

## SOME OBSERVATIONS ON VITAMIN C DEFICIENCY IN ACUTE MENTAL DISORDER.\*

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It is well known that gross impairment of nutrition is a not infrequent finding in the newly-admitted psychotic patient. Some of these cases present a state of mental confusion which is directly attributable to a condition of semi-starvation brought about by personal neglect and refusal of food. Obvious clinical signs of malnutrition are present, such as anorexia, emaciation, coated tongue, constipation, and ketonuria. Rapid mental improvement frequently occurs as a result of a liberal diet and relief of gastro-intestinal stasis. But it is equally important to recognize the mild and less obvious forms of malnutrition.

Recent advances in the study of nutrition have served to emphasize the widespread effects of a defective diet in the production of disorder of all systems of the body, thus giving rise to many minor disturbances of the well-being. Indeed, it has been maintained that the majority of mankind lives on a diet which modern research has shown to be defective in one or more of its dietary essentials.

In regard to the vitamins, clinical and biochemical tests are now being used for the detection of the early stages of deficiency in these factors, with the result that a wide field of research has been opened up, stimulating investigations from all branches of medicine.

Since Svirebely and Szent-Gyorgyi (1) in 1932 showed experimentally that vitamin C was identical with ascorbic acid, numerous studies have been made mainly upon its excretion in the urine and the relationship to vitamin C nutrition. The vitamin is essential to healthy cell-life, and in addition to its specific action of regulating the colloidal condition of intercellular substance in all mesenchymal structures it has an important respiratory function, since it forms an oxidation-reduction system in the cell. It is stored in high concentration in the pituitary gland, the suprarenal cortex, the corpus luteum, the interstitial cells of the testes, the tonsils and, to a lesser degree, in the liver, spleen, etc.

Gross deficiencies of vitamin C lead to the development of scurvy—a condition which is now seldom seen. But it has been suggested by Hess (2),

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Parsons (3) and others that slighter degrees of deficiency are of common occurrence, and produce a condition of latent scurvy or hypovitaminosis C analogous to latent tetany. It is claimed that this condition represents a wide zone of deficiency without the appearance of scurvy, where physiological processes are subnormal and the individual suffers from a reduced vitality, excessive tiredness, lack of appetite and vague ill-health.

Such symptoms as these are common enough in psychoneurotic and psychotic patients, who frequently have food fads and fancies leading to a restricted or unbalanced diet. Ungley (4) stresses the importance of psychological factors which influence not only the quantity and quality of the food eaten, but also its assimilation. Bersot (5), in an investigation on mental patients, found that numbers of catatonics, arteriosclerotics and senile cases had hypovitaminosis C, which he regards as a pathological state unfavourable to health.

The determination of the existence or otherwise of latent scurvy has been extensively studied in this country by Harris (6) and his colleagues, by estimating the rate of excretion of ascorbic acid in the urine, utilizing a simple titration method.

The daily level of vitamin C excretion by the kidneys has been found to be remarkably constant (20 to 30 mgrm. per day) when the diet is uniform, the amount varying according to the dietary intake of the vitamin and the degree of saturation of the tissues.

The normal and well-nourished person apparently has reserve stores of the vitamin, and when placed on a vitamin-free diet, the urinary output remains constant for a time and then gradually falls. If, however, a large dose of vitamin is administered, there will be a sharp rise in the urinary output, depending upon the degree of saturation of the tissues.

A low urinary response to a test dose indicates a depleted reserve and a condition of vitamin C subnutrition, whereas a high response is found when the tissues are already saturated.

The daily excretion level and the saturation tests thus constitute different but complementary methods of estimating the vitamin C nutrition of the body.

In the present investigation upon mental patients both methods have been adopted, the urinary ascorbic acid being estimated according to the method of Harris *et al.*, using a modification of Tillman's 2 : 6-dichlorophenol-indophenol method.

