SOME OBSERVATIONS UPON VITAMIN C NUTRITION IN MEASLES, AND IN PREGNANCY.

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Thesis Presented

for the Degree of M.D.

C O N T E N T S.

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SECTION II - PREGNANCY.

CHAPTER I.

THE WORK LEADING TO THE RECOGNITION OF HYPOVITAMINOSIS C.

(a) The Causation of Scurvy.

Scurvy is one of the classical diseases and recognisable references to it are made even in the earliest medical writings. Though frank scurvy was well known and clinically well recognised so long ago it is only comparatively recently that any universal agreement has been attained as to its causation.

The history of scurvy is closely associated with the histories of wars, famines, and expeditions to far places and whenever natural food supplies became difficult to procure scurvy appeared with greatly increased incidence. But it is only two hundred years ago since the therapeutic value of fresh fruit and vegetables became established. Bachstrom in 1734 ascribed anti-scorbutic virtues to fresh fruit and vegetables. In spite of the obvious therapeutic and prophylactic value of these foodstuffs it was not generally conceded that they were directly connected with the causation.

As late as 1916 Johnstone and Moody (1) recovered a diplococcus from scorbutic pigs which when introduced into normal animals produced haemorrhagic lesions/

lesions. Since these animals had been fed on milk and oats which was then known to be an adequate diet for rats it was thought that the diplococcus must be related to the causation of scurvy. Scurvy had first been observed in an experimental animal (the guinea-pig) in 1895 by Smith and in 1907 the disease was produced experimentally in the same animal by Holst and Frolich. Doubt existed as to the value of the infectious theory. This doubt was further encouraged in 1918 by Cohen and Mendel (2), who following the work upon vitamins originated by the discoveries of Sir F.G. Hopkins at Cambridge (3) and Funk in America of the accessory food factors, were able to produce scurvy in guinea-pigs by feeding them on a superior experimental diet deficient only in vitamin C. This work indicated that deficiency of the specific - factor C was responsible for the development of scurvy. In 1920 Parsons (4) further undermined the foundations of the infectious theory by demonstrating that while milk and oats constituted a protective diet for rats it was only because of the complete immunity of this animal to scurvy. This work was confirmed in 1924 by Parsons and Hutton and by Lepkovsky and Nelson (5) and the infectious theory was dropped.

Following upon much research work by Tillmans, Hirst and many others, Waugh and King (6) were able in/

in 1932 to isolate the vitamin in natural form. In the same year Swirbely and Szent-Gyorgyi furnished evidence which seemed to indicate that a substance hexuronic acid and vitamin C were identical. The structure of hexuronic acid was established by Haworth, Hirst and collaborators in 1933 and in the same year Reichstein and Oppenhauser synthesized the vitamin. Various names were given to the substance, in England Vitamin C, Hexuronic acid, Ascorbic acid, and in America, Vitamin C or Cevitamic acid.

Associated with these discoveries has been the gradual but conclusive demonstration of the direct connection between vitamin C deficiency and the development of scurvy both in the guinea-pig experimentally and in the human being clinically. The prophylactic and curative effect of this vitamin in both Infantile and Adult scurvy is now well substantiated.

(b) Sub-clinical Scurvy.

Following upon the discovery of the accessory food factors came, not unnaturally, investigations to discover the optimum individual requirements for these substances. McCarrison (7) and others called attention to the fact that vitamin underfeeding of a chronic nature might occur without being severe/

severe enough to produce the classical symptoms or signs of avitaminosis and so the problem of the hypovitaminoses appeared.

By careful post-mortem examination of 532 children Elliott was able to demonstrate 125 cases of scurvy most of which had been unsuspected during life. The diagnosis rested in most cases exclusively upon histological and radiographic evidence and it was shown that both of these methods might yield definite evidence of scurvy of a recognisable kind.

By this and other works the attention of research workers was therefore directed towards a method of diagnosis for this state of hypovitaminosis C which gave rise to no recognisable symptoms. Gothlin (8) working on the known haemorrhagic diathesis of scurvy was able to demonstrate a decreased capillary resistance to pressure in children in various schools in North Scandinavia. Many of these children were receiving diets poor in Vitamin C. Dalldorf (9) in America had noticed a similar tendency in guinea-pigs during the experimental production of scurvy in these animals. The capillary resistance test is not however entirely satisfactory as it suffers from the disadvantage that it is non-specific and that other conditions modify capillary resistance.

Following the discovery by Tillmans (10) of a chemical/

chemical method for the quantitative estimation of vitamin C other methods of detecting hypovitaminoses C were advanced. These newer laboratory methods, enumerated below, were found to yield reliable results when applied to developed cases of scurvy.

The diagnosis of hypovitaminoses C therefore rests upon laboratory rather than clinical methods. There are no symptoms especially suggestive of this state comparable to the hemeralopia of early vitamin A deficiency etc. Its detection requires special methods. Few or none of the early symptoms of scurvy - weakness, fatigue, palpitation or breathlessness - are present and the condition of the gums is usually satisfactory. The diagnosis therefore rests upon the demonstration of an abnormal state of vitamin C nutrition by one or more of the special methods. The best known of these are:-

1. Capillary resistance.

The capillary resistance to pressure is lowered in subjects of subnormal vitamin C nutrition. There are two recognised methods of performing the test. The principle is the same in both cases namely the increase of the venous pressure by mechanical means for a known period of time. The number of petechiae developed in a given area of skin so affected are counted. The methods are:-

(a) Gothlin's (8) method.) See Appendix
(b) Suction Cup method.) page 62 .

2. Urinary excretion of Vitamin C. (Tillmans, Harris & Ray (11).

The vitamin C content of the urine is estimated by titration against a known solution of 6 : 2 di-chlorophenol-indophenol.

3. Urinary Saturation Test. (Harris & Ray (11).

The effect on the urinary excretion of vitamin C of the administration of a large dose of the vitamin is watched. The vitamin is detected in the urine as above.

4. Blood Plasma concentration of Vitamin C.

(a) Method of Tauber and Kleiner (12) - the reducing power of the cevitamic acid in the plasma is calculated by the use of an acid ferricyanide.

(b) Micro-Method of Farmer and Abt (13) a modification of the above.

5. Intradermal Test. (Rotter (14) and Wilkinson (15).

A known quantity of the dye 6 : 2 dichlorophenol-indophenol is injected intradermally and the rate of decolouration of the dye by the vitamin present in the skin is timed. Delay in decolouration of the dye of any extent indicating sub-normal dermal content of vitamin C. and hypovitaminosis C.

SECTION I. MEASLES.

CHAPTER II.

THE OBJECT OF THE PRESENT INVESTIGATIONS.

To assess the adequacy of the diet of the poorer classes in a "depressed" industrial area to meet the increased usage of vitamin C during measles.

Recently attention has been drawn to the comparatively high incidence of vitamin C subnutrition amongst the hospital class of patient in this and other countries (Harris and Simon Kelly (16), Gander and Niederberger (17). Since the vitamin does not appear to be synthesized within the body it must be ingested and deficiency is therefore directly attributable to dietary inadequacy. (A very limited number of cases of deficiency occurring in persons receiving an adequate amount of the vitamin have been reported (18)).

Furthermore, numerous authors have been able to demonstrate an increased usage of the vitamin during various infectious and pyrexial states (19) (Harris, Abbasy, Gray, Hill, Ellman, Paget etc. (19).

In a community of such circumstances as to suggest hypovitaminoses C, the increased usage of this vitamin associated with an infectious disease would presumedly increase the incidence and severity of/

of hypovitaminoses in the area during an epidemic. Such increased incidence would make it more readily demonstrable.

The commencement in this area (West Cumberland) in the Autumn of 1937 of an epidemic of measles produced such conditions. It was decided to investigate:-

(a) the possible presence of hypovitaminosis C amongst the apparently normal children (chiefly of the poorer classes) of this area.

(b) the possible increase in incidence of such hypovitaminosis C in children of the same area, suffering from measles.

(c) the length of time this increased incidence (if any) persisted during the convalescence.

CHAPTER III.

THE METHOD ADOPTED FOR THE DETECTION OF HYPOVITAMINOSES C, THE SELECTION OF CHILDREN FOR EXAMINATION, ETC.

(a) THE AREA.

The area in which the investigations were conducted is situated on the West coast of Cumberland in the heart of an industrial area which has been classed with South Wales as one of the most "depressed" regions in the British Isles. The average income of most households is low, and the number of children often large. Also as there is no resident Public Assistance Medical Officer many of the poorest families were under the direct care of the author.

As the investigation had for its chief aim the detection of the presence of hypovitaminoses (and of any dietary inadequacy of vitamin C) rather than the actual percentage incidence of hypovitaminoses it was considered legitimate to make a definite bias towards children of the poorer and larger families in the selection of cases. Though this bias would give a false impression of the actual incidence of hypovitaminosis C in the area it could be ignored as no attempt was being made to assess the actual percentage incidence but only to detect if hypovitaminoses C were present or not. As the bias would operate not only/

only in the case of measles but also in the selection of normal children for examination, it was not considered that it would prejudice the demonstration of an increased incidence of hypovitaminoses C following measles, since the groups of children compared (i.e. normal children and sufferers from measles) would be of similar economic circumstances.

(b) DIET.

Since the only source of the vitamin is from the food a demonstration of hypovitaminosis C would generally speaking be considered sufficient to prove a dietary lack and therefore a detailed survey of the actual vitamin content of the diet was not essential for the purposes of the investigation. However a fairly detailed enquiry into the previous dietetic history was made in an attempt to correlate any deficiency which might be detected with an inadequate diet.

For this purpose the findings given by Fellers(20) for the ascorbic acid content of the various foodstuffs were used in association with Hess's dictum that 2.5 mgm. per day (100 International units) will protect a baby and that "the adult need is probably not over 7.5 mgm."(21). From these figures the child's average daily requirement according to his age/

age was calculated and from his known diet and Feller's table it was possible to calculate his approximate average daily intake. The figures so obtained came below the reputed "minimal optimum" intake of 25 mgm. per 10 stone body-weight but as they were used chiefly as a standard for comparison between the various diets this was of little significance. According to the relationship between a child's calculated dietary intake of vitamin C and his actual requirements deducted from Hess's findings his diet was classed as follows:-

Very high vitamin C content.
High " " "
Satisfactory " " " when the two figures were in agreement.
Low vitamin C content.
Very low " " "

(See Appendix page 62)

N.B. Throughout the whole investigation the selection of the diet for cases was left entirely to the respective parents unless advice was specifically asked for; in such circumstances the usual fever diet was suggested, including sweetened orange drinks but the advice having been offered the matter was then left in the hands of the parents.

c./

(c) THE METHOD ADOPTED FOR THE DETECTION OF HYPOVITAMINOSES C.

