Activity 5

Making Decisions in the Face of Uncertainty

At a Glance

Focus: Students analyze a case study about a family's decisions related to testing for particular genetic variations that increase susceptibility to breast cancer and consider how understanding the related science can help people make decisions in uncertain circumstances.

Major Concepts: Our growing understanding of human genetic variation will allow us to identify genes that are associated with common diseases such as cancer. Genetic testing to identify individuals who have variations that make them susceptible to certain diseases can help people make decisions in uncertain circumstances and holds the prospect for more effective prevention and treatment. However, this capability also raises difficult questions that illustrate the personal and social implications of biological research.

Objectives: After completing this activity, students will

- recognize that our understanding of science can help us analyze and make decisions in uncertain circumstances;
- understand that the ability to identify susceptible individuals through genetic screening and testing holds the prospect for more effective prevention and treatment;
- understand that our ability to identify individuals susceptible to particular diseases also raises difficult questions about the uses of genetic information;
- be able to explain that although it is possible to analyze these questions rationally and civilly, people still may disagree on the answers; and
- understand that science can tell us what we can and cannot do, but we depend on an analysis of ethics and public policy (informed by a sound understanding of the science) to help determine what we should do.

Prerequisite Knowledge: Students should understand that cancer is characterized by uncontrolled growth of cells. Students also should understand that all cancer is fundamentally genetic because it results from the loss of genetic control of the cell cycle. That does not mean that all cancer is hereditary. The form of breast cancer that this activity addresses is one of the hereditary cancers, but it is responsible for only about 5 percent of all breast cancers. Most breast cancers arise from somatic mutations and thus are not hereditary.

Basic Science-Health Connection: This activity highlights the remarkable progress scientists are making in identifying genes related to multifactorial diseases such as cancer and focuses students' attention on the implications such discoveries have for personal health and decision making.

Introduction

This activity offers students the opportunity to apply their understanding of human genetic variation to a fictional case study involving a potentially painful set of decisions that various members of a family have to make. Teams of students analyze the case of a woman, Beth, who is concerned that she may carry a variant of either the *BRCA1* or *BRCA2* gene that predisposes to breast cancer. The case study is presented in five segments during which Beth makes two key decisions: (1) to proceed with being tested for altered forms of these genes and (2) after she develops cancer in one breast, not to have a prophylactic mastectomy of the other breast. Students analyze each segment by discussing a set of questions related to the underlying science and to the ethical and policy dilemmas raised by the decisions.

The activity's fundamental purpose is to help students see that an understanding of science and a clear, systematic analysis of options can help us make decisions in uncertain circumstances. Beth has a family history of breast cancer, a form of cancer that kills more than 40,000 women in the United States each year. Information about the presence of the altered gene could help her and her physician be more alert to the possibilities of her developing cancer.

On the other hand, she already is practicing the guidelines recommended to increase the chance of early detection should cancer develop. Furthermore, as students learn, breast cancer related to the presence of an inherited altered gene accounts for only 5 percent of the new cases of breast cancer diagnosed each year, and even if Beth is shown *not* to carry the altered gene, a certain risk of breast cancer remains. Thus, the decision whether to be tested is complex and is made more so by uncertainty related to the normal human genetic variation that exists among humans. Our understanding of genetic factors that can predispose individuals to certain cancers, while increasing, still is far from complete. The question about whether Beth should request prophylactic mastectomy of both breasts after she develops cancer in one breast is equally complex.

Materials and Preparation

You will need to prepare the following materials before conducting this activity:

- Master 5.1, *Making Decisions in the Face of Uncertainty* (make 1 copy per student)
- Master 5.2, *Analyzing the Issues* (make 1 copy per student)
- Master 5.3, *Reference Database* (make 1 copy per student)

Procedure

Tip from the field test. Teachers who tested this activity raised two cautions.

- Students became so engaged in Beth's story that they lost sight of the major messages about genetic variation and its relationship to complex disease. Remind your students that Beth's difficult decisions arise because of progress in basic science that allows us to detect such genetic variations.
- Students tended to confuse the test for mutations in the *BRCA1* and *BRCA2* genes with a test for cancer itself. Be sure to clarify this distinction. The

genetic test identifies forms of the *BRCA1* and *BRCA2* genes that can increase one's likelihood of developing cancer. It is not a test for cancer.

