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# THE DISTRIBUTION OF ASCORBIC ACID IN THE BLOOD

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In this paper we are reporting the results of a study of the distribution of ascorbic acid in the blood in human subjects and in guinea pigs.

## EXPERIMENTAL

Fifty healthy medical students (47 males and 3 females) on self-selected diets and 50 patients (41 males and 9 females) in a municipal hospital were studied. Oxalated blood samples were collected under fasting conditions about 15 hours post-prandial. The ascorbic acid content of the whole blood and the plasma was determined by the method of Roe and Kuether (1). The concentration of ascorbic acid in oxalated whole blood and plasma was also determined by the same method in guinea pigs upon an apparently adequate diet (2) made up to contain different levels of ascorbic acid.

## RESULTS

The results of our studies with healthy human subjects are shown graphically in Figure 1. Since all bloods were collected approximately 15 hours after food intake, the values may be considered as representing equilibrium conditions. The distribution ratio of ascorbic acid in the plasma to that in the whole blood follows a characteristic pattern. At whole blood levels below 0.6 mgm. per 100 ml., the plasma concentration was lower than the whole blood concentration in all cases. At whole blood levels ranging from 0.6 to 0.9 mgm. per 100 ml., the plasma concentration was either equal to, or slightly greater or less than, the whole blood concentration; in other words, at these levels, the plasma and whole blood concentrations approached each other very closely. At whole blood levels above 0.9 mgm. per 100 ml., the plasma concentration was higher than the whole blood concentration in all instances, except one.

The results shown in Figure 2 with 50 hospitalized patients suffering serious illness are in striking contrast to those obtained with healthy human subjects. In these patients, the ascorbic acid of the plasma was lower than that in the whole blood in all cases. The clinical diagnoses made in this group of patients were as follows: Pulmonary

tuberculosis, hyperthyroidism, syphilis, glomerulonephritis, portal cirrhosis, hepatitis, diabetes mellitus, carcinoma, pernicious anemia with cellulitis, cystitis, pyelonephritis, duodenal ulcer, Addison's disease, rheumatoid arthritis, and cardiovascular heart disease.

In Figure 3 is shown the relation of the level of ascorbic acid in the plasma to that in the whole blood in 52 guinea pigs fed an apparently adequate diet containing different levels of ascorbic acid. The same pattern of distribution ratio of ascorbic acid in the plasma to that in the whole blood was observed in the guinea pigs as in our healthy human subjects. The results are not so clear-cut, however. We think this was due to the fact that smaller samples of blood were collected from the guinea pigs than from the human subjects, especially the scorbutic pigs, which probably influenced the precision of the analytical data obtained.

## DISCUSSION

Pijoan and Eddy (3) found the ascorbic acid content of the plasma higher than that in the whole blood in 12 normal subjects with high ascorbic acid blood levels. Heinemann reported that the concentration of ascorbic acid is consistently higher in whole blood than in plasma or serum (4, 5), in fasting subjects. Stephens and Hawley (6) observed that the concentration of ascorbic acid was higher in the plasma than in the whole blood in 12 of 19 normal subjects. With 10 normal subjects having whole blood concentrations above 0.8 mgm. per 100 ml., Butler and Cushman (7) found the concentration of ascorbic acid in the plasma higher than in the whole blood in 3 subjects, lower in 4 subjects, and the same as in the whole blood in 3 subjects. With 8 subjects having whole blood concentrations lower than 0.23 mgm. per 100 ml., Kyhos, Sevringhaus, and Hagedorn (8) found the plasma level lower than the whole blood level in all cases; and, with 9 subjects having whole blood levels above 1.17 mgm. per 100 ml., these