As explained previously (page 5) the diagnosis of hypovitaminoses C rests entirely upon special examination by certain laboratory methods. In choosing a test for the present purpose certain requirements had to be met. The test had to be sufficiently reliable, reasonably simple to perform,and one not requiring too much time. The tests which suggested themselves were, the capillary resistance test, the intradermal test and the urinary excretion and saturation tests. On consideration the capillary resistance test was rejected as it is non-specific (22), and the intradermal test because it gave no opportunity of measuring the degree of hypovitaminoses, and because it is painful. There remained the urinary excretion estimation and the saturation test both devised by Harris and Ray (11).

These authors formulated a method for the detection of the quantity of vitamin C in the urine (a modification of Tillmans method for the detection of the vitamin in body fluids). They made a detailed study of the excretion of the vitamin in normal and abnormal subjects. Their general conclusions were as follows:-

(d) ..

(d) THE PRINCIPLE OF THE URINARY TESTS.

With regard to vitamin C excretion Harris and Ray demonstrated that provided there is no interference with the normal excretory mechanism the quantity of vitamin C excreted daily is directly connected with two factors:- firstly the immediately previous vitamin C intake, and secondly the past intake. They showed that if the immediately previous intake is satisfactory and urinary excretion is below a certain minimal figure the past nutritional history has been unsatisfactory and therefore the subject is suffering from vitamin C subnutrition. If however the immediately previous intake has been low then a low excretory figure is of no significance since it may reflect merely the recent low intake and the past history may be satisfactory. They explain these differences by assuming that the body normally accumulates a certain reserve of vitamin C within its tissues. An intake of the vitamin persistently below the minimal daily requirement necessitates drawing upon body reserves. (this if it continues will result in complete depletion of the reserves and then definite clinical signs of vitamin C deficiency would appear.) They further demonstrate that if an amount of vitamin above the daily requirement of the body be fed to an individual his urinary excretion depends upon the state of his body stores of vitamin C - i.e. his/

his degree of "saturation". If he is fully saturated any excess above the daily requirement is excreted and the urinary excretion figure is above a certain level. If on the other hand he suffers from any degree of unsaturation the excess above the daily requirement is retained by the body to replenish its reserve and the urinary excretion remains low in spite of the excess ingested. In other words a low excretion on a known optimum daily intake of ascorbic acid (recent intake) indicates post-nutritional deficiency - hypo-vitaminoses C.

The proper use of this test however requires:-

(a) control of the vitamin intake for a few days before the actual excretion figure is examined so as to provide a satisfactory "immediately previous intake".

(b) very accurate measurement of the quantity of ascorbic acid in twenty-four hour specimens of urine carefully preserved.

These factors were not easy to comply with in the present work and the saturation test offered certain advantages. The urinary excretion figure was calculated where possible as a check for though a low reading might have little significance since no control was taken of the diet, a high reading on the other hand indicates satisfactory vitamin C nutrition even without such control.

The/

The advantages of the saturation test are that it requires no previous dietetic control. Also the degree of error may be appreciably greater without influencing significantly the validity of the test. The principle involved is essentially similar to that outlined above. It depends upon the varied urinary response to administered doses of ascorbic acid reflecting the state of the body reserve of vitamin C, i.e. "degree of saturation". A large test dose of ascorbic acid is administered to the individual to be tested and the urinary reaction observed. If the individual is unsaturated the excess of cevitamic acid above the daily requirement is retained almost completely and the urinary excretion figure for the vitamin remains correspondingly low. If on the other hand the body is saturated any excess is immediately excreted and a noticeable increase occurs in the quantity of ascorbic acid excreted in the next twenty-four hours. It has been demonstrated that by giving a large test dose a very marked difference in the urinary response of a saturated and partly saturated individual occurs which difference is so great "as to allow of minor technical errors without significantly influencing the validity of the test". Also the degree of unsaturation may be gauged as the amount of vitamin required to be administered before a satisfactory urinary response occurs, since such response occurs only when saturation is reached. The amount of ascorbic acid administered is therefore equivalent to the amount required to/

to replenish the body reserve and therefore equivalent to the total previous deficiency.

One disadvantage attends the saturation test namely that once the degree of unsaturation has been assessed further testing at a later period is likely to be negative as any deficiency present is automatically corrected during the first test. It was therefore necessary to take different cases to assess the degree of unsaturation at various stages of the convalescence from measles. This was not however considered a great handicap as the object was not to study vitamin C nutrition during measles (for this was considered to require greater facilities than were reasonably available.) but merely to ascertain if hypovitaminosis C was present and if so in what approximate proportion at each stage.

(e) THE SELECTION OF CASES AND THEIR DIVISION INTO GROUPS.

Reference has already been made to the bias towards the poorer families (page 9) which bias was considered legitimate for the reasons given.

The cases firstly divided naturally into two principal groups:-

(a) Apparently Normal children - Group 1

(b) Children suffering from Measles - Group 2

GROUP 1./

GROUP 1.

With regard to the former, this group consisted of children attending the surgery for very minor ailments which were non-pyrexial and non-infectious and could therefore be considered as having no influence upon the vitamin C nutrition of the affected child. Volunteers were not asked for because it was considered that the appeal was very likely to be unsuccessful.

GROUP 2.

With regard to the latter; as the chief aim was to investigate the adequacy of the diet to meet the increased usage of vitamin C the actual causation of that demand is of secondary importance. But for the sake of uniformity, and to diminish the number of secondary factors affecting any conclusions which might be drawn from the results obtained it was decided to limit the investigation to unquestionable cases of measles.

The epidemic was extensive and occurred in a crowded population so that ample opportunity was afforded for the selection of suitable cases. Only cases were included which showed:-

(1) Absence of measles in the past history.

(2) The history of or presence of a short coryzal stage (2-5 days) with gradually increasing fever and cough.

(3) The final appearance of a rash of typical form and/

and distribution.

(4) The absence of other signs to cause doubt in the diagnosis.

In about 60% of the cases Koplicks spots were observed but it was not practicable to include only these cases in which these pathognomonic spots were seen as often medical attention was sought only after the rash had appeared.

To attain the third object of the investigation it was necessary to further divide the cases of measles. The aim was "to assess the length of time the increased incidence of hypovitaminosis (if any) persisted during convalescence". This was in reality an attempt to assess the adequacy of the diet of these children to make good the depletion of their body reserves caused by the increased usage of the vitamin during the attack of measles.

Attention will be called to the fact that (page 21) for definite diagnoses of abnormal vitamin C nutrition the saturation test is relied upon in this investigation (the excretion test alone giving no conclusive data as the diet was in no way controlled). Earlier it has been mentioned (page 16 line 3) that the saturation test can be applied once only to any particular patient. Therefore to attempt to assess the/

the state of vitamin C nutrition throughout the convalescence it was necessary to divide the cases of measles into several sub-groups and to examine each sub-group at a different stage of convalescence.

They were divided into four groups as follows:-

Sub-group A. Children (at least 24 hours apyrexial) examined 7 days after the first appearance of the rash.

Sub-group B. Children examined 14 days after " " "

Sub-group C. Children " 28 days " " " "

Sub-group D. Children " 2 months " " " "

With regard to the selection of cases for each sub-group this was done merely by rotation so that as each case was first attended it became A, B, C and D sub-group in sequence.

All the children of the above groups had run a normal and uneventful course entirely free from complications. A complication would in itself presumably increase the demand for vitamin C and so vitiate the result obtained.

Finally though the epidemic was remarkably free from cases developing complications a few of the children developing complications were examined (at varying intervals from the first appearance of the rash) and the results are recorded in a separate table. These children form Group 3.

(f) THE PROCEDURE FOR EXAMINATION OF CASES.

The procedure adopted was firstly to assess the quantity of ascorbic acid excreted daily and then to test for hypovitaminosis by the saturation test. It was necessary to apply the saturation test for though a high daily excretion of cevitamic acid would preclude the possibility of subnutrition in that factor, a low daily excretion is of little significance for as the diet was not controlled it might indicate past nutritional deficiency or merely an immediately recent low intake (a state that might occur in a person in perfect health.)

For correct measurement of the daily excretion of ascorbic acid accurate measurement of a twenty-four hour specimen carefully preserved is required. This however was not practicable in the present investigation and an attempt was made to obtain an approximate figure by collecting only a four-hour specimen and multiplying the figure obtained by six. In an attempt to assess the possible value or degree of fallacy in this method the writer examined his own urinary excretion over a period of twelve days by both methods by collecting the urine for the full twenty-four hours but keeping separate that passed in the four-hour period from 10 a.m. to 2 p.m. However in December Harris and Abbasy (26) published an/

an article suggesting a simplified urine test for estimation of excretion of ascorbic acid by the collection of only a 3 hour period namely the first three hours in the morning. They had satisfied themselves that it was "sufficiently accurate for routine surveys" - therefore following this publication their method for this and also for the simplified saturation test was adopted throughout the investigation.

(1) The daily excretion of ascorbic acid was estimated as follows:-

The patient was asked to empty his bladder at 9 a.m. and to discard this specimen. Any urine passed from then until 12 a.m. was collected and at 12 a.m. the bladder was again emptied and this specimen added to any already collected. The urine was stored in dark glass bottles or if these were not available in ordinary bottles wrapped in several layers of brown paper to exclude the light. The ascorbic acid was further preserved by the addition of glacial acetic acid, - 10% by volume as recommended by Harris and the necessary corrections for dilution made when the titration was performed.

A suggestion has recently been made that glacial acetic acid is not an efficient preservative of ascorbic acid (Fleming and Burrows (27)). But this is not the experience of other authors and though Harris/

Harris admits there is a certain amount of vitamin C lost he considers that the method is adequate for the purpose for which it is advocated - the clinical diagnosis of vitamin C subnutrition. Even Fleming only found a loss of 22% with 5% acetic acid in twenty-four hours. As will be described later all specimens in this investigation were examined at the very latest within four hours of being passed. Also Harris suggests 10% glacial acetic acid whereas Burrows made his tests with 5% acetic acid. Also as the results of the saturation test depend upon a high peak in the urinary excretion a loss of 20% even if it did occur would not greatly influence the significance of the test.

