DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Occupational Health Research & Training Facility
Bureau of State Services
1014 Broadway
Cincinnati 2, Ohio

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Gordon J. Stoppe, M.D.
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Haskell Laboratories
Newark, Delaware

Dear Dr. Stoppe:

Your inquiries regarding hypersusceptibility and lead poisoning have been referred to me by Dr. Stokinger.

In France and Italy, where many employees in the industry come from ethnic groups in which glucose-6-phosphate dehydrogenase deficiency of the erythrocyte is not uncommon, there have been attempts to determine if this inborn error of metabolism was a factor in aggravating saturnism in this segment of the industrial population.

It had been shown by Jonderko in Poland that rabbits and men exposed to lead exhibited a reduction in the glutathione content of the red cell. Finally, two reports show that lead poisoning does, indeed, depress: 1. the glucose-6-phosphate dehydrogenase (G-6 PD) of erythrocytes, together with 2. glutathione (GSH), 3. the ability of red cell glutathione to be restored after incubation with acetyl-phenylhydrazine, (the GSH stability test), and lastly, 4. the ability of the red cell enzyme systems to reconvert methemoglobin into hemoglobin. Apparently lead impairs the development of the erythrocyte so that, among other defects, the enzyme systems which maintain normal membrane and hemoglobin integrity are deficient.

Subjecting to lead exposure such persons, deficient in the normal complement of erythrocyte enzymes, would aggravate the defect and lead to hemolytic effects such as transpire when persons with these inborn errors of metabolism are treated with a number of common drugs as aspirin, acetanilide, sulfas, etc.

Evidence for lead-associated effects on red cell constituents is reported by Rubino, G. F., Coscia, G. C., Perelli, G., and Parigi, A., The Behavior of glutathione, the glutathione stability test and glucose-6-phosphate dehydrogenase activity in lead poisoning (Comportamento del glutatione, del

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test di stabilita del glutatione e dell' altivata glucosio-6-fosfato deidrogenasica nel saturnismio), Minerva Medica 54, 930-932, (1963).

Results of this work are summarized in a table:

Subjects	GSH mg/100ml r.b.c.	GSH after stab. test	G-6-PD units/10^9 red cells
1. Normal	57 ± 6	47 ± 4	277 ± 12
2. Pb-clinical effects acute and subacute	40 ± 9 P < 0.01	35 ± 10 P < 0.01	231 ± 31 P < 0.01
3. Pb exposed, no overt symptoms but Pb and coproporphyria elevated in urine	47 ± 11 P < 0.05	41 ± 8 P < 0.05	245 ± 33 P < 0.05

Unit = Δ .001 O.D./min.

The function of the erythrocyte enzyme systems with respect to restoration of hemoglobin subsequent to its conversion to methemoglobin (Methemoglobin reduction test) has been observed to be impaired in acute lead poisoning: Helen Robin and J. D. Harley, Experience with an extended methemoglobin reduction test. Factors influencing hemoglobin destruction, Blood 27, 395 (1966, Mar). While these authors mention their lead studies, only in passing, referring to another report to be published, they do report that methemoglobin reduction capacity was impaired. Their main thesis is that hemoglobin is destroyed in the conditions of the test and this should be evaluated. Unfortunately they emphasize this while tending to overlook the significant fact that methemoglobin persists longer in defective hemolysates of erythrocytes (in this case, associated with Pb poisoning) than it does in hemolysates of normal blood.

While we have not been able to do extensive lead studies in this laboratory, we have studied effects of other agents on the blood and tissue enzyme systems of animals. We have G6PD deficient subjects available through local hospitals.

The enclosed procedures for G6PD activity and the semi-quantitative methemoglobin reduction test are those we have found satisfactory.

Trusting this information will be useful to you, I am

Sincerely yours,
/signed/
John T. Mountain
Toxicology Section