

### Dehydroascorbic Acid Level in Blood of Patients Suffering from Various Infectious Diseases. (21659)

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The relation of ascorbic acid to diverse physiological conditions has been extensively studied in an attempt to find out the value of ascorbic acid in health and in disease, Banerjee(1), but insufficient reports have appeared on the role of dehydroascorbic acid in diseased conditions. Kellie and Zilva(2) noted that dehydroascorbic acid was not present in the blood under normal conditions. Plant and Bulow(3) and Fujita and Ebihara(4), on the other hand, noted that dehydroascorbic acid content of the blood was more than ascorbic acid. Bartolini(5) observed that the ratio of dehydroascorbic acid to ascorbic acid was lowest in normal human blood, but increased in some diseases. Banerjee *et al.*(6) reported the presence of dehydroascorbic acid in significant amount in tissues of scorbutic guinea pigs and absence of it in the tissues of a normal animal. Nyden(7) noted a significant reduction in the ascorbic acid contents of liver, spleen and adrenals in rats infected with *trypanosoma hippicum* and a marked rise in the ratio of dehydroascorbic acid to ascorbic acid in the plasma. Lund and Elmy(8) noted that the property of the intestine to reduce dehydroascorbic acid to ascorbic acid

was lost in intestinal diseases. Banerjee and Belavady (9) reported that dehydroascorbic acid content of the blood was raised and ascorbic acid content of the blood diminished significantly in patients suffering from typhoid fever. Dehydroascorbic acid was found to be toxic to rats by Patterson(10). It is a paradox that dehydroascorbic acid, which behaves essentially like ascorbic acid in giving protection from or curing scurvy (11, 12), should be toxic in high doses. It was, therefore, of interest to study the dehydroascorbic acid level in blood of patients with infectious diseases which might indicate abnormal conditions in the tissues. The present investigation, therefore, was undertaken to study the dehydroascorbic acid and ascorbic acid contents of blood of patients suffering and convalescing from meningococcal meningitis, acute lobar pneumonia, tetanus, typhoid fever and tubercular meningitis. These values were also estimated in the blood of healthy adults for comparison.

*Methods. Selection of cases.* 25 cases of meningococcal meningitis with purulent cerebrospinal fluid, 25 cases of tetanus with classical symptoms, 23 cases of typhoid fever with

positive blood culture, 22 cases of acute lobar pneumonia and 17 cases of tubercular meningitis with typical symptoms and characteristic cerebrospinal fluid were selected. Blood was withdrawn from these patients before institution of treatment and during convalescence.

Normal subjects selected for investigation were students of Nilratan Sircar Medical College, Calcutta belonging to the same economic and social status as the selected patients.

*Results. Estimation of dehydroascorbic acid and ascorbic acid in blood.* It has been observed that dehydroascorbic acid is very easily formed from oxidation of ascorbic acid present in the blood and other tissues. To guard against this possibility it is essential to deproteinize the blood as soon as it is withdrawn. 3 cc of freshly drawn oxalated blood were added drop by drop to 9 cc of distilled water in a 15 cc centrifuge tube, 3 cc of M-sulfosalicylic acid were added, the mixture was shaken thoroughly, centrifuged and the centrifugate was filtered through a piece of dry absorbent cotton. The filtrate was taken in a microburette and titrated quickly against a solution of 2:6-dichlorophenol-indophenol standardized according to the method of Menaker and Guerrant(13). Ascorbic acid content of blood was thus obtained. In an aliquot of the filtrate hydrogen sulfide gas was passed for 5 minutes to reduce dehydroascorbic acid to ascorbic acid, excess gas was removed by passing a current of nitrogen and the treated filtrate was taken in a microburette and was titrated quickly with the standardized dye. This titration gave the values for both ascorbic acid and dehydroascorbic acid. The difference between the 2 values gave the level of dehydroascorbic acid in the blood. The results are given in Table I.

*Discussion.* During the acute phase in all the diseases investigated, the dehydroascorbic acid level of the blood was considerably increased and the ascorbic acid content diminished. During convalescence dehydroascorbic acid content of the blood went down with a concomitant increase in the ascorbic acid content. These values, however, never reached the normal levels. The accumulation of dehydroascorbic acid in these diseases

TABLE I. Dehydroascorbic Acid and Ascorbic Acid Contents of Blood. (mg/100 cc of blood.)