The 3 hour specimens were collected from the patients homes between 12 a.m. and 12.30 a.m. and taken to the hospital for titration. All titrations were performed personally and were completed between 12.30 a.m. and 1.30 p.m. and any not examined through lack of time were discarded. This test was repeated on the next day and the average finding taken. If the quantity of ascorbic acid excreted was over a certain figure the saturation test was omitted. Harris states "The daily output of vitamin C in the urine of course furnishes a far more stable measure of the state of vitamin C nutrition than does a determination of its mere concentration, since the latter/

latter fluctuates considerably according to the volume of urine. Nevertheless, if a child is known to be excreting neither more nor less than the average bulk of urine, and the concentration of ascorbic acid is found to be consistently above the limit of 0.01 - 0.02 mg. per c.cm. it may be safely assumed that his vitamin reserves are adequate. The same argument applies to an adult, except that the level of 0.02 to 0.03 mgm. per day may be substituted for 0.01 to 0.02 mgm." For this investigation children excreting 0.025 mgm. per c.cm. on the average of the two days examination were taken as being of satisfactory vitamin C nutrition. This allowed a safe margin for slight errors. The quantity of the child's daily excretion of urine was taken to be within normal limits if he excreted a 'normal' amount for the 3 hour period. The possible diuretic effect of cevitamic acid would not affect this reading as it was taken before any acid had been administered (Abbasy, M.A. Biochemical Jour. Vol. XXXI. 1937 No.2 pp.339-342).

The technique for the saturation test used throughout the investigation was as follows:-

The day following the last examination of the excretory rate, a certain known quantity of "Redoxon" powder (crushed tablets) was taken at 10 a.m. and the urine/

Table of Size of Test Dose.

Age (in years)	BOYS. Average Weight.	BOYS. Calculated required Test Dose.	BOYS. Actual Test Dose used.	GIRLS. Average Weight.	GIRLS. Calculated required Test Dose.	GIRLS. Actual Test Dose used.
4	2 st. 3¾ lbs.	157 mgm.	200 mgm.	2 st. 2½ lbs.	153 mgm.	150 mgm.
5	2 st. 6½ lbs.	172 mgm.	200 mgm.	2 st. 5½ lbs.	167 mgm.	200 mgm.
6	2 st. 13½ lbs.	205 mgm.	250 mgm.	2 st. 10½ lbs.	192 mgm.	200 mgm.
7	3 st. 4½ lbs.	232 mgm.	250 mgm.	3 st. 2 lbs.	220 mgm.	250 mgm.
8	3 st. 9½ lbs.	267 mgm.	300 mgm.	3 st. 6½ lbs.	242 mgm.	250 mgm.
9	4 st. 1 lb.	285 mgm.	300 mgm.	3 st. 10 lbs.	260 mgm.	300 mgm.
10	4 st. 6½ lbs.	312 mgm.	350 mgm.	4 st. 2 lbs.	290 mgm.	300 mgm.
11	4 st. 12 lbs.	330 mgm.	350 mgm.	4 st. 8 lbs.	320 mgm.	350 mgm.
12	5 st. 2¾ lbs.	366 mgm.	400 mgm.	5 st. 2½ lbs.	364 mgm.	400 mgm.

urine collected during the 3-hour period 2 p.m. - 5 p.m. with the same precautions as before. The amount of powder administered varied with the age and was calculated on a basis of 70 mgm. ascorbic acid per stone of body weight (see table opposite). In all patients who were not weighed (the majority!) the test dose was taken as that required by the average person of that particular age. (Calculated from average weight). Each Redoxon tablet is equivalent to 50 mgm. of ascorbic acid and no attempt was made to divide tablets so that all test doses were multiples of 50 mgm. and all figures were taken to the nearest multiple of 50 above e.g. so that 269 would become 300 mgm. All the precautions detailed later with regard to the collection, preservation and titration of samples were scrupulously observed.

The sample collected was titrated against 6 : 2 dichlorophenol - indophenol and the ascorbic acid content deduced. With regard to the reading of results for this test the authors state "that a response should occur to the standard test dose" (70 mgm. per stone of body weight) "usually on the first and certainly on the second day" (24). Throughout this investigation therefore no response to the second calculated standard test dose (see table page 24a) is taken as indicating hypovitaminosis C and the total amount of cevitamic acid administered before a satisfactory/

satisfactory urinary response occurred minus the amount of two test doses is taken as indicating the degree of hypovitaminosis in any particular subject.

The titrations.

Titrations were to determine the quantity of ascorbic acid in the urine specimens. They were all performed personally at the hospital. A micro-burette and micro-pipette were used and all the precautions advised by Harris and Ray in the original paper were observed (11). The dye used for the titrations was 6:2 dichloro-phenol indo-phenol obtained from Messrs Roche in tablets each equivalent to 1 mgm. l-ascorbic acid (Eddy and Dalldorf considered this particular tablet of good quality (30)) The dye solution was freshly prepared each day and was of such a strength that 0.05 c.cm. was equivalent to 0.025 mgm. ascorbic acid (see correction by Harris. Lancet Feb. 1935, Vol 1. p.462.) The end point was reached in two minutes and if necessary the dye was further diluted to obtain a definite end-point before 2 c.cm. of urine had been used, etc.

TABLE NO. 1.

Group 1. Apparently Normal Children.

23 examined - 2 hypovitaminoses C.

	Age	Sex	Quantity of Ascorbic Acid Excreted Daily	Amount of Test Dose	Number of Test Doses	Total Quantity of Ascorbic Acid Administered.	Calculated Vitamin C Deficiency	Diet Content in Vitamin C.
1	10	♀	81.2 mgm.	Not required			Nil	V. High
2	9	♀	34.2 mgm.					High
3	6	♂	29.3 mgm.					"
4	7	♂	26.2 mgm.					?
5	6	♀	24.3 mgm.					High
6	6	♀	19.2 mgm.					Satisfactory
7	8	♂	18.7 mgm.					"
8	9	♂	18.2 mgm.					"
9	11	♂	17.9 mgm.					"
10	7	♀	16.5 mgm.					High
11*	11	♂	12.6 mgm.	350 mgm.	1	350 mgm.		Satisfactory
12*	7	♀	11.1 mgm.	250 mgm.	1	250 "		"
13	6	♀	....	200 "	1	200 "		"
14*	6	♂	....	200 "	1	200 "		"
15	8	♂	9.5 mgm.	300 "	1	300 "		"
16	9	♂	5.6 mgm.	300 "	1	300 "		"
17*	7	♂	....	250 "	1	250 "		Low
18	7	♀	....	250 "	1	250 "		Satisfactory
19	8	♀	5.2 ..	250 "	1	250 "		"
20	8	♂	....	300 "	1	300 "		"
21	7	♀	....	250 "	2	500 "		Low
22	7	♂	....	250 "	3	750 "	250 "	"
23	8	♂	....	300 "	5	1500 "	900 "	Very Low

* No.11 - See Page 28a Table 2 No. 12
No.12 - " " 29a " 3 " 2
" 14 - " " 29a " 3 " 8
" 17 - " " 30a " 4 " 12

All later developed measles - and 3 (i.e. No.11, 14, 17 of Table No.1) showed hypovitaminosis C.

CHAPTER IV.

RESULTS OBTAINED IN MEASLES AND DURING CONVALESCENCE.

In all 87 children were examined divided into three groups:-

Group 1. 'Normal' children 23

Group 2. Measles " 58 Sub-group A - 12

" " B - 15

" " C - 15

" " D - 16

Group 3. Children with complications 6.

GROUP 1. "Normal children".

As described previously (page 17, line 1) this group is composed of children who attended surgery for minor ailments. 23 children of both sexes were examined, ages from 6 to 11 years. Ten of these showed a high daily excretory rate for the vitamin and the saturation test was considered unnecessary. Of the other twelve, on all of whom the saturation test was performed, ten responded in a definite but varying manner to the first test dose, one after the second test dose, one after the third and one not until the fifth test dose. The last two therefore came below the standard adopted for this investigation/

investigation and they were taken to show definite hypovitaminoses C. The last, a boy, required 5 test doses of 300 mgm.; his degree of unsaturation therefore was 1500 mgm - 600 mgm. 900 mgm. ascorbic acid. He was a weakly looking individual with a poor appetite though no cause was discovered for his lack of growth and general robustness (weight 2 st. 10 lbs.) His urine was normal to the ordinary tests. He had however a very poor appetite and his mother would not allow him to eat oranges. She gave as a reason that they always caused him to be sick. She had made this 'discovery' three years previously and had not allowed him oranges since. The rest of his diet was small in actual vitamin C content. His deficiency was corrected with Redoxon tablets (one each morning) and since this he has been much better though he has not gained much in weight. (2 st. 13 lbs. 5 months.)

The two children showing hypovitaminosis C also showed a dietary history with poor vitamin C content while conversely the children not requiring test doses had without exception diets high in ascorbic acid content. Most of these ten children were of better working-class families, and they had all daily excretion figures above 15 mgm. per day. One child showed the very high figure of 80 mgm. per day, the rest varied from 16.5 mgm. to 34.2 mgm. This child was pale, puny and anaemic (65% Haemoglobin) and hypovitaminosis/

TABLE NO. 2.

Sub-group A - Children examined 7 days after the first appearance of the rash.

12 examined - 10 hypovitaminosis C.

	Age	Sex	Quantity of Ascorbic Acid Excreted Daily	Amount of Test Dose	Number of Test Doses	Total Quantity of Ascorbic Acid Administered	Calculated Vitamin C Deficiency	Diet Content in Vitamin C.
1.	6	♂	6.12 mgm.	250 mgm.	2	500 mgm.)	Nil	Very high
2.	10	♂	....	300 ..	2	600 ..)		" "
3.	7	♀	3.1 mgm.	250 ..	3	750 ..	250 mgm.	High
4.	8	♂	....	300 ..	3	900 ..	300 ..	"
5.	8	♀	.... To low to estimate.	250 ..	4	1000 ..	500 ..	Satisfactory
6.*	7	♀	....	250 ..	5	1250 ..	750 ..	"
7.	7	♂	....	250 ..	5	1250 ..	750 ..	Low
8.	6	♀	....	250 ..	5	1250 ..	750 ..	"
9.	5	♀	....	200 ..	5	1000 ..	600 ..	Satisfactory
10.	5	♂	....	200 ..	5	1000 ..	600 ..	Low
11.	6	♂	....	250 ..	8	2000 ..	1500 ..	V.Low
12.	8	♀	....	250 ..	10	2500 ..	2000 ..	V.Low

* No.6 See Page 26a Table No.1 Children No.12.

hypovitaminosis had been expected although his dietary history was satisfactory. Careful examination revealed no cause for her under-development until separate night and morning specimens of urine were obtained and then a small quantity of Fehling's reducing substance was found to be constantly present in the morning sample. A blood sugar test showed a raised blood sugar with slow return to normal following the administration of glucose. This case is interesting in view of the finding of vitamin C deficiency in association with diabetes recorded by some authors (Pfleger and Scholl Lancet 1937 vol. II, p.1384; and Weiner Archiv. innere Medizin 1937, vol. 31 No.4.)

GROUP 2.

Group 2 consists, as explained, of children suffering from or convalescent from measles. They were further divided into sub-groups (see page 19).
A total of 59 children were examined and in 26 of these hypovitaminosis C was detected.

