrom in 1734, was one of the earliest to ascribe therapeutic powers to fresh vegetables and about twenty years later we were given our first clear account of the scorbutic

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disease by James Lind in his "Treatise on Scurvy".

Lind went further in his work and showed the value of lemon juice and even went so far as to evolve methods for concentrating and preserving lemon juice. His work received official recognition in 1804 when Sir Gilbert Blaine introduced regulations to ensure the daily consumption of lemon juice in the British Navy. Sixty years later similar measures were adopted by the mercantile marine.

The modern study of Vitamin C dates from 1907 with the demonstration of experimental scurvy in the guinea-pig by Holst and Frölich at Christiana. Their work instituted the modern study of Vitamin C and so made possible its eventual identification.

The first clue to the nature and identity of the vitamin was its instability. Thus, in their attempts to separate Vitamin C from lemon juice, Zilva in England, Bezssonoff in France, and Lawson and King in America, noted how rapidly oxidation destroyed the power of the Vitamin C containing portion. This was borne out by studying commercial methods of preserving antiscorbutic substances where undue loss of Vitamin C was prevented by controlling oxidation.

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In 1922 Zilva noted that the potency of Vitamin could be reduced by 80 per cent in half an hour's exposure to the air if it were made alkaline. On the other hand, he was able to show that although the vitamin was an easily oxidized compound, the process of oxidation could be vastly reduced in an acid medium.

The chase after the elusive vitamin was held up considerably after 1916 by the theory that scurvy was in some way related to an infection. Jackson and Moody recovered a diplococcus from scorbutic guinea-pigs which produced haemorrhagic lesions when inoculated into healthy guinea pigs, and so concluded that infection rather than a dietary deficiency was the causative factor in scurvy.

However, in the following year, 1917, McCallum and Pitz confirmed the production of scurvy in guinea-pigs on a diet of oats and milk alone, but they had found it difficult to believe that scurvy could be due to the lack of a specific substance alone as experience had shown that milk alone was perfectly adequate for the nutrition of all young mammals in the first days and weeks of extra-uterine life. They therefore inclined to the view that a

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focus of infection in the distended caecum was the cause.

Fortunately, Chick and Hume in England were able to show that milk was very poor in antiscorbutic potency and Cohen and Mendel restored attention to the importance of the dietary factor in 1918, by producing scurvy in guinea-pigs fed on a superior experimental diet deficient in Vitamin C and non-productive of caecal impaction. In 1920, Parsons furnished an explanation for McCallum's inconsistent results by showing that while a diet of oats and milk was entirely satisfactory for rats this was due not to the vitamin content of the milk but to the fact that the rat is completely immune to scurvy. (All previous work had commonly been done on rats and it was naturally concluded that the guinea-pig metabolism was more or less identical). Further probing showed that the rat's immunity to scurvy was due to the fact that the animals synthesized the anti-scorbutic substance. This fact has been confirmed by numerous workers since.

Work along this false line of investigation on the infection theory then ceased and more concentrated efforts were brought to bear upon the dietary

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factor which was now generally admitted to be the cause of scurvy. It was realized too that clinical studies were essential in interpreting the results of experimental findings in laboratory animals.

The next important step was taken in 1928 at Frankfort by Tillmanns, who, on having to distinguish between fresh and stale or natural and artificial fruit juices used a dye 2:6 Dichlorophenol-indophenol as an indicator. At an earlier stage Zilva had shown that fresh fruit juices bleach the dye, and now Tillmanns found that this property was not present in stale or artificial juices.

Subsequently Zilva and his co-workers found that they could estimate the reducing or bleaching powers of anti-scorbutic substances with a degree of precision that ran more or less parallel with the earlier biological assays.

Tillmanns repeated these experiments and accumulated evidence to show that the reduction of the dye was due to Vitamin C itself and he went on to state that the dye might be used to measure the concentration of the vitamin and its potency. He further put forward the suggestion that the vitamin

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might well be hexuronic acid a compound known to have similar reducing properties. At this stage his work began to overlap that of Szent-Györgyi, who had already demonstrated the reversible oxidation of hexuronic acid.

Thus in 1928, Szent-Györgyi showed that the adrenal cortex contains a relatively large quantity of a highly reducing substance which is specific for the interrenal system. This substance proved to be a carbohydrate derivative hitherto unknown, a highly reactive isomer of glycuronic acid, the substance therefore falling into the hexuronic acid series. He isolated this new derivative from oranges and cabbages as well, two vegetables known for their antiscorbutic potency. In 1933, Svirbely and Szent-Györgyi published their results of experiments carried out to demonstrate the antiscorbutic properties of hexuronic acid obtained from the suprarenals of the ox.

The acid was administered in doses comparable with the hexuronic acid content of the protective dose of lemon juice. Given in this quantity of 1 mgm. daily, hexuronic acid afforded complete protection against scury in a 90 day test. Since it is generally

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assumed that animals kept free from scurvy for 90 days would remain so indefinitely under identical conditions it was concluded that Vitamin C is a single substance identical with hexuronic acid.

This conclusion was criticized by Zilva who did not think hexuronic acid identical with Vitamin C.

At about this time and independently of Szent-Györgyi, King and Waugh stated that a crystalline preparation of Vitamin C which they had isolated from lemon juice had the chemical and physical properties of Szent-Györgyi's hexuronic acid. The latter criticized their work on the grounds that they made no chemical analysis of their substance and that their claims to its antiscorbutic activity based on the vitality of the experimental guinea-pigs were ill-founded as no post-mortem examinations were made, no weight curves worked out, and an insufficient number of animals observed for too short a period!

Harris and Ray (1932) showed raw suprarenal cortex to be a more powerful antiscorbutic than any natural source hitherto known, possessing three times the activity of fresh orange juice or 30 International Units per gram.

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They found that the degree of activity corresponded precisely with the value predicted on the basis of the relative yields of hexuronic acid obtainable from oranges or fresh supra-renals. From this evidence and other evidence they concluded that Vitamin C was either identical with hexuronic acid or was a substance possessing a close similarity to it in its distribution and in its chemical nature. Their preliminary results showed that in the guinea-pig - a species resembling man and the monkey, but differing from many others, including the dog and the rat, in being unable to synthesize Vitamin C in vivo when none is provided in the food - the Vitamin C activity of the supra-renals is lost with the onset of scurvy. They supposed that Vitamin C plays a special rôle in the physiology of the supra-renal, and thought that the occurrence of distinctive hypertrophic changes in the suprarenals in scurvy to be in keeping with this.

Later, Harris, in association with Mills and Innes (1932) carried out experiments at the same time as Zilva but independently, with a specimen of hexuronic acid provided by Szent-Györgyi to prove its antiscorbutic worth.

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Zilva concluded that the preparation contained Vitamin C but that the identity of hexuronic acid with Vitamin C was not proven as yet.

Harris, using different methods, came to the conclusion that the antiscorbutic action of the hexuronic acid obtained from ox suprarenals was confirmed by means of a striking curative test and by Höjers "tooth" structure method. One mgm. of the hexuronic acid was found to have an activity somewhat greater than 1 cc. of orange juice.

Lastly, in 1932, further evidence of the common identity of Vitamin C and hexuronic acid was brought forward by Moore and Ray. These workers found that a parallel blackening of the fresh suprarenals with Silver Nitrate solution occurred when the guinea-pig was non-scorbutic and normal quantities of hexuronic acid were extractable. On the reverse, they could produce no blackening when the animal was scorbutic. Further, in rats, animals which synthesize Vitamin C, blackening was still obtained even when the rats had been fed on a Vitamin C deficient diet for many weeks. On this evidence, these investigators also felt the common identity of hexuronic acid and Vitamin C to be proven.

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In 1933 using hexuronic acid of which they had extracted over one pound in weight from Hungarian red peppers (Capsicum Annuum) Svirbely and Szent-Györgyi produced evidence to show that the antiscorbutic activity of their pure hexuronic preparation was due to the acid itself and not to a contamination by some more potent substance. They considered therefore, that they had now demonstrated this fact, and that their experiments gave definite proof of the identity of hexuronic acid and Vitamin C.

At about this time as a result of the latest chemical analyses (Cox et al. 1932) (Karrer et al. 1933, Zurich) Szent-Györgyi, and Haworth of Birmingham (1933) agreed that this antiscorbutic substance, identical with Vitamin C and formerly known as hexuronic acid should be known henceforward as "Ascorbic Acid". In contrast to this mode of reasoning, the American Medical Association introduced the term "Cevitamic Acid" expressly to avoid the intentional connotation of antiscorbutic properties.

CHEMISTRY.

Two groups of workers, Reichstein, et al. in Switzerland, and Hirst and Haworth et al. in Birmingham

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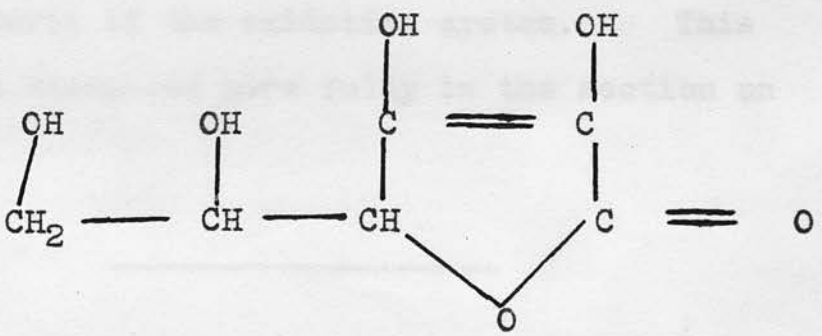
in 1933 almost simultaneously succeeded in the artificial manufacture of Vitamin C.

The following briefly indicate the steps required before the final product is achieved:-

d - galactose → d - galacturonic acid diacetone →
d - galachuronic acid → l - galactonolactone →
l - galactonamide → l - lyxose →
lyxose-phenylosazone → l - lyxosone →
(or l-xylosone) → ascorbic β - ketonitrile →
l - ascorbic acid.

Vitamin C, a carbohydrate derivative with a formula corresponding to $C_6H_8O_6$, is an odourless, white or yellowish-white crystalline powder with a melting point of 189°-192°C.

Its formula may be written thus:-



or a structural model showing the arrangement of the atoms in space, thus:-

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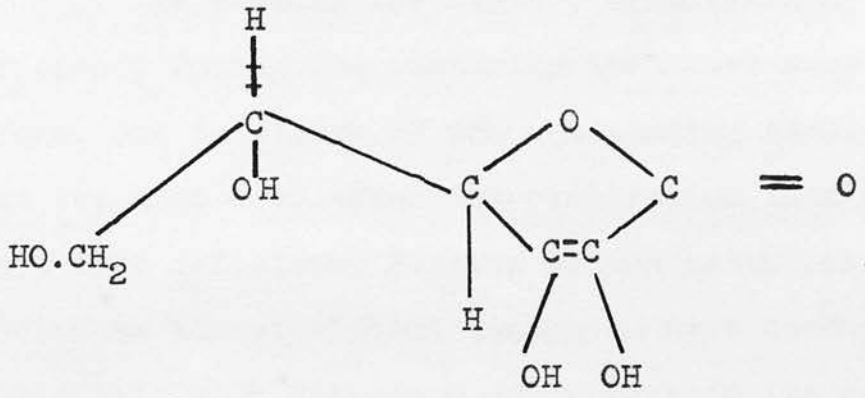

The Vitamin oxidises on exposure to air and light whereas in an inert atmosphere it is quite stable to moderate heat even in alkaline solution.

It has a high reducing property, which is all the more remarkable since the oxidation of the acid is reversible. It is by this reversible oxidizability that the substance probably exerts its biologic activity. It is oxidised and reduced alternately giving off and taking up two atoms of hydrogen thus acting as a hydrogen carrier between different parts of the oxidation system. This question is discussed more fully in the section on Physiology.

PHYSIOLOGY

of

VITAMIN C

In tracing the history of Vitamin C deficiency during the centuries that have gone before, one is struck by one outstanding fact. That is, that even after the realisation that scurvy was a food deficiency disease became established, all clinicians almost without exception were concerned exclusively with Vitamin C deficiency in its most gross form i.e. scurvy. Of recent years more and more attention has been turned to the undoubtedly numerous cases where the deficiency of Vitamin C is less apparent. At a later stage I shall attempt to enlarge upon this aspect of Vitamin C deficiency and stress the importance of its recognition and alleviation. To make these points clear a certain knowledge of the physiology of Vitamin C is most essential, and for the same reason an understanding of the morbid anatomy of the deficiency state is equally vital. For these reasons I shall describe at some length the more important features of these two studies as described by various independent investigators.

Origin and Physiological Function of Vitamin C.

No Vitamin C is to be found in dry seeds, but Fürst (1912) showed that it is produced during the

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germination of seeds, and gradually diminishes in quantity as the seeds ripen. All actively growing parts of the higher plants, all fresh green leaves, algae and even bacteria perhaps contain demonstrable quantities of the Vitamin. A feature of its distribution in plants is that it may occur in equally high concentrations in such diverse parts of the plant as the leaves, the fruit or the root.

Most animals derive their supplies of Vitamin C from the vegetable kingdom, but one commonly used experimental animal, the rat, is able to synthesize Vitamin C. Man, the primates, and guinea-pigs on the other hand, are quite unable to synthesize Vitamin C from the time of conception onwards. Modern evidence goes to show as a result of exhaustive investigation that the Vitamin can be recovered from practically all the tissues of the higher animals and it has been clearly demonstrated that the distribution of Vitamin C in the human being is closely similar to that in the most commonly used experimental animal for this work - the guinea-pig.

In general the concentration of the Vitamin appears to be more or less in direct proportion to the degree of metabolic activity of the particular tissue.

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Thus there is a higher concentration in the individual tissues of the growing child than in those of the adult. Speaking broadly, glandular tissue has the highest concentration, and muscle and stored fat the lowest, with heart, kidney and lungs intermediate. The falling scale for the Vitamin concentration of the various tissues is pituitary, corpus luteum, adrenal cortex, young thymus, pancreas, liver, brain, testes, ovaries, spleen, thyroid, submaxillary, lung, kidney, intestinal walls, heart, muscle, cerebro-spinal fluid and blood.

Using the Silver Nitrate staining reaction for Vitamin C, Gough and Zilva (1933) showed that the pituitary seemed to stain more constantly and intensively than the adrenals, confirming their relation in the above scale, but they went further and showed that in experimental animals and patients very often the adrenals did not stain at all though the subjects were entirely free from symptoms of scurvy.

However, to illustrate once again the general direct relation of concentration of the vitamin to the metabolic activity of the tissue, it has been shown that rapidly growing tumour tissue usually has a high content though this may decrease when necrosis takes place.

..... Supply

Supply of Vitamin C to Infant and Foetus.

Although Cimmino (1938) gives much lower figures, it is interesting to note that the Vitamin C content of human milk is four to five times that of cows' milk when one recalls that the human infant is solely dependent for its vitamin C supplies on its mother, whereas the calf can synthesize it. Thus the infants serum ascorbic acid titre follows that of the mother but has a higher absolute level approximating to that of the milk (Elenby and Christensen 1938).

As regards the foetus and its dependence upon the mother for its supply of Vitamin C, Neuweiler (1938) has shown that blood from the umbilical vein contains 0.1 mgm % more Vitamin C than that from the umbilical artery. Further the **uebro**-placental blood c ontains more than the cubital venous blood of the mother and an intravenous injection of Vitamin C may as much as double the content of the infants blood.

Excretion and Storage.

Excretion of Vitamin C in the urine is continuous, but when the intake ceases the rate of excretion decreases gradually and may finally fail to

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be excreted if the intake is withheld indefinitely.

Administration of Vitamin C to a body so depleted of its reserves results firstly in the restoration of the Vitamin in the various tissues, and secondly in the urinary excretion of the excess. This is a point of some importance and will be expanded at a later stage, for upon it are based the numerous clinical methods of estimating the state of Vitamin C nutrition or "saturation" of any particular subject.

Physiological Functions.

Thus far two specific rôles for Vitamin C in the tissues have been apparently well-established:

(1) The work of Wolbach and his associates (1926) has demonstrated how it regulates the colloidal condition of the intercellular substance or material of mesenchymal derivatives.

(2) Its second rôle is that of a respiratory function in serving as a "hydrogen transport agent between as yet unidentified metabolytes and other carriers of molecular oxygen, by way of two or more oxidase enzyme systems" (King 1936).

In its regulation of the physical state of intercellular substances it is closely associated

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with Calcium metabolism, while the growth and repair of bones, teeth, white fibro-cartilage and fibrous tissue is also clearly influenced by the Vitamin, as will be shown in the discussion on the Pathology of Vitamin C deficiency to follow.

In common with the other vitamins it is concerned with over-all growth of the body as well.

Where the anaemia which commonly accompanies Vitamin C deficiency state is concerned, the fault is believed to lie primarily in the dysfunctioning erythropoietic system rather than in increased haemolysis or faulty haemoglobin production. Mettier, Minot and Townsend (1930) came to the conclusion that Vitamin C can apparently therefore, have a specific effect on erythropoiesis when there has been a chronic lack of the Vitamin.

One of the most striking features of the effect of Vitamin C noted in animal experimental work is of great interest in connection with the work carried out in this particular inquiry. Workers noticed that when guinea-pigs were given diets free from Vitamin C, or diets with a low Vitamin C content, they showed impaired physiological function long before growth was restricted or the signs of scurvy

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appeared. As has been clearly demonstrated by numerous independent workers, this pre-scorbutic state, or state of mild Vitamin C deficiency is of common occurrence among the general population and has proved to be a field of investigation which on the whole has shown close agreement between the individual findings. (Abbasy et al. 1935).

The arteries, teeth and adrenals are especially sensitive to injury by toxins when the Vitamin C stores of the tissues are depleted. Hess (1932) although in agreement with the essential changes that may take place in cases of Vitamin C deficiency, casts doubt upon the very widespread American belief that dental caries is associated with Vitamin C deficiency of a mild type. His views will be referred to again in the section on Pathology.

Vitamin C and Serum Complement.

Marsh (1936) noted that the complement in guinea-pigs disappears or suffers reduction in titre when Vitamin C is withdrawn from the diet, and that it is restored to normal when the Vitamin is included in the diet. He found that these effects took place within seven days or less and therefore suggested

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that it might be the earliest sign of scurvy which in the guinea-pig only becomes manifest in 20-40 days and in man in 4-8 months.

At approximately the same time Horgan (1936) noted that in winter the titre of serum complement of guinea-pigs used for Wassermann Reactions became greatly reduced. In addition he observed that they very often bled to death after cardiac puncture and that they were killed off by epidemics of pneumonia. On investigation he found that they were getting no grass or other fresh green food, and upon his adding mangolds and cabbage to their diet their serum complement rose within seven days to normal titres and they rarely died of cardiac punctures.

More recently Ecker and his associates have shown that the normal activity of complement was dependent on its being present in the reduced state, this oxidation-reduction phenomenon being associated with the amount of Vitamin C in the blood plasma.

Finally, at the moment of writing, work on the relation of Vitamin C to serum complement and antibody formation is being carried out at Durban, Natal, but as yet no publication has been made.

In the consideration of the pathological changes attending the state of Vitamin C deficiency one is more especially concerned with the milder changes occurring and with the earliest changes that can be detected. However, for a full and proper understanding of these early and slight changes and their possible significance, it is necessary to have a comparatively comprehensive knowledge of the grosser morbid effects so that the undeniable earliest changes may be the better appreciated. Thus to illustrate the importance of these primary changes, one may recall how a few years ago the undergraduate was taught to search for and recognise the gross signs of carcinoma ventriculi which at that stage was usually inoperable. We have progressed beyond that crude stage now and efforts are unceasing in attempts to hunt for and interpret the earliest deviations from normality in the endeavour to bring about a cure. From this ideal it is but a short jump to the superior goal of complete prophylaxis. In a less dramatic, but no less important sense the same trend of thought applies to states of Vitamin C deficiency.

Thus the primary morphological effects of Vitamin C deprivation on the tissues occur in the

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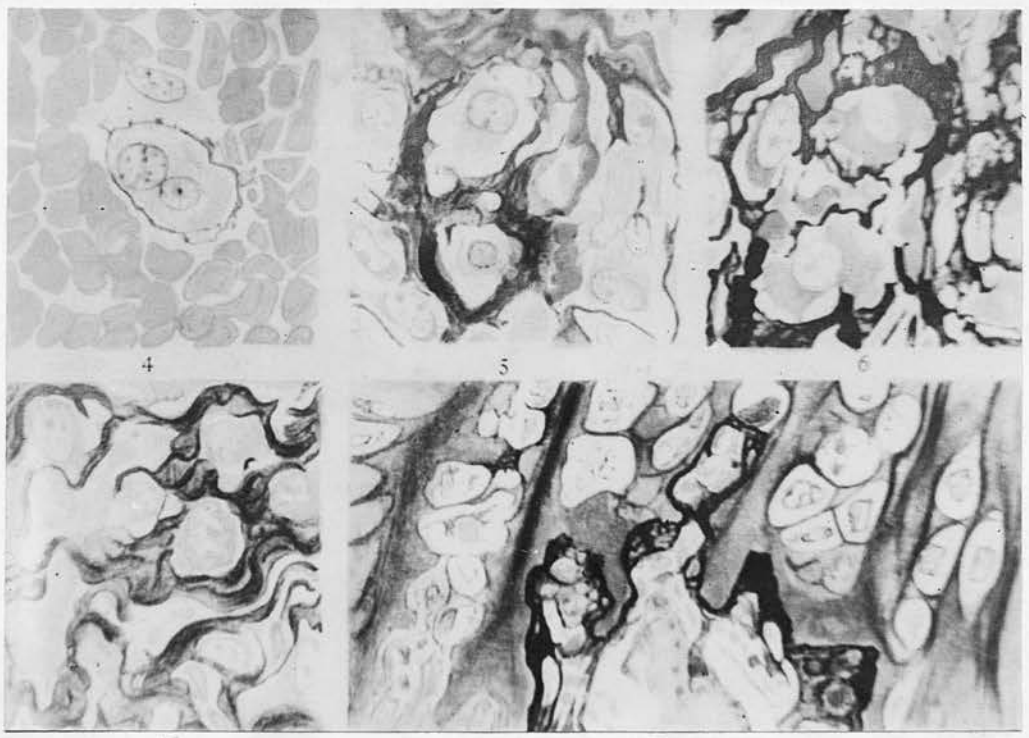

Fig.4. To show collagen in relation to an isolated cell deep within the blood clot.

Fig.5. A field from a group of cells deep within the clot, illustrating collagen deposited by cells that have penetrated fibrin strands.

Fig.6. Showing argyrophile fibrils and their distribution in relation to the cells, similar to that of the collagen.

Fig.7. To illustrate collagen formed by a cluster of cells during a 96 hour repair period.

Fig.8. To illustrate resumption of endochondral bone formation in rib, showing newly formed argyrophile fibrils in presence of homogeneous collagen representing the first stage in formation of the intercellular substance of bone.

Wolbach S.B.1933. Amer.J.Path.9 689.

intercellular substances of certain mesenchymal derivatives. These important changes can best be described in terms of loose connective tissue. Under normal conditions fibroblast cells lie in an amorphous ground substance within which fibrils or a reticulum are formed. These fibrils may become gathered together to form wavy bundles of collagen, and during this process the fibrils appear to become cemented together by a translucent matrix. It is this important stage in the formation of the intercellular cement substances that appear to be completely controlled by Vitamin C.

Thus Wolbach (1926) in his experimental work on guinea-pigs showed that in states of complete scorbutus formation of intercellular materials cannot take place, so that although the ground substance and fibroblasts are present as in health, fibrils and collagen are not. That the production of these important intercellular substances is closely associated with Vitamin C can be shown dramatically in the experimental animal where the production of collagenous substances in the scorbutic animal can be histologically demonstrated within eighteen hours

of the administration of a single dose of Vitamin C (Wolbach 1933).

These observations made on the experimental animal tally closely with the appearances noted in cases of spontaneous scurvy in man. Whether the Vitamin C directly affected the intercellular colloids or the fibroblasts was a point of some uncertainty but Wolbach (1933) was able to show very clearly that the reticulum of argyrophil fibres is always laid down in immediate proximity to the fibroblasts, quite some distance from blood vessels and pre-existing normal tissues.

Further, in the scorbutic experimental animal it is observed that in the process of repair capillaries do not penetrate the injured tissue for any marked distance and they are apparently unable to form new capillaries, although closed columns of endothelial cells accompanied by fibroblasts do form. Oedema may be present and it appears to be formed in vacuoles within the fibroblasts, which thus produce the extracellular fluid.

These defective intercellular materials can be demonstrated in the connective tissues, bones and teeth and are believed to occur in the blood

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vessels.

It must be stressed that in partial depletion there is a tendency for defective materials to be formed in connective tissue and that in complete deficiency of Vitamin C there is nothing of a substantial nature formed as intercellular substances. Further involution of the tissues cannot be studied because the animal dies.

Actual morphological changes in previously normal capillaries have not as yet been detected. That they do occur is a matter of conjecture at the present moment. However, bearing in mind the fact that the capillaries arise in embryonic connective tissue and knowing what we do of defective intercellular substances in Vitamin C deficiency, one cannot be surprised that they are affected and become more fragile than normally. Just where the weakness occurs is uncertain. Either the cement substance binding the living endothelial cells is at fault or the ensheathing connective tissue and collagenous fibres are defective.