1. **Open the activity by asking students whether they know anyone who has had breast cancer. Invite those students who wish to briefly describe their relationship to the individual involved to do so.**

   With approximately 1 in 8 American women developing breast cancer in their lifetimes, it would not be unusual for one or more of your students to be involved personally with this type of cancer. It may be that the student's mother or another family member has had or currently has cancer. For some of those students, discussions of cancer may be disturbing. We suggest that you watch your students for signs of discomfort (for example, tearfulness, reluctance to begin the activity, unusual silence or reticence) and provide appropriate support.

2. **Distribute one copy of Master 5.1, *Making Decisions in the Face of Uncertainty*, to each student. Direct students to organize into teams and select students to read the parts of the various characters. Ask students simply to read the script completely through so they can get a sense of the complete case.**

3. **Distribute one copy of Master 5.2, *Analyzing the Issues*, and Master 5.3, *Reference Database*, to each student and explain that now the class will read the script again, one segment at a time. Suggest that students take notes and list questions that occur to them as they read each segment, then respond to the related questions on *Analyzing the Issues*. Discuss each segment in turn, as students complete it, using the questions on *Analyzing the Issues* as a guide. Address any other questions the students raise as well.**

   If students raise questions about the science or legal/policy issues that you and they cannot answer with the materials provided, suggest that someone pursue those answers outside of class.

Segment 1: Considering the Test

Question 1 What decision does Beth have to make?

Beth has to decide whether to have the test for mutations in her *BRCA1* and *BRCA2* genes. Your students might be interested in the financial aspects of the test. As of mid-1999, when this program was written, the laboratory cost for the combined test for *BRCA1* and *BRCA2* was about $2,500. The costs for the associated genetic counseling were about $250 to $300. Insurance coverage varies depending on the carrier.

Question 2 Who might be affected by Beth's decision?

Beth, her husband, her mother, her sisters, her teenage daughter, and her daughter's future husband (if she marries).

The identification of mutations that predispose individuals carrying them to cancer is an excellent example of how basic research in science yields results that benefit society. As students complete the activity, challenge them to think about the benefits that Beth and her family gain as a result of this knowledge. Ask students to summarize their ideas as you close the activity in Step 4.

Question 3 What arguments support having the test?

This is a good opportunity to make certain that the students understand the underlying science in this case study. Information provided in the *Reference Database* will help students learn about the science.

Beth no longer will be uncertain about her status with respect to *BRCA1* and *BRCA2*. She will be able to make some other decisions, and she will be able to inform other family members about whether they are at risk for carrying a mutated form of one of the genes. Note that Beth says, with respect to a potentially negative genetic test, "You find out that you're safe." Ask students to comment on this remark. Emphasize that this test identifies only one type of risk factor for breast cancer. Simply because one does not have the particular mutations identified in this test does not mean that one "is safe" from developing breast cancer. There likely are other unknown genetic variations that can increase one's risk. Furthermore, only a small proportion of breast cancer is hereditary. Beth's comment about birth control pills provides an opportunity to discuss the constantly changing nature of scientific knowledge and to point out the environmental contributions to cancer.

Question 4 What arguments support *not* having the test?

Beth may not want to know. She also will not have to worry about whether she should share potentially positive test results with other members of the family. She will not have to make tough decisions about detection and/or prevention options (for example, prophylactic mastectomy), none of which is 100 percent effective.

Question 5 What factors do you think Beth and Charlie should consider in making their decisions?

Answers will vary, but be alert for misconceptions about the underlying science.

Segment 2: A Family Question

Question 1 What new facts have you learned about breast cancer?

In testing for genes related to cancer, it is helpful to test a family member who already has had the disease. Not all cancers are heredity. The form of cancer that Beth's mother has may not be heredity. If it is hereditary, it may be associated with a gene not yet identified by scientists.

Question 2 What are some of the family issues that arise in this counseling session?

Beth's mother feels guilty about her breast cancer and about the possibility that she has passed on the associated mutation. The issue of blame also arises, as well as the question of what Beth will do with the information if the test is positive. Note that the counselor stresses the importance of privacy and confidentiality. Emphasize for your students

that genetic counselors are trained to handle the social and emotional aspects of counseling as well as the scientific aspects.