The routine method of examination described on pages 21-25 was followed in all cases.

Sub-group A. consists of boys and girls between 5-10 years old. They were all examined only after they had been twenty-four hours apyrexial. The examination commenced on the seventh day after the first appearance of the rash.

The/

TABLE NO.3.

Sub-group B. Children examined 14 days after the first appearance of the rash.

15 examined - 9 hypovitaminosis C.

	Age	Sex	Quantity of Ascorbic Acid Excreted Daily	Amount of Test Dose	Number of Test Doses	Total Quantity of Ascorbic Acid Administered	Calculated Vitamin C Deficiency	Diet Content in Vitamin C.
1	6	♂	25.2 mgm					V.High
2*	11	♂	10.2 "	350 mgm	1	350 mgm		Satisfactory
3	8	♂	...	300 "	2	600 "		High
4	7	♀	...	250 "	2	500 "		"
5	6	♂	...	250 "	2	500 "		Satisfactory
6	9	♀	...	300	2	600 "		"
7	5	♀	...	200 "	3	600 "	200 mgm	"
8*	6	♂	...	200 "	3	600 "	200 "	Low
9	7	♂	...	250 "	3	750 "	250 "	"
10	7	♀	...	250 "	4	1000 "	500 "	Satisfactory
11	8	♀	...	250 "	4	1000 "	500 "	"
12	5	♂	...	200 "	4	800 "	400 "	Low
13	5	♂	...	200 "	4	800 "	400 "	"
14	9	♀	...	300 "	6	1,800 "	1500 "	V.low
15	8	♂	...	300 "	8	2,400 "	1800 "	"

* No.2 See Page 26a Table No.1 Child No.11

No.8 " " " Table No.1 Child No.14

The results obtained showed a striking difference to those of Group 1. None of these children showed a sufficiently high excretory rate to omit the saturation test. Only two children showed a satisfactory response after the second test dose. The other ten required a varying number of test doses from 3 to 10 (Table 2 page 28a) These ten all required more than two test doses and therefore showed varying degrees of hypovitaminosis C.

The effect of diet was again obvious. Of the two children who showed a satisfactory urinary response after the second test dose, one was an only child and was receiving liberal gifts of fruit from her many relatives and the other was a boy passionately fond of fruit especially oranges. On the other hand the two children who required the largest number of test doses were both of poor families. One a boy aged 6 who required 2000 mgm. cevitamic acid to produce the required response and a girl aged 8 to whom 2,500 mgm. were administered. Their calculated deficiencies were 1,500 and 2,000 mgm. respectively.

Of the twelve children examined ten therefore showed demonstrable hypovitaminosis C.

Sub-group B.

Sub-group B was composed of 15 boys and girls of ages between 5-11 years examined by the routine method 14 days after the first appearance of the rash.

One/

TABLE NO.4.

Sub-group C. Children examined 28 days after the first appearance of the rash.

15 examined - 9 hypovitaminosis C.

	Age	Sex	Quantity of Ascorbic Acid Excreted Daily	Amount of Test Dose	Number of Test Doses	Total Quantity of Ascorbic Acid Administered	Calculated Vitamin C Deficiency	Diet Content in Vitamin C.
1	7	♂	31.6 mgm	-	-	-)		V.High
2	9	♂	20.8 "	-	-	-)		High
3	6	♂	3.59 "	200 mgm	1	200 mgm)		"
4	5	♂	...	200 "	1	200 ")		V.High
5.	10	♀	2.10 "	300 "	2	600 ")		Satisfactory
6	4	♂	...	200 "	2	400 ")	Nil	"
7	5	♀	...	250 "	2	500 ")		Low
8	10	♀	...	300 "	2	600 ")		Satisfactory
9	5	♂	...	200 "	2	400 ")		"
10	9	♂	...	300 "	2	600 ")		"
11	8	♀	...	250 "	3	750 "	250 mgm	Low
12*	7	♂	...	250 "	4	1000 "	500 "	Satisfactory
13	6	♂	...	200 "	4	800 "	400 "	Low
14	5	♂	...	200 "	8	1,600 "	1,200 "	V.Low
15	10	♂	...	350 "	10	3,500 "	2,800 "	V.Low

To low to be estimated

* No.12 See page 26a Table No.1 Child No.17

One boy (aged 6) showed a high daily excretory rate (25.2 mgm.) and no further test was considered necessary. His attack of measles had been mild and his parents were in good working-class circumstances. He was an only child.

One other child responded to the first test dose and four to the second. A further nine were examined and showed calculated deficiencies from 200 - 1800 mgm. ascorbic acid. (The actual number of test doses required for each child is shown in the table (3) on page 29a).

Two of these children showed high degrees of deficiency 1,500 and 1,800 mgm. and in both these cases the families were large and poor.

In this sub-group therefore, nine of fifteen showed vitamin C subnutrition.

Sub-group C.

Again 15 children were examined, of either sex, ages from 5-10. The routine examination was commenced 28 days after the first appearance of the rash.

Two boys showed a satisfactory daily excretory rate and the saturation test was omitted and a further two responded handsomely to the first test dose. All these children were receiving diets high in vitamin C and one of them had been receiving a teaspoonful of Halibut orange q.i.d. at his mother's instigation/

TABLE NO. 5.

Sub-group D. Children examined 8 weeks after the first appearance of the rash.

16 children - 8 hypovitaminosis C.

	Age	Sex	Quantity of Ascorbic Acid Excreted Daily	Amount of Test Dose	Number of Test Doses	Total Quantity of Ascorbic Acid Administered.	Calculated Vitamin C Deficiency	Diet Content in Vitamin C.
1	10	♀	20.2 mgm.	-	-	-	)	High
2	11	♂	18.7 "	-	-	-	)	"
3	5	♀	— "	200 mgm.	1	200 mgm.	)	Satisfactory
4	7	♀	— "	250 "	1	250 "	)	High
5	6	♀	6.2 "	200 "	1	200 "	)	"
6	8	♂	— "	300 "	1	300 "	) Nil	Satisfactory
7	6	♂	— "	250 "	1	250 "	)	"
8	9	♂	— "	300 "	1	300 "	)	"
9	7	♀	— "	250 "	2	500 "	)	"
10	6	♀	— "	200 "	2	400 "	)	Low
11	8	♂	— "	350 "	2	700 "	)	"
12	7	♀	— "	250 "	2	500 "	)	Satisfactory.
13	5	♀	— " Too low to estimate.	200 "	2	400 "	)	"
14	6	♀	— "	200 "	3	600 "	200 mgm.	Low
15	8	♂	— "	300 "	4	1200 "	600 "	V. Low.
16	8	♀	— "	250 "	8	2000 "	1500 "	V. Low.

instigation. Still another six children showed no deficiency as they all responded to the second test dose. Of the five that remained three showed mild degrees of hypovitaminosis C (250, 500 and 500 mgm.) and two showed high degrees (1,200 and 2,800). It is significant that the last two, both boys, again came from very poor families.

Of these fifteen children therefore five showed some degree of hypovitaminosis C.

Sub-group D.

Sub-group D consists of sixteen boys and girls, ages from 5-11 years examined 8 weeks after the first appearance of the rash.

Two showed high daily excretory figures and the saturation test was deemed unnecessary. Of the rest, six responded to the first test dose and five to the second. Another gave a very doubtful response to the second test dose and therefore though a borderline case is classed as having taken three test doses to give a satisfactory response. The remaining three required 3, 4 and 8 test doses respectively and all therefore showed deficiency. Their calculated vitamin lack was 200, 600 and 1,500 mgm. in that order.

Therefore three of the sixteen children in this group were in a subnormal state of vitamin C nutrition.

It is of special interest to note that four of the/

TABLE NO. 6.

Group 3. Children developing complications.

Age	Sex	Complication	Pyrexia	Quantity of Ascorbic Ac. excreted daily.	Amount of Test Dose.	Number of Test Doses	Total Quantity of Ascorbic Acid on Admission	Calculated Deficiency	Diet Content in Vitamin C.
5	♀	Otitis Media	Present	1.1 mgm.	200	6	1,200	800	Satisfactory
7	♂	Axillary Abscess.	Present	"	250	5	1,250	750	Low
4	♂	Broncho-Pneumonia (Tuberculous)	Present	"	200	10	2,000	1,600	Low
8	♀	Otitis Media	Present	1.0 "	250	5	1,250	750	Satisfactory
6	♂	Severe Conjunctivitis	Absent	"	250	6	1,500	1,000	Low
9	♂	Bronchitis	Present	"	300	7	2,100	1,500	Low

the children examined in Group 1 (Normals) and who later contracted measles when they were again examined, three of them showed a definite hypovitamoses C. They are marked with an asterisk in the respective tables:-

Table No.1	p.	(Normal children)	Nos.11,12,14,17.
" "	2	p. (at 7 days)	No. 6.
" "	3	p. (at 14 ")	Nos. 2, 8.
" "	4	p. (at 28 ")	No. 12.

GROUP 3.

Group 3 consists of children showing complications. The incidence of complications throughout the epidemic was low. A few of the cases developing complications were examined at various intervals from the first appearance of the rash. They all showed definite degrees of hypovitaminoses, but as the complication in every case was capable of causing an increased usage of the vitamin it is not possible to surmise whether the complication or the hypovitaminoses came first. The results are tabled on page opposite (Table 6) for interest.

CHAPTER V.

DISCUSSION OF RESULTS.

Harris, Simon. Kelly (31) and others (17) have drawn attention to the relative frequency of hypovitaminoses C especially amongst the poorer classes. This area is one of the most "depressed" in the British Isles and since dietary deficiencies are almost always accompaniments of economic distress it seems reasonable to suspect hypovitaminoses. Schoeder, Harde (A) and others have demonstrated that pyrexia and infections greatly increase the usage of vitamin C. Since these people are on the whole too poor to augment their diet during disease to meet the additional requirements it seems possible that the occurrence of an epidemic of infectious disease would increase the incidence and severity of such hypovitaminoses. These suppositions accord well with the actual findings in this investigation.

In group 1, of twenty-three apparently normal children selected at random, two showed definite vitamin C subnormality, i.e. almost 10% so that hypovitaminoses C appears to be not uncommon amongst the normal children of the area. The percentage appears to be high but it has to be remembered that these were chiefly children of poor families. The percentage incidence of vitamin C subnutrition is however greatly increased/

increased in the children examined subsequent to an attack of measles. These children constituted Group 2 and of 58 examined at various stages of convalescence 26 showed definite vitamin C subnormality - i.e.nearly half of the children examined - 50%. This great increase in the incidence of hypovitaminoses C following measles is even more striking if Group 1 and sub-group A are compared. These groups consist of normal children, and children examined 7 days after the first appearance of the rash, respectively. In the first the incidence of subnormality was 10%, in the second it was 80% - ten of twelve children examined showing definite vitamin C deficiency.

