In Sickness and in Health: A Trip to the Genetic Counselor

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Part I—Pedigree Construction

Greg and Olga were both a little worried. Starting a family presented choices and responsibilities far more long-reaching and complex than anything either of them had encountered before, and sitting here in the reception area of the genetic counselor’s office they were beginning to feel the pressure. They had met four years earlier in the hemophilia clinic where Greg was waiting for his brother Jeff to get an injection of factor VIII, a protein that helps the blood to clot. When a person’s factor VIII level is very low (less than 1% of normal), even the smallest cuts can be troublesome and uncontrolled internal bleeding is common. Complications include swelling, joint damage, and an increased likelihood of neurological complications due to intracerebral bleeding. Even simple surgical procedures such as tooth extractions become far more risky. Jeff’s condition was noted by his pediatrician shortly after birth when his circumcision bled profusely. Since then, Jeff has received monthly injections of factor VIII, either at home or (twice a year) at a clinic where his physical condition is reviewed by a physician’s assistant. At first these injections contained clotting factor isolated from the blood of human donors but, for the last 10 years or so, he has received recombinant clotting factor, which is genetically engineered.

It was in that clinic waiting room that Greg struck up a conversation with Olga, who was waiting for her uncle to finish his exam and receive an injection of clotting factor. Like Jeff, Olga’s uncle also suffered from hemophilia A due to factor VIII deficiency. Beginning with this common experience, Jeff and Olga quickly fell in love and were married the following year. They are now thinking about starting a family of their own, but are concerned about the risks of passing on genetic diseases to their children. They know for example that hemophilia A is an inherited disease, and several of Greg’s relatives suffer from myotonic dystrophy, a muscle weakening disease that also runs in families. As a first step, the genetic counselor has asked them to fill out a narrative history listing their relatives, relationships, and if they were affected by any genetic diseases that they know of. The forms are seen on the following pages.
NAME: Greg

I have one brother and one sister, neither of whom are married. My brother suffers from factor VIII deficiency, but no one else in my family does. My mother has two brothers and one sister. One of my uncles and one of my aunts are affected by myotonic dystrophy. My affected aunt married an unaffected man and they have a young, seemingly unaffected daughter. My other uncle is unaffected, as is my mother. Our primary care doctor has said that because both my mother and uncle are over fifty years old and show no symptoms, they do not have the disease. My father is completely normal. He was adopted from an orphanage and nothing is known about his family. My maternal grandmother was an only child who also suffered from myotonic dystrophy. Her husband (my grandfather) was one of seven children (four boys and three girls). No one in the family seems to know much about the health status of my grandfather or his brothers. Both of my parents are alive but all of my grandparents are deceased.
“Good afternoon” said the woman rising to greet them, “I’m Dr. Ciletti. It’s good to finally meet you in person.”
“Nice to finally put a face to the voice. I’m Greg and this is my wife Olga.”
“Nice to meet you,” Olga said, taking a seat across the desk from Dr. Ciletti. “This whole having-kids thing is more nerve-wracking when you really start to think about it.”
“You’re doing exactly the right thing. There is no sense in worrying about things unless you have to. Maybe I can set your mind at ease a little bit. To begin with, I know that you’re both concerned about factor VIII deficiency and myotonic dystrophy because of the family history. Is there anything else that you’d like to know?”
“Well,” began Olga, “the fact that we both have these diseases in our family and there is a chance that we could pass them on to our children has opened our eyes a little bit, but we’d also
like to know if you can predict other diseases that don’t run in our family. Like my best friend in high school had cystic fibrosis and she died when she was only twenty four, and was sick almost all the time.”

“Okay, well, cystic fibrosis doesn’t look like it is in either of your family histories so it’s probably not worth worrying about. But, we can spend a little time going over the chance that you both carry a gene that has never before shown its face. The first step is we have to convert the family information you two have provided into a graphical representation called a pedigree. From there we can begin to correlate family relationships with the appearance of specific diseases.”

**Before Class on Thursday answer the following questions:**

1. What would a pedigree of Greg and Olga’s families look like? Concentrate simply on family relationships and affected persons.

2. What is the inheritance pattern for hemophilia (Factor VIII deficiency) and myotonic dystrophy?

3. Why does the counselor think that inheritance of cystic fibrosis is not a concern?

**Reference**

Human Genetics for First Year Students: Pedigree Construction

[http://www.uic.edu/classes/bms/bms655/lesson3.html](http://www.uic.edu/classes/bms/bms655/lesson3.html)