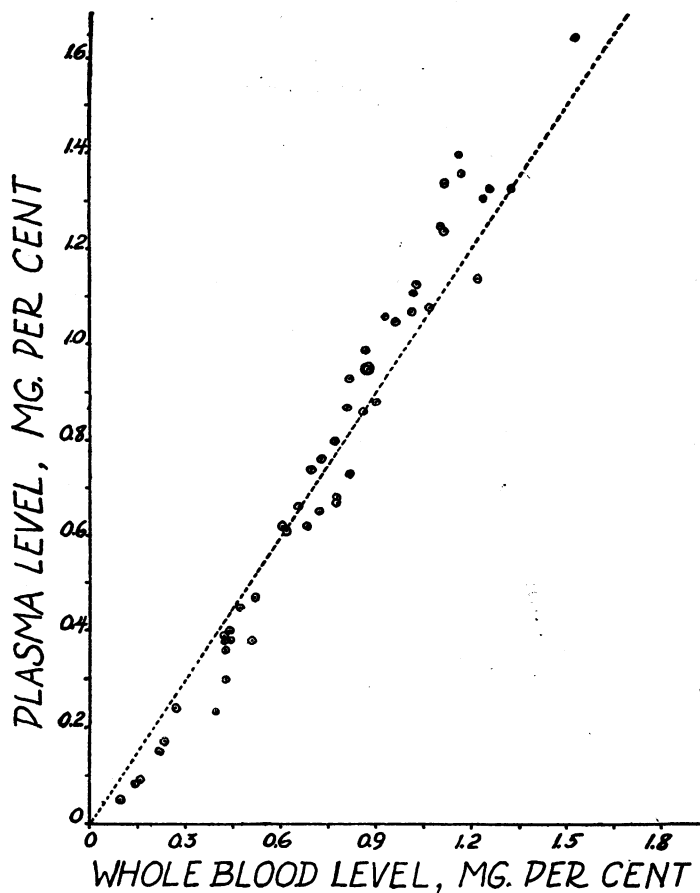


FIG. 1. THE RELATION OF THE LEVEL OF ASCORBIC ACID IN THE WHOLE BLOOD TO THAT IN THE PLASMA IN 50 HEALTHY HUMAN SUBJECTS

authors found the plasma content higher than the whole blood content in 2 instances and lower in 7 instances. Lubschez (9) made a study of whole blood and plasma concentrations of ascorbic acid in 63 subjects. She found that the majority of whole blood values were higher than the plasma values and that the relation between plasma and whole blood concentrations did not show any trend at different levels.

Our data upon subjects having high blood levels of ascorbic acid are in agreement with the work of Pijoan and Eddy (3); and our results with subjects having low blood levels agree with those data in the report of Kyhos, Sevringhaus, and Hagedorn (8) dealing with low blood levels. We are unable to explain the disagreement of our data with Heinemann's results, unless it is due to the different methods of analysis used. It is sug-

gested that some of the opposite results in the literature may be reconciled by a recognition of the effect of the concentration of ascorbic acid in the blood upon its distribution between plasma and whole blood. It also appears desirable for data to be classified on the basis of whether the subjects are healthy or are suffering from some underlying disease that may alter the metabolism of vitamin C.

In our normal subjects the data show that the distribution of ascorbic acid between the plasma and the whole blood is related to the level of ascorbic acid in the blood. At high blood levels the plasma concentration is higher than the whole blood concentration; at intermediate blood levels the plasma and whole blood concentrations are approximately the same; and at low blood levels the plasma concentration is considerably lower than the whole blood concentration.

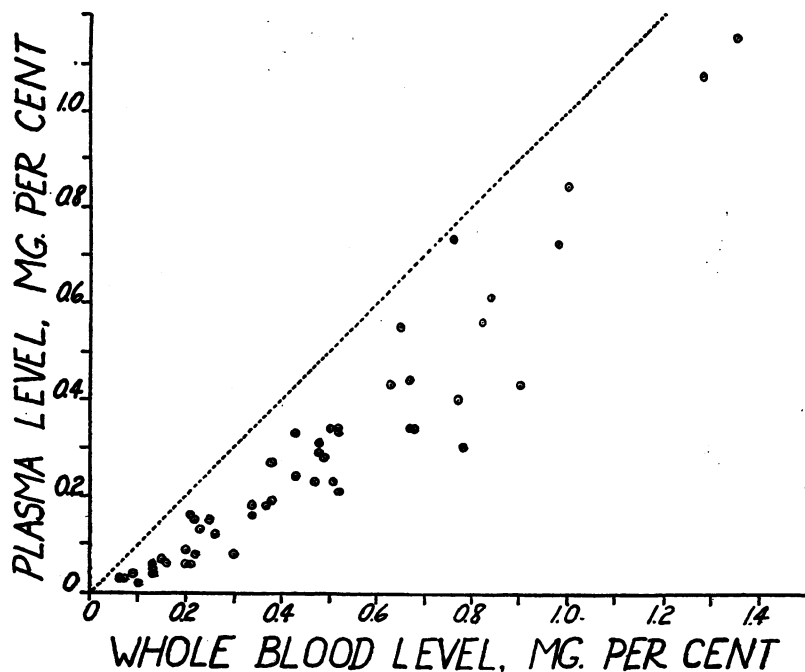


FIG. 2. THE RELATION OF THE LEVEL OF ASCORBIC ACID IN THE WHOLE BLOOD TO THAT IN THE PLASMA IN 50 PATIENTS

In guinea pigs upon the levels of ascorbic acid fed in our studies it has been observed that the concentration of ascorbic acid in the blood varies directly with the intake of this vitamin as shown

