Genetic Testing for Huntington’s Disease

Part 1: A Family Disease

Jenny’s grandmother died of Huntington’s disease. Her parents never talked much about her grandmother’s illness. It was like a “family secret” that nobody wanted to talk about.

Now that Jenny is 18 years old, her mother wants her to see a doctor so she can get a genetic test for Huntington’s disease. Jenny doesn’t understand why her mother insists that she get the genetic test.

Jenny is very worried. She did not realize that she might get Huntington’s (HD) disease from her grandmother. She wonders how she could get HD when her parents don’t have any of the symptoms that her grandmother had.

Jenny did a bit of research on the Internet. Here is what she found out about Huntington’s disease.

Huntington’s Disease

Huntington's disease (HD) is an inherited disease that gradually destroys cells in certain areas of the brain. The loss of brain cells causes symptoms that include uncontrolled movements, loss of intellectual ability, and emotional disturbance.

HD is an inherited disease caused by a defective dominant gene that may be passed from parent to child. A person who inherits one HD gene will eventually develop the symptoms of Huntington’s disease. The symptoms of the disease typically begin at about age 40, but this varies from individual to individual.

The illness is progressive (gets worse with time). Some early symptoms of HD are mood swings, depression, irritability; along with trouble driving, learning new things, remembering facts, or making decisions. As the disease progresses, patients develop uncontrolled body movements that become progressively worse.

At this time, there is no cure for HD. Physicians can prescribe medications to help control the emotional and movement problems associated with HD. These medications have side effects and do not slow or stop the progression of the disease. Persons with HD usually live about 20 years after first showing symptoms.

A genetic test for the HD gene, along with a complete medical history and other medical tests, helps physicians diagnose HD. The genetic test may also be used to determine if a person with a family history of HD has inherited the dominant gene and is likely to develop the symptoms of HD later in life.
1. List three symptoms of HD (Huntington’s disease).

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2. What causes the symptoms of HD?

_________________________________________________________________________
_________________________________________________________________________

3. Jenny’s father doesn’t have any symptoms of HD. Does this mean that he does not have the defective gene that causes HD?

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4. Why might a person who doesn’t have symptoms of Huntington’s disease consider genetic testing?

_________________________________________________________________________
_________________________________________________________________________

5. Many people with a family history of Huntington’s disease spend years thinking about whether or not to get the genetic test. Would you want to have a gene test that told you whether or not you had the gene for Huntington’s disease? Explain why or why not.

_________________________________________________________________________
_________________________________________________________________________
_________________________________________________________________________

6. If you were Jenny, list three questions you would have about Huntington’s disease and genetic testing?
   • ______________________________________________________________________
   • ______________________________________________________________________
   • ______________________________________________________________________
Learn more about Huntington's disease and genetic testing by visiting the following websites:

- **Huntington's Disease: Hope Through Research**

- **Your Genes Your Health: Huntington's Disease**
  http://www.ygyh.org/hd/whatisit.htm
  Be sure to click on the headings in the bar on the left!

- **The Huntington's Disease Outreach Project for Education**
  http://www.stanford.edu/group/hopes/
  Be sure to click on the bars at the top of the page!

- **Huntington's Disease Story**
  http://vids.myspace.com/index.cfm?fuseaction=vids.individual&videoID=2014772897
  A video about a family with Huntington's disease.
Part 2: Jenny’s Chances

When Jenny asks what her chances of getting Huntington’s disease are, her family doctor suggests that she talk with a genetic counselor. Genetic counselors are trained specialists who help people understand information about genetic diseases that run in their families.

The genetic counselor explains that Jenny’s grandmother had one defective “H” gene for Huntington’s disease and one normal “h” gene. Her grandfather did not have Huntington’s disease, so he probably had two normal “h” genes.

The genetic counselor tells Jenny that she can’t inherit the gene “H” for Huntington’s disease unless her father inherited an “H” gene from his mother. So, Jenny’s first question is “What is the chance that my Dad got the Huntington’s disease gene from my grandmother?”

