It's All Greek to Me: Genetics Edition

by
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Part I – Something's Not Right

Dr. James Stephens is a pediatrician serving the Tarpon Springs, Florida, area who is seeing one of his new patients in the clinic today. As Dr. Stephens enters the examination room, he says "kali mera" to Stephania and Nikolaus Stamos, a greeting he uses with a number of his patients who are Greek Americans. Mr. and Mrs. Stamos have brought in their only child, beautiful little Nikoleta. It seems odd to Dr. Stephens that they are here because Nikoleta's one-year checkup is only six weeks away. Nikoleta's parents are very concerned and tell the doctor that the baby has been acting strangely. The father, Nikolaus, is a personal trainer and he suspects that Nikoleta has been anemic for some reason. Originally, Nikoleta had been on a low iron formula because she was experiencing gastrointestinal distress. The parents changed her formula to a high iron formula to see if it would help alleviate her symptoms, but Nikolaus tells Dr. Stephens that it did not. His daughter continues to suffer from general malaise and lethargy, and her skin looks a little pale recently. Nikoleta's parents also tell the doctor that their daughter looks bloated all the time, and seems tired and cranky. Dr. Stephens notices that Nikoleta is not growing as she should. She has not grown significantly since her last checkup three months earlier. Dr. Stephens orders a CBC (Complete Blood Count) panel.

Questions

1. What are the symptoms of anemia?
2. Why did the parents change Nikoleta's formula to a high iron formula?

Part II – The Test Results

Dr. Stephens receives the lab reports and decides to refer Nikoleta to a hematologist. The results are as follows:

	Value	Normal
Hb (hemoglobin)	5g/dL	Male: 13.5–16.5 g/dL Female: 12.0–15.0 g/dL
RBC (red blood cell count)	4.6×10^6 cells/ml	Male: $4.5–5.5 \times 10^6$ cells/ml Female: $4.0–4.9 \times 10^6$ cells/ml
MCV (mean corpuscular volume)	65	80–100
WBC (white blood cell count)	15,000 cells/ml	4500–10,000 cells/ml
Platelet count	250,000	100,000–450,000

Mr. and Mrs. Stamos bring little Nikoleta into the hematologist's office and Nikoleta has her blood drawn. After a few minutes, the hematologist returns to speak with the parents. Even with just a few moments looking at the sample, he knows that there is something wrong. The hematologist reports that he observed severe hypochromia and microcytosis (lightly colored and small cells), fragmented and nucleated RBCs.

The blood sample taken in the office appears as follows:

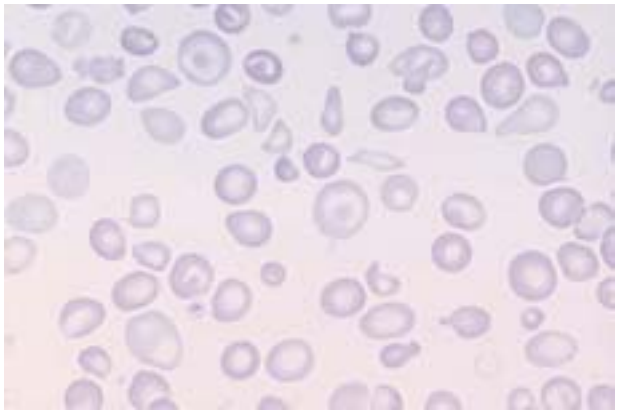

Figure 1A. Nikoleta's red blood cells

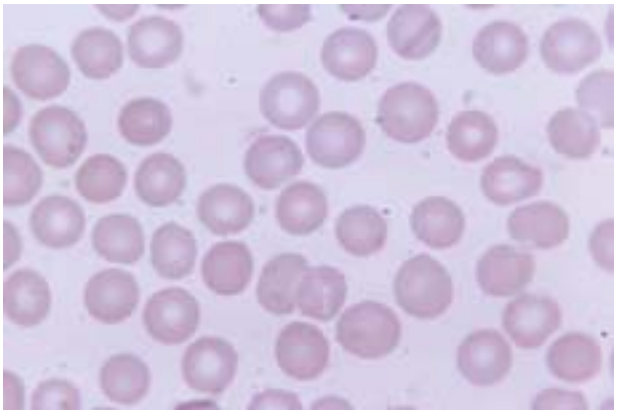

Figure 1B. Normal red blood cells

The hematologist meets with the Stamos family in the exam room. "Mr. and Mrs. Stamos, there are some things that do not look normal in Nikoleta's blood. I am not sure of the cause, but I do know that Nikoleta's red blood cells aren't shaped correctly and they are not the right color. The red blood cells should be very red under the microscope and her red blood cells are light pink."

Mrs. Stamos asks, "Does it matter if her red blood cells aren't red?"

The hematologist replies, "Yes, it does matter. Healthy red blood cells are very red and carry oxygen. Nikoleta's red blood cells aren't able to carry much oxygen to her tissues. Hemoglobin is a molecule found in the blood that is used in oxygen transport. When oxygen is bound to hemoglobin, it gives the red blood cells their characteristic color. There are two proteins involved in the process of carrying oxygen, alpha and beta. You need both of them in order to have properly working hemoglobin. Nikoleta's beta proteins don't function correctly. I have an additional concern as well. Sometimes disorders like anemia can have a genetic basis. I would like to have both of you to give a sample of blood for a complete blood count."

The findings from both parents are mild hypochromia and macrocytic (lightly colored and large cells) anemia. The hematologist gives a diagnosis of erythroblastic anemia for both Mr. and Mrs. Stamos.

Questions

3. Are the lab results of the CBC normal? Which values are normal and which are not?
4. Do red blood cells normally have nuclei?
5. What is the structure of hemoglobin and how is oxygen bound to it?
6. Why was an analysis of Mr. and Mrs. Stamos' blood ordered?
7. What is erythroblastic anemia?

Part III – The Family Returns

Dr. Stephens calls Mr. and Mrs. Stamos and asks that they come in for a follow-up visit. This time the parents meet with Dr. Stephens in his office, not the exam room. After they are seated, Dr. Stephens informs them that Nikoleta's condition is very serious and that it is a genetic disorder.

"Is it our fault?" Mrs. Stamos asks.

"No, not at all. It seems that you and your husband both have mild anemia. The disorder that Nikoleta has is called beta-thalassemia, or Cooley's anemia. It is a recessively inherited disorder. That means that each of you has a "bad" copy of a gene and a "good" copy. During fertilization, the newly fertilized egg receives two copies of each gene: one comes from the mother and one comes from the father. Unfortunately, Nikoleta received the bad copy from both of you. Also, I don't know what you are considering for the future of your family, but because of these findings, I suggest that you see a genetic counselor before deciding to have another baby."

Questions

8. What are the general features of this disease? (Who gets the disease?, etc.)
9. Construct a pedigree for Nikoleta and her parents.
10. Construct a Punnett square to determine the probability that Mr. and Mrs. Stamos will have another child with the disorder.
11. If you were the genetic counselor, what would you suggest to Mr. and Mrs. Stamos concerning having more children? Why?

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