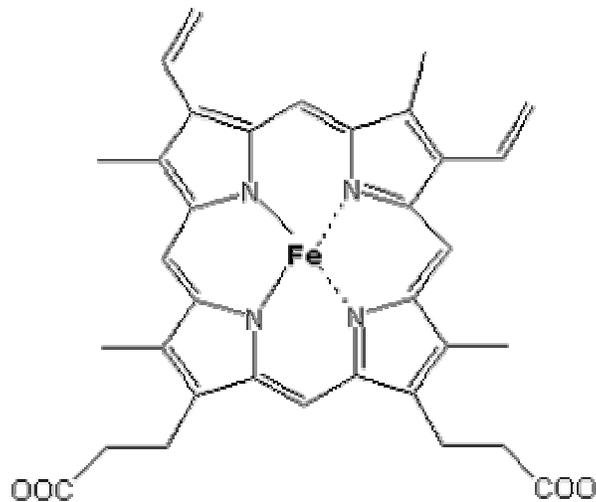


CHEM-342 Introduction to Biochemistry
Final Examination - Group Part
Monday, 26 May 2003
8:45 – 10 PM
H. B. White - Instructor

Group Members

Important - Please read this before you turn the page.

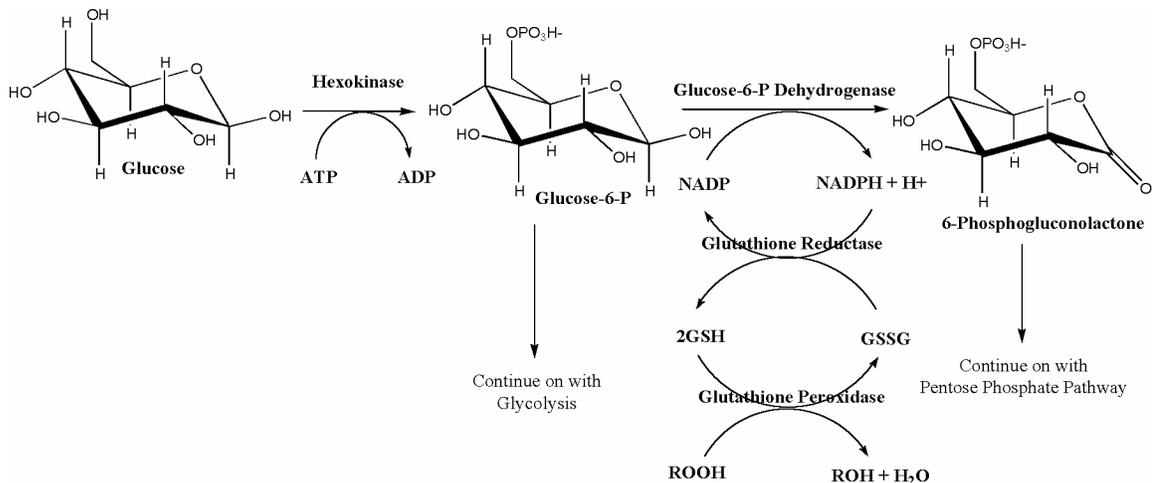
- You must sign your name on this page to receive the group grade.
- You may refer to your notes, course reader, handouts, textbook, or graded homework assignments. Reference books in the course library may be consulted briefly and returned.
- The structure of heme is below.



As with hemoglobin, mutations in the genes encoding any protein can have serious consequences for red blood cells and the health of the affected individuals. One of these proteins is glucose-6-phosphate dehydrogenase (G6PD). G6PD deficiency is the most common human enzymopathy. As noted by Dr. Allison during his visit, one common variant of G6PD appears to provide some protection from malaria. The discovery of this enzyme variant and its mode of action have a long and interesting biochemical history.

For ages some otherwise normal people, usually men living in Mediterranean countries, would have dangerous hemolytic episodes after eating fava beans. Favism, as it is known, is a sex-linked condition. The symptoms include dark or black urine a day or two after eating fava beans, weakness and lethargy, temporary anemia, and jaundice. In the 1920's, primaquine, a then new antimalarial drug related to quinine, was introduced and thought to have no serious side effects. However, when given to people susceptible to favism, the symptoms of favism appeared. Interestingly, after the episode, the physical symptoms disappeared despite the continued use of primaquine. Analysis of the patients who recovered showed an increased proportion of immature red blood cells in their blood.

Much later an electrophoretic variant of G6PD was found to have a high frequency in certain Mediterranean populations exposed to malaria. Characterization of this G6PD showed that it was unstable and lost activity as the red blood cell aged. Individuals with this variant were sensitive to fava beans, primaquine, and a variety of other drugs and chemicals that have nothing to do with malaria. Apparently, these compounds create an oxidative stress in red blood cells and generate peroxides in reactions with oxygen. The peroxides are destroyed using the NADPH generated by G6PD and reactions with glutathione as shown below.



1. (10 points) Based on the properties of the G6PD variant, propose a plausible hypothesis for why people recover from their hemolytic anemia attack despite their continued use of primaquine. Include the evidence in support of your hypothesis.

2. (10 points) The X chromosome carries the gene for G6PD. If the gene for G6PD that confers resistance to malaria occurs at 11 % in a population, predict the percentage of males and percentage of females who are susceptible to favism in that population.
3. (5 points) If you could see molecular detail in the mirror you look in each day, you would discover proteins containing “D”, rather than “L”, α -amino acids. In this D-world, would “D” hemoglobin need a different heme than we have attached to our “L” hemoglobin? Explain your reasoning clearly.

On the back - 5 bonus points for the appropriate chemical model and mathematical derivation of $t_{1/2}$.