To answer her question, the genetic counselor hands Jenny two bags that contain beads to represent genes. She explains that Jenny’s grandmother has both “H” genes and “h” genes. Therefore, when her grandmother produced gametes (eggs), half of her eggs will each carry one “H” gene and half of her eggs will each carry one “h” gene. Jenny’s grandfather does not have Huntington’s disease, therefore he only produced gametes (sperm) that each carry an “h” gene.

The beads in the red bag represent gametes (eggs) produced by Jenny’s grandmother. The red bag contains equal numbers of black beads and clear beads.

- The black beads represent eggs that carry the defective “H” gene that causes Huntington’s disease.
- The clear beads represent eggs that carry the normal “h” gene.

The beads in the blue bag represent gametes (sperm) produced by Jenny’s grandfather. This bag contains only clear beads to represent sperm that carry one normal “h” gene.

The genetic counselor explains that each of Jenny’s grandparents contributed one H gene or one h gene to each of their children. She asks Jenny to randomly draw one bead out of each bag (without looking inside the bag) and combine the two beads to represent one possible “offspring.”

Jenny is very upset when she draws a black bead (H gene) out from the “Grandmother” bag and a clear bead (h gene) from the “Grandfather” bag. She asks, “Does that mean my father has Huntington’s disease?”
The genetic counselor gives Jenny a data table (like the one below) and asks her to fill in the first row by:

- Recording the black bead (H gene) drawn out from the “Grandmother” bag.
- Recording the clear bead (h gene) drawn out from the “Grandfather” bag.
- Putting an X in the box (Hh) that represents the genes that the offspring received.

**Data Table: Possible Offspring**

<table>
<thead>
<tr>
<th>Number of draw</th>
<th>Genes</th>
<th>Offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Jenny’s draw)</td>
<td>H</td>
<td>h</td>
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<tr>
<td>2</td>
<td></td>
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<td>10</td>
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</table>
The genetic counselor then asks Jenny to complete the data table by randomly drawing beads from the “Grandmother” and “Grandfather” bags, and filling in the remaining boxes.

1. Follow these instructions to finish filling in the data table:
   - Draw one gene out from the “Grandmother” bag and record it as black (H) or clear (h).
   - Draw one gene out from the “Grandfather” bag and record it and record it as black (H) or clear (h).
   - Put an X in the correct “Offspring” box to represent the two genes in the offspring (HH, Hh, or hh).
   - Put the beads back in the same bag they came from (Hint: be sure that any black beads go back into the “grandmother” bag)
   - Repeat until the data table is complete

2. Explain why there are no HH offspring.

_________________________________________________________________________
_________________________________________________________________________
_________________________________________________________________________

3. How many of the offspring in your data table are hh? __________

4. How many of the offspring in your data table are Hh? __________

5. Calculate the percentage (%) of the offspring in the data table that have the Hh genes that lead to Huntington’s disease.

\[
\text{Number of Hh offspring} \times 100 = \frac{\text{Number of Hh offspring}}{\text{Total number of offspring}} \times 100 = \text{___}\% \text{ of Hh offspring}
\]

6. Calculate % of the offspring in the data table that have the hh genes and do not have Huntington’s disease.

\[
\text{Number of hh offspring} \times 100 = \frac{\text{Number of hh offspring}}{\text{Total number of offspring}} \times 100 = \text{___}\% \text{ of hh offspring}
\]
Jenny asks, “So if I continue drawing pairs of beads many times, I’d probably get about 50% of offspring with Huntington’s disease and 50% healthy. That means it’s kind of like flipping a coin—heads you get the gene, tails you don’t.”

“But two of my father’s sisters have Huntington’s. Does that mean that my father has a better chance of inheriting the gene or not inheriting the gene?”

7. Does having siblings (brothers or sisters) with Huntington’s disease mean that a person is more likely to inherit a defective HD gene?

_________________________________________________________________________
_________________________________________________________________________
_________________________________________________________________________

8. Would it be possible for all of Jenny’s grandmother’s children to get a defective gene that causes Huntington’s disease?