To explain this great rise in the percentage incidence of vitamin C sub-nutrition there is nothing except the attack of measles. The children were essentially of similar social position etc. Their diets had been altered in no way whatsoever. It is here interesting to recall that four children were examined in Group 1 and found to be in a satisfactory state of vitamin C nutrition, they later contracted measles and when again examined three of them showed appreciable subnormality. (see page 32)

Harris and Ray (11) have made the suggestion that the body normally has a reserve store of vitamin C presumably to meet times of increased demand or low intake. (It seems probable that the classical signs and/

and symptoms of vitamin C deficiency do not arise until this reserve has been depleted and the body requirements for cell metabolism can no longer be met. Before this stage is finally reached there is however the intermediatary period when deficient intake is supplemented from body-reserves - vitamin C nutrition is now sub-optimal - this stage probably corresponds to sub-clinical scurvy - the state of vitamin C nutrition of the body is sub-normal but there are no signs or symptoms of the deficiency as the actual tissue requirements for cell metabolism are still met.)

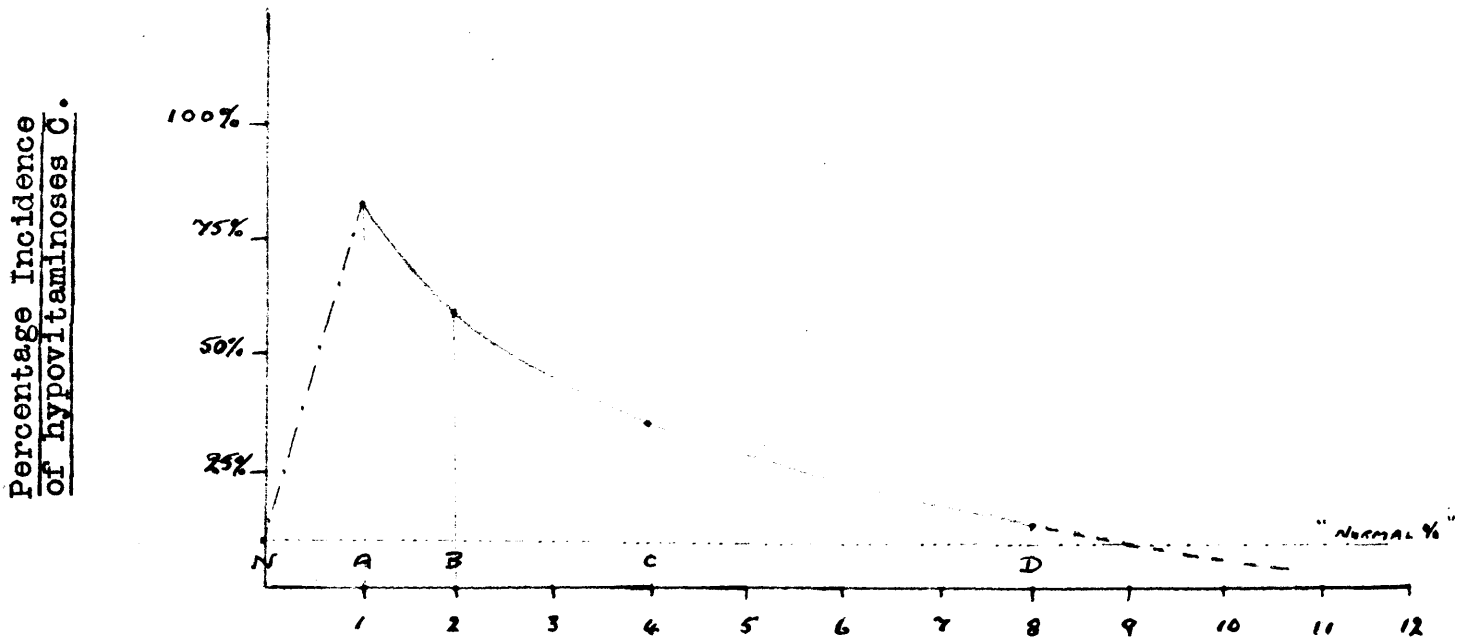
If then the diet of a given individual is just slightly in excess in vitamin content of his daily requirements and his body reserve store full - he will live in a state of equilibrium and of optimal vitamin C nutrition with his daily requirements met and his reserve "untouched". If there is now a sudden large increase in his daily requirements, his intake remaining as before, this increased demand must be met by drawing upon his body reserves which will gradually and progresively become depleted. If this increased demand ceases before his body reserves are entirely exhausted (i.e. while he is still in the asymptomatic stage of subnutrition) and his intake remains as before, he will now again be at equilibrium his intake being once more adequate for his daily requirements - but now at equilibrium with his reserve gone - his stores/

stores depleted. The rate at which he returns to his former optimal state will depend theoretically directly upon the relationship between his vitamin C intake and daily requirements (since any excess of requirement has been found to be retained by the body - presumably to replenish the depleted reserves.) If this excess is high he will return rapidly to his former state, if low he will return slowly. Applied to a number of individuals in whom sub-nutrition of vitamin C had been detected following an infectious disease this principle would indicate that the incidence of hypovitaminosis C would decline at a rate in direct relationship to the amount of ascorbic acid in the diet. If therefore the greatly increased incidence of hypovitaminoses following measles returns only slowly to normal it seems reasonable to conclude that the diet of the children examined is inadequate in vitamin C to meet the increased usage of the vitamin during measles - and also inadequate to return these children rapidly to a satisfactory state of vitamin C nutrition once the attack of measles has passed.

These observations were found to coincide with the results obtained in the investigations. The greatly increased incidence of vitamin C subnormality has been mentioned (page 34). Followed through the convalescence it was found that the subnormality persisted, in certain of the children examined, for a long/

TABLE NO. 7.

A graphic representation of the decline in incidence of Hypovitaminoses C as convalescence progressed.



Weeks from commencement of illness.

Group 1 (N)	Normal children	2 in 22	showed	hypovitaminosis C	= 9%
Sub-group A(A)	at 7 days	10 in 12	"	"	" = 83%
Sub-group B(B)	at 14 "	9 in 15	"	"	" = 60%
Sub-group C(C)	at 28 "	5 in 15	"	"	" = 33%
Sub-group D(D)	at 56 "	3 in 16	"	"	" = 18%

long time after the attack of measles. It was further found that the percentage incidence of vitamin C sub-nutrition gradually and progressively declined as convalescence lengthened (See graphs opposite).
In sub-group A, ten of twelve children examined 7 days after the first appearance of the rash, showed sub-nutrition - approximately 80%. In sub-group B, nine of fifteen children examined at 14 days showed deficiency - approximately 60%. In sub-group C five of fifteen examined at 28 days - approximately 33% and in sub-group D, three of sixteen children examined at 2 months showed subnormality - approximately 20%. So that although hypovitaminoses C is present amongst the children of this area long after measles its incidence gradually and progressively wanes. As deficiency in vitamin C is generally assumed as being directly due to dietary lack it seems reasonable to conclude that the diet of these children in insufficient in vitamin C to meet the increased usage during measles.

The incidence of hypovitaminoses in all groups seems to be surprisingly high so that all calculations, titrations etc. were carefully checked and yet no fallacy was detected. It is to be remembered however that this was really an examination of the poorer classes of a poor area so that the degree of vitamin C sub-nutrition is not perhaps really higher than might/

might be expected. "Sub-clinical scurvy has been estimated to run as high as 22 per cent. among the poorer children of New York". (Eddy and Dalldorf - The Avitaminoses p.198 line 11) while Gothlin found 20-25 per cent amongst the poorer school children of Northern Sweden (8).

It must of course be stated that the suggestion that vitamin C subnutrition is not infrequent among the poorer classes of this country is by no means generally accepted. As late as 1934 McCance in a lecture at King's Hospital said of vitamin C " ..... everyone needs it, but fortunately nearly everyone in this country gets it and gets enough of it". (McCance. The preventive Aspects of Medicine by various authors. p. 110.)

Two possible sources of error in the method used for detection of subnutrition in this paper have to be considered. The first - the presence of other substances in the urine besides l-ascorbic acid capable of reducing 6:2 dichloro-phenol-indo-phenol. Though such substances do exist in normal urine (such as thio-sulphate, ergothionine) Harris (11), Tillmans and many others consider that provided proper care is taken in the preservation of samples and to the details of titration the quantity of these substances is so small as to be of little practical significance. In this connection an advantage of the saturation test may/

may be mentioned - since this test depends upon the demonstration of a large quantity of ascorbic acid in the urine following the administration of the test dose (or doses) the proportion of such other substances even if present will be much smaller and therefore of much less significance than when the estimation of the average quantity of ascirbic acid excreted daily is being used.

Since criticism has been levelled at the method used for preserving the ascorbic acid in urinary samples (see page 22) it must be admitted that if gross loss of the acid did occur the results obtained would be erroneous. But Harris and Abbasy after careful testing consider that the method is adequate for the purpose for which it is advocated. Burrows and Fleming only detected a loss of 22% after samples had been standing for twenty-four hours whereas in the present work they were never allowed to stand longer than four hours; also the criticism of these authors was levelled chiefly at the use of sulphuric acid as a preservative. Here again the advantage of the saturation test is seen for since it depends upon the demonstration of a gross difference in the quantity of ascorbic acid excreted in the twenty-four hours before and after the test dose - the loss of acid will not appreciably affect the relative difference between the quantity of the acid in the two samples.

The second factor for consideration is the absorption of ascorbic acid. Although administration of the acid orally has been the method used in numerous investigations upon hypovitaminosis C (Harris, Abbasy, Paul Wood, Archer, Ellmann etc.) there is some reason to believe that the vitamin so administered is not always well absorbed (Eddy and Dalldorf. The Avitaminosis p. 197). Intravenous injection of cevitamic acid has been used by Neuweiler (21) and others to obviate this difficulty but intravenous injection was not practicable in the present investigation and it is extremely costly.

However, the fact that all the cases of hypovitaminoses C detected during the investigation were sooner or later corrected successfully by the oral administration of cevitamic acid (and a satisfactory high urinary excretion obtained) would seem to indicate that at least a large proportion of the acid was absorbed. The results are calculated on the assumption that all the acid administered is absorbed. It is stated that there is, in certain hypo-chromic anaemias, a diminished absorption of mineral elements as a result of achlorhydria. Whether similar vagaries of absorption exist for l-ascorbic acid has not so far been determined but even if they did this fact would only affect the results of the tests used in the investigation as far as degree and actual incidence/

incidence of hypovitaminosis C are concerned. It could hardly be considered to produce an increased incidence following measles or to affect the return of that increased incidence to the previous standard.