#### TECHNIQUE AND RESULTS.

##### (1) *The Daily Excretion of Ascorbic Acid.*

In the first place, it was decided to estimate the daily output of ascorbic acid in a series of patients immediately after admission. A twenty-four-hour specimen of urine is required, but unfortunately many cases of acute mental disorder are either incontinent or else unwilling to co-operate. It was not

considered advisable to catheterize resistive patients repeatedly, so that the ultimate selection of cases was determined not so much by their state of nutrition as by the amount of co-operation obtained. In the majority, however, we were able to estimate the excretion over a period of forty-eight hours.

The whole twenty-four-hour specimen was collected before testing, and it was found that no appreciable loss of vitamin occurred when concentrated sulphuric acid was added to the urine in the proportion of 2% by volume. Without this the ascorbic acid is rapidly oxidized on standing. The urine, when voided, was immediately measured, sulphuric acid was added, and the specimen placed in a stone jar. At the end of twenty-four hours the ascorbic acid was estimated by titration with indophenol, according to the method of Harris.

Harris and his colleagues used 5% glacial acetic acid for the preservation of the vitamin, although this gives rise to a loss of 20 to 30% in twelve to fifteen hours. They state, however, that this loss is of little practical importance.

There has been much discussion on the best means of preserving the vitamin, and it has been claimed by Johnson and Zilva (7), and Youmans *et al.* (8), that the least loss occurs when the urine is acidified with sulphuric acid to pH<sub>3</sub> and is kept in the dark at ice-box temperature.

The efficiency of sulphuric acid for this purpose was verified by a series of tests which we carried out at the beginning of the present investigation.

In Table I it will be seen that in six experiments with sulphuric acid the amount of titrable substance remained fairly constant over a period of twenty-four hours, whereas there was a marked decrease of this substance when 5% acetic acid was used. Each specimen of urine, immediately after passing, was divided into two parts; 2% sulphuric acid was added to one part and 5% acetic acid to the other.

There is, in fact, a tendency for a slight increase of titrable substance to occur when sulphuric acid is used, due, according to Scarborough and Stewart (9), to the production of extra ascorbic acid by acid-hydrolysis of certain derivatives of ascorbic acid present in the urine.

Harris and Ray state that in normal adult subjects of about 10 st. body-weight, receiving small amounts of fruit, the daily excretion of ascorbic acid is about 20 mgrm. The excretion of 10 to 15 mgrm. suggests a low vitamin diet. Youmans *et al.*, using sulphuric acid as a preservative, also give 20 mgrm. as the lower limit of normal daily excretion.

In five normal individuals selected from the hospital staff we found that the daily excretion varied from 27 to 60 mgrm. (Table II). From these and other estimations we agree that 20 mgrm. per day can be regarded as the lower limit of normal, and in the present investigation we have fixed upon 15 mgrm. as the standard below which the diet is presumed to have definitely contained less than the reputed optimum of vitamin C (estimated by Harris at 25 mgrm.

TABLE I.—*Showing the Relative Efficiency of Acetic and Sulphuric Acids for the Preservation of the Ascorbic Acid Excreted in the Urine.*

Specimen of urine number.	Reducing substance in mgrm. %.			
	Acetic acid 5%.		Sulphuric acid 2%.	
	After 1 hour.	After 24 hours.	After 1 hour.	After 24 hours.
I	3·1	2·0	4·0	4·4
2	3·4	2·1	4·5	4·4
3	3·0	2·0	4·2	4·5
4	2·5	1·9	3·4	4·2
5	1·8	1·2	2·3	2·3
6	2·5	1·4	3·1	3·1

TABLE II.—*Showing the Daily Excretion of Ascorbic Acid in Five Members of the Hospital Staff.*

Initials.	Mgrm. of ascorbic acid excreted in 24 hours.	Previous diet in regard to vitamin C intake.
F. T. T—	27·5	Good.
M. B. B—	30	„
M. N. F—	37	„
M. N. T—	41	Excellent.
E. M. S—	60	Exceptional.

TABLE III.—*Summary of the Daily Excretion of Ascorbic Acid in Mental Patients on Admission.*

Number of cases tested.	Mgrm. of ascorbic acid excreted in 24 hours.			Average excretion.
	Below 15 mgrm.	Below 20 mgrm.	Above 20 mgrm.	
Males	2 (10%)	9 (45%)	11 (55%)	21·1
Females	20 (53%)	30 (79%)	8 (21%)	12·4
Total	22 (38%)	39 (67%)	19 (33%)	15·4

per day, which is equivalent to the greater part of the juice of a moderate-sized orange).