Question 3 What reasons does the genetic counselor give for not testing Jennifer? Do you agree that children under 18 should not be tested?

The counselor's reasons are rather nonspecific, simply that "teenagers often have different perspectives about developing breast cancer." Students' views on the testing of children under 18 will vary. Insist, however, that they provide concrete explanations for their positions and be alert to misunderstandings of the science.

The decision for a health care provider to conduct a genetic test is based on a variety of factors. Health care professionals are trained to reduce risks to their patients, including psychosocial risks. Anxiety and depression may arise in response to a positive test. A similar issue received attention in the mid-1980s, when health care professionals had to decide how to handle testing for exposure to the AIDS virus, HIV. At that point, the connection between a positive test for exposure to HIV and development of the fatal disease AIDS was not yet clear (although the correlation has since been established to the satisfaction of virtually all scientists). Keep in mind that not everyone who inherits an altered form of *BRCA1* or *BRCA2* develops breast cancer; thus, knowing that one carries such an allele may trigger needless anxiety.

Other factors that a health care provider considers when discussing genetic testing include the following questions:

- Can the related disorder, once diagnosed, be treated? In some cases, for example, Huntington disease, there are no treatments currently available that can help a person who tests positive.
- Does the patient exhibit symptoms, or is the order for a test based on family history alone?
- Do the benefits outweigh the harm brought about by knowledge of the test results?

The issue becomes even more complex when the patient to be tested is a minor, that is, under 18 years of age. The request for a genetic test may come from the parents or from the minor. When the minor is an adolescent, the issue becomes particularly complicated because the patient may exhibit a considerable degree of autonomy regarding his or her health care decisions. Experts agree that in these cases the primary goal of genetic testing should be to promote the child's well-being. For example, the child who tests positive may be overindulged or may be treated as a scapegoat. Both of these problems can occur, however, even in the absence of testing. The testing of a child (or indeed any other family member) also has implications for all members of the family. In some cases, this forewarning will be welcomed; in others, it may be

unwanted. Genetic testing of a child will ease some aspects of uncertainty, but people differ greatly in their response to such news.

In the case of genetic testing for mutations in the *BRCA1* gene, most health care providers and genetic testing centers adhere to a policy that denies tests to minors. This denial extends to requests from the parents, who are the legal guardians of the child's health. The psychological effects can be mixed. Whereas some individuals prefer the release from uncertainty, others could view a positive result as a death sentence and react in ways that are destructive to themselves or their families. Genetic testing requires informed consent, and some geneticists argue that this requirement automatically rules out children, and even teenagers, who generally are judged incapable of providing such consent. This view of minors, however, may be far too broad and may not be realistic. Some specialists are beginning to recognize that some adolescents and young children have sufficient autonomy in consent and decision making to make such decisions, and recommend that the desires of these youths should be taken into account. In any event, one must weigh the *balance* of potential harm and benefit in reaching a decision about testing a minor.

One outcome of the current policy is to delay the decision to test until the individual is an adult and can make the decision, rather than letting parents remove this option by making the choice themselves. Note that a *change* in policy most likely would result in *parents* being permitted to make the decision, rather than leaving the decision to the minor in question. Either way, issues of ethical decision making will arise.

Question 4 Beth's mother says, "I'm not sure more information is better." Do you agree with her? Explain your answer.

Answers will vary.

Segment 3: The Test Results

Question 1 Beth and her mother have had the genetic test. What new information have we learned?

Beth and her mother are positive for the *BRCA1* mutation. Beth has a lifetime risk of perhaps about 60 percent of developing breast cancer. This number is down from original estimates, which were as high as 87 percent. Some recent data sugggest an even lower risk figure than 60 percent. In fact, as is often true when a new medical test becomes available, the exact figure is still not yet known. Further, it appears that the exact risk figure may vary, depending upon the exact mutation in the *BRCA1* that an individual woman carries.

Students also have learned that Beth may *not* develop breast cancer even though her test was positive and that Beth can do a number of things (breast self-examinations and mammograms, for example) to help detect any cancer early and, therefore, to begin early treatment.