The direct connection between the diet and the development of hypovitaminosis C was reflected throughout the investigation and such connection seems further to support the adequacy of the tests used since children on diets low in vitamin C showed sub-normal nutrition in that factor while children on high vitamin C diets showed no sub-normality. A short reference to the tables will demonstrate this relationship.

In the first group (page 26) those children who did not require test doses to establish the satisfactory nature of their vitamin C nutrition had good supplies of the vitamin in their diets. Conversely the two boys showing hypovitaminoses C were of poor families and showed a diet of very low vitamin C content. Again in sub-group A. (page 28) the only two children showing no deficiency 7 days after the first appearance of the rash, were receiving exceptionally high amounts of the vitamin while those at the other end of the table had correspondingly low dietary content of ascorbic acid. The same relationship between diet content of vitamin C and development of sub-nutrition in that factor is evidenced in the rest/

rest of the tables not only in Section 1 but also in Section II (the investigations in pregnancy).

Closely associated with the above observation comes the relationship of the economic status of the household to the development of vitamin C deficiency and as is to be expected by far the greater percentage of the children showing deficiency came from poor households. To many of these people fruit in any form even tomatoes is considered more as a luxury than as a necessity of diet and this coupled with the fact that during the winter good fruit is expensive and cheap fruit unattractive seems to have a very adverse effect upon the diet especially that part of the diet which supplies ascorbic acid so that during the winter at least there is danger of them developing deficiency. Although this dietary inadequacy might be corrected by a liberal supply of the vegetables of high vitamin C content namely cabbage and spinach; these vegetables are not eaten to any excess. Also if they are kept at room temperature - at home or in the shop - for any length of time they lose much of the vitamin C content (Eddy and Dalldorf). Further also much of the vitamin may be lost in cooking through oxidation, destruction by salts added, or by solution in the water in which the vegetable is cooked and which is usually discarded.

Much/

Much stress has for some time been laid upon the value of vitamins A and D by the medical profession and by commercial advertisers of foodstuffs. The high content of fresh butter of these vitamins is known by the public and those of them, who give consideration in their family budget to the known requirements of good health appear to have a disproportionate view of the value of fresh butter as opposed to fresh fruit - so that they are apt to purchase fresh butter in preference to fruit which they consider a luxury. If vitamin C deficiency is as prevalent as has been suggested by some authors - margarine and fresh fruit with doses of cod liver oil might perhaps be a more successful method of supplying essentials to a large family with a small income.

Through the investigation careful observation was made of all children showing vitamin C deficiency in an attempt to detect any frequently recurring sign or symptom which might give a clue as to the condition. This scrutiny applied not only to normal children but also to the children who had had measles, for though the fact that the child had recently suffered from measles might partly detract from the value of such a clue, if obtained, if the sign of symptom rapidly disappeared on the administration of ascorbic acid then the inference would be that it was due to the deficiency/

deficiency in that factor and not a specific "after-effect" of measles. Nothing of value was however elicited. Many of the children were tired and listless - more so than children of similar histories but showing no deficiency. Some complained of vague pains, some though bright in the morning tired as the day passed. A few appeared perfectly normal. It is interesting to note that in none was gingivitis detected except where it was associated with one or more grossly carious teeth and the significance thereby obscured. It seemed that the only way to be certain that sub-nutrition did not exist was to apply one of the recognised tests for its detection. The most reliable indications were provided by the dietary history and the child's general health and if either of these was unsatisfactory it was prudent to apply a test, the results of which were often surprising.

CHAPTER VI.

CONCLUSIONS.

From the results obtained it seems reasonable to conclude that:-

(1) Hypovitaminosis C is present amongst the apparently normal children of this area.

(2) That there is an appreciable increase in the incidence of hypovitaminosis following measles in children of the same area.

(3) That the diet of the poorer children of this area is too low in vitamin C during an attack of measles and the convalescence, to meet the increased usage of the vitamin so that the effects of this increased usage are detectable for some time following the attack of measles.

SUMMARY.

1. An investigation has been conducted into the state of vitamin C nutrition of the poorer children of this area (a) normal (b) following measles, using the simplified urinary saturation test to detect ascorbic acid deficiency.

2. Of 23 normal children 3 showed hypovitaminosis C.

3. Of 12 children examined 7 days after the first appearance of the rash 10 showed hypovitaminosis C.

4./

4. Of 15 children examined 14 days after the first appearance of the rash 9 showed hypovitaminosis C.
5. Of 15 children examined 28 days after the first appearance of the rash 5 showed hypovitaminosis C.
6. Of 16 children examined 2 months after the first appearance of the rash 3 showed hypovitaminosis C.
7. All the children with complications that were examined showed hypovitaminosis C.

SECTION II.

OBSERVATIONS ON VITAMIN C NUTRITION DURING PREGNANCY.

CHAPTER I.

INTRODUCTION.

Neuweiler of Berne (32) has demonstrated that a larger quantity of vitamin C is required by a pregnant than a non-pregnant woman to maintain her vitamin C nutrition at the optimum level. Two years later Bucher of Zurich (33) confirmed these results while investigating the possible cause of dental caries occurring during pregnancy in Switzerland. He demonstrated that during pregnancy a much larger daily intake of the vitamin was required to maintain the urinary excretion rate at equilibrium at the lowest quantity indicating satisfactory vitamin C nutrition, namely 13 mgm. per day. (Harris) than was required to obtain the same effect in the non-pregnant woman. He also found that the health of mothers on large doses of vitamin C was superior to that of those on average diets - "no healthy tooth became carious, none of the women receiving vitamin C became anaemic, they suffered less from fatigue, rheumatic and sacral pains and they were much less susceptible to chills."

The demonstration of hypovitaminosis C amongst the hospital class in this country has been mentioned (page 7 line 6) and the comparative poverty of the area in which this investigation was conducted has been described (page 9).

THE OBJECT OF SECTION II.

Having the above facts in mind it was decided to investigate:-

(a) The presence of hypovitaminoses C amongst the non-pregnant and pregnant women of this area.

(b) The possible increase in incidence in pregnant women as compared with the non-pregnant women.

(c) At which of three stages of pregnancy the incidence was highest :-

(a) at the fifth month

(b) at term

(c) during lactation.

METHOD OF INVESTIGATION.

The test adopted was essentially the same as that described in Section 1 (pages 12 - 16) namely the simplified urinary saturation test of Harris and Abbasy (24). In those cases which were examined while in hospital an attempt was made to estimate the daily excretion of ascorbic acid before the test dose was administered. For this estimation the simplified procedure of collecting 3-hour specimens from 8 a.m. - 11 a.m. as suggested by the same authors was used. No attempt was made to make an accurate estimation of the vitamin C nutrition as it seemed impossible to examine a sufficient number of cases and also/

also the collection of 24 hour specimens of urine by patients living at home is not practicable amongst the poorer classes. Even the cases which remained in hospital during the time they were being examined were not so investigated as the collection of total daily specimens of urine was considered too much of an imposition upon the nursing staff of a small over-crowded hospital with no laboratory accommodation.

The actual tests used were the same as those described in the section on measles and all the precautions mentioned there with regard to the collection, preservation and titration of urinary samples were observed. Firstly in a limited number of cases the daily excretory rate was estimated and then on all the saturation test was performed. In this case of course the actual size of the test dose was much larger but complied with the standard of at least 70 mgm. per stone of body weight. 800 mgm. of ascorbic acid (16 crushed Redoxon tablets) was used for all cases.

No attempt was made to make the investigation a representative one of the various social strata composing the practice and again a definite bias was present in the selection of cases towards the poorer classes. The cases examined were either resident at home or in hospital during the investigation. The non-pregnant/

non-pregnant women and the women five months pregnant were generally speaking resident at home and the women at term or in the puerperium were resident in hospital.

The cases were divided into four groups:-

Group 1. Non-pregnant apparently normal women.

Group 2. Women 5 months pregnant - normal.

Group 3. Women at term. "

Group 4. Women in the puerperium "

To these was added a special group:-

Group 5. Women developing complications during pregnancy and in the puerperium.

TABLE NO. 8.

Group 1. Apparently normal non-pregnant women.

22 examined - 1 hypovitaminoses C.

	Age	Quantity of Ascorbic Acid Excreted daily	Number of Test Doses of 800 mgm.	Calculated Deficiency	Diet Content in Vitamin C.	Health.
1	19	31.1 mgm.	-		Very High	Good
2	23	26.1 "	-		High	"
3	30	22.1 "	-		Satisfactory	"
4	18	19.2 "	-		High	Moderate
5	26	16.1 "	-		"	Good
6	21	"	1		"	"
7	24	"	1		Satisfactory	"
8	23	10.1 "	1		"	Moderate
9	29	9.7 "	1		"	"
10	28	"	1	Nil	"	Good
11	18	"	1		"	"
12	23	"	1		Low	Poor
13	22	8.3 "	1		Satisfactory	Good
14	27	"	1		"	"
15	26	"	1		"	"
16	29	7.2 "	1		"	"
17	19	5.1 "	1		Low	Moderate
18	28	"	1		Satisfactory	V. Good
19	20	"	1		"	Moderate
20	26	"	1		"	"
21	23	5.6 "	2		Low	Poor
22	26	" "	5	2.400 mgm.	V. Low.	V. Poor

CHAPTER II.

RESULTS OBTAINED.

GROUP 1. Non-pregnant Women.

Women attending the surgery for very minor ailments were utilised for this investigation. They consisted of nulliparae and multiparae ages from 22-38. 21 were examined.

Five showed a very high concentration of ascorbic acid in a casual specimen and no further test was applied. The titration of casual specimen is not recommended by Harris (11) etc. but in these cases the content of vitamin C was so high as to make hypovitaminoses C highly improbable.

On the rest the saturation test was performed and a very definite response occurred to the standard test dose of 800 mgm. cevitamic acid in all but one subject. The responses varied:-

from 21.5 mgm% ≒ 325.5 mgm per day 37.5% of the test dose
to 42.3 mgm% ≒ 635.5 mgm per day 75% " " " "

In only one case therefore was vitamin C sub-nutrition detected. The subject required five test doses before a satisfactory urinary response occurred (actually six were administered but as the subject vomited within an hour of taking one of the test doses, this dose was omitted from the calculation as it was impossible to say whether or not the ascorbic acid had been/

TABLE NO. 9.

Group 2. Women 5 months pregnant.

21 examined - 2 hypovitaminoses C.