In Table III is summarized the results of our estimations of the daily excretion of ascorbic acid in 58 adult patients shortly after admission, and mainly during the months of late winter and early spring. In this table it will be seen that 53% of the females and 10% of the male patients were excreting less than 15 mgrm. per day, and might, therefore, be said to be in a state of latent or sub-scurvy. The higher percentage of females with low excretion-rates may to some extent be due to chance selection, and the larger

number of patients tested, but a more probable explanation is that malnutrition is, in general, more prevalent amongst the female admissions. A married woman who becomes mentally ill frequently has to fend for herself, and consequently neglects her diet.

Of the 20 females excreting less than 15 mgrm. daily, 10 were suffering from melancholia, 4 from acute confusion, 2 from senile dementia, and 1 each from mania, schizophrenia, epilepsy and dementia paralytica.

Many of these patients exhibited clinical evidences of a scorbutic condition, such as spongy hæmorrhagic gums, submucous hæmorrhages in the mouth, or bruising on the trunk and limbs. There were others who showed no such signs.

Harris, Abbasy and Yudkin in a survey of 55 patients at Addenbrooke's Hospital, Cambridge, found 75% excreting less than the minimum standard of 13 mgrm. of ascorbic acid per day, and apparently none of these showed signs of scurvy. The authors conclude that although so many individuals in certain sections of the population are found to be below the reputed optimum standard in their vitamin C intake, and yet may superficially seem little the worse for it, when extra vitamin is provided their general health and fitness improve.

The consumption of one orange a day is more than adequate to bring the intake of vitamin C up to the level of the reputed optimum, and should, therefore, be included as a routine in all hospital diets. When this is carried out the urinary excretion rapidly approaches a normal level.

In two of our female patients the daily excretion on admission was 9 mgrm. and 11 mgrm., but after two weeks on the ordinary hospital diet their excretion level had risen to 16 mgrm. and 17 mgrm. respectively.

#### (2) *Response to an Intravenous Test Dose.*

The daily excretion of ascorbic acid in the urine is dependent upon the past intake of the vitamin, and this resting level becomes constant when a regular amount of the vitamin has been taken for some time past. It has been shown by Harris and his colleagues that further information regarding the state of vitamin C nutrition can be obtained by the oral administration of test doses of ascorbic acid, followed by an estimation of the rise in the amount excreted in the urine the subsequent twenty-four hours. The degree of response to such a dose indicates the degree of saturation of the subjects.

Archer and Graham (10), on the other hand, prefer to estimate the amount of ascorbic acid which must be given by mouth before the percentage output rises above 75% of the intake, and in a case of scurvy it was found that only 55% was excreted after the administration of 4,950 mgrm. of ascorbic acid in divided doses.

Of the vitamin C taken by the mouth, however, a considerable proportion

is lost in the stool, some is destroyed, and pathological changes in the alimentary tract may seriously affect its absorption. These objections have been overcome by the intravenous method of administering the ascorbic acid.

Ippen (11) described a method in which he gave 100 to 200 mgrm. of ascorbic acid intravenously, and then estimated the concentration of this substance in the urine at hourly intervals for three to four hours. The result was a uniform and characteristic curve rising from the normal 1 to 3 mgrm. % to a maximum after one hour of 5 to 10 mgrm. %. The excretion curve was called positive if rising above 4 mgrm. % and negative if below. It was concluded that a flat curve indicated a deficiency of vitamin C in the organism corresponding to the large field of hypovitaminosis lying between health and avitaminosis.

Portnoy and Wilkinson (12) and Wright *et al.* (13) advocate the administration of 1,000 mgrm. of ascorbic acid intravenously, followed by an estimation of the quantity excreted in the urine during the next six hours. Values below 400 mgrm. are regarded as subnormal.