Remember to emphasize that Beth and her mother were tested for mutations in the *BRCA1* and *BRCA2* genes, not for cancer.

Segment 4: A Diagnosis of Breast Cancer

Question 1 What new information have we learned about Beth?

It is now three years after the genetic test, and Beth has been diagnosed with cancer in one breast. There is a high risk of cancer in the other breast.

Question 2 What major decisions do Beth and her husband discuss in this segment?

First, they discuss whether Beth should have both breasts removed, and second, they consider whether to tell Jennifer that she is at risk for the *BRCA1* mutation. Note that even removal of both breasts does not guarantee that the cancer will not appear elsewhere or even appear in the remaining breast tissue.

Question 3 What do you think Beth and Charlie should do? Why?

Answers will vary, but make certain that students provide sound explanations for their positions. Again, make sure that the science is correct.

Segment 5: Five Years Later

Question 1 What new information emerges in this segment?

Beth has had a lumpectomy, and Jennifer has not been tested. Emphasize that the chance of survival increases with early diagnosis.

Question 2 What is Jennifer's primary concern about the test?

She is concerned that potential employers and insurers will discriminate against her if they find out she has a high relative risk for breast cancer.

Question 3 Do you think employers or insurers should be able to deny employment or insurance to a person who has a genetic predisposition to a disease such as cancer? Explain your position.

Answers will vary. Inform students that at present many states have laws that prohibit health insurers from accessing and using genetic information in a discriminatory way. In addition, the federal Health Insurance Portability and Accountability Act (HIPAA) prohibits those who issue commercial, employer-based, group health plans from discriminating against individuals on the basis of information gained from genetic tests.

Regarding employment discrimination, the Equal Employment Opportunity Commission extends "Americans with Disabilities" protection to individuals who experience discrimination based on genetic information related to illness, disease, or other disorders.

4. Close the activity by challenging students to identify the questions that now face Jennifer, Beth's daughter, about her own health and personal welfare. Encourage students to think deeply about these questions. For each question that they identify as facing Jennifer, have them determine her options and begin to identify arguments that she might use in support of choosing one option over the other. Invite neighboring teams to discuss these questions. Then, use the following questions to stimulate a brief, final class discussion about the activity.

Use students' answers to these questions to assess their understanding of the activity's major concepts.

- **Our understanding of and ability to identify genetic differences among us has increased remarkably in the last few decades and continues to increase. How might Beth's and Jennifer's decisions have been different 50 years ago? What advantages does our knowledge of human genetic variation bring us? What questions does it also raise?**

  Fifty years ago, Beth and Jennifer would not have been faced with the decision about whether to have these genetic tests. They would have had the option of lumpectomy or radical mastectomy if cancer were discovered. Our increased knowledge of human genetic variation has improved our understanding of the relationship between certain variations and disease and enabled us to test for some of these genetic variations. New knowledge and abilities, however, raise questions about whether we should test and about what we should do with the resulting information. The ability to test also raises the question of whether we should or will come to treat people who are genetically predisposed to illness as if they already are sick, even if they are not and may never be. These people are sometimes referred to as the "asymptomatically ill."Ask the students to react to that designation.

Insist that students apply the saying to this activity. Then, to close the module effectively, ask students to apply the saying to our growing knowledge of human genetic variation (in general). Students should see that this knowledge offers us new opportunities and choices, but it also brings new challenges.

- **How does this activity illustrate the old saying that knowledge plus choice equals power?**

  The more we learn about a given situation—for example, our status with respect to the *BRCA1* and *BRCA2* genes—the greater our ability is to make decisions and control our own destiny, so long as the choices are available. The importance of choices emerges in this activity in at least two ways. First, Beth and Jennifer must be confident that information that results from the test will not be used against them. Otherwise they may feel, as Jennifer does, that they are not really free to chose whether to have the test. Second, the general policy not to test children under 18 for mutations in the *BRCA1* or *BRCA2* genes has restricted the choices for people under 18. This limits their access to knowledge about themselves and restricts their power to make decisions about their own lives.

Potential Extensions

Extend this activity by challenging students to connect what they learned in Activity 5 with what they learned in the two preceding activities. For example, ask students to connect Activity 5 with Activity 3 by suggesting how discovering mutations that predispose people to the development of cancer might help scientists develop new approaches to treating cancer. Then, assign students to learn more about this question by reading the article "Making headway against cancer" by J. Rennie & R. Rusting in the September 1996 special edition of *Scientific American*.