_________________________________________________________________________
_________________________________________________________________________
_________________________________________________________________________

9. If Jenny’s father has the Huntington’s disease gene, what are the chances that Jenny will develop Huntington’s disease when she gets older? _________%

10. If Jenny’s father does not have the Huntington’s disease gene, what are the chances that Jenny will develop Huntington’s disease when she gets older? _________%
Part 3: Jenny’s Family History

Jenny knows that the defective (H) gene that causes Huntington’s disease is a dominant gene. If a person has one defective (H) gene, that person will have Huntington’s disease. Jenny hopes that she got two normal genes!

Jenny’s father refuses to be tested to see if he has the dominant gene that causes Huntington’s disease. She wonders if she should get the genetic test. She also wonders if her brother (Jeremy) or other members of her family should consider getting tested to see if they have the defective (H) gene.

The genetic counselor asked questions about Jenny’s family and recorded the information to create a pedigree chart. Jenny explains that none of her mother’s relatives have Huntington’s disease. But, her grandmother (her father’s mother) and two of her aunts (her father’s sisters) have Huntington’s disease. Here is the pedigree chart that the genetic counselor created to represent Jenny’s father’s family.

**Pedigree Chart for Jenny’s Father’s Family**

<table>
<thead>
<tr>
<th>Key:</th>
<th>Huntington’s Disease</th>
<th>NO Huntington’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Female</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**Row 1**

Grandmother [ ]
Grandfather [ ]

**Row 2**

Dad [ ]
Mom [ ]
Frank [ ]
Ann [ ]
Mary [ ]
Jane [ ]
Alice [ ]
Joe [ ]

**Row 3**

Jenny [ ]
Jeremy [ ]
Uncle Frank’s Children [ ]
Aunt Alice’s Children [ ]
1. Jenny’s grandmother had Huntington’s disease, so you know she has one “H” gene that causes Huntington’s disease and one “h” that does not cause Huntington’s disease. Write \( Hh \) in the circle for Jenny’s grandmother.

2. Jenny’s grandfather did not have Huntington’s disease. What genes did he most likely have—\( HH \), \( Hh \), or \( hh \)? Write the genes in the square for Jenny’s grandfather in the pedigree. Explain your answer.

_________________________________________________________________________
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Row 2 on the pedigree chart represents Jenny’s father, his siblings (brothers and sisters) and their spouses (husbands and wives).

3. Which of the individuals in Row 2 are Jenny’s father’s siblings? Explain your answer.

_________________________________________________________________________
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4. Jenny’s Aunt Mary and Aunt Alice have been diagnosed with Huntington’s disease. Write the appropriate genes (\( HH \), \( Hh \), or \( hh \)) in the circles for Mary and Alice.

5. None of the spouses (husbands and wives) of the family members in Row 2 have a family history of Huntington’s disease. They are unlikely to have the gene that causes Huntington’s disease. Write the appropriate genes (\( HH \), \( Hh \), or \( hh \)) in each of the circles and squares representing the spouses in Row 2 (Mom, Ann and Joe).

6. Uncle Frank had a genetic test for Huntington’s disease. His genetic test revealed that he does not have the gene that causes Huntington’s disease. Write the appropriate genes (\( HH \), \( Hh \), or \( hh \)) in the square for Frank.

7. Jenny’s father is 40 years old and Jenny’s Aunt Jane is 42 years old. Neither of them has shown any symptoms of Huntington’s disease. Does this mean that they definitely do not have the gene for Huntington’s disease? Explain your answer.

_________________________________________________________________________
_________________________________________________________________________
Row 3 on the pedigree chart represents Jenny, her brother Jeremy, and her cousins.

8. Is it possible that some of Aunt Alice’s children could develop Huntington’s disease? Explain your answer.

_________________________________________________________________________
_________________________________________________________________________

9. Is it possible that some of Uncle Frank’s children could develop Huntington’s disease? Explain your answer.

_________________________________________________________________________
_________________________________________________________________________

10. Is it possible that Jenny or Jeremy (Jenny’s brother) could inherit the gene for Huntington’s disease? Explain your answer.

