The Chemistry of Cooley's Anemia

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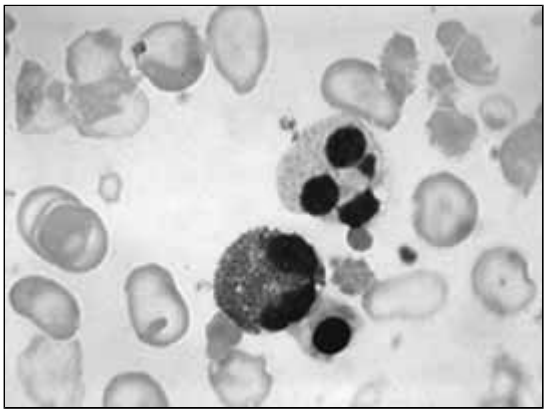

Max and Andrea Foresti are sitting in the waiting room of their family physician, Dr. Mary Litton. A young couple, Max and Andrea have been married just two years and have a son, Peter, whom they are bringing in for a follow-up visit with the doctor. They are concerned because Peter has recently been suffering from a number of infections. Although Peter seemed to be a happy and healthy newborn, he has grown increasingly listless over the past few months. He has lost much of his appetite and his complexion has become pale. Max and Andrea believe that Peter has become anemic due to his poor diet; both Andrea and Max themselves suffered from jaundice as babies.

The family is called in to see Dr. Litton, who, after exchanging pleasantries, reviews Peter's symptoms with them and then says, "You'll remember that when you were last here I ordered some blood work to be done on Peter. The results of the blood work have confirmed a suspicion I had based on Peter's symptoms and some other things you told me. Peter is suffering from thalassemia."

Max interrupts Dr. Litton. "What is thalassemia? I've never heard of that before."

"Well, thalassemia is a genetic blood disorder. In fact, it was your telling me during your last visit that your grandparents had emigrated from Italy that made me suspect thalassemia. Thalassemia tends to affect people of Mediterranean descent."

Andrea, who has grown quite pale, asks anxiously, "What is this thalassemia doing to Peter?"

"Thalassemia causes hemoglobin, the protein in your body that binds and transports oxygen, to be malformed."

"I've heard of hemoglobin. It's the cause of the red color in your blood."

"That's correct. You see, there are two components to hemoglobin called the alpha protein and the beta protein. If the body doesn't produce enough of either of these, then it can't get sufficient oxygen. The two basic types of thalassemia are differentiated based on which of the two proteins that make up hemoglobin are affected. One type is alpha thalassemia, the other is beta thalassemia. There are also various subtypes of each of these two, depending on the amount of protein affected. Some individuals produce some, but just not enough, of either the alpha or beta protein; their red blood cells are smaller than normal and they experience a mild anemia, although many have no symptoms at all.

"In Peter's case, his body is producing none of the beta protein. He has thalassemia major, which is also known as Cooley's anemia. Unfortunately, this is the most severe form of thalassemia. If left untreated, there is a 50 percent chance of death by the age of three."

Max stares at Dr. Litton in disbelief. "Oh, my God. We thought that Peter was just anemic. That's why we started giving him iron supplements."

"Oh, you really shouldn't have done that. Peter's problem is that his body is not producing a protein. It's not that he is getting too little iron. In fact, this is a case where that extra iron may do more harm than good.

"I'm sorry if I shocked you, but there is a treatment, although not a cure, for thalassemia. Because Peter is not producing properly formed hemoglobin, what we will need to do is supply his body with healthy red blood cells. Now, this will mean that he will need to receive blood transfusions for the rest of his life. Most patients with this condition receive transfusions every couple of weeks."

Andrea, looking only a little reassured, asks, "So, blood transfusions are all he will need to do?"

"Well, there is an added complication. When transfusion was first utilized as a treatment for thalassemia it led, initially, to a high survivor rate. But then, after a number of years, even these patients began dying. Most had severe infections or suffered organ failure. About half of the patients died by age 18."

"What was wrong?"

"Well, this is why I am concerned about the iron supplements. You see each unit of whole blood contains a small amount of free iron, a necessary but highly insoluble nutrient. The body has a number of means of binding, transporting, and storing iron. So, if you or I were to receive a blood transfusion we could easily handle this extra iron. Unfortunately, for a patient who is receiving many transfusions over time, this iron accumulates until the body can no longer handle the excess iron. Whereas the normal amount of iron in the body is about 5 grams, these patients can accumulate 60 to 70 grams."

Max jumps in, "But, I thought that iron was good for you."

"Usually it is. In fact, your body normally wants to hold onto as much iron as it can—that's why there is no normal mechanism for excreting excess iron. And that's also the problem. With patients receiving transfusions, this iron overload just can't be handled and the iron begins to precipitate out into the organs, particularly the heart and liver. It can also be the cause of severe infections."

Andrea asks, "Can't anything be done?"

"To help remove this excess iron, patients receiving these regular blood transfusions must also undergo chelation therapy using the drug, deferoxamine[1]."

"Chelation therapy?"

"Yes. Chelators are small molecules that can bind the iron and make it soluble. The chelated iron is readily excreted from the body."

Max asks, "So this is some sort of pill?"

"Unfortunately, no. Deferoxamine is poorly absorbed if taken orally. It is also so rapidly eliminated from the body that it must be administered by a slow infusion to have the appropriate therapeutic effect. A needle is attached to a small subcutaneous pump five to seven times a week for up to 12 hours. It is a difficult and painful procedure."

Andrea sighs. "But, when will all of this be over for Peter?"

"I'm afraid that it will never be over. This is a lifetime commitment for Peter and for you. The blood transfusions will need to be administered on an outpatient basis every two to four weeks. These sessions normally last four to six hours. You will also need to administer the deferoxamine each night by placing a needle under Peter's skin. This is a difficult prospect for most parents who are simply unprepared for such intensive home care."

"So we are committing our child to a life of transfusions and chelation therapy?"

"Yes. Both of these are vital to long-term survival. Unfortunately, many patients, particularly those in their teens, find the treatment so difficult or so burdensome that they stop it altogether. This, of course, leads to early death. But, those patients who are able to continue with therapy have a 90 percent chance of surviving to age 25."

You must now put yourself in the role of one of Peter's parents. You must make a choice as to what treatment you will choose for your child; you might even choose to pursue no treatment at all. Before making this decision, investigate the following questions so that you may make an informed decision. The class will reconvene at a later date to consider your answers to these questions. At that point you will need to come to a decision about Peter's future.

Questions for Investigation and Discussion:

1. What is the basic structure and function of hemoglobin?
2. Which proteins transport and store iron in the body?
3. What is thalassemia and what are its causes?
4. What are the different types of thalassemia?
5. What are the symptoms of beta thalassemia major (Cooley's anemia)? Why don't these symptoms appear at birth?
6. What are the current treatments for thalassemia? What are their problems?
7. What is iron overload? What are its causes?
8. What are chelators?
9. What is chelation therapy and why is this treatment necessary to combat iron-overload?
10. What should Peter's parents do?

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[1] Deferoxamine is also known as desferrioxamine B, or as Desferal®, its trade name.

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