

**CHEM-342 Introduction to Biochemistry**  
**Final Examination - Group (Part II)**  
**Friday, 26 May 2006**  
**12:15 – 1:30 PM**  
**H. B. White - Instructor**

**Group Members**

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**Range 15-26 out of 27,**  
**Average 21.0**

**Important - Please read this before you turn the page.**

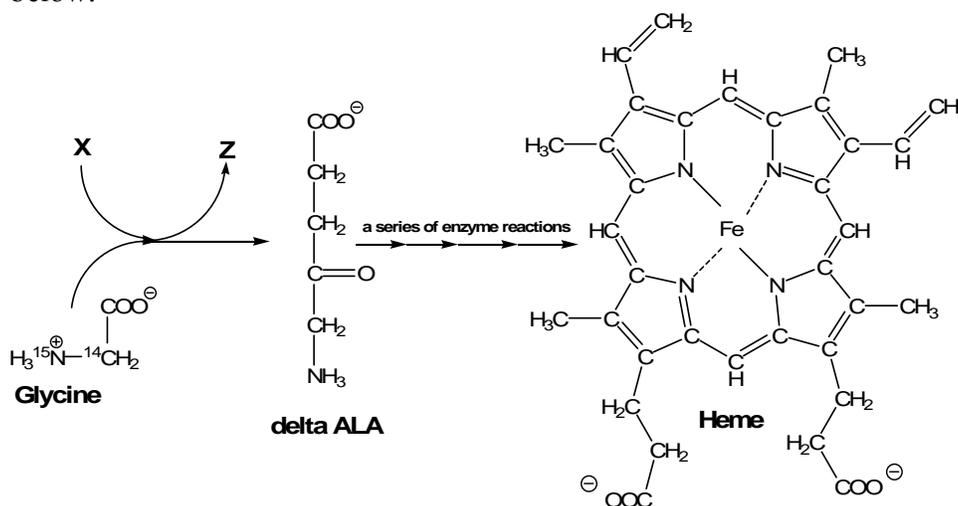
- You must sign your name on this page to receive the group grade. In case of lack of consensus, you may hand in your answer separately from your group for individual grading.
- You may refer to your notes, course reader, handouts, or graded homework assignments. Textbooks and reference books are not permitted.
- In CHEM-342, hemoglobin is a vehicle for learning how to learn by asking questions and pursuing answers to those questions. Undoubtedly you have learned a lot about hemoglobin in the process but you also should be developing habits of mind that will enable you to solve problems in other courses and throughout your life. This part of the final examination provides an opportunity for you and the other members of your group to display problem-solving skills as a team. It is extremely unlikely that anyone in your group or in the class has encountered the information on the following pages. Your answers should display your collective:
  - breadth of knowledge (not limited to hemoglobin or biochemistry)
  - ability to analyze, make connections, and ask probing questions
  - sense of logic and organization
  - skill at generating models (testable hypotheses)



"This place is all right. Two more weeks and I'll be a molecular biochemist."

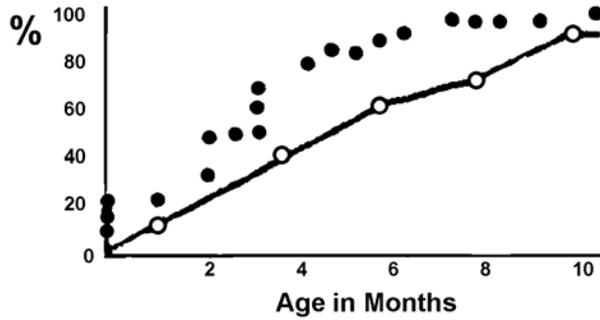
- The fact that nitrogen from  $^{15}\text{N}$ -labeled glycine was incorporated in such high amounts into heme clearly indicated that, unexpectedly, glycine was a biosynthetic precursor of heme. After this initial experiment designed to study protein turnover, Shemin's interest understandably shifted to the biosynthesis of heme. Rather than continuing to experiment on himself, he chose to work with duck red blood cells because, unlike mammalian red blood cells, they were nucleated and thus continued to synthesize heme after differentiation.

Shemin's experiments with Rittenberg showed that the nitrogens from glycine were incorporated into heme, but the experiment provided no evidence for the incorporation of carbon atoms from glycine, an experiment that became possible with  $^{14}\text{C}$ . When  $^{15}\text{NH}_2$ - $^{14}\text{CH}_2$ -COOH was used as a precursor, instead of the expected 1:1 incorporation of labeled nitrogen and labeled carbon they found two atoms of  $^{14}\text{C}$  per atom of  $^{15}\text{N}$  in heme. Other experiments showed that the carboxyl group of glycine was not incorporated at all into heme or  $\delta$ -aminolevulinic acid ( $\delta$ -ALA), an intermediate on the pathway to heme as shown below.



- (4 points) In the space below, make an educated guess at the chemical structures of X and Z based on the information provided. Explain your reasoning.
- (8 points) Predict which carbon atoms in heme are derived from the  $^{14}\text{C}$ -labelled methylene carbon in glycine? Circle each. What is the basis of your deduction?

2. (8 points) Tony Allison in his 1954 article presented evidence that people with the sickle cell trait had resistance to malaria. He also hypothesized that fetal hemoglobin (HbF) confers resistance to malaria and offered the following graph in support of his hypothesis.



“The apparent relationship between the appearance of adult-type haemoglobin (dots) and malarial infection (circles) in the newborn. Each dot represents a test of a single individual using an alkali denaturation techniques (Allison unpublished observation): the circles represent the percentage of Luo children showing malaria parasites (Garnham, 1949).” (Allison, 1954).

Provide a structured logical argument that describes why these data are consistent with malarial resistance in new born humans. If you were a skeptic, how might you interpret these data differently?