_________________________________________________________________________
_________________________________________________________________________

11. Which members of Jenny’s family should consider getting genetic tests to determine if they have the defective (“H”) gene?

_________________________________________________________________________
_________________________________________________________________________

12. Why doesn’t Jenny’s mother need to be tested for the Huntington disease gene?

_________________________________________________________________________
Jenny thought that the genetic counselor would tell her to get the genetic test. But, the genetic counselor explained that genetic counselors don’t tell people what to do. They are trained to help people think about how getting tested, or not getting tested, might affect their future and their family.

The genetic counselor explains that it is important that Jenny NOT rush into getting a genetic test! Before Jenny makes a decision, she needs to understand what kinds of choices she has and what the consequences of these choices might be. Jenny should understand why some people decide to have genetic testing done and why other people decide to NOT get a genetic test.

The genetic counselor encourages Jenny to talk with her father and her brother (Jeremy) about genetic testing. Here’s is Jenny’s conversation with Dad and Jeremy.

1. Read the conversation below. As you read, use two different colors to underline (or highlight) the parts of the conversation that indicate:
   • reasons for getting genetic tests—one color
   • reasons for not getting genetic tests—a second color

   Hint: This is more fun if you can get three people to be readers and play the roles of Jenny, Dad, and Jeremy.

Jenny: Mom is really pressuring us to get tested, but we’re really having trouble deciding about this genetic testing.

Dad: Remember it’s not your mother’s choice or my choice. It’s one you and your brother need to make.

Jeremy: Dad, I don’t want to upset you, but we really need to understand why you never got tested. It’s important to hear your side of things before I make my decision.

Dad: It’s tough to explain. When the doctors figured out your grandmother had Huntington’s disease, there wasn’t any way to test for the HD gene. Once scientists developed the genetic test for the HD gene, I’m not sure why I didn’t get tested.

Jenny: But didn’t you want to know whether you had the gene or not?

Dad: Your mother used to tell me I hid from the problem, hoping it would go away. She wanted me to face the future and plan for it. But I didn’t think I could handle knowing.
Jeremy: It would have been very difficult to take care of Grandma knowing that you had the gene and might end up suffering like she did.

Dad: Even worse, I couldn’t bear thinking I might have passed the HD gene to either of you. I wish I’d known about Grandma’s illness before we had children.

Jenny: Wasn’t it worse to live with the uncertainty—to not know whether you had the gene?

Dad: Maybe, but there were other reasons why I didn’t want the test.

Jeremy: Like what?

Dad: I was afraid that other people might find out about my test results. Imagine what the airline I work for would do if they found out one of their pilots had the HD gene? What would my health insurance company do? There are some laws about privacy and discrimination but I wasn’t sure they would actually protect me.

Jeremy: One article I read said that people could avoid that kind of problem by paying for their genetic testing by themselves so their insurance company and employer wouldn’t find out the results.

Dad: But even if you do that, it would still be a risk to tell anyone the results of the test. Think about who you should tell, and then who they might tell. Your family? Your friends? Your teachers? Your coworkers? Keeping all this as a family secret was the safest thing for me to do.

Jenny: We know about family secrets. You and Mom raised us to say that Grandma had “mental problems.” We weren’t supposed to talk about Huntington’s. Now I understand that you and mom did that to protect us. But it would have been nice to be able to ask my friends for their advice.

Dad: And speaking of friends. If you find out you have the gene, what will you do if you start dating someone seriously? When should you tell that person? Or even should you tell them? Getting tested doesn’t stop the questions; it simply changes the questions that you need to deal with.

Jenny: Maybe I should wait to get tested until I’ve found a boyfriend that I’m really serious about. Or maybe I should even wait to get tested until after I’m married and want to have children. Then my husband could help me decide. Maybe by then they’ll have a cure.