Likewise, connect Activity 5 with Activity 4 by asking students to research how discovering mutations that predispose people to the development of colon cancer has led to the creation of screening and counseling programs that are already saving lives by alerting people to their increased risk and helping them make good lifestyle and health care choices.

Making Decisions in the Face of Uncertainty

Characters
Beth
Charlie, Beth's husband
Genetic Counselor (GC)
Mother, Beth's mother
Jennifer, Beth's daughter

Segment 1: Considering the Test
Beth and Charlie at home

Charlie: Something is bothering you, Beth. What is it?

Beth: I just read a newspaper article about a test for a breast cancer gene. I guess with Mom's diagnosis, I'm worrying about it.

Charlie: But she's a lot older than you.

Beth: When mom was first diagnosed with cancer when she was my age. I remember it, I was 13 years old. It wasn't easy. And I never told you my grandmother died from ovarian cancer.

Charlie: So what did the article say?

Beth: Apparently there is a special kind of cancer that runs in families. If you have a certain form of this gene, you're at a high risk of getting breast cancer. Now they have a test for it.

Charlie: What do they mean . . . high risk?

Beth: I don't know. At least you know that you're more susceptible. Or you find out that you're safe.

Charlie: (Kindly) So go get the test if it'll put your mind at ease.

Beth: But that's just it. I don't know if it would make me feel safer. What if I find out that I do have it? I'll feel doomed.

Charlie: I think we should find out. As soon as possible. You've got a cloud hanging over you as it is.

Beth: A cloud! Do you know how worried I've been all these years? That's why I was so confused about taking birth control pills. At first, they thought it would increase the risk of getting breast cancer, so I didn't take them. Now, I read that it can actually lower the risk of ovarian cancer.

Charlie: Wouldn't you feel better if you knew for sure about that gene?

Beth: I just don't know.

Segment 2: A Family Question
Beth's mother, Beth and a genetic counselor at the genetic counselor's office

GC: I'd like to make sure we all understand what we are here to discuss.

Mother: It's because of me, isn't it?

GC: Beth is interested in having the *BRCA1* and *2* genetic tests. These tests help us identify women who have a genetic predisposition toward breast cancer and we find that we can get more information to help us understand Beth's situation if we first test family members who already have cancer.

Mother: I've already been through the ringer with this disease. What possible good is this test going to do for me?

Beth: This test is for me mother. I have a right to know . . . And for the sake of my family.

Mother: I'm already the family outcast, the one with this condition, who has passed it on to all of you.

Beth: No one is blaming you mother. This is just something our family has to deal with.

GC: Let's not get ahead of ourselves. The first step is to understand what such a test can tell you and then decide if this is information that you want to know.

Mother: What if the family doesn't want to deal with it. Your sisters, aunts and cousins might not want to know all this stuff. It'll be one more thing to have a big family ruckus over.

GC: You will decide who you want to tell. Now we will encourage you to tell your relatives because the information can be useful to them regardless of the result. I can help you think about how to tell them if you decide you want to.

Mother: And if I take the test and it turns out that my cancer was related to one of these mutations, what will you do?

Beth: Well, I'd continue to watch carefully for any signs of cancer, and I'd get Jennifer tested. She's my teenage daughter.

GC: I can understand your concern about your daughter. But there are several reasons why we do not offer testing to children under 18 years of age. The foremost being, that the test results won't change the care we give Jennifer.

Mother: The world has gotten so complicated. I don't know that more information is better. But you are right, I should get tested so that you can have a better idea of what to do. My sister has been wondering if she's at risk as well. After everything I've been through, I'll be able to handle this information.

Beth: I really appreciate this mom. I want to know. I'll either be relieved, or I'll have something real to worry about.

Segment 3: The Test Results

Beth and the genetic counselor in the genetic counselor's office

GC: Beth, the tests show that you and your mother have the *BRCA1* mutation.

Beth: Hmm. I had a feeling about this after my mother's test was positive. So what does this mean for my family and me?