In the present investigation on mental patients Ippen's method has been followed, since it was felt that a simple clinical test was all that could be conveniently attempted on agitated and perhaps resistive patients. The tests were carried out in the morning, three to four hours after a light breakfast and restricted fluids. The urine was voided at 11 a.m., and 200 mgrm. of ascorbic acid injected intravenously. Hourly specimens of urine were then collected, diluted with 5% glacial acetic acid and sent to the laboratory for immediate titration. Fig. 1 illustrates a typical positive curve obtained in a patient whose previous diet had included orange-juice daily.

Ippen also found that a flat or negative curve could, in certain cases, be made to show a peak after the administration of synthetic vitamin C (e.g., redoxon 100 mgrm. or two tablets daily) for a period of ten days. In the following case of sub-scurvy extra vitamin was added to the diet, but it was six weeks before the curve became positive.

CASE I.—J. M—, a female, aged 78, suffering from paraphrenia with delusions of persecution. On admission she was edentulous, anæmic, poorly nourished, and had extensive bruising on the limbs. Her blood-count showed erythrocytes 2,700,000, hæmoglobin 65%, colour-index 0.9. The leucocyte count was 3,500 per c.mm. A test-meal showed normal gastric acidity.

Urinary ascorbic acid averaged 8 mgrm. daily for a period of three days. She was then given the juice of two oranges daily. One month later her blood-count had improved to erythrocytes 4,000,000 and hæmoglobin 74% without the administration of iron. The urinary concentration curve after 200 mgrm. ascorbic acid intravenously was negative.

She was then given in addition to the orange-juice two redoxon tablets daily (100 mgrm.). After 3,000 mgrm. the urinary concentration curve was just positive at 4 mgrm. %, and after a further 1,000 mgrm. the concentration reached 8 mgrm. %.

The amount of ascorbic acid required to be given in order to change a negative into a positive curve thus provides an index of the degree of hypovitaminosis.

After several experiments with Ippen's concentration test we found that more information could be obtained from a single test if the dose of ascorbic acid was increased to 500 mgrm. intravenously. By this means a greater range of responses could be obtained, which appeared to indicate approximately the degree of saturation of the subject. Wright *et al.* also point out that a

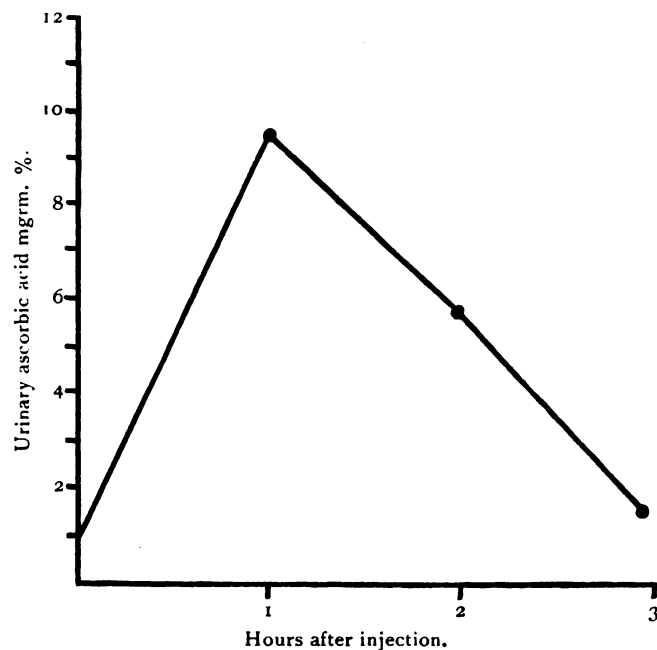


FIG. 1.—Showing the hourly concentration of ascorbic acid in the urine following an intravenous injection of 200 mgrm. Patient, L. G. H—, a female, aged 40, on orange-juice daily.

large test dose has an additional advantage in that it reduces the effects of slight variations in the dietary intake immediately preceding or during the test. The patient may even continue his normal diet without producing important changes in the result.