Jeremy: Would that be fair to your future husband?

Jenny: No. I guess not. Talking to you has just made this more complicated. But I guess that’s good. It makes me realize that I really need to think about what my options are and what the benefits and risks are for those options.
Jeremy: Dad, we understand that if we get tested and one of us has the gene, then that means that you have the gene too. Is that going to be a problem for you?

Dad: Not really because there is something else you and Jeremy need to know. I have been having some problems lately. I’m getting angry and depressed more often. I’ve been noticing these small muscle twitches. I finally went to the doctor and he told me that these might be early signs of Huntington disease.

Jenny: We’re so sorry. We hope you’re wrong.

Dad: I’ve decided that I need to get the genetic test. But I think I know what the results will be.

Jenny: Will you let us know the results?

Dad: Yes, of course, if you really want to know. I’m glad you’re both seeing genetic counselors. The counselors will probably discuss things you should think about before you make your decisions.

Jeremy: My counselor is helping me make lists of benefits and risks for genetic testing. But I’m not sure that’s helping. It’s not a simple matter of just counting up which list has the most benefits or the fewest risks. And also it doesn’t answer the question of when should I get tested—now or when I’m older.

Jenny: We do understand that each of us may make a different decision. We need to choose based on what is important to each of us. But I worry about how my decision might affect my family and even my friends.

2. On the chart on the next page, make a list of the benefits and the risks of getting a genetic test for the gene that causes Huntington’s disease.

Be certain to complete the benefits and risks chart on the next page before you answer questions 3 and 4, below.

3. Not all benefits and risks are equally important to some people. On your chart:
   - Put an “X” in front of the one benefit and one risk that are very important to you.
   - Put an “O” in front of one benefit and one risk that are not important to you.

4. Do you think the benefits of genetic testing outweigh (are more important than) the risks of genetic testing? Explain why or why not.

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<tr>
<th><strong>Benefits</strong> of getting a genetic test for Huntington’s disease</th>
<th><strong>Risks</strong> of getting a genetic test for Huntington’s disease</th>
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Part 5: The Huntington Gene and the Genetic Test

The Huntington Gene

Huntington’s disease is caused by a mutation (a change in the DNA code) in the Huntington gene. The Huntington gene is located on the end of the chromosome number 4.

- On the normal Huntington gene (h) which does not cause the disease, there is a part of the DNA code that has between 11 to 35 copies of three DNA bases, CAG. These are called “CAG repeats” (example, CAGCAGCAGCAGCAG)
- On the mutated (defective) Huntington gene (H) which causes Huntington disease there is an increased number of CAG repeats. There are 40 or more CAG repeats in the mutated (H) gene.
- A Huntington gene with 36 to 39 CAG repeats may or may not lead to Huntington’s disease.

1. Which is longer, a normal Huntington gene (h) or a mutant (H) Huntington gene that causes Huntington’s disease?
2. Explain, in your own words, what a PCR machine does.

_________________________________________________________________________
_________________________________________________________________________

3. The counselor handed Jenny two bags that contain models that represent PCR copies of the Huntington gene from two people.

- Look at the two bags labeled “PCR Huntington Gene Copies from Person A” and “PCR Huntington Gene Copies from Person B.”
- Which person (A or B) do you think has the gene for Huntington’s disease? Explain how you could tell.

_________________________________________________________________________
_________________________________________________________________________

**PCR (Polymerase Chain Reaction)**

The genetic counselor said that scientists could take a drop of Jenny’s blood and use a special machine, called a PCR (polymerase chain reaction) machine, to make many copies of the DNA in her Huntington genes.
4. What does the process of gel electrophoresis do?

Gel Electrophoresis

The genetic counselor explains that the PCR gene copies in a sample are too tiny to be seen. But scientists use a process to visualize the size of the PCR gene copies, called gel electrophoresis. Gel electrophoresis separates the DNA molecules according to their size.