The above passages review briefly the fundamental changes of a morbid character in Vitamin C deficiency and now the anatomical manifestations of

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the deficiency must be considered.

These manifestations are greatly modified by two factors, namely, growth and stress, and immediately their importance in childhood springs to the mind.

Thus growth so affects the clinical picture that for two centuries there was confusion of scurvy and rickets in children and infants and the term scurvy rickets was employed to describe the picture of scurvy complicated by marked bony changes. With decrease in the rate (of degree) of growth, haematomata become less frequent and bone pains gradually decrease in frequency with increase in age. For the same reasons of rapid growth, osteoporosis is most marked in children and is more pronounced in those regions where bony growth is more active. Thus the distribution and degree of severity of the lesions parallels those seen in rickets.

Stress modifies the site of the lesions and governs the degree of involvement of the neighbouring tissues. Thus the site of a haemorrhage is determined by the stress a vessel or vessels may suffer and in older times haemorrhages were seen classically in the shoulders of blacksmiths and in the calf and lumbo-sacral muscles of soldiers.

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These lesions may be modified by other factors such as the coincidence of infectious diseases such as tuberculosis, typhoid and lobar pneumonia and conditions associated with an increase in the metabolic rate. Mettier et al (1930) considered that arteriosclerosis may be a modifying or contributory factor as well.

Whether Vitamin C is directly connected with the phenomena of inflammation is uncertain, but there is evidence to show that there is some relationship to the production of the granular leucocytes or to the increased consumption of Vitamin C by the body in the production of leucocytes as in infections or in leukaemia.

Thus Cuttle (1938) noted that in leukaemia an excessive amount of Vitamin C could be absorbed and retained and that the amount of Vitamin C in the blood cells is increased. These abnormalities bore a direct relationship to the number of circulating leucocytes and he considered it possible that the leucocytes absorb a large amount of Vitamin C. Further, he found that in leukaemia whole blood contained more Vitamin C than the plasma, and the whole-blood Vitamin C fell below the plasma level coincidentally with the

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fall in the leucocyte count. Cuttle came to the conclusion therefore, that the increased requirements for Vitamin C in infections were probably due to the accompanying leucocytosis. This point will be further elaborated in the section devoted to Vitamin C and its relation to disease.

The essential lesions in various structures are briefly described below.

Thus in bones growth ceases and the osseous shell becomes rarefied and widened. The normal junction between diaphysis and epiphysis is replaced by a zone of collagen-poor connective tissue in which are embedded fragments of densely calcified cartilage matrix devoid of osteoid tissue. This zone is commonly spoken of as the "gerüstmark" so characteristic radiologically.

The periosteum may show weakening of its attachments to the bone and where muscular attachments are present there is proliferation of the connective tissue cells in a violent attempt to reinforce the insertion or origin. Under the additional factor of stress haemorrhages may complicate the picture.

In the teeth, the dentine becomes resorbed and porotic, the process commencing with the widening

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of the Tomes canals. The odontoblasts involute and revert to a state indistinguishable from the connective tissue cells of the pulp, and the tooth becomes replaced by a bone-like material, osteo-dentine, which is surrounded by a thin shell of pre-existing dentine. This is the picture in states of extreme deficiency but the various stages are so regular and characteristic that they are mentioned as they illustrate the basis of the Höjer "tooth" method of assessing the degree of Vitamin C deficiency in the experimental animal. The growth of the tooth is also characteristically affected and this knowledge is made use of in the Dalldorf and Zall method for assessing Vitamin C saturation.

The changes in the gums, the haemorrhages into muscles, ecchymoses of the eyelids, characteristic peri-follicular or petechial haemorrhages of the skin, serous effusions, and slight oedema of the ankles are too well-known to be described in detail. Of some importance is the possible enlargement of the heart to which Höjer ascribed the early weakness occurring in scurvy.

Atrophy of the bone-marrow takes place with a resulting anaemia and corresponding reduction of haemoglobin, the picture suggesting a relative aplasia

of the bone marrow, an appearance which Piney confirms (1928). The bone marrow picture is that of a secondary anaemia and after treatment with Vitamin C alone there is marked reactivity of the bone marrow with mitotic figures and increased numbers of nucleated erythrocytes. The reticulocyte response occurs on the 3rd day and reaches its peak on the 8th day (Dry 1933).

The adrenals atrophy as the cortical fat is absorbed during the loss of Vitamin C in the advanced stages of scurvy and this can be clearly shown by staining the split adrenals with a solution of silver nitrate (Bessey, Menten and King 1934). Finally, there is also some atrophy of the lymphoid tissue, salivary glands, kidneys and liver.

Changes in the Central Nervous System are rare and slight. Meyer and McCormick (1928) have described a degeneration of the peripheral nerves and large anterior torn cells, and Hess (1917) (1918) described evidence of vagal disorder in children. Stewart (1925) emphasized the sign of reduction or absence of the knee-jerks as being of importance as an index of nerve lesions.

In this attempt to present a compact yet

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not too detailed a picture of the morbid anatomy of Vitamin C deficiency, it may again be pointed out that although most of the changes are indicative of gross vitamin deficiency lesser changes which can not be demonstrated may be present in cases of less extreme deficiency and will thus betoken a deviation from the normal, which may be manifested in the form of impaired physiological function which investigators have noted in experimental animals.

VITAMIN "C" DEFICIENCY

and its

RELATION TO DISEASE

Ever since the isolation and identification, and later, the synthesis of Vitamin C was accomplished, interest in its possible relation to disease apart from pure deficiency states has been maintained at a high level. As a result of this a great deal of work has been done in attempting to find out what bearing various degrees of Vitamin C deficiency might have on different unrelated diseases.

Thus from the earliest times it has been known that persons suffering from varying degrees of scurvy were especially prone to suffer from infections.

On the other hand it is equally true that very often scurvy itself is precipitated by an intercurrent infection. In striking illustration of this fact Lind (1919) reported how in an institution where there had been no change in the diet for years, an epidemic of a mild febrile illness led to an outbreak of scurvy of epidemic proportions.

In an attempt to determine whether in infectious conditions there was actual depletion of Vitamin C from the body tissues of the infected organism, Harris, Passmore and Pagel (1937) examined the livers and suprarenals of guinea-pigs on standardised diets.

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They found that in acute infections there was a considerable diminution in the amount of Vitamin C present in the suprarenals as compared with controls on the same dietary intake of Vitamin C. In more chronic infections they noted there was a similar though less marked fall in the content of Vitamin C of both adrenals and liver.

Zook and Sharpless (1938) by using artificial fever on guinea-pigs confirmed these findings by showing that fever increases the requirements and accelerates the destruction of Vitamin C.

Turning their attention to the human subject, Abbasy, Harris and Hill (1937) in examining a series of cases of osteomyelitis, noted that in common with other infectious conditions there was a diminished rate of excretion of Vitamin C in the urine and other indications of an apparently increased usage of the vitamin during the infective process. It was noted too, that half-healed cases were intermediate and healed cases were normal in respect of Vitamin C storage, thus providing an interesting comparison with cases of rheumatic fever to be described below. They made the interesting observation, illustrating again how infections cause depletion of tissue Vitamin C,

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that in the series they examined, mild intercurrent diseases such as upper respiratory tract infections and pyrexia caused an immediate and concurrent drop in the urinary output of Vitamin C.

Schroeder and Hande (1935) and Rothstein and Rotish (1935) also showed that Vitamin C is used up more rapidly during fever and considered therefore that ample supplies are indicated during fever and convalescence.

Impressed by certain circumstances common to Vitamin C deficiency states and rheumatic fever, Rhinehart (1936) made various studies of the relationship of Vitamin C deficiency to this condition.

In his experimental work upon guinea-pigs, he found that if their diet was satisfactory in regard to Vitamin C, no heart or joint lesions developed following upon injections of streptococci.

However, if the diet of these inoculated guinea-pigs was scorbutic in character, the changes found were simply an accentuation of what is found in the heart and joints of guinea-pigs on a deficient diet without infection, that is, infection merely intensified the effects of Vitamin C depletion. Further, he found that this bacterial factor is not specific.

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Sendray and Schultz (1936) working independently of Rhinehart, followed the urinary excretion of Vitamin C in a group of cases of rheumatic fever and failed to detect any connection with Vitamin C deficiency and the aetiology of rheumatic fever. However, in contrast to these emphatic conclusions Abbasy, Hill and Harris (1936) decided that in rheumatic fever treatment with Vitamin C in large amounts is of therapeutic and prophylactic value. They examined a large series of children at Queen Mary's Hospital for Children, Carshalton, Surrey, and found that cases of active rheumatic fever showed marked evidence of Vitamin C deficiency as judged by the urinary excretion, whereas convalescent cases showed a milder yet definite state of deficiency. Control cases on the same diet showed a normal state of Vitamin C nutrition. They concluded on these grounds, therefore, that there must be an increased need or destruction of Vitamin C in rheumatic fever as the diets of the cases examined contained an adequate amount of Vitamin C. Finally, they considered that in cases of convalescent and latent rheumatic fever on normal diets, evidence of Vitamin C deficiency might be used as a prognostic point of some significance and a supplementary criterion of diagnosis

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respectively.

In going further into these studies of rheumatic fever and Vitamin C, Schultz (1936) examined the effects of Vitamin C therapy in cases of rheumatic fever. His conclusions as to the value of Vitamin C were not as optimistic as those of Abbasy et al. He took two comparable groups of rheumatic children, and while one group received daily doses of Vitamin C he observed the two groups at intervals during the late winter and early spring.

He found that in the treated group a state of mild Vitamin C deficiency was prevented whereas it was not in the untreated group. But, and here was the important point, in neither group was the incidence of active rheumatic fever favourably affected either by medication with Vitamin C or not.

Over periods of several months and with larger doses of Vitamin C by mouth and by the intravenous route, he found that the clinical manifestations of acute rheumatism were not demonstrably affected. He thus came to the conclusion that Vitamin C deficiency is not a necessary factor in the aetiology of rheumatic fever, but passes no comment upon the advisability of alleviating the state of Vitamin C deficiency in active rheumatic

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fever as Abbasy et al. advise.

In further studies of Vitamin C and its relationship to infection, Abbasy, Harris and Ellman (1937) examined the Vitamin C nutritional states of cases of pulmonary tuberculosis. They found that in in-patients the Vitamin C deficit is quite extreme as compared with controls on a similar diet. Further it was observed that there was a fairly constant correlation between the severity of the disease as assessed by the usual clinical standards including the blood sedimentation rate, and the degree of Vitamin C nutrition. Thus they suggested that Vitamin C should be administered in cases of pulmonary tuberculosis to eliminate conditions of Vitamin C deficiency. Their deductions are open to some criticism however, because the blood sedimentation rate, upon which they base a good deal of their judgment, has been shown by Heise et al (1937) to be reduced very frequently in cases of tuberculosis treated with large doses of Vitamin C, and this guide to progress may be a false criterion when Vitamin C is being exhibited.

Furthermore at a conference on Vitamin C held at Darmstadt, Professor Stepp of Breslau (1934)

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reported that the injection of Vitamin C daily for several days resulted in a definite increase in the amount of plasma albumin and so brought about a significant lowering of the blood sedimentation rate. However, in support of their contention of the value of Vitamin C therapy, Weber (1938) claimed that he had obtained satisfactory results by administering Vitamin C to his pulmonary tuberculosis patients.

It has long been known that in patients with severer degrees of Vitamin C deficiency wound healing takes place slowly and badly, and the previously described fundamental pathological changes as recorded by Wolbach give the morphological explanation for this being so. In Hess' words, in such cases of Vitamin C deficiency, the wounds "assume a haemorrhagic aspect, the edges becoming blue or livid and showing no tendency to heal; even scars which have existed for many years change in colour and show an altered state of nutrition and ulcers long-healed break out afresh."

Lanman and Ingalls (1937) suggested that Vitamin C deficiency in man, even when it is partial may be one of the major causative factors in the cases of wounds breaking down where there is no

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evidence of infection of the wounds and where the patient had been on an inadequate dietary regime. In connection with this it is interesting to record the observation of Dry (1933) who, in an outbreak of scurvy among Rhodesian native railway employees, noted that there was marked delay in wound healing which speeded up noticeably after treatment with Vitamin C.

In 1938 Taffel and Harvey in their experiments, found that their results confirmed the beliefs of Lanman and Ingalls, and Lauber and Rosenfeld (1938) found that the granulation tissue of animals receiving an adequate Vitamin C intake contained Vitamin C, whereas if the animal had been on a deficient diet no Vitamin C could be demonstrated in experimentally produced granulating wounds. They noted too, that healing took place much more quickly where the diet had been adequate.

Much of the work done on wound healing as related to Vitamin C deficiency is applicable to the ever-present attempt to elucidate the aetiological factors taking part in the problem of peptic ulceration.

Thus MacCarrison (1921), Magee, Anderson

and McCallum (1929) Smith and McConkey (1933) had shown in their experimental work that Vitamin C deficiency states in animals predisposed to peptic ulceration.

In a survey of hospital patients, Harris Abbasy, Yudkin and Kelly (1936) noted that a large number of their series with evidence of Vitamin C deficiency were cases of Gastric and Duodenal ulceration - that is out of 74 patients examined 19 were deficient and had Gastric or Duodenal ulcer, the total percentage of deficient cases being 84%. Kelly in Manchester in a similar survey, noted that in eight patients with peptic ulcer, the institution of routine treatment rapidly brought about a Vitamin C deficient state in the patients. Archer and Graham (1936) in their investigations found that six out of nine patients with peptic ulcer had definite degrees of Vitamin C deficiency and they were so impressed with this correlation of ulceration and hypovitaminosis with the certain knowledge that the usual diet of milk, cream, eggs, bread and butter was most lacking in Vitamin C that they advocated the use of adequate quantities of Vitamin C in the treatment of peptic ulceration.

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In support of these findings Ingalls and Warren, using different methods of estimating Vitamin C nutrition, found in twenty (20) patients with peptic ulcer, eighteen or 90 per cent of them showed deficient Vitamin C nutrition. However, in spite of these striking figures they raised the query as to whether so common a condition as Vitamin C deficiency could be entirely responsible.

Stimulated by these reports Portray and Wilkinson (1938) investigated 107 cases, 51 control subjects, 25 cases of peptic ulceration and 31 of haematemesis. Their findings are of great weight and interest for they employed no less than six different tests in each subject to determine the state of their Vitamin C nutrition. They were satisfied that they had shown by these methods that patients with peptic ulcers and haematemesis suffered from a severe degree of Vitamin C deficiency, and on these findings they too advocated the use of large doses of Vitamin C in treatment.

In the same year Bourne (1938) carried out a similar investigation using the indirect method of Göthlin to assess the degree of Vitamin C nutrition. He observed that hospital patients on a dietary regimen for peptic ulceration showed a degree of Vitamin C nutrition significantly inferior to that

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of the control subjects. He also considered that their degree of deficiency bore a fairly definite relationship to the inadequacy of their Vitamin C intake as judged from their dietary histories.

However, Bourne a after his investigations concluded that he could find no satisfactory evidence that the development of peptic ulcer was conditioned by an inadequate moiety of Vitamin C in the daily diet, in spite of the significantly frequent coincidence of ulceration and Vitamin C deficiency. Rao (1938) came to the same conclusion - Vitamin C deficiency is not related to peptic ulcer as a causative or contributory factor.

At this stage a word is necessary about the relationship of Vitamin C deficiency to dental caries. As a result of the work of Hanke (1933) and numerous others the view was commonly held, in America mainly, that Vitamin C deficiency was a causative factor in dental caries, but Hess cast doubt upon this prevalent view. However Dry (1933) made the very striking observation that in cases of frank scurvy among Rhodesian natives, renowned for the excellence of their teeth in common with most pure native races, dental caries was most common. The possible explanation in this case however, was that although natives usually have perfect teeth, this particular group had seen fit to improve on their

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heritage by filing their teeth to sharp points, a measure hardly calculated to be a prophylactic one where dental caries is concerned!

Finally, Sandberg and Dagulf (1939) in Norway, came to the conclusion from their investigations that they had failed to show that Vitamin C is a factor of importance in dental caries.

The foregoing is but a brief review of the work which has been done on this aspect of Vitamin C deficiency, and although most of the results of different investigators are inconclusive and often conflicting it would be rash to dismiss the findings up to date as being of no value and importance without further and more prolonged investigation, if only for the reason that a state of Vitamin C deficiency, no matter of what degree, represents a deviation from the normal and so, on general principles, requires correction.

It will be noted too, that in this Chapter, no mention of scurvy itself as a result of Vitamin C deficiency has been made. This omission is deliberate as the association between the two is historic and in this investigation I have confined myself to a consideration of the less gross forms of Vitamin C

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deficiency, a definition and discussion of which will follow a little later.

To complete the picture of this aspect of Vitamin C, a brief account of its possible and alleged beneficial effects in disease is appended below.

V I T A M I N "C"

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T H E R A P Y.

A variety of conditions favourably influenced by the use of Vitamin C has been reported and additional ones described periodically. However, it is hardly necessary to state that many of these observations may not be substantiated by further experience and investigation.

Thus at a conference on Vitamin C held at Darmstadt in April 1934 it was reported by various independent workers that administration of Vitamin C had favourably influenced such diverse conditions as dysentery, leukaemia, peritonitis, diptheria, haemorrhagic nephritis, acute infections of the respiratory tract, pyuria in children, ununited fractures, and certain forms of pigmentation of the skin. It can be said at the outset that the majority of these conclusions were based upon investigations carried out on very small numbers of cases, in many cases inadequately controlled. However, in view of what has been said in relation to infection and Vitamin C in the foregoing chapter, it is interesting to note how many of these conditions have that factor in common - namely bacterial invasion.

In regard to pigmentation there is no con-

clusive evidence of Vitamin C being beneficial. Thus Morowitz (1934), aware of the fact that patients with Addison's Disease showed a decrease in pigmentation when treated with adrenal cortical preparations by mouth, tried the effect of Vitamin C therapy on a case of chloasma-like pigmentation where scurvy supervened as a result of a diet devoid of Vitamin C. He was successful in curing both the scurvy and the pigmentation and argued that since Vitamin C is present in a high concentration in the adrenals there must be some relationship between this type of pigmentation and Vitamin C deficiency.

Wilkinson and Ashford (1936) found distinct Vitamin C deficiency in three cases of Addison's disease. After administration of large test doses of Vitamin C and cessation of therapy, they found that the degree of Vitamin C subnutrition paralleled the severity of the disease in the three cases. They too argued the normal high Vitamin content of the adrenals might be concerned with the regulation of the skin pigmentation. However, no change in the degree of pigmentation during intensive oral administration

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of Vitamin C occurred, but after the discharge, the pigmentation decreased under treatment with a high Vitamin C diet and intramuscular injections of cortical extracts. They could not decide whether the improvement in the pigmentation was due to the Vitamin C or the adrenal cortex. It should be pointed out, however, in this connection of the probable effects of Vitamin C therapy on pigmentation of this description that pigmentation rarely, if ever, occurs in even the grossest cases of scurvy where there is a most severe depletion of the tissue Vitamin C including that of the adrenals.

The reported value of Vitamin C therapy in bleeding diseases such as Thrombocytopenic purpura haemorrhagica and haemophilia and the isolated cases of 'haemorrhagic nephritis' is extremely doubtful. The cases reported upon were few and uncontrolled and in the case of purpura haemorrhagica the investigators ignored the significance of the well-known spontaneous remissions that occur.

Of some interest, however, is the single case of paroxysmal haemoglobinuria reported by Armentano (1936). This case proved to be highly deficient in Vitamin C and therapy with Vitamin C

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intravenously for several days caused the condition to disappear. He went further and demonstrated in vitro that Vitamin C conferred protection upon the red blood corpuscles. Nevertheless, in this case too, the same objections, based on spontaneous remissions taking place, apply.

The effect of Vitamin C therapy on the stimulation of specific antibody production was studied by Jusatz (1937). He demonstrated that massive doses of Vitamin C injected intravenously clearly increased antibody synthesis in rabbits. Vitamin C given orally was valueless. The observations made on the relation of Vitamin C to the serum complement titre by Marsh (1936) and Horgan (1936) are interesting in this respect, especially in view of the earlier work done by Otto (1936) on the treatment of diptheria and Vitamin C. In 92 cases all were treated with serum but 42 had additional Vitamin C therapy and 50 were used as controls. His results failed to show that Vitamin C had any effect on the condition as regarded the time of disappearance of the diphtheritic membrane and the temperature. It failed to influence the number of complications and fatalities as well, but it did

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on the disease. In experimental work on guinea-pigs, Heise and Martins (1936) gave 5 of them a stock diet and 5 a diet very deficient in Vitamin C. Both sets were inoculated with tubercle bacilli and after being killed showed little or no appreciable difference, thus providing the conclusion that there was no experimental support for the belief that excessive Vitamin C therapy in tuberculosis is of benefit.

The results of investigations into the relation of Vitamin C deficiency and carbohydrate tolerance have provided an interesting study, which further trial may prove to be of practical value.

Thus, working on the knowledge that a great many people existing on ordinary diets have an unsatisfactory state of Vitamin C nutrition, Pfleger and Scholl (1937) found that diabetics being treated with insulin excreted much less sugar in the urine when the Vitamin C nutrition was restored to normal so that the insulin therapy could be reduced by 10-20 units in many cases. Curiously, in mild cases receiving no insulin, the degree of glycosuria was not reduced by increasing

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the Vitamin C nutrition or "saturation".

Investigations carried out in healthy subjects showed the same relation of Vitamin C to insulin. Another interesting point was that where no insulin was being given, but aceto-acetic acid was being excreted in the urine, "saturation" of the subject with Vitamin C led to a reduction of the acetonuria.

Pfleger and Scholl suggested that the action of Vitamin C is due to an increased capacity on the part of the liver to store glycogen and went further to state that all diabetics should be investigated as to the state of their Vitamin C nutrition or that any possible deficiency should be prevented by ensuring an adequate daily intake of Vitamin C.

Bartelheimer (1938) publishing his results of investigations into the Vitamin C nutrition of 30 cases of diabetes mellitus a year later came to the same conclusion i.e. that Vitamin C increases the capacity of the liver for glycogen storage.

Hetenyi (1935) considering the anti-haemorrhagic effects of Vitamin C in its relation to capillary fragility, tried the effect of

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Vitamin C therapy in 7 cases of ulcerative colitis. He was encouraged to try this therapy as dietary histories of these patients suggested that their Vitamin C nutrition was significantly poor, and his results were very encouraging as there was a rapid disappearance of blood and mucus from the stools and great improvement in the general condition. Unfortunately he does not report on their further progress and whether they relapsed or not. Another successful case was reported by Gaehtgens (1937) during his work on Vitamin C deficiency in pregnancy and lactation. In conjunction with Werner (1937) he found that 62% of primigravida were deficient in Vitamin C and that 70% of those who were multipara were deficient. They did not consider that lactation per se increased the Vitamin C requirements, and noted too that a pre-existing Vitamin C deficiency was not accentuated during lactation. They did not state whether these deficient states benefited or not by Vitamin C therapy, save where there was evidence of gastro-intestinal disorder.

In this respect of Vitamin C deficiency in pregnancy, Jaroschka (1938) took the rather

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extreme view that it was a common cause of abortion and prematurity. He found that administration of Vitamin C by mouth to premature children or by injection to the mother is followed by an increase in weight in the infant which is quite striking. He concluded, also, that the mortality of premature infants is appreciably diminished by treatment with Vitamin.

Lastly in connection with pregnancy, Doxiades (1939) reported that in hyperemesis gravidarum 14 cases were successfully treated with repeated orally, intramuscularly and intravenously administered Vitamin C in large doses.

Passing from this condition to severer cases where there is liver damage, Tohaku (1938) working on the assumption that Vitamin C has a great stimulant effect on the formation of glycogen in the liver (cf. note on diabetes above) found that treatment of liver damage e.g. by phosphorus or chloroform poisoning, is best by means of glucose and Vitamin C.

Abbasy (1937) claimed a specific diuretic effect for Vitamin C in human beings and considered its possible clinical applications. He suggested that it might be of use where a mild diuretic or a slow and progressive dehydration is desired. Lueg

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and Hamman (1939) reported that the vitamin had a marked adjuvant effect in the treatment of cardio-vascular disease with diuretics and the digitalis series. They noted that in decompensated cases with oedema little improvement with Vitamin C alone was obtained and that the administration of digitalis or mercurial diuretics did not act effectively. However, a combination of these methods did produce good results.

Where the diuretic factor alone is to be considered, my own results are quite different from those of Abbasy and this point will be discussed at greater length below.

The value of Vitamin C in treatment has been claimed for such diverse conditions as carditis, carcinoma, gout, anaesthesia and others too numerous to mention. Some of the more important have been briefly reviewed and commented upon to illustrate the possible importance of ensuring a normal state of Vitamin C nutrition.

VITAMIN "C" SUBNUTRITION

and its value as an

INDEX OF MALNUTRITION

In the field of nutrition, numerous methods for the determination of Vitamin C deficiency have been evolved, that is, methods for determining whether the patient is "saturated" with Vitamin C or not, for between those cases which have an adequate Vitamin C intake and the palpable scorbutics who are severely deficient in Vitamin C, there is a large group of cases which are markedly deficient in Vitamin C yet frequently asymptomatic.

