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Vitamin C Content of Human Non-Scorbutic Cerebrospinal Fluids.

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Much data have been accumulated regarding the ascorbic acid content in various body fluids and tissues. Little information is to be found concerning the occurrence of vitamin C in the cerebrospinal fluid, and none in the English or American literature. Kasahara and his coworkers[1, 2] and Plaut and Bulow[3, 4] have shown that vitamin C is present in the cerebrospinal fluid of experimental animals. The latter[5] and Monauni[6] have determined the ascorbic acid content of the cerebrospinal fluid of psychiatric patients. Monauni observed seasonal variations and considered 0.5 to 0.8 mg. % as normal for winter and summer months respectively. In an effort to obtain further data, the authors have determined the vitamin C reducing power of the cerebrospinal fluid in 50 ambulatory patients who gave no clinical evidence of avitaminosis C.

The chemical procedure used was the dichlorophenol indophenol method, the technique being a modification of that used by the authors for work with urine.[7, 8] Because of the low protein content of the cerebrospinal fluid, direct titration is possible without preliminary removal of the protein. Two cc. of the fluid are brought to a total volume of 5 cc. with water and adjusted to an approximate pH of 4.7 with 5% acetic acid. If smaller quantities of the fluid are used, the final volume is reduced proportionately. The solution is then titrated with 2:6 dichlorophenolindophenol (2 mg. in 50 cc. of water, one cc. of which is equivalent to 0.02 mg. of ascorbic acid) to a faint bluish red endpoint. 92-100% of ascorbic acid when added in quantities equal to its usual concentration in cerebrospinal fluid was recovered from the fluid by this method.

1 Kasahara, M., and Gammo, H., *Z. f. d. ges. Neurol. u. Psychiat.*, 1937, **157**, 147.

2 Kasahara, M., Tatsumi, M., and Gammo, H., *Ibid.*, 1937, **157**, 149.

3 Plaut, F., and Bulow, M., *Klin. Wchnschr.*, 1935, **14**, 1716.

4 Plaut, F., and Bulow, M., *Ibid.*, 1935, **14**, 1318.

5 Plaut, F., and Bulow, M., *Z. f. d. ges. Neurol. u. Psychiat.*, 1936, **154**, 481.

6 Monauni, J., *Ibid.*, 1937, **157**, 636.

7 Jetter, W. W., and Bumbalo, T. S., *Am. J. Med. Sc.*, in press.

8 Bumbalo, T. S., *Am. J. Dis. Child.*, in press.

TABLE I.
Ascorbic Acid Content of Cerebrospinal Fluid in 50 Cases Showing No Avitaminosis C.

Range $\frac{\text{mg.}}{\text{100 cc.}}$	0.7-1.0	1.1-1.3	1.4-1.6	1.9	2.1
No. of observations	12	20	14	3	1

Thirty-three of the 50 cases were syphilitics. All were under active treatment in the outpatient department and were admitted for routine spinal examination. Involvement of the central nervous system, when present, was asymptomatic. The remaining 17 cases exhibited various types of pathology but all were ambulatory. In these cases, examination of the cerebrospinal fluid was not indicated, the procedure being performed solely for the determination of the ascorbic acid content. As far as could be ascertained, the diets of the patients were adequate in vitamin C. In all of the cases, samples of the cerebrospinal fluid were obtained not later than 3 days after entry to the hospital. The hospital diet contained an adequate ration of vitamin C. The diet before hospitalization was representative of that usually followed by individuals of the class attending the outpatient department of a large city hospital.

Clinical examination revealed no evidence of acute infection in any member of the group. Also, no clinical manifestations of avitaminosis C could be detected. In view of the minimal pathology in all cases, the absence of acute infection and any clinical manifestation of avitaminosis C, we believe that the group may be considered as representative of normal for the purpose of this paper.

The state of nutrition was determined by the clinical condition of the patient and was classified as good, fair or poor. No cases showing definite malnutrition were included in the series. The nutrition was considered good in 26 cases; fair in 18, and poor in 6. No definite correlation between the state of nutrition and the ascorbic acid content of the cerebrospinal fluid could be detected. The majority of cases fell in an age group from 25-65 years. No correlation between age and vitamin C was found.

The ascorbic acid content of the cerebrospinal varied in this series from 0.7 to 2.1 mg. %. Thirty-one fell in the group between 0.9 and 1.4 mg. %. The median of the entire series was 1.2 mg. %. This level of cerebrospinal ascorbic acid of so-called normal individuals is somewhat higher than that reported by Monauni.[6] As yet we have no data establishing a definite level below which symptoms of avitaminosis C will occur. Further work in conjunction with studies of the urinary excretion is indicated. The determination of the

vitamin C content of the cerebrospinal fluid may become an aid in the diagnosis of avitaminotic states.

Conclusion. The ascorbic acid content of the cerebrospinal fluid in a series of 50 ambulatory patients has been determined. All individuals were on a diet adequate in vitamin C and showed no clinical evidence of avitaminosis C or of acute infection. The ascorbic acid content varied from 0.7 to 2.1 mg. % with a median of 1.2 mg. %.

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A New Goiter-Producing Diet for the Rat.

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Diets which consistently produce goiter in rats have been limited to those composed of natural food materials. Modifications of the Steenbock rachitogenic diet have been used successfully by Levine, Remington and von Kolnitz,[1] Thompson,[2] and others. Hellwig[3] has used a diet of 50% rolled oats and 50% corn meal boiled in distilled water. Other diets, composed mostly of the cereal grains or their milling products, have been used with little success.

Attempts to produce goiter in rats with the above diets or modifications of them resulted in failure. It was found that rats of the same colony and under the same environmental conditions that resulted in failure with other diets, readily developed goiter when fed the following diet: soy bean flour (unprocessed) 75.0 parts, dried yeast 3.0 parts, butter fat 5.0 parts, sodium chloride 1.0 part, calcium carbonate 0.5 part, sucrose 15.5 parts, and viosterol 15 drops per kilo of food.

Rats weighing 50-70 gm. were used in the study. More than 150 were fed the diet over a period of 2 years. Enlarged glands were obtained consistently. After 4 weeks on the diet, the glands of many animals were enlarged to 5 times normal size but there were wide individual variations. The weight of the gland in relation to body weight after 8 weeks was rarely greater than the largest glands of the younger group, but the individual variation was much less. The

1 Levine, Harold, Remington, R. E., and von Kolnitz, Harry, *J. Nutrition*, 1933, **6**, 325.

2 Thompson, Juanita, *J. Nutrition*, 1932, **5**, 359.

3 Hellwig, C. A., *Endocrinol.*, 1934, **18**, 197.