When scientists use gel electrophoresis to test PCR gene copies, they:

- Put the DNA sample (gene copies) from one person into a well on an agarose gel. This gel looks like a piece of Jell-O.
- Put the gel into a box filled with a liquid that conducts electricity.
- Turn the electricity on. The electricity causes the gene copies to move out of the wells to form bands at specific places in the gel.

How far the DNA in the sample moves in the gel depends on how large the DNA copies are.

- The DNA copies of normal genes are small so they move farther down the gel.
- The DNA copies of the mutant genes that cause HD are larger so they don't move as far as the normal genes.
5. Which lane (1, 2 or 3) on the gel diagram on the previous page:
   - Contains only long DNA pieces? ________
   - Contains DNA from a person who has both \( H \) and \( h \) genes? ________
   - Contains DNA from a person who does not have genes for Huntington’s disease? ________

Jenny, Jeremy, and their father have decided to undergo genetic testing for Huntington’s disease. A laboratory technician has collected DNA and copied Huntington gene (DNA) samples from Jeremy, Jenny, and Dad. These samples were placed into wells on a gel and the electricity was turned on so that the gene copies moved through the gel.

6. Your lab kit contains a simulated “Electrophoresis Gel for Jenny’s Family” that the technician has prepared. The graphic below shows whose DNA was placed in each of the wells.

   ![Diagram of gel wells]

   **Wells of the gel**
   - 1 – Jenny’s DNA sample
   - 2 – Jeremy’s DNA sample
   - 3 – Dad’s DNA sample

7. You can’t see the DNA (gene) pieces in the electrophoresis gel because DNA is not colored. If you add a DNA stain to the gel, the stain will make the DNA pieces in the gel visible.

8. Stain the “Electrophoresis Gel for Jenny’s Family” by following these steps:
   - Fill the clear plastic tray approximately \( \frac{1}{2} \) full with water.
   - Pour the contents of the “DNA Stain” tube into the clear plastic tray.
   - Use the stirrer to mix the contents of the tray for approximately 30 seconds.
   - Gently place the “Electrophoresis Gel for Jenny’s Family” into the DNA stain in the tray.

9. Observe the colored spots of DNA that appear on the gel. On the diagram of the gel (above), draw the results of the gene testing.
10. Use the information from the electrophoresis gel to complete the “Laboratory Report: Huntington's Disease Gene Testing” below.

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**Laboratory Report: Huntington’s Disease Gene Testing**

**Patient: Jenny Lanahan**

Results: (number of bands) ___________

Analysis: (circle one)
- Two Huntington's disease genes - HH
- Two normal genes - hh
- One Huntington's disease gene and one normal gene - Hh

Likelihood that patient will develop symptoms of Huntington's disease? (circle one)  
- Likely
- Uncertain
- Not likely

**Patient: Jeremy Lanahan**

Results: (number of bands) ___________

Analysis: (circle one)
- Two Huntington’s disease genes - HH
- Two normal genes - hh
- One Huntington’s disease gene and one normal gene - Hh

Likelihood that patient will develop symptoms of Huntington’s disease? (circle one)  
- Likely
- Uncertain
- Not likely

**Patient: James Lanahan (Dad)**

Test Results: (number of bands) ___________

Analysis: (circle one)
- Two Huntington’s disease genes - HH
- Two normal genes - hh
- One Huntington’s disease gene and one normal gene - Hh

Likelihood that patient will develop symptoms of Huntington’s disease? (circle one)  
- Likely
- Uncertain
- Not likely

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11. Now that Jenny, Jeremy, and Dad know the results of their genetic tests, there are many more decisions they may need to make or questions they may have in the future.

List two examples of decisions (related to Huntington’s disease) that each of the family members may need to make or questions they may have. Hint: You may want to read the “conversation” between Jenny, Jeremy and Dad again.

Jenny:
• ____________________________________________________________________
• ____________________________________________________________________
• ____________________________________________________________________

Jeremy:
• ____________________________________________________________________
• ____________________________________________________________________
• ____________________________________________________________________

Dad:
• ____________________________________________________________________
• ____________________________________________________________________