VITAMIN C IN SENILE PSYCHOSES. (A PRELIMINARY REPORT.)*

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THE senile psychoses are in regard to their origin an unsolved problem. Much valid work has been done in the field of anatomy and histology in approaching this problem, but as the mental diseases of old age cannot be separated from the growing old of body and mind generally, this problem is more or less a biological one. The borderline between old age and senile dementia is not a sharp one. In brains of old people without clinical symptoms of dementia there have been found histological changes, such as are usually found in cases of senile dementia. This makes it probable that the extent of degeneration of brain cells alone is not decisive for the appearance of senile psychoses. The finding of the characteristic plaques in the brain of senile psychoses may give evidence of the extent of the process and the severity of clinical symptoms, but it does not tell us anything about their nature and origin. Whether a constitutional factor is decisive or whether the histological changes are a reaction to an unknown noxa is undecided. Heredity may have its share too.

Two considerations aroused our special interest in the problem of origin of senile psychoses. Some authors have discovered the plaques which are always found in senile psychoses in brains of persons who had suffered from alcoholism. That gave us the idea that some toxic factors or disturbances in general metabolism might have their share in the origin of the pathological changes in brains of old people. A further consideration was the fact that in one case of senile dementia it seemed probable from the past history that a sudden incident had precipitated the syndrome of a senile psychosis, or at least had led to a great deterioration. When inspecting the literature we found a series of cases which supported this assumption. We bore in mind that humoral factors might have played their part in the production of senile changes in the brain.

The investigations of biochemists into the nature of the vitamins, especially of the B complex and vitamin C, have taught us that they are important for the maintenance of a regulated and ordered change of energies and metabolism. Their close connections with hormones, especially of the suprarenal gland, is well known. The suprarenal gland contains more vitamin C than

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any other organ of the body. This suggests biological relationship between these two substances. Ascorbic acid with its reducing quality probably protects the cortical hormone from oxidative disintegration. Furthermore the suprarenal cortex is an important factor for the maintenance and increase of the resistance of the body against infections. Especially in acute infections there is a lack of vitamin C, and this has been proved in our own experience. In this connection it may be mentioned that the intracerebral injection of the virus of poliomyelitis in the monkey is stated to be non-infectious when small quantities of vitamin C have been added. The task of the vitamins as catalysts is to prevent the appearance of toxic intermediate products. The removal of creatinuria by vitamin C in progressive muscular dystrophy has been followed by considerations, which lead into the field of psychiatry. According to Jahn the occurrence of creatinuria is characteristic of the metabolism of asthenics. The same author has found creatinuria in schizophrenias of the asthenic type. On the other hand, a low content of vitamin C in the spinal fluid of schizophrenias with catatonic and depressive features has been said to be typical.

Plaut and Bülow have examined the content of vitamin C in different parts of the human brain and at different ages. Normally the brain has a high content of vitamin C. The cortex of old people has only 12% of the content of the cortex of the foetus, whereas the diminution of the content of the cerebellum and the brain-stem is much less in old age. A comparison of different parts of the brain in adults shows a higher content of vitamin C in the cerebellum than in the cerebrum, in the grey matter more than in the white substance. According to Plaut and Bülow the degree of saturation of vitamin C in the body is reflected in the spinal fluid. According to Monauni the vitamin C content of the spinal fluid is dependent on age, the vitamin C content of food and physical diseases. Melka and Klimo have found that the average amount of vitamin C in the spinal fluid depends, too, on the season; the minimum was found in April and May, the maximum in autumn. This fluctuation may be connected with the content of vitamin C in food. Simons has found low values in the spinal fluid of schizophrenias and patients suffering from general paralysis, especially in progressive cases. He considers the reason to be insufficient nutrition or increased consumption.

This paper, being a preliminary communication, contains a full report of our results as to the content of vitamin C in the urine of senile psychoses. Our investigations of vitamin C in the blood and spinal fluid and its relations to metabolism are still in the beginning.

The conditions for estimation of the content of vitamin C in blood are much more complicated than those in the spinal fluid and urine. Zilva and Kellie have found that there exists a competition for the ascorbic acid of the blood between the absorptive tendency of the tissues, which varies with the degree of saturation and the excretory function of the kidneys. In this respect there

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are important individual differences, and as far as it concerns our own investigations in senile psychoses no definite relations between blood and urine content of vitamin C have so far been found.

