DISEASE OF THE MONTH: SICKLE CELL DISEASE

1. What is the mutation in DNA that leads to sickle cell disease? How is this mutation expressed at the protein level, and why is this mutation important?

2. As of 2002, how many hemoglobin variants have been identified? How many have pathologic significance?

3. Estimate the number of African Americans with sickle cell disease. What is the survival advantage for heterozygous individuals with sickle cell trait?

4. What is the most immediate risk for infants diagnosed with sickle cell disease, and how should they be treated, based on this risk?

5. Deoxygenation of erythrocytes leads to a sequence of reactions which play a major role in the pathophysiology of sickle cell disease. What are these processes?

6. Why is the spleen often severely damaged in sickle cell disease, and what are the consequences of this damage?

7. Acute chest syndrome is the leading cause of death in sickle cell disease; what are the specific mechanisms involved?

8. What clinical symptoms are associated with sickle cell disease (The list is long!)?

9. Why are blood transfusions commonly used in therapy of sickle cell disease, and what are the risks involved? How can these risks be minimized? What specific pathological event can be prevented in children by blood transfusion?

10. Hydroxyurea treatment is now one of the most successful therapeutic modalities for sickle cell disease. How is it administered, and what are the proposed mechanisms of action (several!) of the drug? Are there risks involved with hydroxyurea treatment?

11. Nitric oxide inhalation may be beneficial for patients with sickle cell disease. What symptoms may be treated, and how does the nitric oxide work?

12. What is the only curative therapy for sickle cell anemia, and how often is this therapy used? Why?

13. Certain therapies are focused on limiting erythrocyte dehydration. What are these therapies, and how do they work?

14. Sodium butyrate treatment resembles which other treatment in terms of the targeted outcome? How does sodium butyrate work?

15. How is the pain of sickle cell disease treated?
16. Describe common laboratory techniques used in the diagnosis of sickle cell disease. How often are newborns in the U.S. tested for sickle cell disease? Can prenatal diagnosis be performed? How?

17. Why is there such wide distribution in symptoms between patients, when they all have the same underlying defect? What other factors may be important?

Instructions: You will meet with a faculty member in small groups for two hours on September 15 to address these questions. The job of the faculty member is to monitor and organize the discussion. However, we expect that you will have researched these questions and that you will be prepared to present your findings to your group. We recommend that you organize yourselves into sub-groups of 2-3 individuals, and then divide up the responsibilities for the questions. A reasonable formula, based on 15 students per group, and therefore 5 subgroups is as follows:

Group 1: Questions 1-4
Group 2: Questions 5-8
Group 3: Questions 9-10
Group 4: Questions 11-14
Group 5: Questions 15-17

Thus, you only have to be prepared for 3 or 4 questions each, but you are certainly welcome to work on more questions, if you wish. Use MEDLINE, or other search vehicles to research these questions. Please limit your searches to papers and books published in 2002 or 2003. When you present your answers in class, please be sure to cite the references you used. The goal of the session will be to learn from each other such that at the conclusion of the session you will know the answers to all of these questions.