We found that even with a test dose of 500 mgrm. intravenously the maximum concentration in the urine occurred after one hour. This varied from 1 to 560 mgrm. %, and is the only estimation required. A typical curve is seen in Fig. 2.

The test was therefore reduced to the following simple procedure: At 11 a.m. the bladder is emptied, and 500 mgrm. of ascorbic acid in 10 c.c. of triple distilled water is slowly injected into a vein. Exactly one hour later

the bladder is emptied, the urine measured and 5% glacial acetic acid added. Titration is carried out as soon as possible and the concentration of ascorbic acid per 100 c.c. determined.

Unfortunately the injection sometimes produces a diuresis, and if the quantity of urine passed during the first hour exceeds 100 c.c. the result will be an unduly low concentration of ascorbic acid. It is important, therefore, that fluids should not be given for several hours before the test. In one case, for example, with a daily excretion of 24 mgrm., an injection of 500 mgrm. ascorbic acid produced 800 c.c. of urine in one hour, and the concentration was only 18 mgrm. %. A few days later the test was repeated after a restricted fluid intake, when the result was 100 c.c. of urine at 200 mgrm. %.

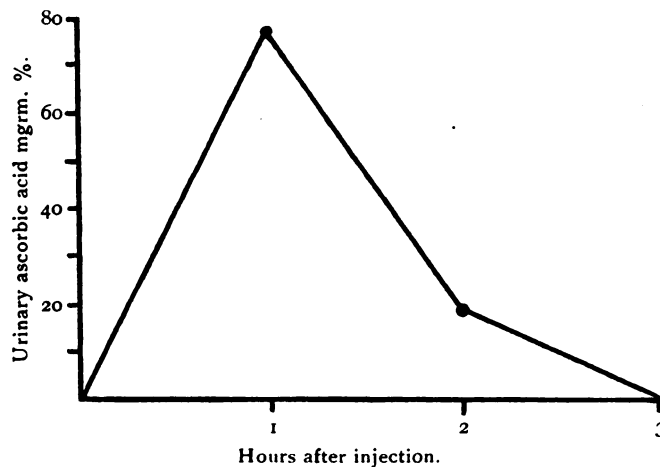


FIG. 2.—Showing the hourly concentration of ascorbic acid in the urine following an intravenous injection of 500 mgrm. Subject F. T. T—, on moderate vitamin C intake.

After carrying out a large number of concentration tests on various patients and comparing the results with the daily excretion level, the conclusion was reached that a concentration of 50 mgrm. % after a test dose of 500 mgrm. represented the minimum normal comparable with Ippen's 4 mgrm. % after a dose of 100 to 200 mgrm. A concentration of between 25 mgrm. and 50 mgrm. appeared to correspond to the lesser degrees of hypovitaminosis C, and below 25 mgrm. % to severe hypovitaminosis or avitaminosis. Table IV shows the results of concentration tests in three healthy adults.

As a contrast we were fortunate in having the opportunity of carrying out tests on the following case of scurvy in which the concentration rose from 10–7 mgrm. % at the onset to 41 mgrm. % when the condition had been cured.

CASE 2.—B. C. D—, a male, aged 47, was found with a petechial rash on arms and legs and painful swellings of the joints of the right ankle and hand. His gums were red, swollen and hæmorrhagic.



TABLE IV.—*Showing the Concentration of Ascorbic Acid in the Urine one Hour after the Injection of 500 mgrm. Intravenously in Three Healthy Subjects.*

Initials.	Daily excretion.	Concentration 1 hour after 500 mgrm. intravenously.	Quantity of urine first hour.	Previous diet.
F. T. T—	. 18.4	. 71 mgrm. %	. 100 c.c.	Moderate fruit.
M. B. B—	. 30	. 120 „	. 40 „	„ „
E. M. S—	. 60	. 660 „	. 40 „	Excessive „

He had been admitted twelve months previously with delusions of persecution and auditory hallucinations. Latterly he had been very difficult with his food and refused to eat vegetables or fruit.

His blood-count gave the following results: red cells 3,500,000 per c.mm., hæmoglobin 75%, colour index 1.0, leucocytes 5,000 per c.mm., platelets 200,000 per c.mm. Urine: trace of albumin and a few erythrocytes.