	Age	Quantity of Ascorbic Acid Excreted daily	Number of Test Doses of 800 mgm.	Calculated Deficiency	Diet Content in Vitamin C.	Health.
1	23	16.1 mgm.	1		Satisfactory	Good
2	19	14.3 "	1		"	"
3	24	10.2 "	1		High	"
4	22	10.1 "	1		"	"
5	19	8.5 "	1		High	"
6	27	8.2 "	1		Good	
7	26	8.2 "	1		Satisfactory	Moderate
8	23	7.5 "	2		"	Poor
9	23	5.1 "	2		Low	Good
10	26	4.1 "	2		Satisfactory	"
11	29	— "	2		"	"
12	21	— "	2		"	"
13	24	— "	2		High	"
14	24	4.0 "	2		Satisfactory	Moderate
15	23	3.2 "	2		Low	"
16	27	— "	2		Satisfactory	Good
17	22	— "	2		"	"
18	23	— "	2		"	"
19	26	2.1 "	2		"	"
20*	24	— "	3	800 mgm.	Low	Moderate
21	22	— "	6	2,600 "	V. Low	Poor

* No. 20 - developed mastitis in puerperium - see pages 55a and 57 .

been absorbed.) She, therefore, received 4,000 mgm. of cevitamic acid and if 1,600 mgm. (the amount of two test doses, which may be required to give a satisfactory response even with normal vitamin C nutrition) is subtracted a deficiency of 2,400 mgm. remains. She was a poor woman who had had several pregnancies in rapid succession though she was not at the time pregnant. She was anaemic (Hb. 62% Red cells 3,500,000). She was given Ferri et Amm. Citras XXX grs. t.i.d and advised to take an orange a day. On examination in four weeks she was much improved - Hb. 75% Red cells 4,220,000.

Of these twenty-one women only one was suffering from hypovitaminosis C.

GROUP 2. Women 5 months pregnant.

This group was composed of 21 primiparae and multiparae ages from 21-34.

In twelve of them casual specimens of urine were titrated almost immediately on being passed but the concentration of the vitamin was so small that the results were ignored. All cases in the group therefore received test doses. Seven responded to the first test dose, twelve to the second, one to the third, and one to the sixth. So that the last two alone showed vitamin C subnormality. Of the first seven it is interesting to note that five of them had been taking high fruit diets of their own accord in view of their pregnant state.

The/

TABLE NO. 10.

Group 3. Women near term.

21 examined - 2 hypovitaminoses C.

	Age	Quantity of Ascorbic Acid Excreted daily	Number of Test Doses of 800 mgm.	Calculated Deficiency.	Diet Content in Vitamin C.	Health.
1	21		1	-	High	Good
2	25	4.38 mgm.	1	-	"	"
3	24	3.28 "	1	-	Satisfactory	"
4	22	— "	1	-	"	Moderate
5	23	3.28 "	2	-	"	"
6	19	— "	2	-	High	Good
7	27	— "	2	-	"	"
8	26	3.12 "	2	-	"	"
9	22	— "	2	-	Satisfactory	"
10	22	4.28 "	2	-	"	"
11	26	2.76	2	-	"	Moderate
12	25	— "	2	-	"	Good
13	23	— "	2	-	"	"
14	24	— "	2	-	Low	Moderate
15	28	— "	2	-	Satisfactory	Good
16	25	— "	2	-	"	"
17	25	2.56 "	2	-	"	Moderate
18	27	2.40 "	2	-	"	Poor
19	24	— "	2	-	"	Satisfactory
20*	22	— "	4	1,600	Low	Poor
21	25	— "	6	3,200	V. Low	"

* No.20 - developed mastitis in puerperium - see pages 55a and 57 .

The two cases showing subnormality had poor dietary histories. Practically their only possible source of the vitamin was cooked potatoes, turnips and cabbage; tinned fruit of inferior quality, and very occasionally an orange.

GROUP 3. Women at or near term.

This group consisted of 21 women, multiparae and primiparae, ages from 19-33. They were mostly admitted to hospital because of "unsatisfactory housing conditions".

At first an attempt was made to ascertain their rate of vitaminC urinary excretion but as the diets were in no way controlled the figures obtained, though low, were of little actual significance. Only eight were examined by this procedure as usually labour was imminent when the patients were admitted to hospital and it was considered prudent to perform the saturation test before the opportunity was lost. The rates of urinary excretion of ascorbic acid of these eight were:-

Quantity Ascorbic Acid in 3 hour specimen.	Calculated Quantity in 24 hour specimen.
.30 mgm.	2.4 mgm.
.32 mgm.	2.56 "
.34 "	2.76 "
.39 "	3.12 "
.41 "	3.28 "
.41 "	3.28 "
.51 "	4.28 "
.53 "	4.38 "

TABLE NO. 11.

Group 4. Women in Puerperium.

11 examined - 1 hypovitaminoses C.

	Age	Quantity of Ascorbic Acid Excreted daily	Number of Test Doses of 800 mgm.	Calculated Deficiency.	Diet Content in Vitamin C.	Health
1	22	11.1 mgm.	1		Satisfactory	Good
2	21	8.1 "	1		"	"
3	25	7.3 "	1		"	"
4	19	7.1 "	1		High	"
5	26	7.0 "	1	Nil	Satisfactory	Good
6	25	— "	2		Low	Moderate
7	23	— "	2		Satisfactory	"
8	27	5.2 "	2		High	Good
9	27	4.1 "	2		Satisfactory	Moderate
10	23	— "	2		Low	"
11	22	"	5	2,400 mg.	V. low	Poor

On these and on a further thirteen the saturation test was performed using on successive days the test dose of 800 mgm. until a satisfactory urinary response occurred. Four responded to the first test dose, 15 to the second, one to the fourth and another to the sixth. The last two came below the standard adopted for satisfactory vitamin C nutrition. They appeared to be in fairly good health. In one of them (she requiring 6 test doses) a definite lack of vitamin C bearing substances was evident in her diet. She rarely ate oranges, never took lemon or grape-fruit and ate all tomatoes "well-fried". In the other the probable cause of the deficiency remained obscure as her present and past diet seemed to contain a satisfactory quantity of the vitamin C containing foodstuffs.

GROUP 4. Women examined during the puerperium.

All the women examined in this group were in hospital and in the first fourteen days of the puerperium. None of these cases had been examined previously during the pregnancy because, as explained in Section I (page 16) any examination by the saturation test results automatically in the correction of any existing deficiency.

Eleven multiparae and primiparae, ages from 20 to 32 were examined.

Five/

TABLE NO. 12.

Women developing complications.

	Age	Complication	Number of Test Doses of 800 mgm.	Calculated Deficiency	Further Treatment.	Result.
1	22	Perineal tear which broke down - Resutured.	5	2,400 mg.	8 Redoxon tablets + 2 night and morning for 1 week.	Sound union with 2nd repair.
2	25	Pruritus Vulvae.	4	1,600	2 Redoxon tablets night and morning for 1 week.	Improved.
3	24	Mastitis	Not examined		4 Redoxon daily for 10 days.	Normal, not accelerated recovery.
4	21	Mastitis				

Five responded to the first test dose, five to the second test dose and one to the fifth. The last alone, therefore, was suffering from vitamin C subnormality. She was a large flabby woman, not very fond of vegetables or fruit, but with an otherwise voracious appetite. (Reference is again made to her on page 56).

GROUP 5. Women developing complications during pregnancy or in the puerperium.

The local hospital serves as an ~~urgency~~ emergency hospital for maternity cases of the surrounding district but normal cases are also admitted on account of "unsatisfactory housing conditions".

The investigation of this group was originally commenced in an attempt to see what influence, if any, vitamin C subnutrition had upon the incidence and progress of complications. So many complications are however associated with toxaemia, infection or pyrexia, conditions which in themselves cause a greatly increased usage of vitamin C (19), that the methods used for the detection of ascorbic acid nutrition in the present investigation were inadequate for this purpose and the original intention had to be sacrificed.

A few cases were examined and the results are of interest and they are recorded here.

Firstly/

Firstly Mrs A, already mentioned in Group 4 (Table No.11 page 54a, No.11). She had a perineal tear at the birth of her child which was sutured immediately but gave way on the fourth day though the wound was apparently aseptic - it however appeared blue and the granulation tissue was rather swollen and oedematous. On examination by the saturation test she required 5 test doses to give a satisfactory response, so that she showed a calculated deficiency of 2,400 mgm. The surgeon decided to stitch the perineum again and this was done on the eighth day. On the day previous she was given 8 redoxon tablets and on each succeeding day for a week 2 tablets night and morning. It is interesting to note that the repair healed well this time and she was discharged from hospital in 14 days from the second stitching. There was a noticeable change in the appearance of the wound following the second repair, it being red as opposed to the previous blue oedematous appearance. This is reminiscent of the difference Ingallis demonstrated in experimental abdominal wounds in scorbutic and well-fed guinea pigs (Lanman T.H. and Ingallis T.H. 1937 Ann. Surg. 105, p.616.)

The second case was a woman at the sixth month of pregnancy suffering from severe pruritus vulvae for which no cause could be discovered locally or generally/

generally. On the application of the saturation test she was found to have a calculated deficiency of 1,600 mgm. ascorbic acid. She was given 2 Redoxon tablets night and morning for a week (200 mgm. cevitamic acid) and though the pruritus did not disappear it was greatly improved. The significance of the effect of the tablets was however obscured for the condition was so severe as to make it impossible not to use also local applications.

During these investigations four women developed acute mastitis in the puerperium, two of whom had shown a deficiency earlier to the pregnancy (Tables Nos. 9 and 10).

The other two had not been examined for subnutrition before parturition. Their state of vitamin C nutrition during the mastitis was not examined because it was considered that the associated pyrexia would vitiate the results. "Redoxon" was administered to all these women in doses of 200 mgm. daily by mouth (2 tablets night and morning). But though their recoveries were entirely satisfactory it was not possible to say that they were accelerated - though they were quicker than many treated by identical methods but without the "Redoxon" tablets.

TABLE NO. 13.

	Hypovitaminosis	Number Examined	Response after first test dose.
Group 1.			
Normal women	1	22	2
Group 2.			
Five months pregnant	2	21	14
Group 3.			
Near term	2	21	17
Group 4.			
During Lactation	1	11	6

CHAPTER III.

DISCUSSION.

Definite hypovitaminoses C was detected in the non-pregnant and in the pregnant women of this area (1 in 22 in the former, 5 in 53 in the latter). But there was no appreciable difference in the incidence in the two groups. Further no difference was observed in the incidence of hypovitaminoses C at the three stages of pregnancy investigated, namely, at the fifth month, at term and during the puerperium. The results are rather surprising in view of the poor financial circumstances of many of the subjects and of the findings of several workers (32) (33).