GC: Two things. For your family, it means that you could pass this mutation to your children. For your own health, it means you have an increased risk of developing breast and ovarian cancer and possibly at a younger age.

Beth: Is there anything I can do about it, to improve my odds?

GC: You can continue to watch yourself closely and get regular checkups. We might want you to start having mammograms earlier than you normally would. If you do develop cancer, early detection greatly improves your chances that the treatment will be effective. In addition, some people consider preventive surgery, but that is a tougher decision to make.

Beth: I see. I know my sister is going to want to get tested. If her results are negative does that mean she is safe?

GC: If she doesn't have the mutation then she probably has about the same risk of developing breast cancer as other women without the mutation.

Beth: What about my children?

GC: Your son and daughter each have a 50 percent chance of having the mutation we see in your family. You probably will want to think about whether you want to share this information with them. Nothing at this time indicates that we would change their medical care in any way.

Beth: You're right. I need to think about all of this for a while. Jennifer would probably want to know. But my son is only 12. It might cause him to worry rather than help him.

GC: Take your time adjusting to this news. We can meet again to discuss how you're doing and what you want to tell your children. Do you have any concerns?

Beth: It's just that now I feel so different from other people.

GC: Everyone is different. Just as people vary in their physical appearance, they also vary in their susceptibility to disease. What you are feeling is perfectly normal. It may take a while for you to accept it. Give yourself some time. Talking with some of your family memebers, even your mother, may help.

Beth: At least now I know some of the cards I've been dealt.

Segment 4: A Diagnosis of Breast Cancer

Beth and Charlie three years later, in the living room

Charlie: I felt the oncologist was encouraging. It's really good that we caught it early.

Beth: Ever since Mom got her results, I knew I was going to have the mutation too. I knew this was going to happen.

Charlie: Well, it's just the roll of the dice.

Beth: Yeah, just chance . . . It was a relief that Aunt Susan tested negative for both genes. At least my cousins don't have to worry. And now that I know that I have cancer, I'm actually a little relieved.

Charlie: Relieved?

Beth: Now I can focus on something specific. You know, I'd been thinking about having both my breasts removed, even before the cancer. Now I have a real reason to do it.

Charlie: Beth, you've got to stay positive. Medicine is getting better. They have a whole treatment plan worked out for you. They said there wasn't any trace of cancer in the your other breast.

Beth: But the risk is high.

Charlie: Well, we have time to decide about that.

Beth: I know Jennifer is going to take this hard.

Charlie: She's a strong girl.

Beth: You know, we probably should tell her about my positive gene test too. I know we felt that she was too young when I got tested, but maybe now maybe she really should get the test.

Charlie: She's barely 19, she's doing so well in college. This is going to be a lot for her to handle all at once.

Beth: But I wanted to know everything I could.

Charlie: She's still young. We've got some breathing room. Let's just take things one step at a time.

Segment 5: Five Years Later

Beth and Jennifer in the kitchen

Jennifer: You seem to be back to your old self.

Beth: Yeah, I feel good. I didn't know it would take so long for my energy to come back.

Jennifer: You look great too.

Beth: Thanks. It's been a year since the lumpectomy and so far it looks like I've been cured. How about you? Have you given any more thought to the test?

Jennifer: Sure, I think about it. I'm young and I live my life like I'm at a high risk anyway.

Beth: You've been doing the self-checks?

Jennifer: Of course, once a month. And I go to the doctor twice a year. The nurses even know the name of my cat.

Beth: We were so worried about how you'd handle all this information.

Jennifer: Well, now I'm more worried about what other people know about me.

Beth: Other people like whom?

Jennifer: You know I've started interviewing for jobs.

Beth: They can't ask you about personal stuff, can they?

Jennifer: Maybe not, but after I'm hired I want to make sure that I get my health insurance. I don't want to go in with this test on my record.

Beth: That sounds like discrimination.

Jennifer: For the insurance companies it's just business. Anyway, I just don't need to know about this gene, at least not now.

Beth: It's up to you, but I can't help still being your mother.

Analyzing the Issues

Use this worksheet to take notes while you read the script, *Making Decisions in the Face of Uncertainty*, a second time. List any questions that occur to you. Be prepared to discuss these questions at the time your teacher indicates.

