BRIEF COMMUNICATION

Glucose-6-Phosphate Dehydrogenase Deficiency and Red Cell Glutathione Peroxidase

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The activity of glutathione peroxidase (GSH Px), glucose-6-phosphate dehydrogenase (G-6-PD), hexokinase, and glutamic oxaloacetic transaminase (EGOT) was measured in 78 blood samples. GSH Px activity was not found to correlate with hexokinase or EGOT activity, indicating that it was not a strongly age-dependent enzyme. Although modest elevations of GSH Px activity were observed in the red cells of patients with a variety of hematologic disorders, the most consistent and striking increases in activity were observed in G-6-PD-deficient subjects.

The activity of numerous enzymes has been measured in G-6-PD deficient erythrocytes. Some deviations from normal have been observed, most notably an increase in activity of glutathione reductase, and a decrease in NADPH diaphorase activity. Both of these enzymes oxidize NADPH, a product of the G-6-PD reaction.

Glutathione peroxidase (GSH Px) catalyzes the oxidation of reduced glutathione (GSH) by peroxides:

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R-O--OH + 2 \text{GSH} \rightarrow R-OH + \text{GSSG} + \text{H}_2\text{O}
\]

This reaction is also closely related to the generation of NADPH, since NADPH is required to maintain GSH in the reduced form. It is, therefore, surprising that GSH Px activity in G-6-PD deficiency has received only scant notice.

Although we have studied many samples of G-6-PD-deficient blood in the past decade, we have not routinely measured the activity of other enzymes, such as GSH Px, in G-6-PD-deficient red cells. Recently, we had occasion to review the results of all of the GSH Px assays carried out on patients with hemolytic and other hematologic diseases. It immediately became apparent that G-6-PD-deficient red cells invariably showed increased GSH Px activity, and this finding has been confirmed in every sample from G-6-PD-deficient subjects that subsequently became available.

MATERIALS AND METHODS

Blood was obtained from patients with a variety of hematologic disorders, including hereditary spherocytosis, sickle cell anemia, pyrimidine 5'-nucleotidase deficiency, the anemia of chronic azotemia, hemolytic-uremic syndrome, congenital dyserythropoietic anemias types I and II, aldolase deficiency, and hereditary persistence of fetal hemoglobin. Many subjects had hemolytic anemias of undetermined origin. All samples assayed for GSH Px within the past 2 yr were included, except those from patients with \(\alpha\)-thalassemia which also showed increased GSH Px activities and which will be the subject of a separate report. The dearth of samples...
RESULTS

The results of the study are summarized in Fig. 1. Each value has been plotted against the hexokinase activity of the same sample as an indicator of red cell age. Similar results were observed when the GSH Px activity was plotted against EGT. GSH Px activity was not age dependent: no correlation with hexokinase or EGT was found. Regression analysis showed that the correlation coefficient of regression of GSH P x activity on hexokinase activity was only 0.0297 (t = 0.25; p > 0.4) and for GSH P x on EGT 0.173 (t = 1.45; p > 0.05), but the correlation coefficient for EGT on hexokinase, two clearly age-related enzymes, was 0.547 (t = 5.39; p < 0.0005). Most of the patients examined had hemolytic anemia, and the red cell hexokinase activity was therefore increased. Modest increases of GSH P x activity were found in the red cells of many patients with varying hematologic disorders. However, the highest values observed were those in G-6-PD-deficient subjects, with and without hemolysis, and the activity of the enzyme was increased in all G-6-PD-deficient subjects investigated, even in heterozygotes. Because of the existence of a GSH
G-6-PD AND RBC GSH Px

Px polymorphism in persons of Mediterranean origin, the average level in Mediterranean subjects was only about 75% of that of Northern European subjects. One of the hemizygotes for G-6-PD Mediterranean displayed much lower GSH Px activity than the other hemizygous G-6-PD-deficient subjects. This individual was of Ashkenazi Jewish origin, a population in which the frequency of the gene coding for low GSH Px activity (GSH Px'), is quite high.

DISCUSSION

The cause of increased GSH Px activity in G-6-PD deficiency is not clear. It is attractive to speculate that elevated levels of peroxides in developing erythroblasts induce synthesis of the detoxifying enzyme, GSH Px. Indeed, there are data which suggest that exposure to peroxides, either by direct feeding or as may occur in vitamin E deficiency, results in increased GSH Px activity in experimental animals. On the other hand, normal GSH Px levels have also been reported in vitamin E deficiency, and it has been suggested that erythroblast G-6-PD levels are nearly normal in the mild, A-type of deficiency. At present, therefore, the possibility that peroxides induce GSH Px activity must be considered a speculation.

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REFERENCES

Glucose-6-phosphate dehydrogenase deficiency and red cell glutathione peroxidase

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