As a valid and reliable procedure the saturation test of the urine, which has been introduced by Harris, Roy and Ward, has proved useful and sufficient for clinical purposes. Though the method is not exact enough for the estimation of the daily need of vitamin C, it is sufficient and reliable for the calculation of the degree of saturation. For this purpose 300 mgm. of ascorbic acid are given daily by mouth until bodily saturation is reached, that is to say, until a distinct increase of the excretion follows. The number of the days is counted until about 50% of this quantity is recovered in a 24 hours' specimen of urine. We titrated with dichlorphenolindophenol as suggested by Tillmans. The objection which has been made to this test that it is not specific enough can be broadly met by observing rules considering the chemical characteristics of the ascorbic acid. This is the more important as critical reviews of biochemists consider the results obtained as being for the most part faulty, the protection from oxidation having not been sufficient.

Before describing our procedure, the cases which had to undergo the test may now be shortly described. Among the seven patients, aged from 72 to 82, were six women and one man. They displayed more or less deterioration of the mind and had no obvious physical diseases. For a control we took one epileptic and two normal persons.

From each patient the 24 hours' urine was collected. Bedridden patients were given the bed-pan every two hours. To each specimen $\frac{1}{10}$ of the volume glacial acetic acid was immediately added. The next day the same procedure was carried out, but instead of glacial-acetic-acid 22% sulphosalicylic acid plus glutathione were added. The latter is an albuminous by-product, and also has a protective function in the body, as it inhibits to a certain extent the efficiency of ferments which cause oxidation of ascorbic acid. When added to the urine, glutathione forms a relatively stable compound with heavy metals, nearly always found in traces in the urine, and which otherwise would oxidize ascorbic acid. At a pH of 2–3, the speed of oxidation of other reducing substances slows down and estimation of ascorbic acid can be carried out without interference, if titration ensues within 2–3 minutes. The result was several times a relevant loss of vitamin C in those cases where acid alone had been added as protection from oxidation. This fact caused us to divide the freshly passed specimens of the patients and control persons into four parts. The first portion was examined immediately, the second without any protection several hours later, and the third and fourth with the reagents just mentioned also after several hours. We got nearly identical results from the examination of freshly passed and immediately examined urines and those portions containing acid plus glutathione. The patients were all on normal diet. From the third day onwards the patients and control persons got each

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day 300 mgm. ascorbic acid, until saturation was reached. Every case of senile psychosis showed a significant delay until the required excretion of about half the intake had been obtained. Of the controls, two of them on the same diet as the patients showed a saturation after two to five days, whereas in senile psychoses saturation was reached only after eight to eleven days. Thus we got a deficit of about 2,400 to 3,300 mgm. of vitamin C. A deficit of 1,000 mgm., or at the most 1,500 mgm., may be regarded as pathological. In one case there was a sudden drop of vitamin C content after a completed saturation, although the daily intake of 300 mgm. of ascorbic acid had been continued. First we had no explanation for it, and investigation showed that a failure in the method could be excluded. Next day there was a rise of temperature, and a fortnight later the patient died from pneumonia. The increased consumption of vitamin C had been doubtlessly caused by the infection. In another case we gave cortin plus 300 mgm. ascorbic acid at the same time in order to see whether a shortening of time until saturation occurred. No such result followed.

As we had to counter the question whether there was a delayed resorption in aged people we gave in two cases 200 mgm. vitamin C by injection, when saturation had not been reached after five days. In both cases no increase of excretion resulted. The other question whether there is an increased need of vitamin C in aged people has to be left open. An increased need would be in contradiction to rules in general metabolism of ageing cells.

As to our investigations of spinal fluids we have no definite results yet; the number of cases in which lumbar punctures could be made is still too small. A high content of vitamin C was present in the spinal fluid in two cases—one aged person and one control—after saturation in the urine had been reached. The quantity was greater than that which is usually found in the spinal fluid of non-saturated persons. Immediate titration of the spinal fluid is essential.

The delay of saturation in aged people shows the existence of a hypovitaminosis. We do not venture to state whether the tendency to infections, the delayed healing of fractures in old age, belonging as well to the picture of a hypovitaminosis, are due to the deficiencies of vitamin C in old age, and we certainly cannot assume at this stage that the vitamin C deficiency is important for the aetiology of the senile psychoses. But I think further investigations along these lines are worth while, especially if we consider the manifold relationships of vitamin C to vital functions. It may yet be that tracing of normal and pathological activity of vitamins and hormones may be of value in psychiatry.

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