Segment 1: Considering the Test

1. What decision does Beth have to make?

2. Who might be affected by Beth's decision?

3. What arguments support having the test?

4. What arguments support *not* having the test?

5. What factors do you think Beth and Charlie should consider in making their decisions?

Segment 2: A Family Question

1. What new facts have you learned about breast cancer?

2. What are some of the family issues that arise in this counseling session?

3. What reasons does the genetic counselor give for not testing Jennifer? Do you agree that children under 18 should not be tested?

4. Beth's mother says, "I'm not sure more information is better." Do you agree with her? Explain your answer.

Segment 3: The Test Results

1. Beth and her mother have had the genetic test. What new information have we learned?

Segment 4: A Diagnosis of Breast Cancer

1. What new information have we learned about Beth?

2. What major decisions do Beth and her husband discuss in this segment?

3. What do you think Beth and Charlie should do? Why?

Segment 5: Five Years Later

1. What new information emerges in this segment?

2. What is Jennifer's primary concern about the test?

3. Do you think employers or insurers should be able to deny employment or insurance to a person who has a genetic predisposition to a disease such as cancer? Explain your position.

Reference Database

Breast Cancer—Causes

A person's cells contain a variety of genes that normally work together to control cell division so that more cells are produced only when the body needs them. The transformation of a cell from normal to cancerous requires that the cell experience several separate changes (mutations) in the genes that control division. When such changes occur in breast or other tissue, cells keep dividing even when new cells are not needed, and a tumor may form.

Breast Cancer—Definition

Cancer is a group of more than 100 diseases that occur when cells become abnormal and divide without control or order. This abnormal division may produce a tumor that can be benign (not cancerous) or malignant (cancerous). Malignant tumors can invade, damage, and destroy nearby tissues and spread to other parts of the body.

There are several types of breast cancer. The most common begins in the lining of the milk ducts of the breast. Another type begins in the lobules where milk is produced. If a malignant tumor invades nearby tissues (for example, lymph nodes in the area), it is known as invasive cancer.

Breast Cancer—Detection

The earliest sign of breast cancer is usually an abnormality that shows up on a mammogram (a special X-ray of the breast) before it can be felt by the woman or a health care provider. When breast cancer has developed to the point where physical signs and symptoms exist, these symptoms may include a lump, thickening, swelling, distortion, or tenderness in the breast, or skin irritation or dimpling.

The value of mammography is that it can help health care workers identify breast abnormalities that may be cancer at an early stage before physical symptoms develop. Many studies have shown that early detection increases survival and expands treatment options.

Most breast lumps are not cancerous, but only a physician can determine this. When a woman has a suspicious lump, or when a suspicious area is detected on a mammogram, further tests are typically done to make a definite diagnosis.

Breast Cancer—Incidence

Breast cancer is the most frequently diagnosed nonskin cancer and the second most common cause of death for American women. Approximately 178,000 new cases of invasive breast cancer were expected to be diagnosed in the United States in 1998. This number translates to an incidence rate of about 110 cases per 100,000 women.

About 1,600 new cases of invasive breast cancer were expected to be diagnosed in men.

Breast Cancer—Managing Risk

What are the options available to a person who is found to have a mutation in a *BRCA1* or *BRCA2* gene? The National Cancer Institute (NCI) lists the following options:

Surveillance. If cancer develops, it is important to detect it as soon as possible. Surveillance methods for breast cancer may include mammography and a clinical breast examination. Some health professionals recommend self-examination, but this should not be used to replace clinical exams. Surveillance for ovarian cancer include pelvic ultrasound, certain blood tests, and clinical examination. Surveillance can sometimes help detect cancer at an early stage, but it does not guarantee a cure if cancer is found.

Prophylactic surgery. This type of surgery involves the removal of as much of the at-risk tissue as possible in order to reduce the chances of developing cancer. Preventive mastectomy (removal of healthy breasts) and oophorectomy (removal of healthy ovaries) are not, however, a guarantee against developing cancer.

Risk avoidance. Particular behaviors that are believed to decrease cancer risk include limiting alcohol consumption and increasing regular exercise. Research results on the benefits of these behaviors are based on studies in the general population; the effects of these actions on people with *BRCA1* or *BRCA2* mutations are unknown.