The daily excretion of ascorbic acid was found to be only 10 mgrm., and the urinary concentration one hour after 500 mgrm. intravenously was estimated at 10.7 mgrm. %.

He was placed upon a high vitamin diet, containing orange-juice and three redoxon tablets daily. Three weeks later his general condition was much improved, his gums were almost normal and the rash was rapidly disappearing. The urinary concentration test had increased to 21 mgrm. %.

After a further month of treatment the rash had completely disappeared, but there remained some slight pain and swelling of the right wrist. The urinary concentration test now gave 41 mgrm. %.

The ascorbic acid concentration test was then carried out on a series of 38 mental patients shortly after their admission to the hospital. In 8 cases the results were in the hypovitaminosis zone between 25 mgrm. and 50 mgrm. %, and in 6 cases the concentration was below 25 mgrm. %.

In many of these patients a preliminary estimation of the daily excretion level was carried out, and it was found that cases excreting above 20 mgrm. per day invariably gave a concentration of above 50 mgrm. %, whereas in those under 15 mgrm. per day the concentration test was below 25 mgrm. %. The following is a summary of the six patients with latent scurvy in which the ascorbic acid concentration test was below 25 mgrm. %.

CASE 3.—E. W—, a female voluntary patient, aged 55. A chronic alcoholic with recurrent melancholia. Said to eat little when "on the drink", and had been drinking heavily previous to admission. Physical condition fair; no clinical evidences of scurvy. The ascorbic acid concentration test resulted in 24 mgrm. %. On the hospital diet and extra orange-juice she quickly recovered and was discharged one month after admission.

CASE 4.—B. W—, a female voluntary patient, aged 54, suffering from diabetes, heart failure and melancholia. Ascorbic acid concentration test yielded 19 mgrm. %. She died two months after admission.

CASE 5.—M. C—, a female, aged 72, confused, resistive and difficult to feed. Extensive bruising on limbs, red gums and injected tonsils. The

ascorbic acid concentration test resulted in only 10 mgrm. %. She was discharged improved two months after admission.

CASE 6.—G. H—, a female temporary patient, aged 25. A case of puerperal mania. On physical examination she exhibited a dry skin, scattered bruises on trunk and limbs, spongy and hæmorrhagic gums. The tongue was dry and furred, the pulse rapid, but the temperature normal. A blood-count showed erythrocytes 2,450,000, hæmoglobin 65%, colour index 1.3, leucocytes 8,500 with 83% polymorphs. The non-protein nitrogen was 32 mgrm.%. The urine contained a trace of albumin and the deposit showed a few erythrocytes. There was no evidence of uterine sepsis.

The ascorbic acid concentration test resulted in 17 mgrm. %. She eventually died from exhaustion and heart failure.

CASE 7.—E. M. O—, a female temporary patient, aged 44, admitted with melancholia and confusion. She had the idea that her food had been poisoned. Physically she was thin and under-nourished, had a dry skin and sordes on lips. The gums were red, and the tonsils and palate injected. She was edentulous.

The ascorbic acid concentration test produced 20 mgrm. %. She was discharged, recovered, three months after admission.

CASE 8.—L. A. F—, a female temporary patient, aged 22. She was seven months pregnant and in a state of acute mania, with confusion. Her conversation was more or less incoherent. Physically she was thin and poorly nourished, there were sordes on the lips, a dry furred tongue and constipation. The gums were red and swollen; palate injected. A blood-count showed: erythrocytes 3,560,000, hæmoglobin 80%, colour index 1.1, leucocytes 9,000 with 78% polymorphs. The non-protein nitrogen was 37.5 mgrm. %. The urine showed a trace of albumin and a few granular tube-casts.

The ascorbic acid concentration test two days after admission was completely negative, and showed less than 1 mgrm. % one hour after the intravenous injection of 500 mgrm. Four days later it was 25 mgrm. %. After one month on a liberal diet with added orange-juice, the concentration test had risen to 93 mgrm. %.

The patient improved physically, but mentally she gradually drifted into a state of schizophrenia.

