

BLOOD GLUTATHIONE IN LEPROSY¹

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Since the discovery of glutathione by Hopkins in 1920 (2) much work has been centered around this interesting sulphur compound, which represents a thermostable oxidation-reduction system and which is assumed to have some important part in the physiologic oxidation-reduction processes of the cells. Voegtlin and Chalkley (8) state in substance that, chemically, SH (reduced) glutathione is a tripeptide composed of glycine, cysteine and glutamic acid. The relation between SH glutathione and S-S (oxidized) glutathione can be presented as follows:



where R represents the complex organic radical linked to the sulphur. The arrows indicate the possibility of converting one form into the other by oxidation and reduction respectively.

The readiness with which this substance participates as an intermediary in tissue oxidations (1, 3), and its widespread distribution throughout the body (7), justify the emphasis that has been placed upon its biological importance. Variations in the glutathione content of various tissues have been found to be related to their metabolic activity as well as to their rate of growth (6).

Normal human blood contains from 15 to 41 mg. of glutathione per 100 cc., with an average of 34 to 39 mg. (5, 9). Most of it is found to be in the reduced state, but treatment of blood filtrates with zinc-dust or other reducing agents will increase the apparent amount present. Thompson and Voegtlin (6) hold that nearly all of the glutathione is present in the reduced form, for they could demonstrate an increase of only about 5 percent on reduction. Woodward and Fry (9) found after zinc-reduction the presence of 4 to 11 mg. percent oxidized glutathione.

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INVESTIGATION REPORTED

Since leprosy produces pathological changes in many tissues of the body, and since glutathione exercises real functions in the chemical dynamics of the cell, it is not unreasonable to suppose that any quantitative alterations in the tissue content of that substance may be accompanied by changes in the quantity of it present in the blood. It seemed of interest to investigate what differences, if any, could be found between the reduced and the oxidized glutathione contents of leprosy individuals.

The 96 patients selected varied as regards type, duration and state of progression of the disease, and their ages ranged from 20 to 50 years. Similar determinations were performed on the venous bloods of 15 apparently healthy men and women, employees of this institution, their ages ranging from 25 to 50 years.

Analytical methods.—Approximately 5 cc. of blood were collected from a cubital vein, potassium oxalate being used as the anticoagulant, and the filtrate was made immediately. Both reduced and total glutathione were determined according to the method of Woodward and Fry (9). Ten cc. aliquots of the sulphosalicylic acid filtrate of oxalated venous blood were titrated with potassium iodate before and after treatment with zinc dust and the reduced and total glutathione contents of the blood were calculated; the difference between the two titrations expressed oxidized glutathione. The analyses were completed within an hour.

FINDINGS

The figures for the total and reduced glutathione in the non-leper control group are given in Table 1. They correspond with those reported by other workers with this method, though the average for the reduced glutathione is slightly lower than usual. Zinc reduction and subsequent titration have given increases over the reduced glutathione figures—i.e., apparent oxidized glutathione figures—of 6 to 15.3 mg. percent. This is slightly higher than the figures reported by Woodward and Fry, which range from 4 to 11 mg. percent.

TABLE 1. Control determinations (15 cases); glutathione in mg. per 100 cc. whole blood.

| Range of findings | Total glutathione | Reduced glutathione | Oxidized glutathione |
|-------------------|-------------------|---------------------|----------------------|
| Minimum..... | 30.7 | 24.3 | 6.0 |
| Average..... | 39.3 | 27.1 | 11.5 |
| Maximum..... | 49.0 | 36.7 | 15.3 |

The findings with the bloods of the patients, classified according to the various stages of activity of the disease, are given in Table 2. These figures show that the average findings for the reduced glutathione, though slightly higher than in the controls, still fall within the normal range. Of the arrested, improving and stationary cases, two each showed a definite increase in the oxidized glutathione. Of the 59 cases that were becoming worse, 17 showed values for oxidized glutathione that were considerably higher than those of the controls.