Of recent years therefore, we have come to concern ourselves less with the occasional isolated cases of manifest scurvy, which are usually easily recognised, and have directed our attention to the undoubtedly numerous cases of ill-defined Vitamin C deficiency for which numerous terms have been suggested e.g. sub-clinical scurvy, subscorbutus, latent scurvy, the praescorbutic state etc., all of which are best grouped together under the term "Vitamin C subnutrition" or "Vitamin C deficiency."

It is to this group of "silent" Vitamin C deficiency states that so much attention has been directed by various workers of late. Their investigations have gone to show how frequently such cases of Vitamin C subnutrition are associated with

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ill-balanced and inadequate dietaries in both children and adults, particularly those who are so frequently and vaguely described as suffering from malnutrition.

The criteria of "saturation" have been ascertained and numerous independent workers have been encouraged to find how close is the agreement between their separate findings (Abbasy et al.1935) though Hess (1932) did not agree with Göthlin's criteria which are described at a later stage.

Some of these methods, to be enumerated below, and which are definitely established apply both to manifest and to latent avitaminosis C. In accordance with the ideals of present day preventive medicine, the search has proceeded for methods which would detect the earliest manifestations of Vitamin C deficiency - that is long before the comparatively gross clinical signs of scurvy appear. One has only to reflect on the morphological changes occurring in Vitamin C deficiency states - "a failure of the integrity of the epithelium of the blood vessels" (Hess 1921) "due to a lesion of the endothelial cells or their cement substance" (Wolbach and Howe 1926) to realise the possible implications of such a state going unrecognised and unchecked.

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After work commencing as far back as 1914 (Hess), Göthlin (1931) went into the possibility of discovering milder deficiencies in Vitamin C nutrition, that is a deficiency "such as lies between the smallest deviation from a normal Vitamin C level and the highest deviation possible without giving rise to actual symptoms of the disease" (Göthlin 1931). When I come to discuss his methods one will realise that even this ideal is open to criticism as his method still leaves undetected, according to other investigators, a large group of deficient cases. (Hess 1932); (Meyer 1923); (Öhrell 1928).

From what has been said in the chapters on the relation of Vitamin C deficiency to disease, and its use in therapy, and from what will be described below in the chapter on Vitamin C and human requirements it will be strikingly obvious how common and how widespread these deficiency states are. In connection with this feature I would like to quote at some length from Abbasy, Yudkin and Kelly's paper (1936).

"Since so many individuals in certain sections of the population are found to be below the

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reputed standard in their Vitamin C intake and yet may seem little the worse for it - superficially at any rate - critics may perhaps argue that the accepted standard is unnecessarily high. We think, however, that it would be a mistake to rush to this conclusion too hastily. A comparison may justly be made here with the accepted standard for the intake of iron and with the prevalence of "subclinical" nutritional anaemia. Laboratory tests have shown that a large proportion of subjects in poor-class districts may show some degree of nutritional anaemia compared with the accepted standards. Such individuals may exhibit no clear-cut symptoms of illness, yet when extra iron is provided their general health and fitness improves, as evidenced for example by their diminished morbidity rate. A similar state of affairs may well be true of Vitamin C and indeed many suggestions have been made in the clinical literature in the past that a state of latent or subclinical scurvy is not uncommon."

Thus in the same publication, Harris et al (1936) reported that in a group of hospital patients, medical and surgical, which they examined, no less than 84 per cent of the total proved to be deficient

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in Vitamin C nutrition. As will be shown below my investigations into a similar but much larger group tend to confirm these figures. Their results obtained from 30 children showed a similar high proportion of deficiency states as revealed by a diminished urinary excretion of Vitamin C. These results confirmed preliminary conclusions on children reached at three other centres - London, Birmingham, and at Manchester (Kelly).

These same workers considered that they had shown that the daily output of Vitamin C (which is used as an index of the Vitamin C nutrition of the individual) is governed by the past dietary intake of the subject and that contrary to some supposition there is little individual variation between different subjects or between subjects on different basal diets. My investigations into a group of 63 children on a standard common diet do not bear this contention out by any means however.

The figures which these workers (Harris et al) give, nevertheless, suggest that the intake of Vitamin C of this class of the population (lower working classes) is generally below the reputed optimum as it is also below that of normal subjects, usually middle-class,

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who have been examined in earlier tests in England, Holland, Germany and the United States of America.

Their findings were in keeping with the conclusions which they had based on a study of the diet sheets, namely that about half the population (England) receives less than its reputed optimum allowance of Vitamin C.

Göthlin (1931) found varying degrees of Vitamin C deficiency ranging from 6-20 per cent of the population of children in various localities, and on inquiring into their diets discovered inadequacy of antiscorbutic foodstuffs in their daily intake.

Dalldorf (1933) using a similar method of investigation in a group of children from poor homes found the incidence of subclinical forms of scurvy to range from 35-66 per cent.

Other significant reports of Vitamin C deficiency states of the subclinical or latent type come from Dalldorf (1933); Nordenmark (1934); Schultzer (1934); Gedda (1932); Ross (1931) and Molitch (1935). The greater number of these cases responded immediately to therapy with antiscorbutic foods, showing that the disorder was primarily due

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to a specific form of malnutrition (King 1936). However, in connection with this latter fact, it must be pointed out that the Vitamin C deficiency may not necessarily be due to an inadequate intake. Thus in addition to those cases where there is an increased demand for Vitamin C as in infection, and those where there is an idiosyncrasy for Vitamin C-rich foods, there is a rare group of cases which appear to be unable to utilize the Vitamin C ingested, which would normally be quite adequate. Wright and Lilienfeld (1936) advance the following possible explanations:-

(1) Anacidity or imbalance of the gastric secretion. In connection with this theory it is interesting to consider the in vitro experiments of Mahlo (1936). He showed that the normal gastric mucosa is able to absorb Vitamin C and to protect it against oxidation by ferments. The mucosa serves as a protective colloid for Vitamin C, and subacid and anacid gastric mucosae although they are able to adsorb Vitamin C are unable to prevent oxidation taking place. The same worker in conjunction with Mulli (Mahlo and Mulli 1936) showed that oxidation of the Vitamin C is brought

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about by a specific peroxidase in the stomach contents, which is inhibited by normal gastric juice. Their observations supported those of Schroeder and Einhauser (1936) namely, that normal gastric mucosa contains a ferment which prevents the oxidation and destruction of Vitamin C and possesses qualities which protect Vitamin C against oxidation. In cases of achylia gastrica, carcinoma ventriculi, pernicious anaemia etc., the gastric mucosa lacks these qualities and Vitamin C is destroyed so that an adequate quantity is ingested but never assimilated.

(2) Bacterial destruction of Vitamin C in upper intestinal tract. Again, here the experiments of Stepp and Schroeder (1935) are of interest for they showed that pathological flora in the upper small intestine can decrease or prevent the absorption of Vitamin C and can thus perforce increase the Vitamin C requirements above the normal intake.

(3) Inflammatory changes in the intestinal mucous membrane.

(4) Accelerated action of the intestinal tract due to a variety of causes including the abuse of laxatives.

(5) Use of oily laxatives which may hold

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the Vitamin C and prevent absorption.

(6) Changes which take place after absorption and render the Vitamin C inert. Some of these explanations may be applicable to those reported cases where intensive treatment with Vitamin C per os was unavailing yet completely effective when given parenterally.

The first morbid effect of a relatively slight deficiency in Vitamin C nutrition is an increase in the capillary fragility and the appearance of petechiae (Hess, Göthlin, Dalldorf). Lind considered that the appearance of petechiae was the most constant symptom of all and that it occurred in the mildest cases. Recent work tends to confirm this view, though a comparative study of the blood-plasma levels of Vitamin C by various investigators would suggest that there is quite a wide gap in the scale of Vitamin C deficiency which remains undetected by this indirect means of assessing the degree of saturation with Vitamin C.

The increase in capillary fragility as evidenced by the appearance of petechiae may be preceded by a prodromal period of lassitude, weakness and irritability. Then petechiae of the skin, nose and other cavities appear and are the

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first morbid expression of Vitamin C deficiency and are related to what is known now as the state of sub-clinical scurvy. Estimation of the blood Vitamin C concentration shows a very significant fall in the daily urinary excretion which decreases and fails to rise sharply after the injection of a test done of Vitamin C.

Thus the state of subclinical scurvy appears to be a definite pathological condition although the deviation from health is slight. However, it may be reasonably concluded that the anatomical effects of Vitamin C deficiency are very prompt in occurring, especially in the young, and that they occur if we include these vascular changes in the mildest states of deficiency (Dalldorf 1938).

As we have seen that clinical reports agree that subclinical scurvy, judged either by direct chemical tests or by the indirect method of measuring capillary fragility, is common, it can be assumed that the morphological stigmata due to the same deficiency are likewise common. These changes represent a deviation from normality and as such, on general principles require correction.

VITAMIN C

REQUIREMENTS.

After the use by Tillmanns (1928) of a dye 2:6: Dichlorophenolindophenol as an indicator to distinguish between fresh and stale fruits and vegetables, and later recognition of its close relationship to Vitamin C for which it is practically a specific indicator, much work was done to employ this dye in chemical tests for the estimation of Vitamin C in body fluids and tissues. Following the perfection by Harris, Ray and Ward (1933) of Tillmanns' 2:6 Dichlorophenolindophenol method, investigators were provided with a relatively simple test with whose assistance they could proceed by means of surveys to estimate what the human requirements of Vitamin C are.

The standards of Vitamin C nutrition or saturation were based mainly on the daily urinary excretion of Vitamin C and the response to test doses of the vitamin, and on the levels of Vitamin C in the blood. Later, attempts were made to correlate these findings with Vitamin C concentrations in the cerebro-spinal fluid, and throughout this period workers have endeavoured to show a relationship between the standards of the direct dye tests and the standards of the indirect capillary fragility

..... test

test with varying success and somewhat conflicting conclusions.

Before the various methods of estimating Vitamin C nutrition are discussed some mention of the Vitamin C requirements of man is necessary and also some description of the work done to determine these standards and figures.

In 1933, Harris, Ray and Ward, investigating the excretion of Vitamin C in the urine and its dependence on the dietary intake, noted that in normal individuals the amount of Vitamin C excreted in the urine was surprisingly constant and generally in the neighbourhood of 30-33 mgm. per day.

They found that a normal individual after a single large dose of Vitamin C e.g. 600 cc. of orange juice, showed a sharp rise in the concentration of the urinary Vitamin C reaching a maximum in about three hours, 8 or 10 times the normal concentration. The concentration then rapidly falls and within a day or two reaches normal levels again where it remains remarkably steady even if the individual is kept on a restricted Vitamin C diet for a week or two.

They concluded that this apparent normal daily output of 33 mgm Vitamin C was in excess of

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the reputed minimum daily requirement for man which had long been held to be one ounce of orange or lemon juice i.e. approximately 20 mgm. Vitamin C.

Their most important conclusion however was that they considered their technique i.e. titration of the urine against the dye 2:6 Dichlorophenol-indophenol, might have possible applications in the diagnosis of cases of Vitamin C deficiency of the sub-clinical scurvy group.

Johnson and Zilva (1934) on the whole agreed with most of these conclusions. They considered, however, that the urinary excretion of Vitamin C under normal conditions is variable and conditioned by the amount stored in the body and consumed in the diet.

They made the important observation, moreover, that when the store of Vitamin C in the body is complete, a more or less constant level of urinary excretion is brought about and that this level varies with the daily intake of Vitamin C.

Further, on discontinuing the intake of Vitamin C a subject who is saturated may yet remain in this condition for some time despite the fact that his urinary excretion drops to a very low level.

..... Conversely

Conversely, when the subject is saturated and a large dose of Vitamin C is given the rate of urinary excretion rises rapidly to a maximum in 3-4 hours and gradually returns to its initial rate in 24-36 hours.

Another practical point they made was that diuresis induced by excessive intake of water does not influence either the rate or level of the urinary output of Vitamin C. This is an important fact to recall when Vitamin C saturation tests, to be described below, are used.

Göthlin (1934) attempted to estimate the daily human requirement of Vitamin C from known guinea-pig standards. On the basis that the degree of susceptibility to microscopic scorbutic alterations in the teeth in guinea-pigs and the prescorbutic reduction in the strength of the cutaneous capillaries in man are approximately the same, he showed that to prevent the earliest onset of Vitamin C deficiency, an adult of 60 Kg. requires a daily dose of Vitamin C 14-20 times as large as a guinea-pig weighing 0.3 Kg. requires to protect itself against microscopic scorbutic alterations in the teeth. Calculating the minimal prophylactic dose for guinea-pigs he

..... estimated

estimated that a 60 Kg. man requires 19-27 mgm. Vitamin C daily to prevent Vitamin C deficiency as evidenced by abnormal capillary fragility. It will be seen that these figures agree fairly well with those reported by Harris et al.

Extending their investigations to children and repeating their examinations, Abbasy, Harris, Ray and Marrack (1935) again showed that as a rule the urinary excretion of Vitamin C bears a direct relationship to the intake thereof. They also confirmed their earlier observation that in individual subjects there is little variation in their daily output when they have been on the same daily intake for a time.

Accepting the reputed minimum dose of Vitamin C needed to prevent earliest symptoms of hypovitaminosis in adults as being 25 mgm. daily, they noted that in normal adult subjects of about 10 stone the addition to a diet fairly low in Vitamin C of 3 oranges per day (90 mgm.) leads to an excretion of 50 mgm. Vitamin C, of 1.5 oranges (45 mgm.) to an excretion of 30 mgm., and of 0.5 orange (15 mgm.) to 15 mgm. excretion daily. On this evidence they

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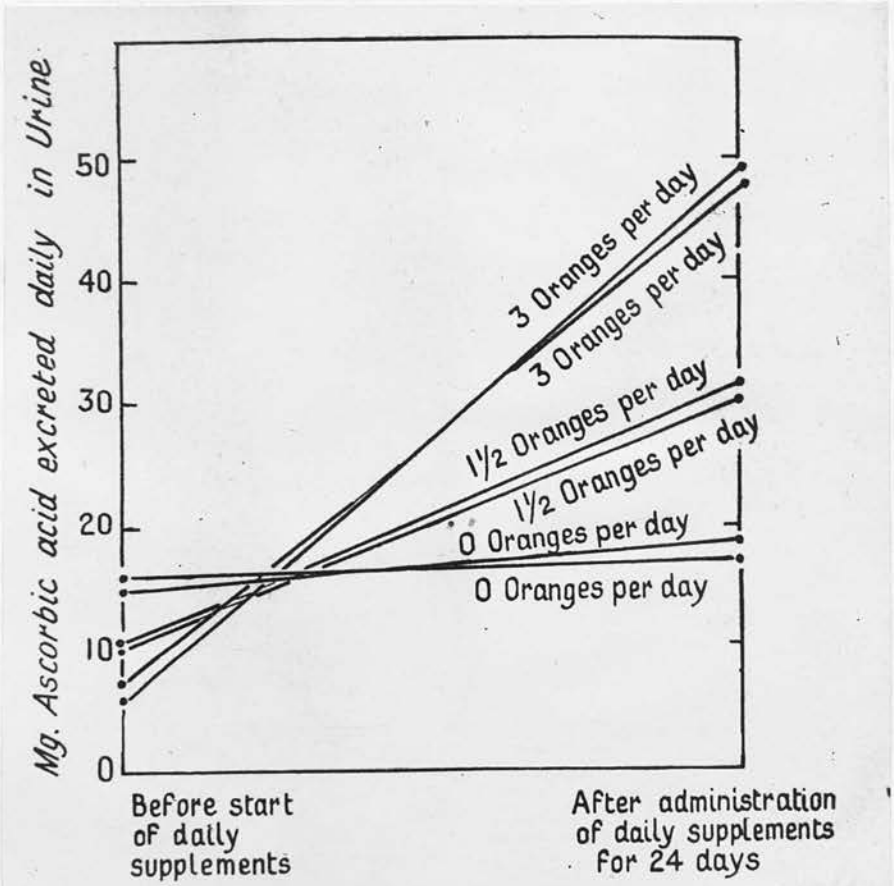

FIG. 1.—Effect of graded doses of orange juice on the day-to-day excretion of vitamin C in the urine. (The orange juice was titrated daily to determine its vitamin C. Average value, approximately: 90 mg. ascorbic acid for 3 oranges: 45 mg. ascorbic acid for 1½ oranges.)

Reprinted from the paper:-

"Diagnosis of Vitamin "C" Subnutrition by Urine Analysis".

Abbasy, Harris, Ray and Marrack. 1935. Lancet 229 ii. 1399.

raised the presumption that the diet should be considered unduly low in Vitamin C whenever the daily excretion falls below 10-15 mgm. daily per 10 stone body weight. Note, their minimum standard of normality as assessed by urinary excretion estimations has dropped from 30-33 mgm. to 10.15 mgm.

They calculated that the average daily excretion of Vitamin C of normal adults in England receiving small amounts of fruit and other sources of Vitamin C to be about 20 mgm. and further, found that although in general the needs of children and infants seem to be greater, their daily excretion tallies with adults according to body weight.

Finally, they made the comment, that judging from excretion figures, deficient intakes of Vitamin C are by no means uncommon.

Van Eekelen (1936) estimated the blood Vitamin C concentration corresponding to the state of Vitamin C saturation and considered it to be in the region of 1.3 mgm. per cent. When this level was exceeded the excess is rapidly excreted in the urine. Under normal conditions she considered that adults weighing 70 Kg. required 60 mgm. Vitamin C daily - more than twice the previously reputed minimum intake.

..... King

King (1936) still considered 25-40 mgm. Vitamin C a satisfactory daily intake for adults, but he added a rider to the effect that an estimated allowance in dietary sources should be well above the minimum requirements because of individual variations and because of the risk of loss before the food is eaten.

By the addition of the assessment of the response to a test done of Vitamin C in normal adults to the usual 24 hour output of Vitamin C estimation, Harris, Abbasy, Yudkin and Kelly (1936) concluded from tests carried out on 6 adult volunteers that it must be presumed that the individual's Vitamin C nutrition is deficient if he excretes less than 13 mgm. Vitamin C daily in the urine, and fails to respond on the first or second day to a test dose of 700 mgm. Vitamin C (per 10 stone body weight) with a steep rise in the urinary output of Vitamin C.

Youmans et al.(1936) brought evidence forward to suggest that a daily urinary excretion of Vitamin C of 20 mgm. be taken as the lower limit of normal daily excretion and an excretion of 30 per cent of a test

dose (600 mgm. Vitamin C) be taken as the lower limit of saturation.

An investigation into the magnitude of the maximal Vitamin C reserve in saturated individuals was made by O'Hara and Hanck (1936). They placed four normal women on a diet adequate in all respects save where Vitamin C was concerned; this was limited to 5 mgm. daily. They found that the amount of Vitamin C necessary to restore the tissues to saturation after a month on this diet ranged from 2,200 to 2,800 mgm. They formed the conclusion that the tissue reserves at saturation appeared to be from 2,500 to 3,000 mgm.

However, Nisenson and Cohen (1937) in investigating a case of adult scurvy by a study of the urinary excretion came to the conclusion that these figures were much too low, and investigation of normal subjects confirmed their viewpoint. They also quoted figures given by other workers as being the daily constant outputs of Vitamin C in healthy adults on adequate diets and they are closely akin to their own, e.g. Nisenson and Cohen 15-30 mgm; Ahmad 23-35 mgm; Hawley 15-28.

..... Finally

Finally, Lind, Sieck, With and Clemmensen (1937) in examining 4 cases of Vitamin C deficiency also came to the conclusion that the tissue reserves at saturation level were much higher than those quoted by O'Hara and Hanck and suggested that they were in the neighbourhood of 4,000 to 4,500 mgm.

Using the indirect method of determining the degree of Vitamin C nutrition, namely the capillary fragility test, Göthlin et al (1937) set out to determine the indispensable requirements of Vitamin C of the physically healthy adult.

They carried out experiments on four schizophrenics over a period of 6-8 weeks. They were placed on a basal Vitamin C diet and additions of extra Vitamin C were made every 3 weeks. Throughout the experiment progress was followed by means of the capillary fragility test, and they came to the following conclusions as to the indispensable daily requirements for subjects of varying body weights:-

50	Kg.	requires	19-24 mgm. Vitamin C.
60	"	"	23-29
70	"	"	27-34
80	"	"	31-38
90	"	"	35-43

It will be noted that these figures are more or less in accordance with the majority of

..... other

other investigators.

These figures are in striking contrast to those of Codvelle, Simonnet and Marand (1938) who concluded that the human body probably requires daily 100 mgm. Vitamin C. They themselves query this figure for they go on to state that most people on a so-called normal diet cannot possibly obtain this quantity of Vitamin C especially in winter time. The authors do not comment on the general agreement among the findings of other investigators.

Schroeder's (1939) figure for the daily requirements of Vitamin C falls in between these two extremes namely 50 mgm.

The work of Rietschel and Menschning (1939) also provides an extreme opinion. One of the authors starved himself of Vitamin C for 100 days and the blood level of Vitamin C fell practically to zero without any apparent ill-effects. They concluded that the Vitamin C requirements of man are very small, but cast doubt upon this opinion in their very next words by stating that synthesis of Vitamin C in the body itself is not to be considered, a possibility which an overwhelming amount of authoritative evidence makes extremely unlikely.

..... Kellie

Kellie and Zilva (1939) in human experiments considered that the minimum daily dose necessary for saturation is between 30 and 50 mgm.Vitamin C. However, they go on to say that previous results in guinea-pigs indicate that about half this amount is probably sufficient to maintain good health, thus bringing their conclusions into line with the commonly held view, i.e. 25-30 mgm. Vitamin C daily.

The figures for the daily human requirements of Vitamin C given by Smith (1938) are rather high but he admits that the normal requirements lie between wide limits. Using various methods, he concluded that the minimal daily amounts for good nutrition are 20 mgm. for infants; 40 mgm. for children, and 50-60 mgm. for adults.

In America, Merrian and Batchilder (1938) examined the daily urinary excretion of Vitamin C in 250 normal college women and found that two groups examined at different seasons of the year gave the following figures:- 15-22 mgm. and 27-33 mgm. Vitamin C per 24 hours. It will be seen that these figures are well above the minimal daily normal output laid down by Abbasy and Harris et al, and therefore denote adequate Vitamin C nutrition.

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In weighing the evidence thus supplied by various independent workers using various methods of investigation into the daily requirements of Vitamin C sufficient to maintain good health and to provide a reasonable reserve, one is struck on the whole by the comparatively close agreement of their individual results. If it is agreed with Smith that the normal requirements lie between rather wide limits one can conclude that the optimum daily requirement of Vitamin C is between 20 and 40 mgm.

As regards an index of adequate Vitamin C nutrition, any daily urinary excretion of Vitamin C less than 13 mgm. should be considered indicative of Vitamin C deficiency.

Evidence of Vitamin C deficiency brought to light by various saturation tests will be discussed below.

SOURCES

of

VITAMIN 'C'

In a consideration of adequate nutrition in general it should be remembered that we are concerned with the problem of supplying numerous factors in proper proportions and this can be solved only by the use of a variety of foodstuffs.

Thus where Vitamin C is concerned one must not take the extreme view and condemn an otherwise excellent food product because it has a low Vitamin C value; because many foodstuffs with many excellent nutritional qualities are found to have naturally low antiscorbutic properties. On the other hand, it is better to conserve the Vitamin C value of the general food supply than to depend entirely upon a special source, although, of course, in certain districts and at certain times of the year this measure may be made essential.

The Vitamin C value of any particular diet is dependent primarily on two factors:-

(1) The natural antiscorbutic power of the particular plant or animal tissue, and

(2) The consequences of aging, storing and preparation which occur before its use as a food.

..... Ignorance

Ignorance of one or both of these factors plays a great part in the Vitamin C intake, adequate or otherwise of large sections of the general population.

A third significant factor might perhaps be mentioned. Thus Smith (1938) pointed out that as the weekly expenditure on food increased the estimated Vitamin C content of the diet increased almost without exception in any one particular area. An exception were farmlands and country communities where they have a high vegetarian diet very commonly. These observations tally very closely with my findings in the Cape and provide an explanation for the unexpected results which I obtained.

In the opinion of the previously mentioned investigator, complete saturation with Vitamin C in the growing child is the ideal to be sought after since in the event of an increased demand or decreased supply the Vitamin C depôt is presumably larger than in a state of partial saturation. He too argues that since Vitamin C is so intimately concerned with cellular metabolism, particularly in the growing child, liberality in allowance throughout the entire period of growth is to be desired.

..... Among

Among the richest sources of Vitamin C are oranges, lemons, grape fruit, either raw or canned, tangerines and mandarins, tomatoes, raw or canned; fresh strawberries, green peppers (Szent-Gyorgyi), raw cabbage and spinach.

In connection with some of these it is interesting to note that the amount of Vitamin C is proportional to the amount of sunlight received during ripening (Mituda 1938). This means that the wide spread practice of plucking fruits some time before they are properly ripe for purposes of export often results in a sacrifice to no little degree of their antiscorbutic properties. Further, in view of the fact that the orange is so often used as a unit of Vitamin C supply in everyday language, the report of the Bureau for Home Economics of the U.S.A. Department of Agriculture is of some importance. The Bureau found that the Vitamin C content of several varieties of oranges in California and Florida, varied within fairly wide limits i.e. from 0.40 mgm. to 0.5 mgm. per c.c.