Subjects	Dehydro-ascorbic acid	Ascorbic acid
Normal (28)	.06 ± .01*	.87 ± .02
Meningococcal meningitis		
Acute cases who did not survive (8)	.95 ± .06	.27 ± .03
Acute cases who survived (17)	.61 ± .04	.43 ± .02
Convalescent cases (11)	.19 ± .02	.53 ± .01
Tetanus		
Acute cases who did not survive (13)	.73 ± .04	.36 ± .01
Acute cases who survived (12)	.41 ± .03	.52 ± .02
Convalescent cases (12)	.15 ± .02	.74 ± .02
Lobar pneumonia		
Acute cases who did not survive (7)	.68 ± .04	.30 ± .02
Acute cases who survived (15)	.40 ± .02	.43 ± .01
Convalescent cases (13)	.16 ± .01	.59 ± .02
Typhoid fever		
Acute cases who did not survive (4)	.56 ± .07	.24 ± .01
Acute cases who survived (19)	.35 ± .02	.45 ± .02
Convalescent cases (15)	.15 ± .01	.68 ± .03
Tubercular meningitis—chronic (17)	.33 ± .07	.50 ± .03

Figures in parentheses indicate No. of subjects  
\* Mean ± stand. error of mean.

might be due either to the conversion of ascorbic acid to dehydroascorbic acid or to failure in the reduction of dehydroascorbic acid to ascorbic acid. Glutathione and ascorbic acid may have considerable influence in controlling the maintenance of proper oxidation-reduction potential in the cells. It may, therefore, be possible that glutathione content is decreased in diseased conditions which results in the failure of reduction of dehydroascorbic acid to ascorbic acid. This suggestion is based on observations of Prunty and Vaas(14) of an inverse relation of red cell glutathione content and the level of plasma ascorbic acid in man.

Sayers *et al.*(15) observed that injection of ACTH in rats and guinea pigs produced a transient fall of ascorbic acid in the adrenal cortex while the other tissues were not affected. Stefanini and Rosenthal(16) observed a fall in plasma ascorbic acid level and

a low urinary excretion of ascorbic acid in 2 patients treated with ACTH. It is, therefore, probable that adrenal cortex may be involved in the production of dehydroascorbic acid. It has been observed by Cornforth and Long (17) that corticotrophin and cortisone facilitate the oxidation of ascorbic acid to dehydroascorbic acid. Further, Long and Miles(18) had suggested that cortisone desensitizes by facilitating the oxidation of ascorbic acid to dehydroascorbic acid and that there is a shift in the equilibrium of ascorbic acid to dehydroascorbic acid to the right. So the accumulation of dehydroascorbic acid in the blood of patients investigated might be due to the stimulation of adrenal cortex by ACTH, which may be produced in increased amount during these infections.

Whatever the mechanisms of the accumulation of dehydroascorbic acid in the blood it might be suggested that the toxic manifestation of the disease might be partly due to the toxic action of accumulated dehydroascorbic acid as shown by Patterson in rats (10). During the present study it had been observed that patients whose blood dehydroascorbic acid was high succumbed. It is, therefore, suggested that estimations of dehydroascorbic acid content of the blood should be undertaken in all cases of acute infection.

*Summary.* 1. Dehydroascorbic acid and ascorbic acid values of blood were estimated in healthy subjects and in patients suffering from meningococcal meningitis, tetanus, acute lobar pneumonia, typhoid fever and tubercular meningitis. These values were also determined in surviving patients during convalescence. 2. There was statistically significant increase in dehydroascorbic acid and a diminution in ascorbic acid values of blood of patients suffering from above mentioned diseases. During convalescence, the dehydroascorbic acid level diminished with a concomitant increase in the ascorbic acid level of the blood. 3. Significance of the rise of de-

hydroascorbic acid level of blood in acute infectious diseases has been discussed. It has been suggested that the estimation of dehydroascorbic acid content of the blood should be undertaken for prognostic purpose.

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