#### DISCUSSION.

It must be remembered that in a given subject the level of vitamin C excretion in the urine depends upon many factors apart from the intake and degree of saturation of the tissues. An intake which is sufficient for a normal person may prove insufficient because of abnormal conditions in the body. This may give rise according to Engelkes (14) to so-called conditioned scurvy.

Defective absorption of the vitamin may occur as a result of intestinal disorders, or it may be destroyed by intestinal bacteria. Increased consumption of the vitamin occurs in infections, hyperthyroidism and pregnancy, where there is increased metabolism and an excess of katabolic processes.

Renal scurvy results when a low renal threshold for ascorbic acid leads to a too rapid excretion by the kidneys (Mawson (15)). Pinotti (16) has shown that in experimental nephritis there is a rise in the concentration of urinary ascorbic acid.

Dietetic scurvy has been studied by several investigators, who have shown that the prescribed diets for gastric ulcer, colitis and nephritis, etc., sometimes lead to vitamin C subnutrition and even frank scurvy (Platt (17)).

There is also a tendency for the vitamin C content of the tissues to fall with increasing age, owing possibly to the increased pH of the tissues. Ascorbic acid has been shown to be diminished in an alkaline urine. Decomposition occurs if many organisms are present in the urine.

The symptoms of frank scurvy are well known, and the time required for the development of this condition in an adult on a vitamin-free diet is four to eight weeks. One of the earliest signs is the appearance of a hæmorrhagic gingivitis, which, in an experimental subject (O'Hara *et al.* (18)), developed during the fourth week of a low vitamin C diet.

Other clinical signs suggesting vitamin C subnutrition are submucous hæmorrhages in the roof of the mouth, hæmorrhages in the skin and conjunctiva, anæmia and the presence of erythrocytes in the urine. Unfortunately the typical lesions of the gums do not develop when the teeth are absent, and in other cases it may be obscured by the presence of pyorrhœa alveolaris. Some authors believe that increased capillary fragility, although not pathognomonic, is the earliest definite evidence of scurvy (Góthlin (19)).

The lesser degrees of hypovitaminosis C are often symptomless, but it is this group which is at present the subject of much controversy. Zilva (20) has stated that there is no clinical or laboratory evidence that unsaturated persons are in a worse state of health than saturated ones, and that to apply to this zone of unsaturation such an expressions as "hypovitaminosis C", latent or potential scurvy, etc., is not justified in the present state of our knowledge. On the other hand, Parsons and others consider that these states are important. It is evident that much research is still required on this subject.

With regard to the present investigation we are convinced that vitamin C deficiency is of common occurrence amongst mental hospital admissions, and the addition of extra vitamin to their diet constitutes a rational and important part of the treatment.

For the purpose of description the cases of vitamin C deficiency studied may be divided into three groups.

In the first group may be placed the toxic confusional cases in which there is usually an extreme degree of hypovitaminosis, and symptoms of sub-scurvy, such as hæmorrhagic gingivitis, are frequently found. They are usually physically ill and have gastric-intestinal disturbances which favour the development of conditioned scurvy.

The second group is the largest and includes a high percentage of admissions, in which the ascorbic acid excretion tests reveal a mild degree of hypovitaminosis. They are mostly melancholics in whom there has been little desire to eat. They usually show no symptoms of scurvy, but appear to benefit from a high vitamin diet.

In the third group we have a small number of patients who have rigidly excluded fruit and vegetables from their diet, as a result of some food-fad or delusion. They are examples of self-induced dietetic scurvy in which symptoms develop rapidly. Case 2 is an example of this group.

In the majority of the cases investigated the low ascorbic acid excretion was merely symptomatic of a general nutritional deficiency. Because a diseased person shows vitamin deficiency, it does not follow that the disease is the result of the deficiency, and there is no definite evidence that a causative relationship exists between vitamin C deficiency and mental disorder.

There is no doubt, however, that there are a large number of cases in which general malnutrition constitutes an important secondary ætiological factor. Psychological symptoms, such as anxiety and fear, frequently give rise to loss of appetite and anorexia. Impaired nutrition then leads to gastro-intestinal disturbances and a vicious circle is formed. These cases improve mentally when the vicious circle is broken, and it is probable that the administration of vitamin C plays an important part in the process.