Grapes, both in the fresh state and the form of bottled grape juice are widely consumed in

this country. The fresh grapes contain useful quantities of Vitamin C, and specially prepared bottled grape juice contains 15 mgm. Vitamin C per litre. This value drops rapidly after the bottle is open and if the grape juice is preserved with sulphite it is powerless to prevent the onset of scurvy in guinea-pigs on a scorbutic diet. (Busing and Raabe 1938).

Properly prepared green leaf vegetables have good Vitamin C values in spite of the relatively large losses sustained during cooking or canning. In this group may be classed cabbage, spinach, brussel sprouts, kale, broccoli and vegetable greens such as turnip, beet and dandelion leaves. The losses sustained in cooking and home canning may be quite severe as the Vitamin C is most unstable save in the case of acid vegetables like tomatoes. Thus boiled cabbage is depleted by one half of its natural content and boiled carrots lose nearly all their potency. It has been shown that short or rapid cooking at high temperatures is better than long cooking at low temperatures e.g. stewing, and milk too should be brought to the boil rapidly, boiled for 5 minutes and rapidly cooled to avoid loss of the already low Vitamin C content.

..... Apples

Apples, bananas, pineapples and potatoes, green beans, and green peas, although containing much less stores of Vitamin C, are nevertheless important sources because of the large quantities usually included in the diet e.g. potatoes. In connection with the latter it should be noted that, contrary to general belief, the highest concentration of Vitamin occurs in the centre of the tuber, and not just beneath the skin as is so widely taught (Krörer and Völksen 1938).

The lettuce group has a lower Vitamin C content than is generally believed, but since they are consumed raw and in fairly large quantities, they compare favourably with cooked vegetables, such as kohlrabi, turnips, parsnips and cauliflower.

Dry cereals and legumes of all varieties are devoid of Vitamin C, but quantities of the Vitamin can be made available by soaking the seeds in water for 24 hours and then keeping them moist and in contact with air for 48 hours at room temperature; during this time they germinate and produce small roots. Even when cooked, beans, peas or lentils so treated possess the same value as most fresh vegetables. Four ounces daily effected a cure in the case of scorbutic

Serbian soldiers and the British committee on accessory food factors has recommended the use of sprouting seeds as an antiscorbutic supply in times of famine.

Dried fruits and vegetables lose nearly all antiscorbutic properties, and cooked muscle meat is practically free from Vitamin C although experience shows that if consumed raw now in large quantities it does prevent and cure scurvy e.g. in Eskimoes on a diet devoid of greens for long periods; and Step Nánsson, the polar explorer. Liver is very much superior to lean meat and butter, eggs and cheese contain no Vitamin C at all.

Recent work has demonstrated that destruction of Vitamin C in foodstuffs usually parallels injury to other qualities of the food such as flavour, colour and other vitamins (King 1936).

In cooking and preparation emphasis must be made of the unfavourable influence of contact with copper utensils, access to air, prolonged heating, alkalinity, disruption of cell structure, exposure to light, pressure cooking - an increasingly common practice nowadays, and boiling in cold water. Added to these are the deteriorating effects of

..... pickling

pickling, salting, curing and fermenting.

In the vast majority of households and particularly the poorer ones, many of these faults are committed daily and result in a huge loss of Vitamin C which would otherwise be rendered available, e.g. stewing vegetables and meat in cold water and adding bicarbonate of soda.

In this country the usual Vitamin C supplies are not so subject to seasonal variations as in Northern climes, but ignorance and economic stress still play a very important part in bringing about inadequate Vitamin C consumption as will be illustrated below.

A list is appended of the Vitamin C content of various foods in terms of milligrams per hundred grams. Unless otherwise stated these figures represent values for fresh, uncooked foods. To convert the Vitamin C values into terms of International Units multiply by 20.

In addition a shorter, graphical representation of the relative Vitamin C values of the more commonly used foodstuffs is included.

..... Food

FOOD	MGM. VITAMIN C	FOOD	MGM. VITAMIN C
Apples	25-5	Lettuce, green leaf	10
Bananas	8	Lettuce, head	5
Green Beans	10	Lime juice, fresh	30
Beefmuscle (cooked)	trace	Liver, cooked	10
Beets	5	Milk, human	6
Butter	0	Cow's milk, raw - fresh	2
Cabbage, young green	40	Cow's milk, pasteurized	0-1
Cabbage, old	20	Cow's milk, dried	5
Carrots	3	Nuts	0
Cauliflower	30	Onion	10
Cheese	0	Orange juice, fresh	50
Corn, dried	0	Orange juice, canned	45
Cucumber	2	Orange syrup	0
Eggs	0	Parsnips	5
Grass, fresh, green	60	Peas, green	15
Grape Juice	trace	Peaches, fresh	7
Grape fruit juice, fresh	40	Pears, fresh	3
Grape fruit juice, canned	30	Peppers, green	180
Jelly	0	Pepper, red, ripe	230
Kale	50	Pineapple, fresh	25
Kohlrabi	70	Pineapple, canned	10
Leek	15	Potatoes, new	15

..... Lemon

FOOD	MGM. VITAMIN C	FOOD	MGM. VITAMIN C
Lemon juice, fresh	60	Potatoes, old	7
Lemon juice, canned	50	Pumpkin	5
Quince	5	Tomato juice, fresh	30
Radishes	12	Tomato juice, canned	25
Spinach, fresh	60	Turnips	30
Squash	3	Watercress	50
Tomatoes	25	Watermelon	5

METHODS OF INVESTIGATING

VITAMIN "C" NUTRITION.

Before the chemical constitution of Vitamin C was discovered and before the pure substance became commercially available, the only methods of diagnosing cases of Vitamin C deficiency barring the therapeutic test method, were indirect ones. Such indirect tests were based on the knowledge of the haemorrhagic diathesis present in cases of manifest scurvy and found expression in the form of testing the degree of fragility of the cutaneous capillaries. The fragility of the capillary wall was tested by increasing the pressure within the capillary. This was done by raising the intra-capillary pressure either by blocking the venous return by means of a tourniquet, or by applying negative pressure to an area of skin by means of some form of suction cup.

Thus as early as 1914 Hess in America demonstrated the increased fragility of the blood capillaries in scurvy by means of a tourniquet test and later he explained this phenomenon on the assumption that this weakness of the capillary

endothelial cells to form intercellular cement substance. It is interesting to note how closely this theory corresponds with the experimental work of Wolbach et al. many years later.

Put in another way, it will be seen that this detection of increased capillary fragility means the recognition of the first morbid effect of Vitamin C deprivation, and although the test was first used to provide contributory evidence in cases of obvious scurvy, it was soon realised that it could be used to discover cases of less severe Vitamin C deficiency. Hess in his classic treatise in 1920 had already stated that the test was not specific for scurvy but that it was positive in the majority of cases of scurvy, and it became generally accepted that capillary fragility leading to the appearance of petechiae was one of the earliest detectable manifestations of the effects of a scorbutic diet.

Thus, in 1928, Öhnell demonstrated the value of such a capillary resistance test in detecting so-called "latent" cases of scurvy i.e. the milder forms of Vitamin C deficiency where the diets had been lacking in or entirely devoid of Vitamin C.

Göthlin (1931) went into the possibility of using this method of discovering much milder cases of Vitamin C deficiency. He used his own modification of a method to diagnose cases of Scarlet Fever without a rash by means of a Bier's compression band, used by Rumpel as long ago as 1909. This method depending on the application of positive pressure will be described in detail in the next chapter.

Thus by dietary experiments on a man and on a woman whose capillary resistances to rupture were initially normal he was able to show that subsistence on a diet extremely poor in Vitamin C. gradually gives rise to a condition of increased capillary fragility. The change proved to be reversible, for with increasing doses of fresh orange juice the strength of the cutaneous capillaries slowly returned to normal.

It was on this work and that of earlier workers that Göthlin based his method of ascertaining indirectly whether an individual's supply of Vitamin C is sufficient or not. However, in view of the criticism of his method which was to follow, it must be noted that from the very first he was quite conscious that in disease, the capillaries may become fragile from causes other than a simple deficiency of Vitamin C, and so he was well aware that his test should be mainly used for healthy individuals. He expressed this conception of his in

the title of his publication of that year (1931): "A Method of Establishing the Vitamin C Standard and Requirements of Physically Healthy Individuals by Testing the strength of their Cutaneous Capillaries",

Since 1931 the use of the capillary test, either by positive or by negative pressure, has developed and has been used extensively.

Dalldorf (1933) made use of the test, in investigating a group of children. He used the negative pressure (suction) method employing the special instrument of da Silva and Mello.

In his paper he quoted other factors which could influence the capillary resistance placing them in two groups. (1) Those directly damaging the endothelium and (2) Those indirectly affecting the capillaries. Thus:

(1) (a) Poisons, such as opium, neoarsphenamine, carbon monoxide, etc.

(b) Toxins as in Scarlet Fever, diphtheria, polyarthritis, etc.

(c) Metabolic products as in anaemia, acetonuria, etc.

(d) Scurvy.

(2) (a) Physiological variations as in menstruation.

(b) Endocrine diseases as in exophthalmic goitre.

(c) Diseases of the Spleen and Reticulo-endothelial System.

This is a very wide and comprehensive classification, and rarely enters into consideration in group surveys of subjects. In the large number I examined, none of the cases could be included in this classification.

Dalldorf in his experiments noted how the normal capillary fragility varied for different people, but did not consider this a limitation destroying the value of the test, and it could be used for single readings of large groups of children where individual differences would be submerged, and where single cases were being examined repeated readings could be taken.

He concluded, therefore, that the Capillary Resistance Test as estimated by the suction (Hecht) method could be used as a device for diagnosing Vitamin C deficiency and in a group of children from poor homes he found this deficiency to vary between 35 and 66% using this method. It may be noted again that in a survey of groups of children in various localities Göthlin(1931) using the positive pressure method found deficiencies ranging from 6 - 20%.

Greene (1934) in evaluating the Capillary Resistance Test in the diagnosis of Vitamin C deficiency, also found variations for individual children, and in contrast to Dalldorf, he considered this a serious limitation of the test where individuals were concerned.

Finally, in company with Hess, he decided that the test is only useful as negative evidence of Vitamin C subnutrition, as they both considered that while an increase in the number of petechial is far more common in individuals suffering from latent subclinical or active scurvy, the reaction could not be used as evidence of a deficiency in Vitamin C intake. These views are more or less in accord with my results and will be discussed more fully.

Molitch (1935) carried out 969 tests on 418 boys using Göthlin's technique and came to the conclusion that although he did not consider the test specific he adjudged it the best available method for recognition of subclinical scurvy. In his results he found that only 4.3% of the boys showed evidence of Vitamin C deficiency and he attributed this small number of positives to the very adequate diet on which the children lived.

In 1935, Dalldorf working in conjunction with Russel confirmed his earlier results and conclusions, i.e. that capillary fragility represents a mild form of Vitamin C deficiency. They further recorded the observation that the parenteral administration of Vitamin C has a prompt and prolonged effect on the capillary resistance of individuals

whose capillaries are fragile as a result of dietary inadequacy or faulty absorption of Vitamin C.

The individual normal variation was stressed by other investigators in the following year. Anderson, Hawley and Stephens (1936) examined 100 normal subjects by means of the suction method and found a high degree of variation. Moreover, they noted that increasing the intake of Vitamin C did not affect the capillary fragility. However, as these normals were presumably saturated or partially saturated, one would not expect the capillary fragility to be affected by further intake of Vitamin C.

In deciding on the relative merits of the two capillary fragility tests, one must pay due attention to what Göthlin (1937) had to say about his own method in particular. Thus he pointed out that most of the adverse criticism directed towards capillary fragility tests, such as that of Anderson, Hawley and Stephens (1936) mentioned above, and that of Abt, Farmer and Epstein (1936) referred to the suction method of Hecht and not his positive pressure method. He went on to point out that the basis of the positive pressure procedure is clear and

unassailable, whereas this can by no means be said of the suction technique.

Further in attempting to correlate the capillary fragility tests with other direct tests, Liebmann, Wortis, and Wortis (1938) decided that the "suction" method is of very little use as it gave a very high percentage number of positives in normal cases (63%), whereas, if indirect methods of determining Vitamin C had to be used, Göthlin's positive pressure method was preferable, bearing in mind its limitations.

However, in spite of the evidence slightly in favour of Göthlins method it will be seen that it has certain drawbacks, the biggest of which, according to my results, is that a large proportion of Vitamin C deficiency states remain undetected by this method. When we come to consider the Vitamin C levels of the blood, and compare the findings with Vitamin C saturation and excretion tests this objection will be made more plain.

However, before passing on to the other methods of assessing Vitamin C nutrition, Göthlins considered publication of 1937 should be studied in some detail, for here he sums up the value of his

capillary fragility test.

Thus he states that if a healthy person shows subnormal strength of the capillaries this is to be regarded as evidence of a subnormal supply of Vitamin C, whereas if a person has capillaries of normal strength his indispensable requirements of Vitamin C are satisfied. He carefully points out that he has not assumed that a person with fewer petechiae should be held better supplied with Vitamin C than another with more petechiae when both the petechial indices are below the border value. But he has assumed that if in one and the same person the number of petechiae diminish to a significant extent, this diminution is evidence of increase in his Vitamin C supply.

He still thinks as a result of his very wide experience of the test that it can be advantageously used in those cases where there are no means of making blood Vitamin C estimation or where venu-puncture cannot be carried out, or where time is limited. In conclusion, he holds the view that the capillary test is of its

greatest value in mass investigations where it is desired to ascertain whether the requisite qualities of Vitamin C are present in the regular diet.

These views would appear to be substantiated up to a point by my own investigations, but, as I hope to make plain below, perhaps the biggest limitation of the test is the fact that although negative evidence of Vitamin C deficiency is fairly reliable, even this merit is detracted from by virtue of the fact that the test does not detect the very large upper level group of mild Vitamin C deficiencies for which we must resort to the direct methods of investigation now enumerated.

DIRECT METHODS OF INVESTIGATION.

Some little time has been spent on tracing the development and utilization of the indirect methods of assessing Vitamin C nutrition, and the reports of various workers show that the value of these methods is still sub-judice or at least somewhat variable.

However, with the use by Tillmanns in 1928 of the dye, 2:6: dichlorophenolindophenol

to differentiate between fresh and stale fruit, and with the realization that this test was based on the direct relationship between the dye and the Vitamin C contained in the fruit, methods were rapidly evolved for measuring the Vitamin C saturation level of any individual by directly measuring the amount of Vitamin C in the various tissues.

These various methods will be briefly described and commented upon, and in the next chapter, the tests I have used in this survey will be described in more detail.

1. Intradermal Test: Many hopes were entertained that with this test we were provided with a rapid, simple and reliable bedside test for Vitamin C deficiency. It depended on the decolorisation of an intradermal injection of a solution of the dye which is brought about by the strongly reducing Vitamin C present in the skin of the individual to be tested. However, evidence produced by various independent workers and my own investigations into a large series of cases show quite conclusively that in its present form this

test has no constant relationship to Vitamin C saturation.

2. Estimation of the Vitamin C contained in a single Specimen of Urine. This is a very rough-and-ready and usually unreliable guide to the individual's Vitamin C saturation. The variation in the concentration of the urine and other factors affecting diuresis are entirely neglected and the test rendered virtually useless.

3. Estimation of Daily (24 hour) Urinary Output of Vitamin C. The total urinary output for the 24 hours is collected and each specimen analysed immediately for its Vitamin C content, or the various specimens are suitably preserved and the Vitamin C content estimated at the end of the day. The work of Harris et al (1936) shows that 13-18 mgm. Vitamin C excreted per 24 hours is the minimal normal output for a healthy adult in a satisfactory state of Vitamin C nutrition. This test is infinitely more reliable than the previous one, but the main objections here are that the test is too time-consuming and that such

low concentrations of Vitamin C in the urine are difficult to estimate accurately by the usual methods of titration.

4. Estimation of Blood Vitamin "C".

A specimen of venous blood is withdrawn, potassium oxalate added and the plasma treated with trichloracetic acid. Titration with the dye is then carried out. The normal figures for the fasting level given by various workers vary very slightly and 0.66 - 1.85 mgm. per 100 cc. can be taken as the average fasting level. Anything less than 0.5 mgm. is to be regarded as subnormal (Pijoan and Klemperer, van Eekelen et al). This test is comparatively simple and exact and it is reliable, but the objections here are the necessary venupuncture and laboratory facilities though these may be considered outweighed by the speed and simplicity of the procedure.

5. Blood Vitamin "C" Absorption Curve Method.

This test is superior to the foregoing one being more precise and reliable as several readings are made. After the fasting level is ascertained, an intravenous injection of Vitamin C is made and

the rise and fall of the blood vitamin C followed by making repeated tests on specimens of venous blood taken at graded intervals. Here again, though the test is probably the most scientific, the time factor and numerous venupunctures are distinct disabilities, especially in group surveys.

6. Estimation of Cerebro-Spinal Fluid Vitamin "C" Content. This test is chiefly of experimental interest and rarely if ever is of clinical value and certainly has no place in large scale surveys.

7. Vitamin "C" Saturation Tests.

It has been shown by various workers that the output of Vitamin C in the urine varies with the dietary in a peculiar manner. Thus normal, well-nourished human subjects were found to behave as though they had quite appreciable reserve stores of the Vitamin, for when the Vitamin was temporarily withheld from their diet they continued to excrete it for a time at an almost steady rate.

On the other hand, when a large dose of Vitamin C is administered to such an individual, his apparently well-filled reserves permit him, as it were, to dispense with some of the surplus and

excrete it into his urine with the result that a sharp peak is seen in the curve of his urinary response. In other words they found that the urinary output depended both on the immediate Vitamin C intake and also on the past nutritional history, or on the state of the Vitamin C "saturation" of the individual, as it has since been expressed. (Harris and Day 1935).

This knowledge has formed the basis of various "saturation" tests. All these tests are based on the response of the body, by way of urinary excretion, to varying doses of Vitamin C, for the response in terms of urinary excretion to a large dose of Vitamin C administered orally has been widely used during the past few years as an indication of the Vitamin C saturation of the body. (Harris and Day, 1935); (Johnson and Zilva, 1934); (Abbasy, Harris, Day and Marrack, 1935); (Youmans, Corlette, Akeroyd and Frank, 1936).

The amounts and media (i.e. orange juice, tomato juice, crystalline Vitamin C) have varied with different workers and the methods of administration have differed too, being either oral or intravenous, most commonly the former. There is

no point however in describing in detail the slight variations in technique used by independent workers, as all the methods are essentially the same in principle, although objections apply to each of them. In essence the saturation, excretion test means, first, an estimation of the normal 24 hour urinary excretion and then of the percentage of a large dose administered which is excreted in a given time. Certain precautions must be taken before interpreting the results e.g. the subject must be afebrile and free from any form of nephritis. The question of absorption from the gut will be discussed in the next chapter.

In addition to these commonly used and established methods of investigation, various other methods have been introduced by independent workers who have used other dyes as indicators for the presence of Vitamin C, and even indirect physicochemical methods. However, few of these have been extensively used, and few of them have the merits of simplicity and bedside adaptability.

None of them was considered as being of use for the purposes of this survey and nothing is to be gained by dwelling on them.

METHODS USED IN INVESTIGATING VITAMIN "C" NUTRITION IN PRESENT SURVEY.

In embarking upon this survey of hospital-class subjects and European and non-European school children, one had to bear several considerations in mind when deciding on the methods of investigation to be used.

Where the clinical material was concerned the biggest factor was that of time. The children, for instance, could only be investigated during the normal hours of a school-day, and only on one day at that. Secondly, any intravenous procedures would have to be of the minimum and carried out with the greatest care and dexterity, as any reports of pain or discomfort filtering back to the school or institution would have had disastrous psychological effects on the subsequent subjects.

Where I was concerned, the time factor was also most important, for in addition to ones duties as Acting Medical Registrar, there were those of lecturing in the Department of Physiology, and so 24 hour tests and those that are longer had to be excluded. Further ,as every single detail of the various technical procedures, titration of urines,

clinical examinations, dietary histories etc. had to be carried out alone and unaided by me, the methods selected had to be relatively simple and non-time-consuming.

Bearing these conditions - only a few of them have been mentioned - in mind therefore, three tests for Vitamin C nutrition were decided upon - one indirect test and two direct tests. They were respectively:-

(1) The Capillary Fragility Test (Göthlin)

(2) The Intradermal Test (Rotter)

(3) The Five-Hour Urinary Excretion Test after an Intravenous Test dose. (Wright, Lilienfeld and MacLenathen).

Three tests were selected because I hoped thus (a) to obtain cross-references by three different methods on each subject and (b) to determine the comparative values of these tests in relation to one another and to previous work done by other workers. This was considered to be of particular importance in regard to the Capillary Fragility Test and the Intradermal Test, which have been the subject of much controversy. Further,

all of these tests could be carried out at the bedside and required only the additional facilities of the ordinary side-room with a few instruments of greater precision than usual.

These three tests and the various points of technique are now described at some length.

(1) The Capillary Fragility Test.

Hess (1920) found the "capillary resistance test" to be positive in scurvy, and also stated that it forms a clue in the diagnosis of latent scurvy, a conclusion confirmed by Öhnell.

Hess, however, only applied the test in cases of manifest or latent scurvy, and Göthlin went a step further and inquired into the possibility of revealing much milder deficiencies of Vitamin C by means of this test. By his work, using this test, which has been described above, Göthlin considered that he had developed the capillary strength test into "a nutritional hygiene test by means of which, in a great many cases, individual Vitamin C standards can at any time be directly ascertained."

Description of Apparatus.

The following are the main instruments required for determining the strength of the cutaneous capillaries.

(1) A rubber stamp with a raised ring 60 m.m. in diameter for imprinting a coloured circle in the ante-cubital fossa of the elbow. An ink pad is also necessary.

(2) A large Politzer bag with an air-tight connection with its nozzle.

(3) A screw-compressor designed to act upon the Politzer bag so as to raise the necessary pressure within the cuff tourniquet.

(4) An ordinary Baumanometer cuff to produce constriction of the veins of the upper arm.

(5) A mercury manometer, preferably one with low readings, conspicuously marked at 50 m.m. Hg. An ordinary Baumanometer suffices adequately.

(6) A many-limbed glass or metal junction tube to link up the manometer, the Politzer bag and two Baumanometer cuffs.

(7) An air-pump, derived from a Baumanometer, interposed between the Politzer bag and the many-branched junction tube.

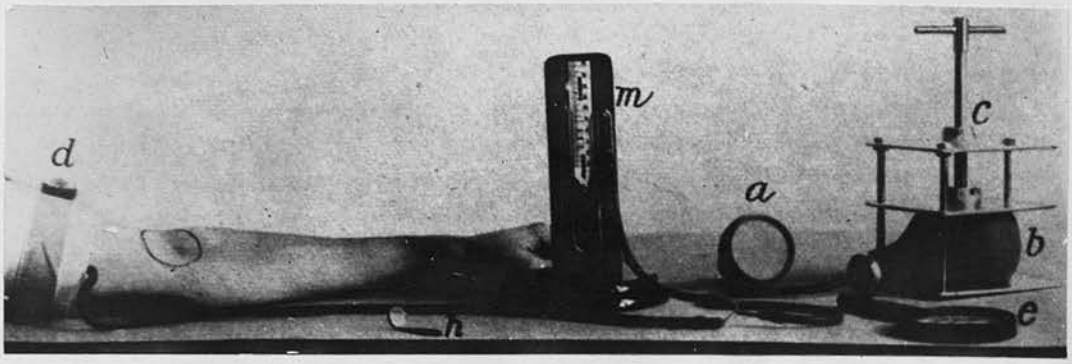


Illustration of apparatus employed by Göthlin in his Capillary Fragility Test.

For the purpose of the present survey an extra Baumanometer cuff and an air-pump were added.

Reprinted from the paper:-

"Outline of a Method for the Determination of the Strength of the Skin Capillaries and the Indirect Estimation of the Individual Vitamin C Standard".

G.F. Göthlin. 1933. J.Lab.Clin.Med. 18. 484.

(8) A circular plane glass set in a holder to be used for compressing apparent petechiae and thus to differentiate between true petechiae which will not fade and hyperaemic red spots which will disappear on pressure.

(9) A magnifying lens of 5D with which to examine the circular demarcated area for petechiae.

(10) A watch with a second hand or a stop-watch for timing the period at which the pressure on the arm is maintained.

(11) Pens with coloured inks to mark off petechiae present before and after the test is carried out, to avoid confusion.

Method of Carrying out the Test.

The test is carried out at a room temperature between 16°C and 21°C., the subject having been at rest for the preceding 3 hours at least.

The petechiae must be counted in broad daylight - a condition which was easily satisfied in this country.

Most important of all, the arm to be tested is placed in the plane of the heart. This was most satisfactorily ensured by having the

subjects sitting on an adjustable chair with the arm resting on an adjacent table. During the test the patient is instructed to sit perfectly still and not to move his arm.