TABLE 2. *Findings in lepers, according to the stage of activity of the disease.*

| Groups (Cases and findings) | Total glutathione | Reduced glutathione | Oxidized glutathione |
|--------------------------------|----------------------|------------------------|-------------------------|
| <i>Arrested</i> (11 cases) | | | |
| Minimum..... | 30.7 | 18.4 | 9.2 |
| Average..... | 46.9 | 31.7 | 15.2 |
| Maximum..... | 58.2 | 43.0 | 30.7 |
| <i>Improving</i> (11 cases) | | | |
| Minimum..... | 33.2 | 21.4 | 4.3 |
| Average..... | 42.4 | 29.3 | 12.9 |
| Maximum..... | 55.1 | 43.0 | 21.7 |
| <i>Stationary</i> (15 cases) | | | |
| Minimum..... | 30.7 | 21.4 | 5.5 |
| Average..... | 42.7 | 29.6 | 17.8 |
| Maximum..... | 55.1 | 39.8 | 21.4 |
| <i>Retrograding</i> (59 cases) | | | |
| Minimum..... | 30.0 | 15.2 | 5.4 |
| Average..... | 43.8 | 30.5 | 13.4 |
| Maximum..... | 58.2 | 43.0 | 24.4 |

In Table 3 the findings are arranged according to the state of progression (or "degree of advancement") of the disease. This analysis of the figures gives averages for both reduced and oxidized glutathione that approximate those in Table 2. Of the 16 early cases, only one showed a slight increase in the oxidized glutathione; of the 47 moderately advanced cases, 9 showed definite increase; and of the 22 far advanced cases, 11 showed such increases.

In the entire series (Tables 2 and 3) the findings for both forms of glutathione fluctuated within comparatively wide limits. The reduced glutathione ranged from 15.2 mg. to 46 mg. per 100 cc. of whole blood, while in the controls the range was only from

24.3 mg. to 36.7 mg. The oxidized glutathione in the patients' bloods ranged from 4.0 mg. to 30.7 mg., as against 6.0 mg. to 15.3 mg. in the controls. All of the 96 cases showed normal values for reduced glutathione. Definite increase in the oxidized glutathione was found in 23 cases.

TABLE 3. Findings in lepers, according to the state of progression of the disease.

| Groups (Cases and findings) | Total glutathione | Reduced glutathione | Oxidized glutathione |
|---------------------------------------|----------------------|------------------------|-------------------------|
| <i>Arrested</i> (11 cases) | | | |
| Minimum..... | 30.7 | 18.4 | 9.2 |
| Average..... | 46.9 | 31.7 | 15.2 |
| Maximum..... | 58.2 | 43.0 | 30.7 |
| <i>Early</i> (16 cases) | | | |
| Minimum..... | 30.7 | 18.4 | 6.0 |
| Average..... | 42.8 | 30.7 | 11.7 |
| Maximum..... | 52.1 | 43.0 | 18.5 |
| <i>Moderately advanced</i> (47 cases) | | | |
| Minimum..... | 30.7 | 16.2 | 4.0 |
| Average..... | 43.0 | 29.8 | 13.5 |
| Maximum..... | 58.0 | 46.0 | 24.6 |
| <i>Far advanced</i> (22 cases) | | | |
| Minimum..... | 30.7 | 15.2 | 6.0 |
| Average..... | 44.6 | 29.9 | 14.1 |
| Maximum..... | 56.8 | 39.8 | 21.6 |

SUMMARY AND CONCLUSIONS

Bloods from 96 lepers, between the ages of 20 and 50 years, representing various types and stages of progression and activity of the disease, were examined for total, reduced and oxidized glutathione. Bloods from 15 normal men and women between the ages of 25 and 50 years were similarly examined, as controls.

The reduced glutathione showed no appreciable deviations either in regard to the range of variations or in the average values. No correlation can be traced between the amount of this form of glutathione and the stages of progression or of activity of the disease.

Definite increase in the oxidized glutathione was found in 23 of the cases, chiefly in the retrograding group of cases and in those that were moderately and far advanced.

It is known (4) that factors are present in the tissues which

promptly reduce the oxidized glutathione whenever its concentration is raised above an equilibrium value. Since the increase of oxidized glutathione was most marked among the patients in whom the disease had progressed for a longer time, there would seem to be a tendency towards excessive tissue destruction which may result in an unbalanced tissue equilibrium with a loss of the oxidized glutathione from the tissues.

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