It must be noted however that the test dose was large (800 mgm. ascorbic acid) and further that if a response occurred after the second test dose vitamin C nutrition was considered normal. It was observed that most of the non-pregnant and lactating women responded to the first test dose, while the greater proportion of the women examined when five months pregnant or near term required two or more test doses to give a similar response. If therefore one test dose is taken as an arbitrary standard a marked difference is evidenced between Groups 1 and 4 as opposed to Group 2 and 3 as is shown in Table No.13 page 58a. This/

This seemed to indicate that had a more detailed method been used for the detection of hypovitaminoses C more cases of subnormality (of mild degree) would have been detected amongst Groups 2 and 3. In this connection it is interesting to quote from one of Harris's earlier writings - "For an adult of average weight a dose of about 600 mg. seems suitable. The response will vary according to the "state of saturation" of the subject, depending upon the amount of vitamin C in his past diet. If the test doses show no appreciable response - indicating a low degree of saturation - further information may be obtained by giving a second dose on the next day, in order to distinguish between severe and more moderate degrees of vitamin deprivation" - this refers to the test when the full twenty-four hours quantity of urine passed following the test dose is examined. It will be remembered that in this investigation the simplified saturation test was used of which Harris says "a response should occur usually on the first and certainly on the second day".

The influence of diet in the production of states of vitamin C subnormality was again obvious and no case of hypovitaminosis C was detected where there was a satisfactory dietary history.

Two possible sources of fallacy connected with the test used for the detection of hypovitaminosis C in/

in this investigation were mentioned in Section I. They were firstly, inadequacy of the method adopted for the preservation of the ascorbic acid in the urinary samples and secondly irregularities in the absorption of cevitamic acid administered orally. If such factors were operating the tendency would be to increase the number of subjects showing hypovitaminosis C - since these were few it is unlikely that the mentioned fallacies even if operable would materially effect the significance of the results obtained.

Further it is to be noted that those subjects in whom hypovitaminosis C was detected the deficiency was of high degree - too severe to arise purely as error due to loss of cevitamic acid by inadequate preservation of that factor. Since accepted methods of preservation were used and since urinary samples were titrated at the very latest within four hours of being passed, the loss from this source could only be of slight degree.

With regard to the question of the absorption of ascorbic acid administered orally, it seems pertinent to observe that since high urinary responses were obtained in all subjects sooner or later, absorption however slow must have occurred so that the essential difference between a subject who responded after the second test dose and one who required more than that number remains.

CONCLUSIONS.

Hypovitaminosis C is present amongst the non-pregnant and pregnant women of this area;as estimated by the simplified urinary saturation test the incidence of hypovitaminoses C is no greater amongst pregnant than it is amongst non-pregnant women and further that as judged by the same test there is no appreciable difference in incidence of hypovitaminosis C at the three stages of pregnancy investigated, namely at the fifth month, at term and during lactation.

SUMMARY.

An investigation has been conducted, into the state of vitamin C nutrition of a number of non-pregnant and pregnant women of a "depressed" area, using the simplified urinary saturation test.

1. of the non-pregnant women investigated
   21 showed no deficiency.
   1 " hypovitaminosis C.
2. of women pregnant 5 months
   19 showed no deficiency.
   2 " hypovitaminosis C.
3. of women at term 19 showed no deficiency.
   2 " hypovitaminosis C.
4. of women during lactation
   10 showed no deficiency.
   1 " hypovitaminosis C.

APPENDIX.

METHODS FOR TESTING CAPILLARY RESISTANCE.

Gothlin's Method (Gothlin, G.F. Skand. Arch. f. Physiol. 225, 1931)

A rubber arm band of the kind used with sphygmomanometers is placed about the arm and inflated to a pressure less than the diastolic pressure of the pulse (Gothlin uses three pressures, 35, 50 and 60 m.m. Hg. to make the test more quantitative). The pressure is maintained for 15 mins. To interpret the test a circular area is imprinted on the skin over the anticubital fossa with a rubber stamp and the number of petechiae in this area counted. Using a circle of 60 m.m. diameter Gothlin found that healthy Scandinavians had fewer than five petechiae when a pressure of 50 m.m. Hg. was used. More than eight petechiae are considered sub-normal.

Section Cup Method (The Avitaminosis. Eddy and Dalldorf p. 313 2nd Ed.)

"A satisfactory method is to use a small bicycle pump connected to a manometer and a small glass cup which is placed on the skin area to be tested and by means of which various negative pressures can be exerted on the capillaries."

Vitamin/

Vitamin C value of common food-stuffs.

(Average vitamin C unitage per 100 grams of food-stuff in International units)

1 international unit = 0.05 mgm. l-ascorbic acid.

Foodstuff.	International units per 100 gram.
Almond	1,000
Apples	150
Apricots, fresh	80
" dried	200
Artichoke, Globe	180
" Jerusalem	nil
Asparagus, green	400
" bleached	400
Banana	200
Barley	nil
Beans, dried, pint	nil
" Kidney	
" Lima fresh	
" dry	
canned	
haricot	
Blueberry	230
Brussels sprouts	550
Butter	nil
Cabbage	1,000
Carrots	200
Cauliflower	500
Celery, green	150

Foodstuff.	International units per 100 grams.
Celery, bleached	100
Cherries	75
Cranberries	250
Cucumbers	250
Currants, black	3,900
Dates, dried	nil
Figs, fresh	40
" dried	nil
Gooseberries	250
Grapes	35
Grape-fruit	650
Leeks	250
Lemons	805
Lemon juice	1,000
Lentils	nil
Lettuce, green	80
" bleached	70
Mandarins	520
Melons	50
Milk, whole	50
" skim	nil
" dried	
" evaporated	
" condensed	
Onions	150
Oranges	800
Orange juice	900

Foodstuff.	International units per 100 grams.
Parsley	1,500
Parsnips	350
Peaches, white	120
" yellow	175
Pears	40
Peas, green	400
" dried	nil
Pineapples	nil
Pineapple juice	200
Plums	100
Potato, sweet	100
" white	150
Prunes, dried	160
Radish	500
Raisins	nil
Raspberries	350
Rhubarb	400
Spinach	1,000
Strawberries	600
Tangerines	500
Tomatoes, green	250
" ripe	300
Turnips	140
Turnip greens	1,000
Walnuts	nil
Watercress	1,000
Water melon	150

Foodstuff.	International units per 100 grams.
Wheat, whole	nil
" flour	
" bran	
Bacon	nil
Bread	
Cheese	
Chicken	
Cream	
Eggs	
Fish	
Flour	
Haddock	
Ham	
All meats	

DIET.

In the above table a detailed list of the common foodstuffs and their vitamin C content per 100 gram is given (Eddy and Dalldorf. The Avitaminosis 2nd Ed. p. 316). It will be noticed that the highest values per unit weight are supplied by black currents, orange/

orange juice, parsley, lemon juice, cabbage, spinach, turnip greens, watercress, almonds, oranges and lemons in this order. That bread, all meats, all fish, cheese, cream and eggs supply none of the vitamin and milk very little.

The vitamin is water soluble, labile and destroyed by oxidation especially heating in the presence of oxygen, though heat itself has no detrimental effect. It is also destroyed by soda, bicarbonate and citrate so that it would appear that cooking might be very detrimental to the vitamin. Recent work by McCance however has shown that the danger is not as great as formerly believed.

The modern methods of canning and rapid chilling do not destroy the vitamin.

REFERENCES.

1 Eddy, W.H., & Dalldorf, G. The Avitaminosis 2nd Ed. p.162.

2 " " " " 2nd Ed. p.163

3 Price, F.W., Text-book of Medicine p 458.

4 Parsons, H.T., J. Biol. Chem., 59, 97 (1924).

5 Lepkovsky, S, & Nelson, M.T., Ibid 59:91 (1924).

6 King, C.G., & Waugh, W.A., Sci. 75, 357, 630(1932)

7 McCarrison, R. Lancet 1931 vol.I, p. 1151.

8 Gothlin, G.F., Skand. Arch. Physiol. 65, 24.

9 Eddy, W.H., & Dalldorf, G. The Avitaminosis 2nd Ed. p.197.

10 Tillmans, J., Hirsh, P., Jackish, J., Zeits f. Unters d. Lebens 1932 lxii. p.93.

11 Harris, L.J., Ray, S.N., Lancet 1935 vol.I, p.71.

--- --- Ibid 1935 vol.II, 1399.

12) Eddy, W.H., & Dalldorf, G. The Avitaminosis 2nd Ed.
13) pp. 310-311.

14 Rotter, H., Nature 1937, 193, 717.

15 Portnoy, B., Wilkinson, J.F., B.M.J. 1938 vol.I, p.328.

16 Harris, L.J., Abbasy, M.A., Yudkin, J., Simon Kelly Lancet 1936 Vol. II, p. 14.

17 Gander, J., & Niederberger, W., Munch. med. Wochenschrift 1936, No.34. p.1386.

18 Eddy, W.H., & Dalldorf, G. The Avitaminosis 2nd Ed. p. 199.

19 Harris, L.J., Abbasy, M.A., Gray Hill, N., Lancet 1936, Vol.II,1413.

--- --- --- Ibid 1937 Vol.II,177

--- --- Ellman P. " 1937 Vol.II,181

--- Passmore, P., Paget, W., Lancet 1937 Vol.II, 183.

--- Abbasy, M.A., Ray, S.N., and Marrack, J.R., Ibid 1935,Vol II,1399.

20 Fellers, C., Am. J.P.H., 25: 1340 (1935).

21 Eddy, W.H., & Dalldorf, G. The Avitaminosis 2nd Ed. p. 172.

22 --- --- " " p. 197.

24)
)
25) Harris, L.J., Abbasy, M.A., Lancet 1937, vol.II,
) p. 1429.
26)

27 Fleming, G.W.T.H., Burrows, T.E., B.M.J. 1938, Vol.I, 333.

29 McCarrison, R. Lancet 1931 Vol.I, p. 1151.

30 Eddy, W.H., & Dalldorf G. The Avitaminosis 2nd Ed., page 308 line 17.

31 Harris, L.J., Abbasy, M.A., Yudkin, J., Simon Kelly. Lancet 1936, Vol.II, p.16

32 Neuweiler, W. Klinische Wochenschrift 1935, No.50 1793.

33 Bucher, A. Munch. med. Wochenschrift 1937 No.19 p. 734.

Bell, A.D.C. Lancet Vol I, p. 547.

Engelkes, H. Ibid 1937, Vol.II, 1285.

Archer, H.E., Graham, G., Ibid 1936, Vol.II, 364.

Abbasy, M.A., Biochem. J. 1937, No.2 p. 339.

Larzarus, S. B.M.J. 1937, Vol.II, p.1011.

Harris, L.J. Analyst 1934 p. 93.

" " Nature 1933 CXXXI, 27.

A Schroeder, H. Klin. Woch. 1935 XIV, 484.*

Harde, E., Rothstein, I.A., and Ratish, H.D.: Proc. Soc. Exp. Biol. med. 1935, XXXII, 1088. *

McCance, R.A. The Preventive Aspects of Medicine p. 110.

* References taken from article by Harris in lancet see 1935 vol.II 1399.