The coloured ring is then impressed upon the ante-cubital fossa and the area of skin so demarcated carefully inspected with the lens and plane glass for any petechiae or capillary ectasiae which may already be present. These are marked off by spots of coloured ink to prevent confusion in counting the petechiae after the test is completed.

The tourniquet is next firmly applied about the upper arm, care being taken to ensure that the lower edge of the cuff lies at least one inch above the proximal edge of the circle.

The pressure in the cuffs is rapidly raised to 50 m.m. Hg. by means of the air-pump, and any minor adjustments made with the screw compressor. (In this survey two patients were tested at the same time).

The time is carefully noted, the pressure kept constant for 15 minutes and at the end of that

period sharply released. After a minute or two and before half an hour has elapsed any petechiae present are counted.

Throughout the survey, in the capillary fragility test, this single reading on each subject was taken, i.e. 50 m.m. Hg. for 15 minutes. The other readings which Göthlin recommends were not considered to be of any value in the present survey.

According to Göthlin, if his technique outline above is adhered to, and a pressure of 50 m.m. Hg. for 15 minutes does not produce more than 4 petechiae in the encircled area we may conclude that the Vitamin C standard is normal, whereas if a pressure of 50 m.m. Hg. produces more than 8 petechiae, the Vitamin C standard is definitely inferior.

This modified scale resolves itself into the following table:-

(+) 8 petechiae	-	positive (definite deficiency)
5-8 "	-	transitional.
4 (-) "	-	negative (no deficiency).

However, as I shall point out below, when compared with results obtained by direct means, it will be seen that these standards set by Göthlin are too low i.e. by his capillary test only fairly severe degrees of deficiency are detected, and great numbers of milder deficiency states go unrecognised.

According to Göthlin cases of simple arterio-sclerosis and pulmonary tuberculosis are not debarred from the test, but cases of acute infectious disease such as measles and scarlet fever should not be tested for at least 2 months as a reduction in the strength of the capillaries in these cases has been found, which may persist for some time. Göthlin (1933) says that at the time of writing the reason for this is unknown, but in view of the work done later on the increased consumption and loss of Vitamin C in pyrexia and the need for Vitamin C in convalescence, a reasonable explanation for the reduction in the strength of the capillaries may be this state of Vitamin C deficiency arising after the incidence of one of the acute infectious diseases.

The test cannot be used in albuminuric conditions, as here too there is a reduction in the strength of the capillaries.

Finally, Göthlin concludes that "this method may be used as a test of the individual Vitamin C standard by physicians, hygienists and dentists in their practice. It can also be used in the statistic examination of groups (e.g. in the army, in boarding schools, in orphanages, in old people's homes, in asylums and in prisons) in order to ascertain whether the diets in use provide a sufficient supply of Vitamin C."

2. The Intradermal Test. (Rotter).

Göthlin's Capillary Fragility Test is an indirect test for Vitamin C nutrition. The next two tests are direct ones and of these two the Intradermal Test is perhaps the more direct one.

Rotter (1937) while determining the Vitamin C content of urine taken from healthy and diseased individuals by means of the dye 2:6 Dichlorophenolindophenol conceived the idea of attempting to perform a similar test on the living organism.

With this purpose in view, he injected minute sterile quantities of a solution of the dye into the soles of healthy and scorbutic guinea-pigs and observed that the dye was decolorised much more rapidly in the healthy animals and much more slowly in the scorbutic ones.

A dye like methyl blue injected simultaneously remained unchanged in colour, so he was satisfied that the discolorisation of the dye 2:6 Dichlorophenolindophenol was due to reduction and not resorption. Next he showed that this decolorisation was brought about by the presence of Vitamin C in the skin. By further detailed experiments he was able to show that the time of decolorisation depends on the amount of Vitamin C present in the individual. He concluded that a decolorisation time of 5 minutes indicates saturation with Vitamin C, a time of more than 10 minutes, deficiency in Vitamin C and a time of 5-10 minutes a normal content of Vitamin C in the body.

Rotter's method and technique for his Intra-dermal Test are as follows:-

The necessary materials are a sterile solution of the dye 2:6 Dichlorophenolindophenol, a 1 c.c. tuberculin syringe graduated in hundredths of a cubic centimetre, and an intradermal needle.

The dye solution contains 2 mgm. of solid 2:6 Dichlorophenolindophenol in 4.9 c.c. distilled water, a solution which was found to be bacteriologically sterile.

The site for the injection is chosen on the skin of the forearm where there is an area free from hairs and small superficial veins. The skin is cleaned with ether, stretched between the fingers of the left hand and the needle inserted intradermally. Of the solution, 0.01 c.c. are injected and a wheal 2 m.m. in diameter is raised. This causes a transient, sharp, burning sensation, and unless the subject is warned beforehand he is apt to pull away and spoil the injection.

The times of injection and complete disappearance of the colour are noted. This procedure needs a certain amount of practice for the point at which decolorisation becomes complete is often difficult to recognise with certainty.

For this reason, both forearms were injected and the mean time for decolorisation taken as a reading.

Portnoy and Wilkinson (1938) in a series of 103 cases formed the opinion that the intradermal test might be of value as a rapid clinical test for Vitamin C deficiency. A few months later, the same two workers, in investigating the incidence of Vitamin C deficiency in cases of peptic ulceration by various methods again came to the conclusion that the results of the intradermal test agreed very closely with those of the other direct and indirect tests. (Portnoy and Wilkinson 1938).

However, a few months later in the same year, 1938, Poncher and Stubenrauch stated that in their work they were quite unable to confirm the conclusions of Portnoy and Wilkinson. In a series of 40 patients they checked the decolorisation times against the Vitamin C plasma levels and found no correlation whatsoever. Jetter (1938) carrying out similar comparative experiments also failed to find any correlation between plasma Vitamin C levels and decolorisation times.

Lastly in my own investigations, as will

be illustrated below, comparison between Vitamin C Saturation Tests and the Intradermal Test again failed to bring any correlation whatsoever to light in a series of 99 cases.

The 5-Hour Urinary Excretion Test following an Intravenous Test Dose.

During the last few years the response to a large test dose of Vitamin C administered orally, measured in terms of the urinary excretion, has been commonly used as an indication of the state of Vitamin C saturation of the body.

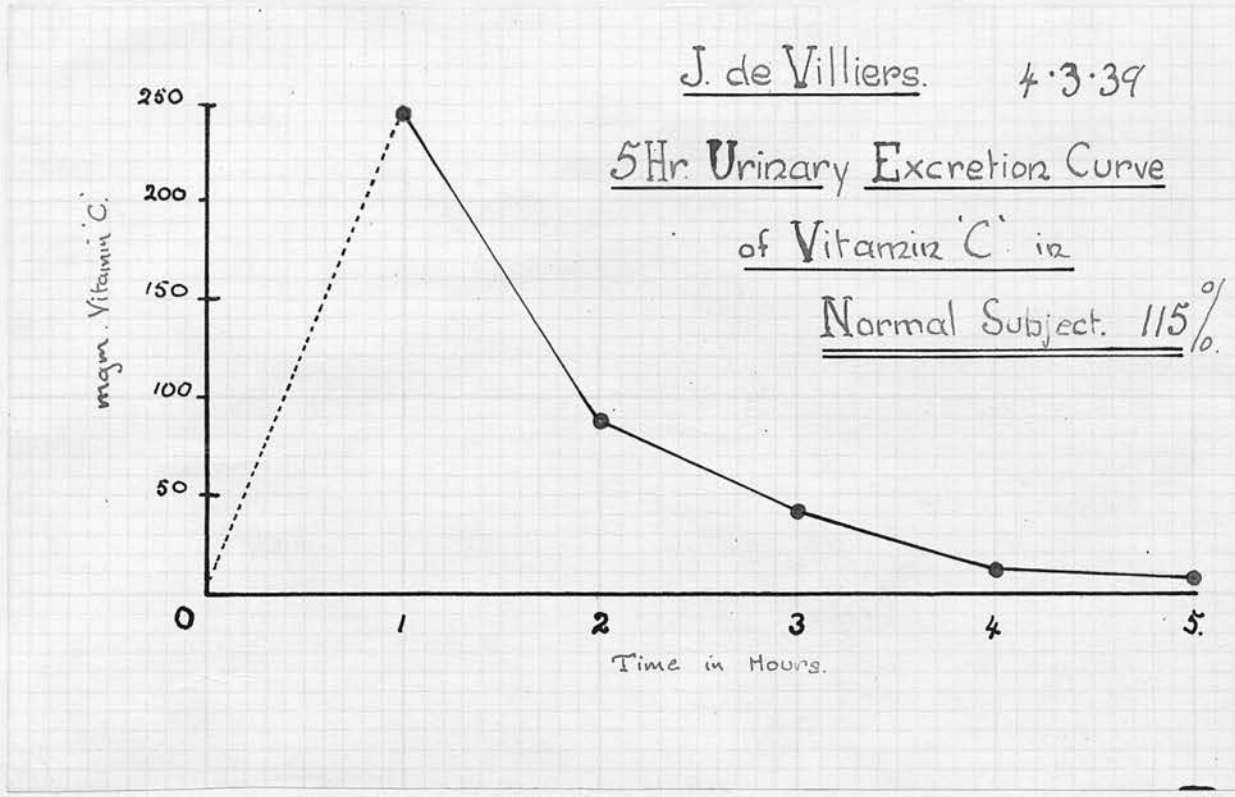
In most series of investigations, the test done was given orally and often repeated. This factor made the test very prolonged, and hence unsuitable for mass examinations. Another undesirable factor of the oral dose is the variation in absorption and utilization of Vitamin C from the gastro-intestinal tract due to various factors mentioned above e.g. anacidity, purgation, inflammation, etc.

In pointing out these objections Wright, Lilienfeld and MacLenathen evolved a less time-consuming test whereby the urinary excretion of Vitamin C was measured during the period of 5 hours

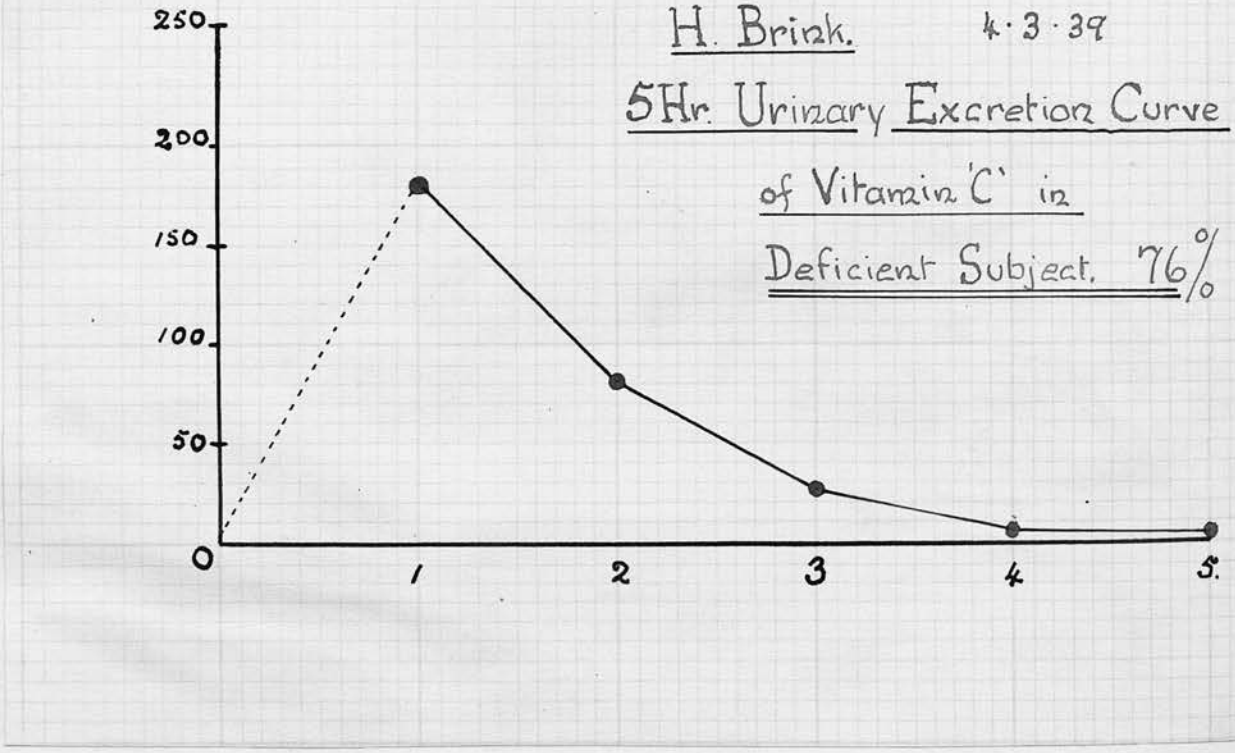
following a massive intravenous dose of crystalline Vitamin C in solution.

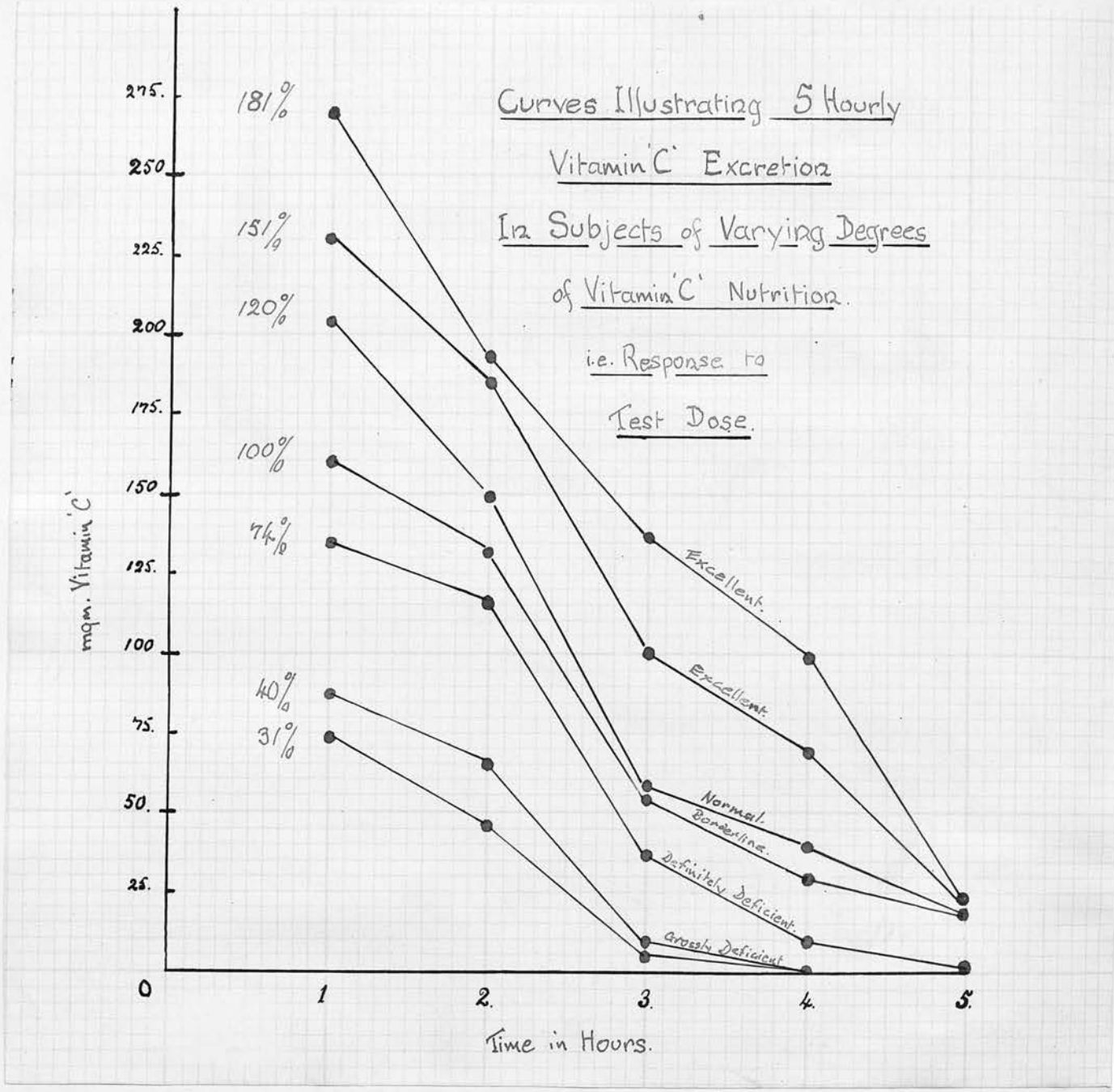
Thus by carrying out experiments on human subjects they found that following the intravenous injection of 1 Gram of Vitamin C there was a fairly sharp and steady rise in the curve of urinary excretion of Vitamin C which reached its peak between the first and second hour. Thereafter there is a rapid fall in the rate of excretion until the fifth hour by which time by far the greater portion of the total 24-hour return of Vitamin C is excreted. (Vide charts on opposite page). Thus individuals in a normal state of Vitamin C nutrition excreted at least 500 mgm. of the 1000 mgm. test dose in the 24 hours following injection. The important finding in their experiments lay in the discovery that during the first 5 hours, 80% or more of the total 24 hour return of Vitamin C, was excreted in the urine i.e. 400 mgm. or more. This observation was verified in a series of 55 tests carried out on persons of varying degrees of Vitamin C saturation.

The advantages of their method are as follows:



Graphic Record of two subjects:
J. de V. of normal Vitamin C nutrition, and
H.B. of deficient Vitamin C nutrition,
to illustrate 5 Hour urinary excretion of Vitamin C.





Graphic Record of 5 Hour Urinary Excretion in Subjects of varying degrees of Vitamin "C" Nutrition.

Note varying response to test dose of 1000 mgm. Vitamin C.

difficult. In this survey, each subject was investigated at the Groote Schuur Hospital where the difficulty did not arise therefore.

(3) Rolli, Friedman and Rubin (1938) when investigating the mechanism of Vitamin C excretion by the human kidney, pointed out that a sudden rise in the blood level of Vitamin C brought about by a large intravenous dose might render the tubules incapable of resorbing Vitamin C from the glomerular filtrate. Thus large quantities of Vitamin C would escape in the urine and so give a false impression of the degree of Vitamin C saturation of the body. However, this danger would appear to be exaggerated for in this survey the rate and mechanism of urinary excretion followed very closely that investigated by Wright, Lilienfeld and MacLenathen in their original investigations.

Method of Carrying out the 5-Hour Test.

All subjects were investigated at the Groote Schuur Hospital, Cape Town. In the case of the school children, they were brought to hospital at 8 a.m. each morning, having had a breakfast restricted to (Vitamin C (non-containing foods. They

were then weighed and immediately before the test made to void urine which was discarded.

The three tests were carried out simultaneously on all subjects (i.e. Capillary Fragility Test, Intradermal Test and 5-Hour Excretion Test), the intravenous dose being adjusted according to the body weight on the basis of 1 Gram Vitamin C to an individual of 70 Kilograms body weight. This worked out approximately at the rate of 14 mgm. per Kilogram body weight, a standard comparable to that adopted by Sloan (1938) in his paper on a comparison of the methods used for detecting subclinical scurvy. The scale of doses is presented on the opposite page.

The time of injection is noted and all urine voided during the subsequent 5 hours including the specimen passed at the end of the fifth hour is collected, measured and preserved in dark brown, stoppered bottles containing 10% glacial acetic acid, or immediately titrated according to the method of Harris, Ray and Ward (1933) which is a modification of Tillmann's original method. During the test fluids could be freely taken if desired as this has no apparent effect on the total Vitamin C excreted in the 5 hours (Sloan 1938) and usually a light meal is

WEIGHT.		DOSE.		NUTR.
Kg.	lbs.	c.c.m.	mgm.	100%
70.	150.	10.	1000.	400.
66·5.	142.	9·5.	950.	380.
63.	135.	9.	900.	360.
59·5.	127.	8·5.	850.	340.
56.	120.	8.	800.	320
52·5	112.	7·5.	750.	300.
49.	105.	7.	700.	280.
45·5.	97.	6·5.	650.	260.
42.	90.	6.	600.	240.
38·5.	82.	5·5.	550.	220.
35.	75.	5.	500.	200.
31·5.	67.	4·5.	450.	180.
28.	60.	4.	400.	160.
24·5.	52.	3·5.	350.	140.
21.	45.	3.	300.	120.
17·5.	37.	2·5.	250.	100.
14.	30.	2.	200.	80.
10·5.	22.	1·5.	150.	60.
7.	15.	1	100.	40.
3·5.	7.	0·5.	50.	20.

Vitamin "C" Dosage Table for 5 Hour Urinary Excretion Test.

Preparations used:-

Bayer's "CANTAN"

La Roche's "REDOXON FORTE"

in sterile ampoules of 5.3 c.c. each.

Each c.c.m. = 100 mgm. = 2,000 I Units Vitamin "C".

served halfway through the test consisting of bread and butter, biscuits or cake.

Titration is carried out rapidly, being repeated three times for each subject, the mean being taken as the final figure from which the total urinary excretion of Vitamin C is calculated. In all cases the final figure is expressed as a percentage of the normal 5 hour excretion of 400 mgm. Vitamin C following a dose of 1000 mgm., 400 mgm. being taken as 100%, e.g. a child of 35 Kilograms would receive an injection of only 500 mgm. A urinary excretion of 200 mgm. Vitamin C would therefore again be expressed as 100%.

The dye 2:6 Dichlorophenolindophenol was obtained in the solid form and standardised against Vitamin C, which had itself been standardised against 0.01 N Iodine solution, every 3 months.

The solution of dye itself was freshly made up twice weekly, 0.025 grams of the dye being treated with 10 ccs. boiling water at a time and then decanted into a 50 cc. volumetric flask. The dye when wholly dissolved gave one 50 c.c. of indicator of 0.05% strength. After standardisation therefore, 1 cc dye solution proved to be equivalent

to 0.238 mgm. Vitamin C, and for each titration 0.5 cc. of the solution is used as an indicator. Throughout the titration the technique of Harris et al (1933) was vigorously carried out, an essential point being rapidity of titration to obtain a sharp end-point, as slow titration leads to an ill-defined end-point and hence incorrect calculations. All the bi-weekly preparations of the fresh dye solution and the periodic standardisations were carried out by myself at the Bio-chemistry Laboratory under Dr. Linder's watchful eye, and the daily titrations at the Groote Schuur Hospital.

Throughout the series of over 500 cases no untoward results followed the large intravenous doses of Vitamin C.. All that was ever complained of was the actual needleprick and pain after injection was never complained of.

In their work, Wright et al. took the figure 100 or over as being the expression of normal Vitamin C nutrition i.e. a man of 70 Kilograms weight, in a state of normal Vitamin C nutrition would in the 5 hours following an intravenous injection of 1000 milligrams Vitamin C, excrete 400 mgm.

or more, a figure represented by 100% or more.

For the purposes of this survey a modified scale of Vitamin C nutrition was employed, as we were interested in the variations to be found in the various groups investigated.

For this purpose six groups of Vitamin C nutrition will be referred to, to facilitate reference to the different methods of investigation used, as the standards used by the various investigators are not always identical, and in the discussion this will become most apparent when comparing the value of Göthlin's Capillary Fragility Test with that of the 5 hour test.

The scale is as follows:-

VITAMIN C NUTRITION TABLE.

125% and over	-	Excellent.
110-125%	-	Normal.
100-110%	-	Borderline.
90-100%	-	Slightly Deficient.
50-90%	-	Definitely Deficient.
50% or less	-	Grossly Deficient.

In all cases where an unduly low Vitamin C nutrition was discovered the renal system was inves-

tigated to satisfy myself that the low excretion was not due to some fault in the kidneys.

Dietary History.

Each case was intensively interrogated as to his customary diet, the weekly average being recorded. Particular attention was applied to the antiscorbutic foods in the diet. Thus, one usually asked for an account of the average days meals. Then the subject was further requested to state how much fruit he got, how many tomatoes, what vegetables and how they were prepared and so on in greater detail, so that a fairly accurate and detailed assessment of his diet could be made.

These diets were then classified and referred to as follows for convenience:-

SCALE OF DIETS.

Excellent	-	E
Good	-	G
Fair	-	F
Poor	-	P

Finally each case was subjected to a thorough clinical examination so that any abnormal findings could be correlated with the Vitamin C

nutrition where the connection seemed to be of any significance. In addition, one was desirous of discovering whether there is any reliable parallel between individual nutrition in general and Vitamin C nutrition. For this purpose each individual's general nutrition was assessed by the usual methods and classified into one of four groups as follows:-

SCALE OF GENERAL NUTRITION.

Excellent	-	E
Normal	-	N
Slightly Subnormal	-	S.S.
Bad	-	B

RESULTS

In commencing this Vitamin C nutrition survey it was decided to investigate about one hundred ward cases, both European and non-European, first of all. This was done with the intention of familiarising oneself with the technique and to discover what the general level of Vitamin C nutrition in hospital class patients was. The work of Göthlin (1931), Dalldorf (1933), Molitch (1935) etc., and of Harris et al. more recently had shown large groups of unsuspected Vitamin C subnutrition to occur in the general population, particularly in school children.

At the same time it was intended to investigate a number of people on so-called normal, healthy diets. They were to be used as controls and were drawn from members of the hospital staff, ones colleagues, and medical student volunteers.