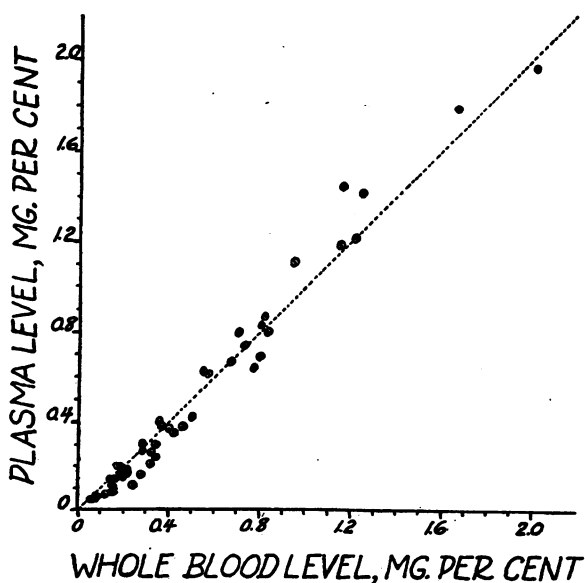


FIG. 3. THE RELATION OF THE LEVEL OF ASCORBIC ACID IN THE WHOLE BLOOD TO THAT IN THE PLASMA IN 52 GUINEA PIGS

in Figure 3 (2). In normal human subjects it is well-accepted that the blood level of ascorbic acid parallels the dietary intake of the vitamin up to a point where massive doses are administered (10 to 14). The unexplained effect of massive doses of ascorbic acid, observed by Wilson and Lub-schez (14), was not present in our normal human subjects. In view of the evidence upon the relation of intake to the blood level of ascorbic acid and our observations upon the effect of blood level upon the distribution of ascorbic acid in blood, it is suggested that the change in the ratio of the concentration of ascorbic acid in the plasma to that in the whole blood in our normal subjects (Figures 1 and 3) was due to a parallel variation in the intake of ascorbic acid.

The results of our studies with 50 patients, showing that the concentration of ascorbic acid in the plasma was lower than that in the whole blood in all instances, are of considerable interest. The concentration of the ascorbic acid in the plasma would be expected to be lower than that in the whole blood in patients with whole blood levels below 0.6 mgm. per 100 ml., since this distribution was observed in normal subjects with similar blood levels. However, the plasma con-

tent was lower than the whole blood content in 15 subjects with blood levels above 0.6 mgm. per 100 ml. Furthermore, comparison of Figure 2 with Figure 1 clearly shows that, at the same whole blood levels, the ratio of the plasma concentration to the whole blood concentration is considerably lower in the patients than in the healthy subjects. Therefore, in the patients, other factors, not in operation in the healthy subjects, contributed to the production of a concentration of ascorbic acid relatively lower in the plasma than in the whole blood. The most probable explanation of this finding is that in patients with serious illnesses there is a greater need for ascorbic acid because of the underlying pathologic processes, and this need is supplied by a more rapid withdrawal of the vitamin from the plasma than occurs in healthy subjects.

#### SUMMARY AND CONCLUSIONS

1. A study of the distribution of ascorbic acid in the blood in human subjects and in guinea pigs has been made.

2. In 50 fasting healthy human subjects, the following was observed: At whole blood levels of ascorbic acid below 0.6 mgm. per 100 ml., the plasma content was lower than the whole blood content; at whole blood levels about 0.6 to 0.9 mgm. per 100 ml., the concentration in the plasma was approximately the same as in the whole blood; at whole blood levels above 0.9 mgm. per 100 ml., the plasma content was higher than the whole blood content.

3. In 52 non-fasted guinea pigs the distribution of ascorbic acid between the plasma and the whole blood followed the same pattern as observed in healthy human subjects.

4. In 50 hospitalized fasting patients with various diseases, the concentration of ascorbic acid in the plasma was lower than that in the whole blood in all instances.

5. It is suggested that in normal subjects the change in the ratio of the ascorbic acid in the plasma to that in the whole blood is due to a parallel variation in the intake of ascorbic acid and that in patients both dietary intake and underlying pathologic processes operate to produce the resulting pattern of distribution of ascorbic acid in the blood.

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