

Living With Her Genes: Early Onset Familial Alzheimer's Disease

by

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Part I—Confronting the Future

Suzanne, a woman in her early 30s, has learned the devastating news that her 38-year-old sister, Karen, has been diagnosed with early-onset familial Alzheimer's disease (EOFAD) through the use of a genetic screen. Karen started experiencing symptoms such as progressive memory loss, confusion, poor judgment, and language problems in her late 30s. Karen is no longer able to care for her two children and is in a nursing home, where she may live another 10 or more years, although her state will deteriorate with time. This is similar to what Suzanne's dad experienced before he died of Alzheimer's-related complications when he was just 42. Suzanne is distraught, both by the thought of losing her sister and by the fact that she may be carrying the gene for this disease herself. Since she is a genetic counselor, she understands the pattern of inheritance of the gene for this autosomal dominant hereditary disease, and its implications for her own life.

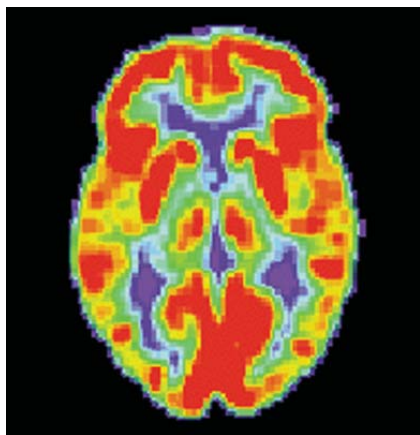
Scientists working on the Human Genome Project have identified three gene mutations responsible for EOFAD. Clinical testing for these mutations is available, and tests on Karen revealed that she has one of these mutations, called APP. This is a relatively rare mutation, affecting only 5% of people diagnosed with EOFAD. Suzanne knows that she has a 50% chance of having inherited this gene mutation herself. She and her husband, David, are struggling with the decision of whether Suzanne should be tested, since they know that no effective treatment or cure for EOFAD exists and the probability of having inherited the gene and remaining unaffected is very small. In addition, there are implications for insurance coverage, potential discrimination by employers, and the likelihood that family and social interactions will change. And, if Suzanne carries the gene, her children have the same 50% chance of inheriting it.

What should Suzanne do? Should she be tested?

Questions

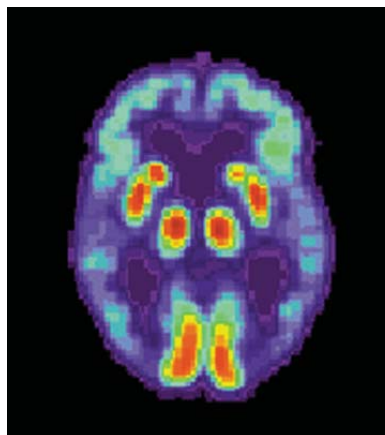
1. Who are the characters in this real-life scenario? What medical situation does each of them face? Draw a pedigree for this family, following the EOFAD trait.
2. Exactly what is Alzheimer's Disease? Is it the same as EOFAD? After looking at the PET scans in Figures 1 and 2 below and doing some reading, discuss how the brain is affected and how this leads to particular symptoms in Alzheimer's Disease.
3. What is a genetic counselor? What background/education does Suzanne have?
4. Who covers the cost of genetic testing? Is this approved by most insurance carriers? If the test is paid for by an insurance company, who owns the resulting information?
5. Why is this decision such a struggle for Suzanne and David? Explain how the implications noted at the end of Part I could impact the lives of Suzanne and her family.

Figure 1



PET scan of unaffected brain.

Figure 2



PET scan of Alzheimer's brain.

Resources

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Part II—A New Dilemma

Suzanne and David decided that Suzanne would take the diagnostic test. In preparing for a possible positive result, they increased the value of Suzanne's life insurance and purchased the best long-term care policy available. They also prayed together and promised each other that the test results would not change them, only prepare them for the future.

The doctor swabbed the inside of Suzanne's cheek to obtain some cells. The DNA was extracted from these cells and tested for the gene. Suzanne's test came back positive—she had inherited the gene mutation APP from her father. When they got the news, Suzanne reacted with tearful stoicism, David with stunned silence.

Suzanne and David now have a new dilemma. They have always wanted to have children, but understand that each of their children now has a 50% chance of inheriting the disease. In addition, it is likely that Suzanne will not be able to raise (or even recognize) her children as her disease progresses. This would have an impact on all of them—Suzanne, David, and any children they might have.