It is as well to commence with the fifteen male and female adult, European, controls who were investigated by means of the 5-hour test.

..... Vitamin C

VITAMIN C NUTRITION

Adult, European Controls.

Name	Sex	Age	Date	Diet	% Vitamin C Nutrition.	
A.P.	F	30	14.11.39	E	187	
A.S.	F	20	14.11.39	E	169	
A.K.W.	F	19	14.11.39	G	145	
D.B.	M	24	20. 5.39	G	138	
Self	M	26	1. 4.39	G	129	Excellent
Self	M	26	30. 8.39	G	127.5	
J.M.	F	28	14.11.39	G	127	
J.duT	M	25	6. 4.39	G	127	
A.M.	F	23	14.11.39	G	126	
J.L.	M	33	30. 8.39	G	122.5	
J.L.	M	33	11. 8.39	G	112.5	Normal
C.vanZ.	M	30	22. 4.39	G	110.5	
S.B.	M	26	11. 8.39	G	108	Borderline
R.McL.	M	26	6. 4.39	G	105.7	
A.D.	M	52	22. 4.39	G	97.5	Slightly Deficient.

According to the scale of Vitamin C nutrition described in the previous chapter, of the 15 adult controls of all ages, and both sexes, the Vitamin C nutrition of 9 is ranked as being Excellent

of 3 " " " " Normal

of 2 " " " " Borderline

of 1 " " " " Slightly Deficient.

The average for the group of controls proved to be 128.8% i.e. Excellent.

It is worth pointing out that the two highest figures, those of A.P. and of A.S., were provided by two stenographers who for months past had lived on orange juice for breakfast with fresh-fruit lunches at midday and a chiefly vegetarian diet at night. All the other diets were classed as being Good. None of the other tests were carried out on the controls.

WARD CASES EUROPEAN AND NON-EUROPEAN.

Turning to the Ward Cases, 58 European and 54 non-European patients were examined. They were drawn from the various wards of the Groote Schuur Hospital, Medical, Surgical and Orthopoedic and were investigated within a day or two of admission or only after several weeks stay in hospital so that it was ensured that the Vitamin C nutrition estimation was based on a steady diet.

The full European list including the Capillary Fragility Test (C.F.T.) and the volume of urine passed during the 5-Hour Test is appended below

VITAMIN "C" NUTRITION

OF EUROPEAN WARD CASES (58).

Patient	C.F.T.	Diet	5 Hour Excretion Test: Volume Urine.	Total mgm. Vit.C. Excreted.	%Nutrition.	
M.G.	2	Ex.	350	700	175	Excellent
R.J.	5	G	303	606	151	
E.D.	0	F	162	291	146	
E.V.	0	G	130	580	145	
H.L.	6	F	210	573	143	
W.J.	-	Ex.	440	553	138	
M.G.R.	7	G	190	507	127	
E.P.	-	G	116	490	123	Normal
R.L.	10	G	420	462	116	
M.G.	0	G	153	459	115	
C.P.	4	G	900	450	112	
S.S.	1	G	440	440	110	
F.U.	12	F	150	450	112	Borderline
H.H.	2	G	175	420	105	
M.H.	1	G	207	414	104	
H.B.	-	P	303	400	100	
J.M.	-	G	176	399	99.5	Slightly Deficient
v.d.W.	6	G	130	390	98	
M.W.	4	G	318	382	95	
J.W.	17	F	470	376	94	
F.N.	0	F	218	371	93	
A.v.B.	0	G	230	368	92	
R.B.	0	F	202	363	91	
P.de W.	3	G	727	363	91	
M.L.		F	545	359	89	Definitely Deficient
H.R.	0	F	268	348	85	
F.G.	2	F	325	270	81	
M.S.	2	F	215	323	81	
A.S.	0	G	160	320	80	
R.H.	1	F	186	316	80	
J.de V.	-	F	189	304	76	
F.E.	6	F	305	305	76	
A.F.	0	F	300	300	75	
B.G.	0	F	98	295	74	
F.M.	-	F	566	284	71	
H.F.	3	F	651	280	70	
A.W.	7	F	116	278	70	
M.C.	-	P	74	266	67	
G.A.	0	F	200	266	66	
M.H.	-	P	146	248	62	
W.L.	0	F	285	246	61	
L.T.	2	P	137	240	58	
H.E.	3	P	190	228	57	
S.R.	10	F	155	219	55	
G.O.	15	P	140	220	55	
R.W.	0	F	218	218	54	
C.W.	6	P	215	215	54	
C.H.	0	F	69	207	52	
B.C.	6	P	210	210	52	
W.W.	0	F	370	203	50	
B.S.	-	P	158	142	50	
F.S.	5	P	260	195	49	Grossly Deficient
S.K.	12	F	291	178	44	
A.R.	1	P	265	174	43	
W.D.	4	F	100	170	42	
J.Z.	5	F	42	168	42	
L.G.	0	P	100	150	38	
C.W.	0	P	225	150	38	

It will be noted that of these 58 cases

7	can	be	grouped	as	Excellent
5	"	"	"	"	Normal
4	"	"	"	"	Borderline
8	"	"	"	"	Slightly Deficient
27	"	"	"	"	Definitely Deficient
7	"	"	"	"	Grossly Deficient

The Average for the 5-Hour Test is 84%.

The Average for the C.F.T. is 3.5 Petechiae.

The Average Total Urinary Output for 5 Hours 267 cc.

Excluding the Borderline cases 72.4% showed deficient Vitamin C nutrition.

The corresponding non-European list of results is appended here.

VITAMIN "C" NUTRITION

OF NON-EUROPEAN WARD CASES (54).

Patient	C.F.T.	Diet.	5-Hour Excretion Test: Volume Urine.	Total mgm. Vit.C Excreted	%Nutrition	
J.P.	-	G	137	618	155	Excellent
B.F.	-	G	170	606	152	
F.C.	-	G	73	560	140	
E.A.	1	G	320	544	136	
H.McM.	0	G	165	495	124	Normal
A.N.	0	F	220	480	120	
A.I.	0	F	165	460	115	
M.L.	0	G	90	450	113	
A.G.	1	G	415	441	110	
M.F.	3	G	160	432	108	Borderline
M.N.	0	G	105	420	105	
L.G.	0	G	139	417	104	
M.v.E.	2	G	153	413	103	
G.A.	0	G	440	406	102	
O.B.	0	Ex.	67	804	101	
A.S.	0	F	185	202	101	
W.F.	0	G	127	381	95	Slightly Deficient
I.W.	4	F	190	370	93	
N.M.	0	F	95	370	93	
F.B.	2	F	285	370	93	
H.N.	0	G	94	364	91	
E.Mc.	2	G	730	352	88	Definitely Deficient
D.v.W.	5	F	117	351	88	
E.S.	0	F	124	335	84	
P.A.	1	F	242	314	79	
F.S.	2	G	333	313	78	
M.v.R.	12	F	102	306	76	
T.N.	0	F	100	300	75	
N.M.	1	F	421	148	74	
A.L.	0	P	95	285	71	
L.R.	0	F	380	285	71	
J.S.	-	G	182	278	70	
H.H.	-	F	115	268	67	
P.W.	0	F	190	253	64	
W.M.	0	F	380	253	63	
L.C.	0	F	168	252	63	
A.W.	4	P	75	225	56	
E.W.	7	F	172	223	56	
M.de B.	-	F	50	214	54	
J.P.	0	P	210	210	53	
P.H.	0	F	340	214	53	
R.K.	0	F	105	198	50	
A.D.	0	P	130	195	49	Grossly Deficient
S.M.	0	P	170	191	48	
E.M.	0	P	195	179	45	
K.L.	0	P	270	180	45	
L.R.	0	P	170	89	44	
M.J.	-	G	191	167	42	
C.W.	-	F	61	166	42	
v.G.	0	P	215	161	40	
W.S.	0	P	310	155	39	
A.A.	-	P	118	134	34	
S.S.	0	P	210	115	29	
J.v.R.	0	VP	78	117	29	

It will be noted that of these 54 cases:

4 can be grouped as Excellent

5 " " " " Normal

7 " " " " Borderline

5 " " " " Slightly Deficient

21 " " " " Definitely Deficient

12 " " " " Grossly Deficient

The Average for the 5-Hour Test is 79%.

The Average for the C.F.T. is 1 Petechia.

The Average of the Total Urinary Output for 5 Hours is 195 cc.

Excluding the Borderline cases, 70.4% showed deficient Vitamin C nutrition.

It is interesting to note at this stage a point which will be commented upon later.

Of the European cases, 11 were peptic ulcer cases whose average Vitamin C nutrition was 87.3%.

Of the non-European cases, 4 were peptic ulcer cases whose average Vitamin C nutrition was 114%.

A series of 112 European and non-European Ward cases, admitted to hospital for a variety of ailments, having been investigated, one proceeded to examine different groups of European and non-European children aged 8-16 years.

The following groups of school children were

examined by two or more of the Vitamin C nutrition Tests.

1.	The All Saints Home	European	63 cases
2.	The Observatory Boys' and Girls' Primary School	European	46 cases
3.	The Battswood Secondary School.	Non-European	107 cases
4.	The Battswood Primary School	Non-European	50 cases
5.	Salt River, Cecil Road, Primary School	Non-European	57 cases
6.	St.George's School, Athlone	Non-European	12 cases
7.	Duinefontein School,Athlone	Non-European	24 cases
8.	St.Paul's School,Rondebosch	Non-European	11 cases
9.	St.Andrew's School, Rondebosch	Non-European	10 cases

The total number of school children so examined was 380.

The total number of cases examined, school children, ward cases and controls was 507.

1. ALL SAINTS HOME - 63 CASES.

All these children, male and female, drawn from an orphanage, and all on the same diet for months on end, were subjected to all three tests - Capillary Fragility Test (C.F.T.); Intradermal Test (I.D.T.); and the 5-Hour Excretion Test.

The following is a full list of results arranged in descending order according to the 5-Hour Test.

VITAMIN "C" NUTRITION
of
ALL SAINTS HOME (63 CASES).

Name	Diet	IDT	CFT	5-Hour Excretion Test: Volume Urine	Total mgm. Vit.C Excreted	% Nutrition.	
D.M.	G	6	2	216	336	186	
E.C.	G	6	2	280	280	157	
C.F.	G	7	2	400	300	166	
W.G.	G	-	-	335	251	154	
J.L.	G	4	2	345	276	153	
J.R.	G	7	0	515	226	150	Excellent
L.D.	G	8	1	174	290	145	
S.S.	G	10	1	389	260	144	
S.v.Z.	G	9	0	215	258	143	
P.S.	G	7	4	595	247	137	
K.S.	G	7	0	330	247	137	
M.P.	F	3	2	635	257	129	
V.L.	G	-	-	176	204	127	
S.S.	F	6	2	590	295	122	
J.C.	F	10	0	310	242	121	
F.D.	G	10	3	190	190	119	
I.G.	F	9	2	565	187	117	
I.A.	F	15	0	570	324	116	
R.F.	F	5	0	195	228	114	Normal.
N.F.	F	5	3	477	159	113	
S.R.	F	4	3	560	224	112	
H.B.	F	7	3	495	247	112	
A.A.	F	6	1	780	358	112	
M.S.	F	6	4	960	220	110	
A.B.	F	6	2	440	176	110	
E.T.	F	8	6	360	262	109	
P.C.	F	-	1	135	195	108	
V.M.	F	4	0	585	260	108	
D.G.	F	-	0	306	193	107	
S.M.	F	10	4	433	172	107	
V.S.	F	6	6	130	169	106	
P.C.	F	-	2	360	190	105	
B.D.	F	6	8	473	188	104	
R.F.	F	5	0	344	187	104	Borderline
M.leR.	F	8	0	260	208	104	
D.P.	F	4	0	860	334	104	
D.B.	F	10	1	520	208	104	
G.G.	F	8	1	525	227	103	
R.H.	F	6	0	444	184	102	
G.D.	F	-	0	219	164	101	
E.S.	F	8	0	385	291	101	
H.S.	F	7	6	490	243	101	
H.K.	F	9	0	275	220	100	
R.R.	F	6	0	376	282	100	
L.duT.	F	4	4	400	180	100	
C.G.	F	-	2	177	177	98	
F.H.	F	6	0	535	177	98	
R.L.	F	-	2	645	194	97	Slightly
O.D.	F	11	1	680	272	97	Deficient
G.deV.	F	6	2	265	212	96	
B.S.	F	4	0	660	227	94	
V.M.	F	4	0	750	180	90	
K.B.	F	7	0	430	287	88	
G.P.	F	6	0	485	138	86	
I.McA.	G	9	0	378	135	84	
G.B.	F	9	4	465	130	83	Definitely
B.H.	F	8	2	480	164	82	Deficient
H.v.R.	F	6	2	415	208	80	
H.W.	F	9	2	575	189	79	
A.W.	F	10	0	705	157	78	
G.H.	F	4	1	805	248	77	
W.v.N.	G	5	1	230	159	73	
J.W.	G	4	1	290	130	72	

Of these 63 cases it will be seen that

13 can be grouped as Excellent

12 " " " " Normal

20 " " " " Borderline

7 " " " " Slightly Deficient

11 " " " " Definitely Deficient.

The average for the 5-Hour Test is 110.4%

The average for the C.F.T. is 1.6 petechiae.

The average for the I.D.T. is 6.7 minutes

The average total Urinary Output for 5 hours is 442 c.c.

Excluding the 20 Borderline cases 28.6% showed deficient Vitamin C nutrition.

During the course of this investigation several of the boys were provided by chance with an extra supply of oranges each day for three weeks and hence an interesting subsidiary discovery came to light, showing how the addition of two or three oranges each day for a few weeks rapidly improved the Vitamin C nutrition. My attention was drawn to this by noting after several weeks work that the percentages had suddenly increased in a number of cases. Closer inquiry then revealed that 16 of the boys had been having the extra oranges. The remaining 16 boys remained on the usual institutional

diet. The effect of the extra Vitamin C in the diet can be shown as follows:-

	16 cases Before Treatment	16 cases After Treatment
5 Hour Test	105.5	135
C.F.T.	2.4	1.3
I.D.T.	5	7

Reference may be made here in advance to the lack of correlation between the 5 Hour Test and the Intradermal Test. This point will be expanded in the discussion to follow.

2. OBSERVATORY BOYS' AND GIRLS' EUROPEAN PRIMARY SCHOOLS.

These cases, 46 in number were taken from a higher economic and social grade of school children to serve as a series of European controls for the other groups of non-European children who were drawn from a very much lower social stratum. In this group, which was the last to be examined, the Intradermal Test was not carried out as it had proved to be fallacious and had been discontinued.

The following is the full list of results arranged in descending order according to the 5-Hour Test.

VITAMIN "C" NUTRITION

of

OBSERVATORY PRIMARY SCHOOL (EUROPEAN) 46 CASES.

Name	Diet	C.F.T.	5 Hour Excretion Test: Volume Urine	Total mgm. Vit.C. Excreted.	% Nutrition.	
M.L.	G	1	150	450	204	Excellent
J.B.	Ex.	0	390	312	195	
D.W.	Ex.	0	65	390	195	
F.I.	Ex.	0	356	301	190	
D.S.	Ex.	8	125	375	188	
M.A.	G	0	150	450	187	
P.H.	Ex.	0	440	330	183	
J.S.	G	0	130	390	177	
E.K.	G	0	145	435	167	
S.K.	G	0	360	336	166	
R.v.D.	Ex.	2	215	322	161	
E.McN.	Ex.	0	335	288	160	
R.M.	Ex.	0	95	285	160	
A.H.	G	0	115	315	157	
K.S.	G	0	90	270	150	
J.P.	G	0	110	264	146	
R.T.	G	2	240	288	144	
H.S.	G	0	160	480	141	
A.B.	G	3	460	396	141	
K.W.	G	2	145	246	136	
D.T.	F	0	440	404	135	
J.M.	G	0	175	298	135	
E.T.	G	0	80	240	133	
A.B.	G	0	120	360	130	
D.M.	G.	0	95	285	129	
J.V.	F	0	120	204	127	
P.M.	G	0	120	204	127	
C.H.	F	0	95	228	126	
N.D.	F	0	221	190	119	Normal
R.H.	F	0	140	210	116	
J.M.	G	0	85	255	116	
D.W.	P	0	142	230	115	
M.M.	P	0	100	306	115	
N.C.	G	0	220	220	113	
G.J.	P	0	150	270	112	
M.S.	F	0	100	200	111	
A.R.	F	0	315	210	105	Slightly Deficient
G.S.	G	0	110	187	104	
E.B.	P	0	215	185	103	
S.G.	G	1	180	306	102	
R.S.	P	0	160	320	100	
E.S.	P	2	210	210	95	Definitely Deficient
J.K.	G	0	100	170	94	
N.S.	P	0	310	232	89	
R.F.	G	0	145	145	80	Grossly Deficient
E.M.	F	1	160	120	60	

Of these 46 cases it will be seen that:-

28 can be grouped as Excellent

8 " " " " Normal

5 " " " " Borderline

3 " " " " Slightly Deficient

2 " " " " Definitely Deficient.

The Average for the 5 Hour Test is 135.6%

The Average for the C.F.T. is 0.5 Petechiae

The Average Total Urinary Output for 5 hours is 186 c.c.

Excluding the 5 Borderline cases, 10.8% showed deficient Vitamin C Nutrition.

3. BATTSWOOD COLOURED SECONDARY SCHOOL. (107 cases)

These children were, for the coloured community, of a superior socio-economical status. That is, their parents were permanently employed, were assured of a constant income and hence the children were well-dressed and well fed, the diet being planned on European lines.

The full list of results is appended below. For the sake of convenience, separate lists have been made for the sexes, but the final averages and calculations are based on the total number of children.

VITAMIN "C" NUTRITION

of

BATTSWOOD COLOURED SECONDARY SCHOOL

M A L E S (89 Cases)

Name	Diet	C.F.T.	5-Hour Excretion Test: Volume Urine.	5-Hour Excretion Test: Total mgm. Vit.C Excreted.	5-Hour Excretion Test: % Nutrition	
v.d.B.	G	1	770	369	205	
S.de J.	G	1	286	286	204	
H.C.	Ex.	0	470	470	198	
S.J.	Ex.	0	260	312	195	
H.M.	G	0	286	386	193	
C.R.	G	4	260	347	192	
L.H.	G	0	423	423	192	
N.W.	Ex.	0	330	420	190	
T.D.	Ex.	1	328	302	189	
R.P.	G	0	245	375	187	
G.M.	G	0	485	446	185	
A.C.	G	0	99	297	185	
H.J.	G	0	875	576	181	
H.C.	G	3	390	360	180	
R.D.	G	4	1009	504	180	
P.O.	G	0	350	396	180	
G.A.	G	0	638	640	177	
A.J.	G	6	552	368	176	
F.A.	G	0	235	282	176	
R.D.	G	2	482	384	175	
B.P.	F	0	420	420	175	
P.P.	F	0	163	489	174	
H.C.	G	0	480	384	174	
I.T.	G	0	295	392	173	
J.G.	G	0	450	414	172	
L.T.	Ex.	1	480	413	172	
H.R.	G	0	275	310	172	
L.P.	G	0	360	310	172	
H.C.	G	0	532	372	170	
G.M.	G	0	405	540	170	
v.d.B.	B	0	170	340	170	
W.B.	F	0	452	272	169	
A.O.	F	0	602	301	167	
W.S.	G	1	595	397	167	
M.S.	G	0	740	296	164	
G.S.	G	0	150	260	162	
E.D.	G	0	415	357	162	
C.S.	G	6	390	292	162	
F.H.	G	0	130	260	162	
J.A.	Ex.	0	480	480	160	Excellent
G.T.	F	1	265	318	159	
D.L.	G	0	380	285	158	
R.de V.	G	0	345	346	157	
L.A.	G	0	340	408	157	
G.J.	F	0	505	378	156	
H.F.	F	0	156	312	156	
L.E.	G	0	260	312	156	
E.P.	F	1	595	309	154	
A.J.	F	0	215	365	153	
N.T.	G	0	526	368	153	
H.B.	G	0	920	475	152	
J.L.	F	0	181	272	151	
J.A.	G	0	266	452	150	
V.H.	F	0	270	360	150	
A.H.	F	0	150	300	150	
D.P.	F	0	315	236	147	
A.N.	G	1	294	294	147	
L.S.	F	0	180	234	146	
A.K.	G	0	540	232	145	
P.J.	F	5	249	230	144	
G.G.	G	0	200	260	144	
B.R.	G	2	470	470	142	
J.R.	F	3	278	256	142	
G.R.	G	3	545	278	139	
J.B.	F	0	425	221	138	
G.M.	G	0	432	209	136	
E.C.	F	0	160	272	136	
D.F.	F	0	540	273	136	
F.J.	P	0	350	350	135	
J.v.B.	F	0	285	213	134	
C.H.	G	2	663	402	134	
A.H.	G	1	745	525	134	
M.A.	G	1	195	600	133	
A.W.	P	0	240	240	133	
E.S.	F	0	430	396	132	
C.M.	F	0	370	234	130	
C.R.	F	0	200	179	128	
V.H.	F	2	150	300	125	
E.M.	F	0	500	220	122	
J.F.	F	0	845	338	121	
V.M.	G	0	239	288	120	Normal
S.H.	P	0	435	215	119	
G.W.	P	0	390	234	117	
I.B.	F	8	170	221	110	
F.T.	F	1	545	218	109	
E.A.	G	0	230	345	105	Borderline
J.P.	F	4	370	185	102	
G.F.	P	0	440	189	94	Slightly Deficient
A.J.	P	0	280	184	66	

VITAMIN "C" NUTRITION

of

BATTSWOOD COLOURED SECONDARY SCHOOL

F E M A L E S (19 Cases)

Name	Diet	C.F.T.	5-Hour Excretion Test. Volume Urine.	Total mgm. Vit.C. Excreted.	% Nutrition	
M.S.	Ex.	0	343	243	203	
M.M.	Ex.	0	525	350	194	
A.H.	Ex.	0	424	365	182	
D.F.	G	0	273	328	182	
K.A.	G	0	145	216	180	
V.N.	G	0	280	240	170	
E.A.	G	0	300	450	161	
E.J.	G	0	418	226	161	Excellent
R.C.	G	0	410	353	160	
I.N.	G	0	150	450	160	
R.E.	G	0	170	289	159	
M.B.	G	0	330	396	156	
H.B.	G	0	470	329	149	
M.T.	G	0	210	354	148	
B.P.	F	5	465	265	147	
v.d.H.	G	0	260	312	142	
M.M.	G	5	195	253	140	
E.C.	F	2	150	300	136	

It will be noted that of these 107 cases,

96 can be grouped as Excellent

6 " " " " Normal

3 " " " " Borderline

2 " " " " Slightly Deficient.

The average for the 5 Hour Test is 155%

The average for the C.F.T. is 0.7 Petechiae.

The Average Total Urinary Output for 5 Hours is 376 ccs.

Excluding the 3 Borderline cases, 1.9% showed deficient Vitamin C nutrition.

4. BATTSWOOD PRIMARY COLOURED SCHOOL 50 CASES.

These children, of a younger age group, come from a similar coloured community to the one just dealt with. The close agreement between the average percentage Vitamin C nutrition of the two groups is quite striking.

The full lists of results for male and female subjects is appended below, the final averages and calculations being based as before on the total number of children.

VITAMIN "C" NUTRITION

of

BATTSWOOD (PRIMARY) COLOURED

M A L E S (20 Cases)

Name	Diet	C.F.T.	5 Hour Excretion Test: Volume Urine.	Total mgm. Vit.C. Excreted.	% Nutrition	
D.A.	Ex.	0	270	270	193	
R.H.	G	4	320	213	177	
J.S.	G	0	400	320	177	
J.D.	G	0	270	294	163	
B.W.	G	0	255	195	163	
J.S.	G	2	130	260	162	Excellent.
E.H.	G	0	170	291	161	
H.M.	G	2	210	252	158	
T.F.	G	0	250	213	151	
R.D.	G	1	90	270	150	
C.I.	G	0	245	294	147	
A.W.	G	3	285	342	143	
E.P.	F	0	195	234	130	
A.L.	F	0	240	221	122	Normal.
J.J.	P	0	260	237	118	
P.L.	F	0	240	240	109	Borderline.
R.E.	P	0	120	214	106	
L.v.d.H.	P	5	105	179	98	Slightly Deficient.
W.W.	P	0	175	149	93	
C.L.	F	0	215	183	91	

VITAMIN "C" NUTRITION

of

BATTSWOOD PRIMARY COLOURED SCHOOL

F E M A L E S (30 Cases)

Name	Diet	C.F.T.	5 Hour Excretion Test			
			Volume Urine.	Total mgm. Vit.C. Excreted.	% Nutrition.	
O.C.	G	2	505	429	238	
L.A.	G	0	535	428	195	
R.J.	G	0	575	310	194	
R.H.	Ex.	0	255	382	191	
L.L.	F	1	176	299	187	
J.B.	G	0	445	253	181	
M.D.	G	0	380	359	179	
J.J.	G	0	335	285	177	
V.J.	G	0	470	352	176	
J.G.	G	0	285	222	176	
I.H.	F	2	247	247	176	
E.de V.	G	1	435	348	174	
D.C.	G	3	260	312	173	Excellent
R.S.	G	0	160	272	170	
E.R.	G	0	270	270	169	
R.de V.	G	1	520	369	168	
C.M.	G	0	403	300	166	
H.J.	G	0	440	264	165	
C.B.	G	0	345	345	157	
J.S.	G	0	280	280	155	
H.R.	G	0	165	210	150	
J.C.	F	0	240	206	147	
M.T.	F	0	400	320	145	
M.F.	F	0	395	261	144	
I.S.	G	0	165	198	141	
M.A.	G	1	370	184	131	
F.A.	P	1	260	156	130	
C.S.	F	0	160	208	115	Normal
L.W.	P	0	560	185	102	Borderline
E.L.	P	0	195	141	88	Slightly Deficient

It will be noted that of these 50 cases

40 can be grouped as Excellent

3 " " " " Normal

3 " " " " Borderline

3 " " " " Slightly Deficient

1 " " " " Definitely Deficient

The Average for the 5 Hour Test is 153.4%

The Average for the C.F.T. is 0.6 Petechiae.