Chemoprevention. This approach uses medication (such as tamoxifen) and micronutrients (such as dietary retinoids, vitamin E, and selenium) to reduce the risk of developing cancer. Tamoxifen is a drug used to prevent a recurrence of cancer in women who already have been diagnosed with cancer. In these women, tamoxifen has also been shown to reduce the risk of new cancers from developing in the other breast. Studies are currently underway to determine whether high-risk women in the general population can benefit from taking tamoxifen as a prevention for breast cancer.

Gene therapy. At present, mutated genes cannot be repaired. Some day, however, it may be possible to fix or manipulate the genes or sets of genes that cause or increase one's risk of cancer and other diseases.

Breast Cancer—Related Genes

Approximately 5 to 10 percent of women with breast cancer have a hereditary form of the disease. These women have inherited an altered form of one of the several genes involved in the control of cell division. For example, scientists believe that inherited mutations in the *BRCA1* and *BRCA2* genes are involved in 30 to 70 percent of all inherited cases of breast cancer. Although inheriting one of these mutated genes does not guarantee that a woman will develop breast cancer, it does increase her risk.

Scientists now have tests that can detect mutated *BRCA1* and *BRCA2* genes with 90 to 95 percent accuracy. Current technology has limited sensitivity and will miss some mutations. However, when someone with a cancer diagnosis and a family history of the disease has been tested and found to have a mutated *BRCA1* or *BRCA2* gene, the family is said to have a "known mutation." Others in the family can now be tested to see if they have that mutation. Once a mutation is identified within a family, the testing of relatives at risk is close to 100 percent accurate.

A positive test indicates that a person has inherited a known *BRCA1* or *BRCA2* mutation and has an increased risk of developing breast and ovarian cancer. In addition, evidence from several studies has shown that a man with a mutated *BRCA1* or *BRCA2* has a small increased risk of developing prostate cancer. However, a positive result only provides risk information and does not indicate whether or when cancer might develop. A positive result also does not provide any information about how a woman will respond to medical treatment should cancer be diagnosed. **It is important to note that many, but not all, women who inherit a mutated *BRCA1* or *BRCA2* gene will develop breast or ovarian cancer.**

Both men and women who inherit a mutated gene, whether or not they develop cancer themselves, can pass the mutation on to their sons and daughters.

A negative *BRCA1* or *BRCA2* test will be interpreted differently, depending on whether a family mutation is known. If a known mutation is not found in certain family members, those individuals do not have an increased risk for breast cancer based on family history and cannot pass the family risk on to their children.

However, in cases where no *BRCA1* or *BRCA2* mutation has previously been identified in a family, a negative test is not very informative. It is not possible to tell whether the person actually has a mutation but the test missed it (false negative) or whether the result is a true negative. Furthermore, a woman may have a mutation in a gene other than *BRCA1* or *BRCA2* that increases her cancer risk, but is not detectable by this test.

Breast Cancer—Risk Factors

Overall, American women have a 1 in 8 chance of developing breast cancer sometime in their lifetimes.

No one knows why some women develop breast cancer and others do not. Over the years, however, researchers have identified certain characteristics, called risk factors, that influence a woman's chance of developing the disease. For example, the risk of developing breast cancer increases with age. The risk also is higher in women who have a personal history of breast cancer or a family history of breast cancer. Other factors that can increase a woman's risk of developing breast cancer include early onset of menstruation, late menopause, recent use of oral contraceptives, and never having children or having the first live birth at a late age.

Most women will have one or more risk factors for breast cancer. However, many women who develop breast cancer have no known risk factors other than growing older, and many women with known risk factors do not get breast cancer.

Breast Cancer—Survival

The five-year survival rate for localized breast cancer (cancer that has not spread) has increased from 72 percent in the late 1940s to more than 95 percent today.

If the cancer has spread regionally, however, the five-year survival rate is 76 percent. If it has spread to distant sites, the rate is 21 percent.

Breast Cancer—Treatment

Depending on the medical situation and the patient's preference, treatment may involve lumpectomy (removal of the tumor) and removal of the lymph nodes under the arm; mastectomy (removal of the breast) and removal of the lymph nodes under the arm; radiation therapy; chemotherapy; or hormone therapy. Sometimes two or more treatment approaches are used in combination.