Should they have children?

Questions

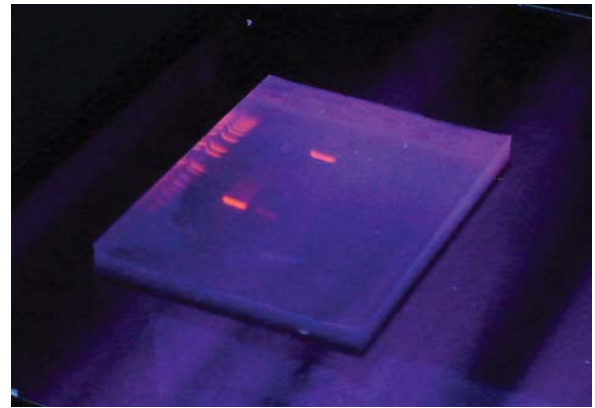
1. What role is played by meiosis, oogenesis, and spermatogenesis in human reproduction? How is it possible that 50% of Suzanne's eggs will be carrying the mutated APP gene?
2. What is DNA? A gene? An allele? How do genes determine traits?
3. The APP gene codes for a particular protein. Why does a mutated APP gene lead to problems in the brain? What are the two other genes (and their resulting gene products—the proteins) that, when mutated, can lead to EOAD? How does each protein play a role in brain function?
4. Suzanne and Karen are carrying a mutated APP gene that they inherited from their father. What is a mutation? How do mutations occur? Are mutations always passed along to the next generation? Explain.
5. The gene for this disease was located due to the efforts of scientists working on the Human Genome Project. What was the main objective of this project? How was it funded? Was it successful? Please explain.
6. How is genetic testing accomplished? How is the DNA extracted from the cells, and how are testing companies able to pinpoint particular alleles? What procedures, depicted in the photos below, are used to find genes? How does this work?

Figure 3



Polymerase Chain Reaction with extracted DNA.

Figure 4



Agarose gel electrophoresis of DNA fragments.

7. Why did Suzanne and David have to prepare for potentially negative ramifications?
8. What are the arguments for and against this couple having children? What ethical issues arise for this couple as they contemplate the future of their family?

Resources

Start by looking up information in your text and notes, especially for questions 1 and 2. Then use these additional sources to answer the questions in Part II.

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Part III—PGD?

Suzanne and David decided to have children. They wanted to ensure that their children would not inherit Suzanne's disease, and are now considering whether to utilize a process known as pre-implantation genetic diagnosis (PGD). This process involves *in vitro* fertilization (IVF) and genetic testing of the resulting embryos for the APP mutation. Only embryos without the mutated APP gene would be implanted. The others would be discarded.

Should Suzanne and David have PGD?

Questions

1. What is *in vitro* fertilization? Does it carry risk? How is the procedure accomplished?
2. Who has access to IVF/PGD? What would obstacles to access be? Are these procedures typically covered by insurance?
3. Do women egg donors undergoing IVF incur any risk? If yes, what might those risks be? What about the risks for the sperm donor? Why do people decide to continue with IVF knowing about potential risks?
4. What are the arguments/ethical issues surrounding this couple's use of IVF/PGD to determine the inheritance of this particular disease gene? If screening for disease genes is okay, is it also okay to screen for the sex of the child? If not, how would you describe the differences between the two types of screening? What about other traits, such as physical attributes and intelligence? Please explain.

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Part IV—Conclusion

Suzanne and David did undergo two cycles of PGD. In the first cycle, the two embryos tested were found to have the mutated APP genes. In the second cycle, four unaffected embryos were put into Suzanne’s uterus and one of those embryos successfully implanted. Genetic testing of this fetus through chorionic villi sampling at week 10 of the pregnancy confirmed that the baby did not have the APP mutation. Suzanne gave birth to a healthy baby girl in 2000.

Questions

1. What are typical IVF success rates? Please explain.
2. Do insurance companies typically pay for IVF? Why or why not? Are there some “conditions” that are covered and others that are not?
3. What is chorionic villi sampling (CVS)? How is it generally accomplished? How does CVS compare to amniocentesis as a form of obtaining fetal genetic information? Are there risks involved in either of these testing types?
4. What are possible next steps for this family? What strategies/agencies, etc., will they need to help them cope?

Resources

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