The Average Total Urinary Output for 5 Hours is 294 c.c.s.

Excluding the 3 Borderline cases, 8% showed deficient Vitamin C nutrition

5. SALT RIVER, CECIL ROAD, PRIMARY COLOURED SCHOOL (57 Cases).

This group of coloured children was very similar to the two foregoing groups from the Battswood Schools. Whereas the latter were representative of the suburban community, the Salt River group were taken from a central urban area, where a kitchen garden is an impossibility and food prices somewhat higher.

A full list of results, both male and female arranged in descending order of nutrition is here appended, the final calculations being as before

VITAMIN "C" NUTRITION

of

SALT RIVER, CECIL ROAD, COLOURED SCHOOL (57 Cases).

Name	Diet	C.F.T.	5 Hour Excretion Test: Volume Urine.	Total mgm. Vit.C. Excreted.	% Nutrition.	
J.J.	Ex.	0	300	510	255	
L.V.	G	0	485	344	191	
F.J.	G	0	412	309	171	
M.M.	G	4	237	204	170	
F.K.	G	0	180	270	169	
F.H.	Ex.	1	247	370	168	
E.J.	F	1	195	331	166	
C.A.	G	0	235	400	166	
M.P.	F	2	225	300	166	
A.F.	G	2	345	297	165	
K.D.	G	1	470	256	160	
E.D.	G	0	240	192	160	
K.L.	F	0	85	255	159	
S.J.	F	0	295	317	159	
R.I.	F	0	425	283	157	
E.J.	G	1	255	306	153	Excellent.
J.A.	G	2	340	272	151	
J.T.	G	0	180	360	150	
A.M.	F	0	375	206	147	
S.M.	G	0	252	378	145	
S.W.	G	0	260	312	142	
B.C.	G	12	190	285	142	
H.B.	F	0	175	225	140	
J.H.	F	0	380	253	140	
K.G.	G	0	140	420	140	
E.C.	F.	1	230	276	138	
E.S.	F	0	480	221	138	
S.J.	F	0	205	273	137	
J.C.	F	0	145	217	136	
K.M.	F	0	355	240	133	
H.B.	G	0	120	288	131	
J.M.	F.	2	315	252	126	
J.F.	F	0	225	300	125	
R.B.	F	1	215	198	124	
P.W.	F	0	150	150	122	
J.A.	F	0	245	267	121	
C.S.	F	0	215	172	121	
L.P.	F	0	280	168	120	
R.B.	F	0	160	192	120	
G.C.	F	2	240	288	120	Normal.
T.D.	F	0	95	142	119	
R.A.	F	2	165	275	118	
Y.D.	P	0	316	237	118	
R.W.	G	0	135	230	115	
R.H.	F	0	185	277	115	
J.S.	F	0	540	297	114	
E.K.	F	0	65	156	114	
A.R.	F	0	830	199	110	
I.D.	F	0	260	260	108	
C.McN.	F.	0	555	300	107	
D.J.	P	0	98	147	105	Borderline.
A.S.	F	0	205	246	102	
J.R.	F	0	100	200	100	
N.B.	F	0	165	151	94	
D.V.	F	0	205	205	93	Slightly Deficient.
S.S.	P	0	100	109	91	
I.McN.	G	0	257	193	88	Definitely Deficient.

It will be noted that of the 57 cases,

33 can be grouped as Excellent

15 " " " " Normal

5 " " " " Borderline

3 " " " " Slightly Deficient

1 " " " " Definitely Deficient

The Average for the 5 Hour Test is 136%

The Average for the C.F.T. is 0.6 Petechiae

The Average Total Urinary Output for 5 hours is 282 ccs.

Excluding the 5 Borderline cases, 7% showed deficient Vitamin C nutrition

6. ST. GEORGE'S COLOURED SCHOOL ATHLONE (12 cases).

These children were drawn from a vastly inferior social community. Unemployment was the rule rather than the exception and employment at best only temporary. Their homes, however, were situated in the country and in nearly every case, a small kitchen garden to provide green vegetables, far from being an impossibility became an economic necessity, the diet of these people being almost wholly vegetarian, fats and first-class proteins being quite beyond their means.

The full list of results is appended below.

VITAMIN "C" NUTRITION

of

ST. GEORGE'S COLOURED SCHOOL, ATHLONE (12 Cases).

Name	Diet	C.F.T.	5 Hour Excretion Test: Volume Urine.	Total mgm. Vit.C. Excreted.	% Nutrition.	
M.J.	F	0	520	312	195	
D.A.	F	0	158	288	160	
D.S.	G	0	448	224	160	
H.C.	F	0	375	281	156	
A.C.	F	0	460	184	153	
E.A.	F	0	105	178	149	Excellent.
W.B.	F	0	155	206	148	
L.J.	F	0	182	198	142	
D.K.	F	0	185	222	139	
M.S.	F	0	350	192	137	
J.J.	F	0	240	180	112	Normal.
I.R.	F	0	85	127	106	Borderline.

It will be noted that of these 12 cases,

10 can be grouped as Excellent

1 " " " " Normal

1 " " " " Borderline

The Average for the 5 Hour Test is 146%

The Average for the C.F.T. is 0 Petechiae

The Average Total Urinary Output for 5 Hours is 272 ccs.

Excluding the single Borderline case, no cases showed deficient Vitamin C nutrition.

DUINEFONTEIN COLOURED SCHOOL, ATHLONE (24 Cases)

This somewhat larger group was similar in all respects socially and environmentally to the previous group of St. George's school children. If anything, poverty was even more marked in this group which was the poorest one encountered.

The full list of results is appended below.

VITAMIN "C" NUTRITION

of

DUINEFONTEIN (COLOURED) SCHOOL, ATHLONE (24 Cases)

Name	Diet	C.F.T.	5 Hour Excretion Test: Volume Urine.	Total mgm. Vit.C. Excreted.	% Nutrition.	
S.A.	F	0	150	225	187	Excellent.
I.P.	G	0	495	297	148	
M.K.	F	0	130	173	144	
K.F.	F	0	215	258	143	
M.I.	G	0	345	197	140	
P.M.	F	0	240	192	136	
B.T.	P	0	220	189	135	
H.P.	G	0	200	160	133	
F.J.	F	0	215	185	127	
A.J.	F	0	250	200	125	
L.B.	P	0	120	204	113	Normal.
D.A.	F	3	150	150	112	
H.C.	P	0	180	180	112	
J.I.	F	0	515	190	106	Borderline.
A.P.	P	0	350	210	105	
W.C.	P	0	330	125	104	
S.R.	P	0	105	157	98	Slightly Deficient.
C.K.	F	0	195	156	97	
G.R.	P	0	125	166	92	
K.F.	P	0	605	199	90	
A.F.	P	0	670	124	88	Definitely Deficient.
A.G.	P	0	500	150	75	
J.F.	P	0	140	84	70	
S.R.	P	0	70	60	50	

It will be noted that of these 24 cases,

10 can be grouped as Excellent
3 " " " " Normal
3 " " " " Borderline
4 " " " " Slightly Deficient
4 " " " " Definitely Deficient

The Average for the 5 Hour Test is 113%
The Average for the C.F.T. is 0 Petechiae
The Average Total Urinary Output for 5 Hours is 271 c.c.s.
Excluding the 3 Borderline cases, 33.3% showed deficient Vitamin C nutrition.

8. ST. PAUL'S COLOURED SCHOOL, RONDEBOSCH (11 Cases).

This small group and the one to follow, fall in between the Battswood, or Salt River, and Athlone Schools economically and socially speaking. That is, the community lay in that area where town becomes suburbia, and employment was fairly regular though of a temporary nature.

The full list of results appears below.

It will be noted that of these 11 cases,

5 can be grouped as Excellent

3 " " " " Normal

1 " " " " Borderline

2 " " " " Slightly Deficient.

The Average for the 5 Hour Test is 130%

The Average for the C.F.T. is 0.5 Petechiae.

The Average Total Urinary Output for 5 Hours is 266 c.c.s.

Excluding the single Borderline case, 18% showed deficient Vitamin C nutrition.

ST. ANDREWS COLOURED SCHOOL, RONDEBOSCH (10 Cases).

This group is similar in all essentials to the previous one - St. Pauls School.

A full list of the results is appended below.

VITAMIN "C" NUTRITION

of

ST. ANDREWS COLOURED SCHOOL, RONDEBOSCH (10 Cases)

Name	Diet	C.F.T.	5 Hour Excretion Test: Volume Urine.	5 Hour Excretion Test: Total mgm. Vit.C. Excreted.	% Nutrition.	
M.F.	G	0	280	260	162	Excellent.
N.F.	G	0	305	284	158	
L.H.	F	0	120	204	146	
J.S.	F	2	340	226	141	
G.B.	P	0	340	226	141	
A.v.D.	F	4	115	196	140	
ML.	F	0	120	180	130	
J..B.	F	0	440	167	119	Normal.
L.C.	F	0	300	200	111	
J.v.D.	F	0	90	180	100	Borderline.

It will be noted that of these 10 cases,

7 can be grouped as Excellent

2 " " " " Normal

1 " " " " Borderline

The Average for the 5 Hour Test is 135%

The Average for the C.F.T. is 0.6 Petechiae

The Average Total Urinary Output for 5 Hours is 245 c.c.s.

Excluding the single Borderline case, no cases showed deficient Vitamin C nutrition.

DISCUSSION

and

CONCLUSIONS.

S U M M A R Y.

Before embarking upon a consideration and discussion of the foregoing results, a word must be said of the blood plasma levels of Vitamin C to enable us to compare and to assess the relative values of the three Vitamin "C" nutrition tests which I have employed in this survey.

So far little or no mention has been made of blood Vitamin C levels. Various independent workers have investigated this aspect of Vitamin C nutrition and have arrived at figures which are fairly close in agreement.

Thus to quote but a few, in 1934, at a conference on Vitamin C held at Darmstadt (Wright and Lilienfeld 1936) Professor Gabbe of Bremen reported the normal blood Vitamin C to be between the figures 0.7 and 1.2 mgm. % with values rising or falling 30-50% as the Vitamin C intake rises of falls.

Baumann (1937) gives a somewhat higher upper limit of normal and a somewhat lower limit of normal, giving a wider range of normality i.e. 0.45 - 2.6 mgm.%. He regarded a figure below 0.45 mgm.% blood Vitamin C as being indicative of Vitamin C deficiency.

Pijoan and Klemperer's (1937) figures are 0.65 - 2 mgm.% and they give the following scale of values:-

1.5 - 2 mgm. % Vitamin C in blood - Saturation.
0.72 - 1.3." " " " " " - Normality.
0.27 - 0.52" " " " " " - Deficiency.

Portnoy and Wilkinson (1938) in a paper on the relationship of Vitamin C deficiency to peptic ulceration give the normal range of blood Vitamin C as being 0.60 - 1.85 mgm.%, with levels of 0.14 - 0.59 mgm.% occuring in patients with peptic ulcers or haematemesis.

Van Eekelen (1936) gives the normal blood level as being 1.3 mgm.% with the deficiency level falling somewhere between 0.2 and 0.4 mgm.%. He regarded 13 mgm.% as being the upper limit of normal, that is, approaching saturation level.

One will note that there is a very close agreement between the lower figures of normality and between the figures given as indicating Vitamin C deficiency. The agreement between the upper levels is not so close: vide 2.6 mgm.% (Baumann) and 2 mgm.%

(Pijoan and Klemperer) though the latter workers do give the range of normality as 0.7 - 1.3 mgm.%, stating that 2 mgm.% is indicative of saturation.

In connection with these unusually high upper levels of normality the work of Faulkner & Taylor (1938) is interesting. From their experiments they concluded that the output of Vitamin C in human urine is dependent upon the serum level of the Vitamin and found that Vitamin C is a threshold substance with a critical level of excretion in the vicinity of 1.40 mgm. %. A maintained value of blood Vitamin C at or above this level corresponds to the state of saturation described by Harris.

Sifting this evidence then we find that there is fairly general agreement about the lower limit of normality i.e. 0.7 mgm.% blood Vitamin C. Bearing in mind the renal threshold value of blood Vitamin C the upper level can be taken as being 1.3 mgm.% blood Vitamin C. From the same evidence we can deduce that anything below 0.7 mgm.% blood Vitamin C represents a slight but definite deficiency and anything below 0.4 mgm. most definite evidence of Vitamin C deficiency.

Wright et al in evolving their 5 Hour Urinary Excretion Test based their standards on such blood Vitamin C levels. Thus 100% nutrition as determined by the 5 Hour Test corresponds approximately with a blood Vitamin C level of 0.7 mgm.% - the lower limit of normality. Note, this figure, 100%, by no means represents saturation with Vitamin C which would have to be represented by the figures 150 - 200% by the 5 Hour Test.

It was the wide limits of normality which made me adopt the rather complicated 5 Hour Test scale of nutrition, for the figure 100% is apt to give a false impression of the subject's Vitamin C nutrition as has been shown by comparison with the blood Vitamin C figures. Therefore 100-110% levels have been grouped as Borderline cases and 110-125% levels as representing Normal Vitamin C nutrition, a conservative standard. 125% Levels have been termed Excellent, though even this does not represent complete saturation and only the upper limits of normality.

Descending the scale, the classification of Slightly Deficient, Definitely Deficient and Grossly Deficient is less important than the upper levels, as the grouping is an artificial one and all these cases could be placed together, simply, as the Deficiency group.

The reason for my employing this detailed descending scale was to enable me to attempt to correlate the 5 Hour Test results with those obtained by means of the Capillary Fragility Test, for as I have mentioned before it appeared to me that one of the greatest objections to the Capillary Fragility Test is that it fails to select the milder cases of Vitamin C Deficiency. Thus, if the blood Vitamin C figures are proven and accepted, and the ideals of prophylaxis are to be kept in mind such a failing in the test is a serious disadvantage, for as is borne out by my results, large numbers of Vitamin C deficient cases are missed and their health thereby possibly jeopardised.

This point may be further emphasized by referring to Göthlin's paper entitled "When is Capillary Fragility a Sign of Vitamin C Subnutrition in Man?" of 1937. Thus he himself points out that,

judging from parallel determinations made by Degeller and by van Eekelen of blood Vitamin C values, his method (C.F.T.) does not reveal Vitamin C deficiency until the blood Vitamin C is as low as 0.1 mgm.%. In other words, therefore, if 0.7 mgm.% is the lower limit of normality of Vitamin C nutrition, all cases with blood Vitamin C levels ranging from 0.2 mgm.% to 0.7 mgm.% will remain undetected by the Capillary Fragility Test. This group represents, possibly, the mildest degree of Vitamin C deficiency but it represents a departure from the normal and should be rendered capable of recognition. This is not possible by means of the Capillary Fragility Test. Furthermore, Göthlin recognises the fact that this test is only to be used where the infinitely more accurate blood Vitamin C or urinary excretion tests cannot be employed for one reason or another. Thus he suggests that the Capillary Fragility Test is of its greatest use in large mass surveys, where venupunctures and tedious urinary estimations are objections. However, even in this sphere, the test would appear to have

limitations, for as is visible from a glance at any one of the tables of results e.g. Ward Cases (European), in the milder cases of deficiency at any rate, there is no constant relationship between Vitamin C nutrition and the number of petechiae produced by the fragility Test. For example, we have such discrepancies represented by cases R.L. and F.V. both of Normal Vitamin C nutrition as determined by the 5 Hour Test yet both recorded as Vitamin C deficient cases by the Capillary Fragility Test. At the other extreme we have such cases as C.W. and L.G. registering no petechiae yet each proving to show only 38% Vitamin C nutrition. These examples can be repeated numerously as the individual variation in response to the Capillary Fragility Test seems to be unpredictable and hence the Test in mass surveys would have very distinct limitations. So much so, in fact, that its only reliable use appears to be aptly summed up in Göthlins own statement where he assumes that if in one and the same person the number of petechiae for the same pressure treatment diminishes to a significant degree this diminution is evidence of an increase in his supply of Vitamin C (by the same

token a rise in the number of petechiae in the same person would indicate a decrease in his supply of Vitamin C.)

Furthermore, as Göthlin himself admits, and as my own results show, the petechial index cannot be used to compare the Vitamin C nutrition of one person with that of another e.g. a person with a petechial index of 2 is not necessarily in a better state of Vitamin C nutrition than one with an index of 4, though both of them would be classed as having normal Vitamin C nutrition. A glance at any of the group lists of results will make this point clear. This disability taken in conjunction with the foregoing objections to the Capillary Fragility Test led one to the conclusion that the test is by no means a satisfactory one, and at best, is only to be resorted to when the more accurate, yet less facile tests cannot be employed.

The position of the Intradermal Test is even less satisfactory than that of the Capillary Fragility Test. The Capillary Fragility Test did give fairly reliable negative evidence of gross Vitamin C deficiency and in only one series of 58 Ward Cases (European) did it give but two false

positives, i.e. R.L. and F.V. There were no other false positives in the remaining groups examined. However, it must be stressed again that even the value of this fairly reliable negative evidence is greatly detracted from because the milder degrees of Vitamin C deficiency are completely missed.

These objections apply in even greater degree to the Intradermal Test for here one could be certain neither of positive nor of negative evidence of Vitamin C deficiency.

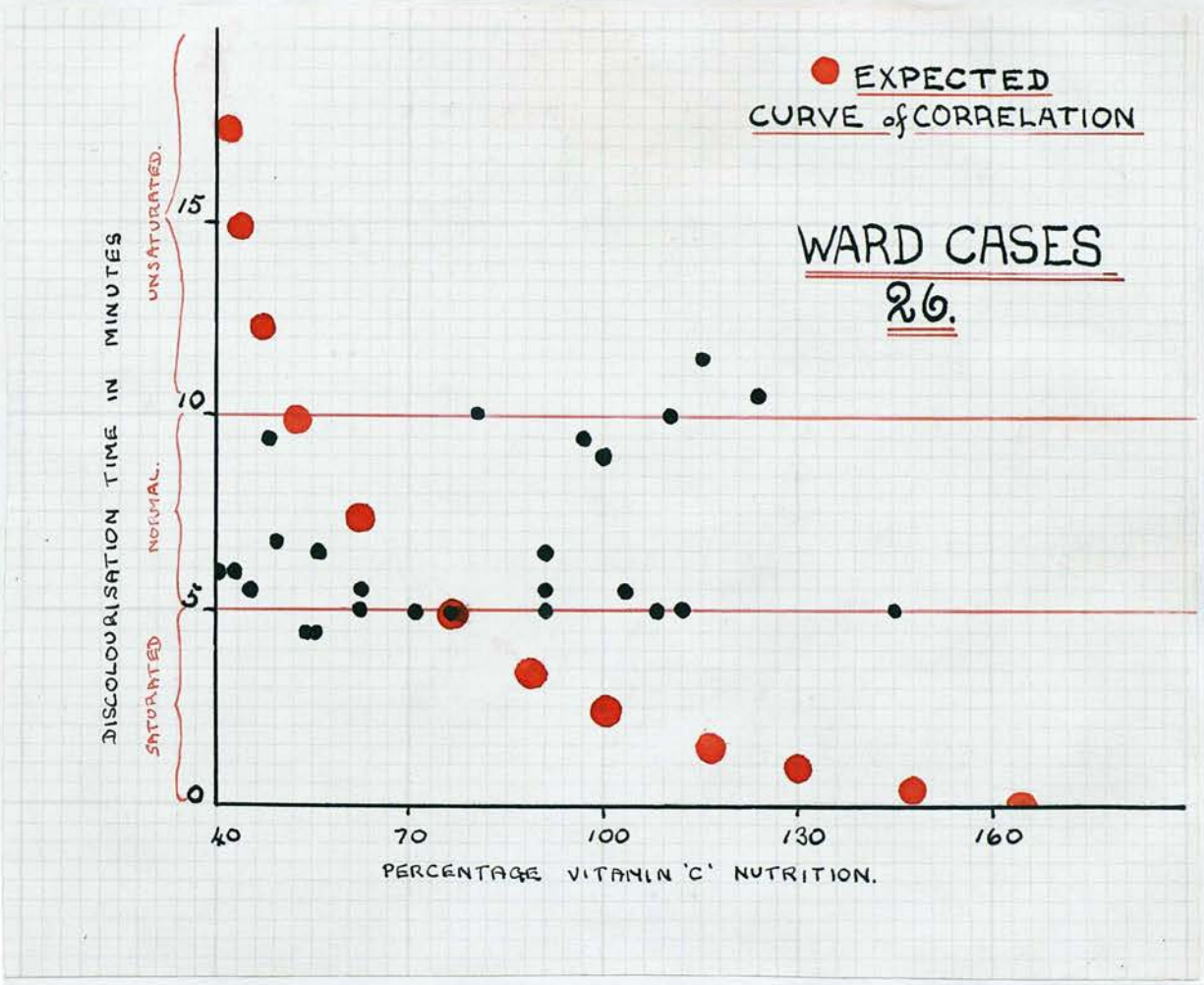
Portnoy and Wilkinson (1938) in their paper on the Intradermal Test of Rotter accepted the latter's standards i.e.

(1) Decolorisation in less than 5 minutes - Saturated.
(2) " " 5 - 10 minutes - Normal.
(3) " " more than 10 mins. - Deficient.

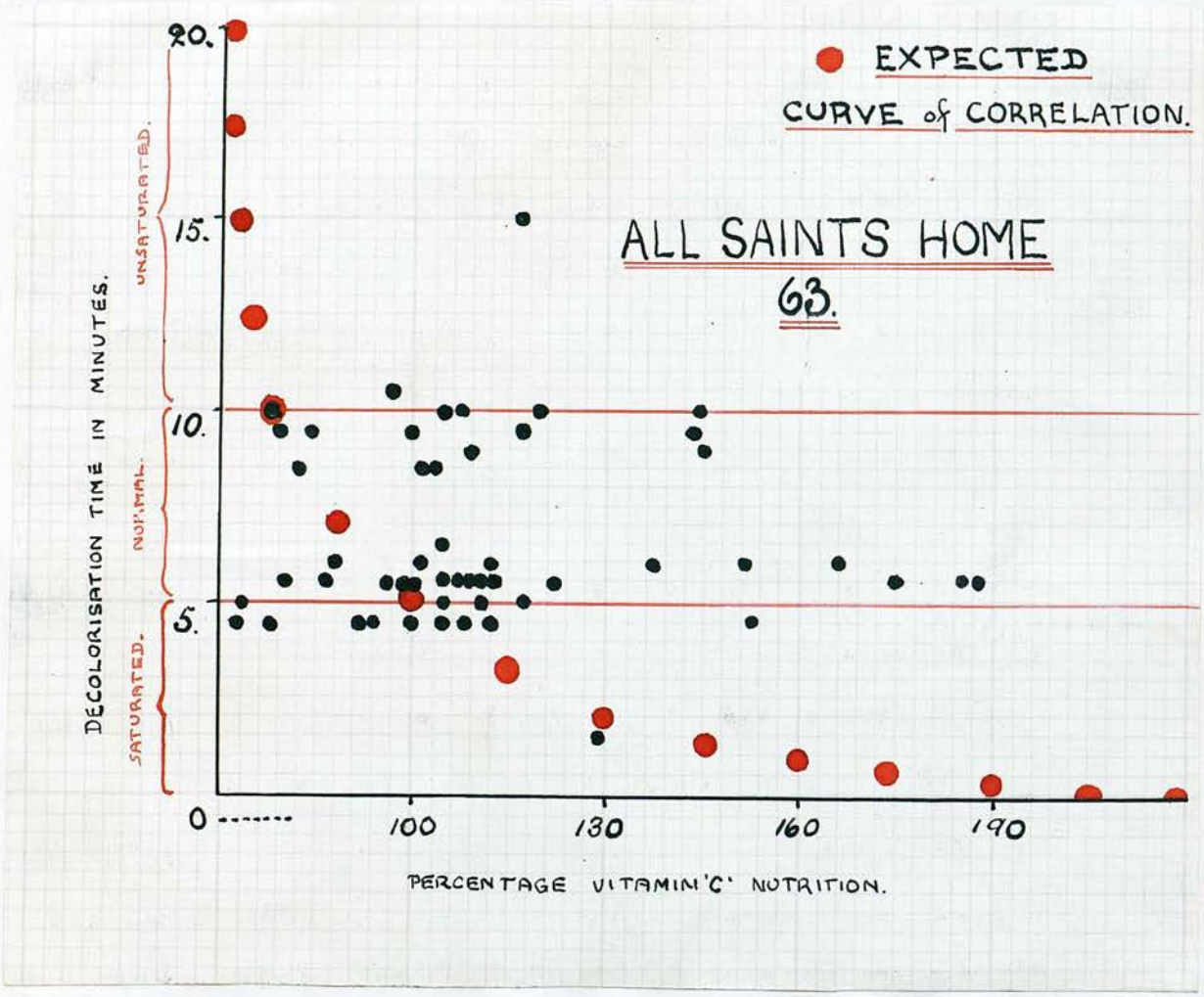
The corresponding blood Vitamin C values for these three groups were

(1) 1.32 - 2 mgm.% Blood Vitamin C.
(2) 0.72 - 1.3 " " " " "
(3) 0.27 - 0.52 " " " " "

In an investigation into 103 patients they concluded that the decolorisation times bore a constant parallel to the corresponding blood Vitamin C values.