#### SUMMARY.

An investigation has been made to determine the incidence of vitamin C deficiency in mental hospital admissions, utilizing as an indication of this condition the estimation of the daily excretion of ascorbic acid in the urine, and the urinary response one hour after an intravenous test dose of 500 mgrm. of ascorbic acid.

Of 58 patients examined, 39 (67%) were found to be below the minimum normal standard of 20 mgrm. per day. In 22 cases the daily excretion was below 15 mgrm. Deficiencies were found to be more prevalent amongst the female admissions.

In response to the test dose of ascorbic acid, 14 out of 38 patients gave results indicating varying degrees of vitamin C deficiency. It is suggested that this simple test is a reliable indication of the state of vitamin C nutrition, which can readily be carried out, even in the absence of co-operation by the patient.

Vitamin C deficiency can usually be demonstrated in the toxic confusional psychoses, particularly in puerperal cases. Lesser degrees of deficiency are found mainly in melancholic and senile states. A case of frank scurvy is described.

In the present state of our knowledge there is no evidence of any direct causal relationship between vitamin C deficiency and mental disorder, and when a deficiency is found it is usually part of the general malnutrition. In these cases the administration of the vitamin frequently plays an important part in bringing about the mental as well as the physical recovery of the patient.

The subject of hypovitaminosis C is beset with many problems, which can only be elucidated by accurate and patient research.

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## REFERENCES.

- (1) SVIRBELY, J. L., and SZENT-GYORGYI, A.—*Biochem. Journ.*, 1932, xxvi, p. 865.
- (2) HESS, A. F.—*Journ. Amer. Med. Assoc.*, 1917, xlviii, p. 235.
- (3) PARSONS, L. G.—*Lancet*, 1938, i, p. 123.
- (4) UNGLEY, C. C.—*Ibid.*, 1938, i, p. 875.
- (5) BERSOT, H.—*Ann. Méd.-psychol.* (pt. 1), 1936, xciv, p. 187.
- (6) HARRIS, L. J., and RAY, S. N.—*Lancet*, 1935, i, p. 71.
- (6a) HARRIS, L. J., ABBASY, M. A., and YUDKIN, J.—*Ibid.*, 1936, i, p. 1488.
- (7) JOHNSON, S. W., and ZILVA, S. S.—*Biochem. Journ.*, 1934, xxviii, p. 1393.
- (8) YOUMANS, J. B., CORLETTE, M. B., AKEROYD, J. H., and FRANK, H.—*Amer. Journ. Med. Sci.*, 1936, cxc, p. 319.
- (9) SCARBOROUGH, H., and STEWART, C. P.—*Biochem. Journ.*, 1937, xxxi, p. 2232.
- (10) ARCHER, H. E., and GRAHAM, G.—*Lancet*, 1936, i, p. 710.
- (11) IPPEN, F.—*Schweiz. Med. Wochenschr.*, 1935, xix, p. 431.
- (12) PORTNOY, B., and WILKINSON, J. F.—*Lancet*, 1938, i, p. 554.
- (13) WRIGHT, I. S., LILIENTHAL, A., and MCLLENATHAN, E.—*Arch. Inter. Med.*, 1937, lx, p. 264.
- (14) ENGELKES, H.—*Lancet*, 1935, ii, p. 1285.
- (15) MAWSON, C. A.—*Ibid.*, 1938, i, p. 890.
- (16) PINOTTI, F.—*Klin. Wochenschr.*, 1935, xiv, p. 1289.
- (17) PLATT, R.—*Lancet*, 1936, ii, p. 366.
- (18) O'HARA, P. H., and HAUCK, H. M.—*Journ. Nutrition*, 1936, xii, p. 413.
- (19) GÖTHLIN, G. F.—*Skand. Arch. Physiol.*, 1931, lxi, p. 225.
- (20) ZILVA, S. S.—*Lancet*, 1937, ii, p. 1509.