Graphic Record of Ward Case Group (26 Cases) to show lack of correlation between results of Intradermal Test and 5 Hour Excretion Test.

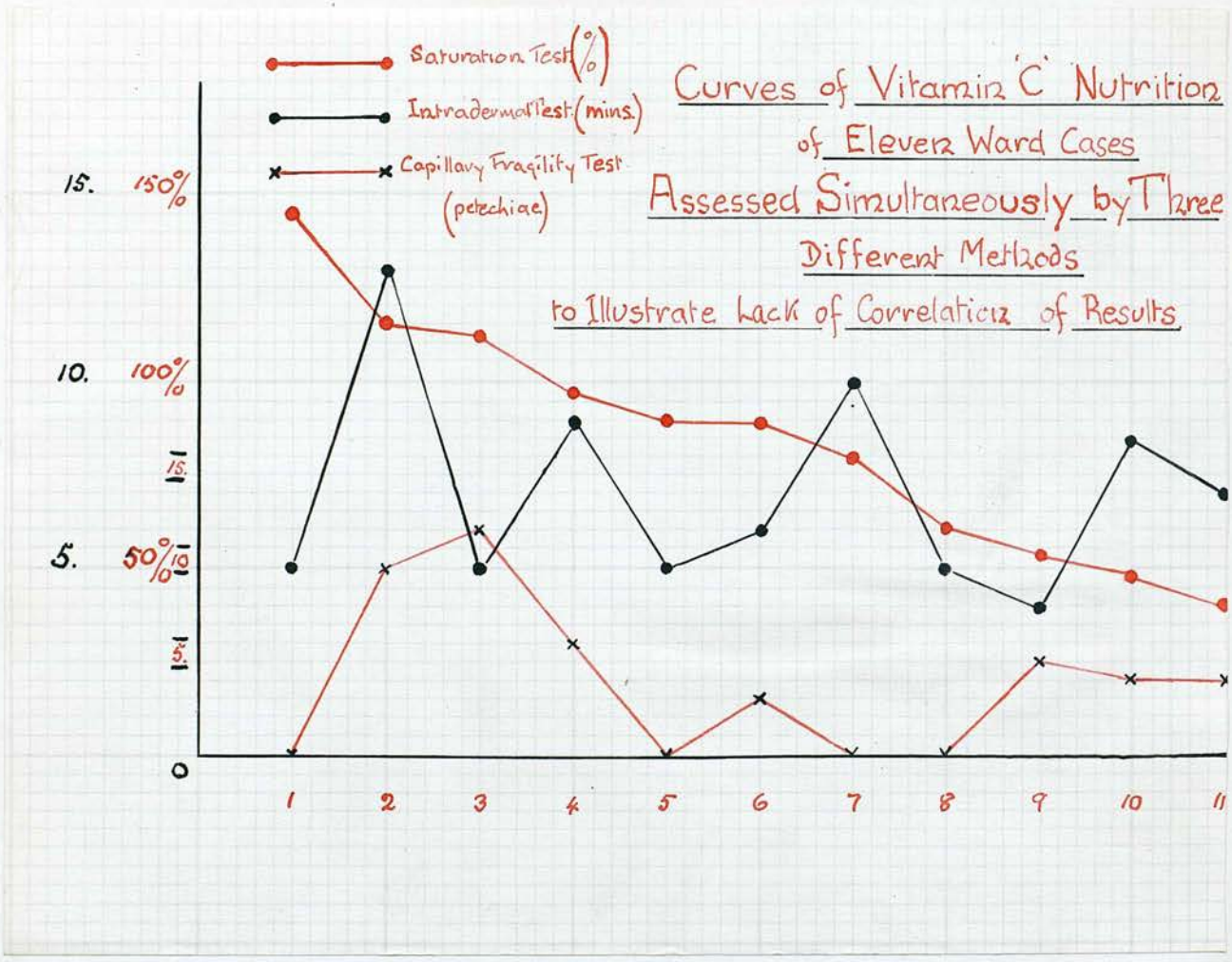


Graphic Record of All Saints Group (63 Cases) to show lack of correlation between results of Intradermal Test and 5 Hour Excretion Test.

However in my series of 89 cases, using the 5 Hour Excretion Test as a guide, I could find no correlation whatsoever, (See two graphs opposite) both in a series of 26 adults and in a series of 63 children.

Extreme instances of fallacies are seen in the Ward Case groups (26 cases) both European and non-European, illustrated by cases R.E.S., H.M., with I.D.T. figures of 13 and 11 minutes (deficiency) respectively, yet with Vitamin C nutrition of 115.6 and 124% (normal) respectively. At the other end of the scale we have cases C.W. and E.W. with I.D.T. figures of 4 minutes (saturated) yet with Vitamin C nutrition of 54 and 56% (Definitely Deficient) respectively. Similar numerous examples can be drawn from the All Saints group (63 cases).

To make the complete absence of reliance that can be placed on the Intradermal Test finally clear, one may refer to the incidental experiment carried out on 16 All Saints cases where extra Vitamin C was supplied to them in the form of orange juice in large quantities for some days. Their percentage Vitamin C nutrition rose from the central average of 105.5% to 135% - a remarkable improvement from the



Graphic Illustration of lack of correlation between Capillary Fragility Test and Intradermal Test, and the 5 Hour Urinary Excretion Test. Tests carried out simultaneously on Eleven Ward Cases.

Borderline Grade to the Excellent Grade. However, the decolorisation time instead of falling, as would be expected, actually rose from 5 minutes to 7 minutes.

In no wise could I find any evidence whatsoever to justify placing any reliance on the Intradermal Test in its present form. The utter lack of correlation between decolorisation time and Vitamin C nutrition is well illustrated by the two aforementioned graphic records.

Finally the lack of correlation between the three tests is illustrated graphically by 11 (eleven) random Ward Cases where the 5 Hour Excretion Test estimations of Vitamin C nutrition have been arranged in a descending scale. (See graph opposite).

Relation of Diet to Vitamin C Nutrition.

When one comes to consider the part that diet plays in Vitamin C nutrition, and the actual results of the nutritional survey, some interesting facts emerge.

Thus it will be seen that the lowest

group averages appear in the two Ward Case groups (European and non-European) and in the All Saints group. The highest group averages appear in the two Battswood School groups both non-European. Thus, if one has proceeded to reason on a socio-economical basis, one is surprised to find the poorer non-European groups in an infinitely better state of Vitamin C nutrition than the presumably more well-to-do Europeans. The real explanation for this apparent anomaly would appear to lie in two factors - (a) ignorance, and (b) economic stress. The first, ignorance, shows its malign effect in the European group of hospital cases, the second, economic stress, shows its beneficial effect in the non-European groups. (This argument does not apply to the non-European group of Ward Cases, as they were a heterogeneous group drawn from all parts of the town proper and usually in an extreme degree of poverty).

Thus the European Ward Case group, of a moderately good economic status, confined its diet to one composed largely of starchy foods, canned and preserved foods with very little in the way of

fresh fruit and green vegetables. Thus although there is an abundance of these two foodstuffs at a low price available in this country, through lack of knowledge the family budget is squandered on a more expensive yet less nutritious diet.

On the other hand, though these factors would apply equally well under other circumstances to the two country Battswood School groups, we find that owing to economic stress, these families live on a diet mainly vegetarian in nature, meat, preserved foods and other factory produced foods often being beyond their reach. Thus larger quantities of green vegetables which can be cheaply bought are consumed and, in many cases, consumed raw to save cooking expenses, e.g. mainly carrots, tomatoes and cabbage. Further-more, the economic stress is frequently eased, particularly in suburban and country districts, by the small kitchen garden which in almost every case adds its quota of fresh vegetables and sometimes fresh fruit to the family table.

This assumption gains further support as we examine the results in other groups. Thus in the

admittedly small Duinefontein and St. George's groups living in a country district, extreme poverty was the rule (they were far and away the two most penurious groups examined) I found a surprisingly high standard of Vitamin C nutrition, viz., 113 and 146% respectively. This on investigation proved to be due to the fact that these children lived almost exclusively on a home-grown vegetarian diet. (In this report there is unfortunately no room for a discussion of other glaring nutritional defects).

As we approach nearer the city's centre, although the economic position improves the Vitamin C nutrition falls, though not below normal, as is strikingly shown by the Salt River, St. Paul's and St. Andrew's School groups which showed figures of 136%, 130% and 135% respectively. It is in these groups that I would suggest that ignorance of what a physiological diet should be, plays a part. This is seen again in the All Saints group with an average of only 110.4%. This large group of cases had been on a standard diet which could only be classed as Fair, from the Vitamin C standpoint, there being little or no fresh fruit or fresh vegetables included in the diet. If the 16 cases who

by chance received extra oranges over a period are excluded the average Vitamin C nutrition falls sharply to 101.8% which strictly reflects their true state of Vitamin C nutrition. (N.B. Even this figure excludes the very large number of Borderline cases in this group, viz. 20).

It will be noted that the control group of European Observatory school children, fall into the near-city category. Thus, although the economic status was quite satisfactory and an adequate diet available, through partial ignorance as to what constitutes first-class foodstuffs, the Vitamin C nutrition although normal, is lower than that of the poorer non-European groups at the Battswood schools. This is shown, too in the group of 15 adult European controls, who although on a diet accepted as normal, only averaged a Vitamin C nutrition of 128.8% The only two controls who approached actual saturation, which is the ideal, were the stenographers A.P. and A.S., whose diet consisted very largely of orange juice, fresh fruit and an abundance of fresh vegetables giving them Vitamin C nutritions of 187% and 169% respectively.

Where the Vitamin C nutrition of <u>groups</u>

is being assessed, as opposed to that of individuals, the average dietary history is quite a reliable guide as has been illustrated above, but at best this is an extremely rough and ready method. This method applied to the individual, however, is quite valueless. This is ideally and very vividly illustrated in the All Saints group, where, if we exclude the 16 cases who received extra Vitamin C in the form of oranges, each child had been on a standard diet for many months past, all being in apparent good health. In the remaining 47 cases the Vitamin C nutrition ranged from 129% to 77% i.e. the children, in spite of receiving identical quantities of Vitamin C apparently absorbed it and utilized it in widely divergent degrees, so that while some showed a Normal degree of Vitamin C nutrition others showed a Definitely Deficient degree of nutrition.

Thus it is emphasized that where any Vitamin C nutrition survey is being carried out in any school, institution or district, reliance as to the degree of nutrition should not be placed upon a mere inquiry into the dietary

habits alone, but should be supplemented by one of the proven chemical tests for Vitamin C nutrition in order to discover those cases, who owing to faulty absorption and utilization of Vitamin C show a deficiency in this Vitamin.

Vitamin C Deficiency and Peptic Ulceration.

Only a brief reference will be made to this point in passing as a very small number of cases were investigated and the results inconclusive.

Thus in 11 European Ward Cases examined, suffering from peptic ulcer and from haematemesis, the average Vitamin C nutrition proved to be 87.3% which is Definitely Deficient, yet actually higher than the average for the total number of cases.

In 4 non-European cases of peptic ulceration the average Vitamin C nutrition proved to be 114%, very much higher than the general average for the whole group, and in the grade of Normality.

If any conclusions are to be drawn from these figures, they are that Vitamin C deficiency of a mild nature appears to play no constant part in the aetiology of peptic ulcer.

Vitamin C and Diuresis.

Though no detailed study of the possible diuretic powers of Vitamin C as reported by Abbasy (1937) and other workers, was made, the following figures for the average 5 Hour excretions of urine after the test dose in the various groups of school children are of interest.

I was unable to attribute any specific diuretic property to Vitamin C as used in the proportions for the 5 Hour Test dose, which is a comparatively large amount, many times in excess of the normal daily requirement. However, if the average figures for the groups are studied in chronological or seasonal order from mid-winter to mid-summer, it must be admitted that it is something more than coincidence that produces this falling scale as we advance from the cold of Winter to the heat of Summer.

All Saints	442 ccs -	August.
Battswood Secondary	376 "	September.
Battswood Primary	294 "	Early October.
Salt River	282 "	Late October.
St.George's	272 "	Early November.
Duinefontein	272 "	Early November.
St. Paul's	266 "	Late November.
St. Andrew's	245 "	Late November.
Observatory	186 "	Early December.

And so one comes to the conclusion that this gradual variation in the urinary output after administration of Vitamin C is due to variation in the seasonal temperature, and that no diuretic effect was noted.

In summing up the state of Vitamin C nutrition in the Cape Peninsula one finds that of a total of 507 cases, 124 or 24.6% proved to be definitely deficient.- Excluding the 112 Ward Cases, where pathological factors were at work, and the 15 control cases, one still finds that of the total of 380 school children in apparent good health, 80, or 21.1% showed definite Vitamin C deficiency. Conservative standards were taken and all Borderline cases were excluded, so that these figures are significant.

In view of the fact that Vitamin C deficiency is so common and can be so easily remedied it is strongly recommended that this widespread deficiency be cofrected. No reference has been made to the general nutrition and clinical appearance of the subjects, yet it is worth placing on record how many fell short of the normal standard in this survey.

Already at nearly all these schools which

were examined, a daily ration of milk is supplied to each child at no great expense or inconvenience, and the beneficial results have been gratifying. In view of the small daily requirements of the growing child, 20-40 mgm. Vitamin C, the easy and palatable manner in which it can be administered, the rapidity with which a state of normality, or even better, saturation, can be reached and maintained, it is suggested that one orange daily, or every second day be made available to any school or institution where, after investigation, Vitamin C deficiency is discovered to be prevalent.

It is beyond the scope of this investigation to discuss the necessity or otherwise of remedying such Vitamin C deficiency states, though sufficient has been said in the earlier chapters to make it plain that these mild deficiency states are to be avoided, as a low reserve of Vitamin C is very rapidly even further diminished to a dangerous level by even mild infections or poverty and the general bodily resistance thereby greatly impaired. In short, these deficiency states represent a departure from the normal standards of sound health and therefore should be corrected.

Table of Summarised Results of the 12 (twelve) groups of cases investigated for Vitamin C Nutrition in the Cape Peninsula.

	GROUP.	No. of Cases.	3 Hour Test.	% Deficiency Cases.	Deficiency Cases.	C. F. I.	I. D. I.	3 Hour Output.	SEASON.
1	WARD CASES. (Euro.)	58.	84.	72.4.	42.	3.5.	—	267.	SUMMER AUTUMN
2	WARD CASES (non-Eur.)	54.	79.	70.4.	38.	1.	—	195.	SUMMER AUTUMN.
3	CONTROLS.	15.	128.8.	6.6	1	—	—	—	—
4	ALL SAINTS (Euro.)	63.	110.4.	28.6.	18.	1.6.	6.7	442.	WINTER.
5	OBSERVATORY (Euro.)	46.	135.6	10.8.	5.	0.5.	—	186.	SPRING.
6	BATTSWOOD SEC.ay (non-E.)	107.	155.	1.9.	2.	0.7.	—	376.	WINTER.
7	BATTSWOOD PRIM.y (non-E.)	50.	153.4.	8.	4	0.6.	—	294.	WINTER SPRING.
8	SALT RIVER (non-Eur.)	57.	136.	7.	4.	0.6	-	282.	WINTER SPRING.
9	ST. GEORGES (non-Eur.)	12.	146.	0.	0.	0.	-	272.	SPRING.
10	DUINEFONTEIN (non-Eu)	24.	113.	33.3.	8.	0.	-	272.	SPRING.
11	ST. PAULS. (non-Eur.)	11.	130.	18.	2.	0.5.	-	266.	SUMMER.
12	ST. ANDREWS. (non-Eu.)	10.	135.	0.	0.	0.6.	-	245.	SUMMER.
*	GRAND TOTAL	507.	—	24.6.	124.	—	—	—	—

S U M M A R Y.

1. A series of 507 cases in the Cape Peninsula, South Africa has been investigated for Vitamin C nutrition.

2. Of the total number of cases, 124 or 24.6% showed marked evidence of Vitamin C deficiency.

3. Of the total number of school children, 380, European and non-European, 80 or 21.1% showed marked evidence of Vitamin C deficiency.

4. Of these children, the Europeans showed a greater percentage of cases of deficiency than the non-European viz., in 109 European cases 23 or 21.1% were deficient, whereas in 271 non-European cases 20 or 7.3% were deficient.

5. During the survey no evidence that Vitamin C has a specific diuretic action appeared.

6. Of the 15 cases examined, there was no conclusive evidence that Vitamin C deficiency plays a constant part in the aetiology of peptic ulcer.

7. The survey was carried out by employing three tests:-

(1) The Capillary Fragility Test.

(2) The Intradermal Test.

(3) The 5-Hour Urinary Excretion Test in response to a Test Dose of Vitamin C,

and the results obtained from them compared.

8. No correlation could be found between these three tests.

9. The Capillary Fragility Test proved

(a) to vary with each individual,

(b) to fail to detect a very large group of mild Vitamin C deficiency cases

(c) to be far from suitable for making an accurate survey of the state of Vitamin C nutrition of any particular group of people, though in any one individual it may have its uses.

10. The Intradermal Test proved to be wholly unreliable in its present form and is considered quite unsuitable for any estimation of Vitamin C nutrition in the human subject.

11. The high incidence of Vitamin C deficiency appears to be due in part to economic conditions and in part to lack of knowledge as to what constitutes

an adequate, well-balanced diet containing all the essential foodstuffs and food factors.

12. It is suggested that the prevalence of Vitamin C deficiency in school children be remedied by the daily (or thrice weekly at least) administration of one orange or its equivalent, and that although Vitamin C Saturation level is the ideal, at least levels of Normality be attained and maintained.

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Liebmann, Wortis & Wortis	1938	Amer.J.of Med.Sci.		196	388
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Lind	1919	Med.J.Aust.		2	107
Lund, Sieck, With & Clemmensen	1937	Klin.Wschr.		16	748
Lueg & Hamman	1939	Med.Welt		No.4	116

M.

Mahlo	1936	Dtsch.Med.Wschr.		62	96
Mahlo & Mulli	1936	Münch.Med.Wschr.		83	1276
Marsh, F.	1936	Nature, Lond.		137	618
McCollum, E.V. & Pitz, W.	1917	J.Biol.Chem.		31	229
McGovern,Gannon,Wright I.S.	1939	Amer.J.Med.Sci.		197	310

M.

Messerlii & Heiman	1938	Rev.de Hyg.		60	20
Mettier,Minot,Townsend	1930	J.Amer.Med.Ass. Part ii		96	1089
Meyer, A.W. & McCormick, L.	1928	Stanford Univ.Press.			
Mitchell, Merrian & Batchelder	1938	J.Home Econ.		30	645
Mituda, H.	1938	J.Agr.Chem.Soc.Japan		14	1335
Molitch	1935	J.Lab.Clin.Med.		21	43
Moore & Ray	1932	Nature, Lond.		130	997
Morawitz	1934	Klin.Wschr.		13	324
Muller	1939	Klin.Wschr.		18	299

N.

Neuweiler, W.	1938	Klin.Wschr.		17	1650
Nisenson & Cohen	1937	Amer.J.Med.Sci.		194	63

O.

O'Hara & Hanck	1936	J.Nutrit.		12	413
Ohnell	1928	Acta med.Scand.		68	176
Otto	1936	Klin.Wschr.		15	1510

P.

Parsons, H.T.	1924	J.Biol.Chem.		59	97
Perry, B.	1935	Lancet		2	426
Platt	1936	Lancet	131	2	366
Poncher & Strubenrauch	1938	J.Amer.Med.Ass.	111		302
Portnoy & Wilkinson March 12th	1938	Brit.Med.J.			554
Portnoy & Wilkinson	1937	Nature, Lond.		139	717
Portnoy & Wilkinson Feb. 12th	1938	Brit.Med.J.			328

R.

Rao, M.N.	1938	Ind.J.Med.Res.	26	171
Rhinehart	1936	J.Lab.Clin.Med.	21	597
Rietschel & Mensching	1939	Klin.Wschr.	18	273
Rietschel	1938	Klin.Wschr.	17	1787
Roberts,Blair,Bailey	1937	J.Paediatrics	11	626
Rolli,Friedman & Rubin	1938	J.Clin.Invest.	17	765
Ross, S.	1931	Med.J.S.Afr.	2	596
Rothstein & Ratish	1935	Proc.Soc.Exp. Biol., N.Y.	32	1088
Rotter, H.	1937	Nature, Lond.	139	717

S.

Sandberg & Dagulf	1939	Nordisk Medicin	1	603
Scheer	1938	Münch.Med.Wschr.	88	256
Schultz	1936	J.Clin.Invest.	15	384
Schultzer, P.	1936	Acta Med.Scand.	88	317
Schultzer, P.	1937	Biochem.J.Part ii.	31	1934
Schultzer, P.	1933	Lancet 225	2	589
Schroeder, H.	1939	Münch.Med.Wschr.	86	133
Schroeder, H.	1938	Dtsch.Med.Wschr.	64	1693
Schroeder, H.	1935	Klin.Wschr.	14	484
Schroeder, H. & Einhauser	1936	Münch.Med.Wschr.	83	923
Schroeder & Harde	1935	Klin.Wschr.	14	484
Sendray & Schultz	1936	J.Clin.Invest.	15	369
Sendray & Muller	1939	J.Clin.Invest.	18	135
Shepp & Schroeder	1935	Klin.Wschr.	14	147
Sloan, R.A.	1938	J.Lab.Clin.Med.	23	1015
Smith & McConkey	1933	Arch.intern.Med.	51	413
Smith, S.	1938	J.Amer.Med.Ass.	111	1753
Stewart, R.M.	1925	J.Psychol.Neurol,Lpz.	6	191
Sure, B.	1933	The Vitamins in Health and Disease. London, Ballier, Tindall & Cox.		
Svirbely & Szent-Györgyi	1932	Biochem.J. Part i.	26	865
Svirbely & Szent-Györgyi	1933	Biochem.J. Part i.	27	279
Szent-Györgyi	1928	Biochem.J. Part ii.	22	1387
Szent-Györgyi	1933	Nature, Lond.	131	225
Szent-Györgyi & Haworth,W.	1933	Nature, Lond.	131	24

T.

Taffel & Harvey	1938	Proc.Soc.Exp. Biol., N.Y.	38	518
Taylor	1937	Lancet	1	973
Tillmanns, J.	1930	Z.Untersuch.Lebensm.	60	34
Tohaku	1938	J.Exp.Med.	35	65

V.

Van Eekelen, M.	1936	Biochem.J.	30	2291
Van Eekelen, M. & Heinenn	1938	J.Clin.Invest.	17	293
Van Wendt	1938	Skand.Arch.Physiol.	80	398
Vestergaard & Sturup	1936	J.Amer.Med.Ass.	108	852

W.

Watanahe	1938	Tohoku J.Exp.Med.	35	61
Weber, H.	1938	Wien.Klin.Wschr.	51	1191
Wilkinson & Ashford	1936	Lancet	2	967
Williams & Green	1939	Med.J.Aust.	1	145
Wilson	1938	Lancet	1	667
Wolbach, S.B.	1933	Amer.J.of Path.	9	689
Wolbach & Howe	1926	Arch.of Path.	1	1
Wood	1935	Lancet	229	1405
Wortis, H.Liebmann,Wortis,S.	1938	Amer.J.Med.Sci.	196	384
Wright & MacLenathen	1939	J.Lab.Clin.Med.	24	802
Wright, I.S.	1938	Ann.intern.Med.	12	516
Wright & MacLenathen	1938			
Wright, I.S., Lilienfeld,A., MacLenathen, E.	1937	Arch.intern.Med.	60	264
Wright, I.S.	1937	Applied Phys.	Oxf.Med.Pub.	
Wright, I.S., Lilienfeld,A.	1936	Arch.intern.Med.	57	241

Y.

Youmans, Corlette, Ackeroyd & Frank	1936	Amer.J.Med.Sci.	191	319

Z.

Zegler & Koff	1936	Z.Klin.Med.		130	178
Zilva, S.G.	1932	Nature, Lond.		129	943
Zilva, S.G.	1932	Arch.Dis.Childhood	63	21,	241
Zilva, S.G.	1933	Arch.Dis.Childhoof	65		145
Zilva, S.G.	1935	Arch.Dis.Childhood		16	253
Zbok & Sharpless	1938	Proc.Soc.Exp. Biol., N.Y.		39	233