MENDELIAN GENETICS, PROBABILITY, PEDIGREES, AND CHI-SQUARE STATISTICS

INTRODUCTION

Hemoglobin is a protein found in red blood cells that transports oxygen throughout the body. The hemoglobin protein consists of four polypeptide chains, two alpha chains and two beta chains. Sickle cell disease (also called sickle cell anemia) is caused by a genetic mutation in the DNA sequence that codes for the beta chain of the hemoglobin protein. The mutation causes an amino acid substitution, replacing glutamic acid with valine. Due to this change in amino acid sequence, the hemoglobin tends to precipitate (or clump together) within the red blood cell after releasing its oxygen. This clumping causes the red blood cell to assume an abnormal "sickled" shape.

Individuals who are homozygous for the normal hemoglobin allele (HbA) receive a normal hemoglobin allele from each parent and are designated AA. People who are homozygous for normal hemoglobin do not have any sickled red blood cells. Individuals who receive one normal hemoglobin allele from one parent and one mutant hemoglobin, or sickle cell allele (HbS), from the other parent are heterozygous and are said to have the "sickle cell trait." Their genotype is AS. Heterozygous individuals produce both normal and mutant hemoglobin proteins. These individuals do not have sickle cell disease and most of their red blood cells are normal. However, due to having one copy of the sickle cell allele, these individuals do manifest some sickling of their red blood cells in low-oxygen environments. People with sickle cell disease are homozygous for the sickle cell allele (SS genotype); they have received one copy of the mutant hemoglobin allele from each parent. The resulting abnormal, sickle-shaped red blood cells in these people block blood flow in blood vessels, causing pain, serious infections, and organ damage.

PROCEDURE

1. Watch the film *The Making of the Fittest: Natural Selection in Humans*. While watching, pay close attention to the genetics of the sickle cell trait and the connection to malaria infection.
2. Answer the following questions regarding genetics, probability, pedigrees, and the chi-squared statistical analysis test.

QUESTIONS

MENDELIAN GENETICS AND PROBABILITY

1. If two people who have the sickle cell trait have children, what is the chance that a child will have normal red blood cells in both high- and low-oxygen environments? What is the chance that a child will have sickle cell disease? Write the possible genotypes in the Punnett square.

In high- and low-oxygen environments:

Normal Red Blood Cells: ____________

Sickle Cell Disease: ____________

   a. What is the chance that a child will carry the HbS gene but not have sickle cell disease? ____________________

   b. What are the chances that these parents will have three children who are homozygous for normal red blood cells? (show work) ____________________________

   c. What are the chances that these parents will have three children who have both normal and mutant hemoglobin beta chains? (show work) ____________________________

   d. What are the chances that all three of their children will show the disease phenotype? (show work) ____________________________

   e. What are the chances that these parents will have two children with the sickle cell trait and one with sickle cell disease? (show work) ____________________________

   f. In the cross above, if you know that the **child does not have sickle cell disease**, what is the chance that he/she has the sickle cell trait? ____________________

2. An individual who has the sickle cell trait has children with an individual who does not have the HbS allele.

   a. What are the genotypes of the parents? _____________________

   b. Show all possible genotypes of their children in a Punnett square. State the genotype and phenotype ratios of the offspring.

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   c. What are the chances that any one of this couple's children will have sickle cell disease? ___________________

   d. If this couple lives in the lowlands of East Africa, what are the chances that one of their children would be resistant to malaria if exposed to the malaria parasite? __________________

3. If a woman with sickle cell disease had children with a man who has the sickle cell trait:

   a. What are the genotypes of the parents? ____________________

   b. What is the genetic makeup of the gametes the mother can produce? ___________

   c. What is the genetic makeup of the gametes the father can produce? ___________

   d. Show all possible genotypes of their children in a Punnett square and summarize the genotype and phenotype ratios of the possible offspring.

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   e. What are the chances that any one of this couple's children will have sickle cell disease?
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   f. If this couple moves to the lowlands of east Africa and has children, which of their children would be more likely to survive? Explain your answer.

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4. In humans, blood type is a result of multiple alleles: I^A, I^B, and i^O. A few simple rules of bloodtype genetics are: I^A is dominant over i^O. I^B is dominant over i^O. I^AI^B are codominant.
Two parents heterozygous for type A blood and who have the sickle cell trait have children. Answer the following questions:

   a. What is the genotype of the parents? ____________________

   b. What are the genetic makeup of all the possible gametes they can produce? ____________________

   c. Complete the dihybrid Punnett square to determine the frequency of the different phenotypes in the offspring. Note: Consider blood type and normal vs. mutant hemoglobin in the various phenotypes.

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5. Now, let's try a different way of solving a dihybrid cross. Because of Mendel's (2nd) Law of Independent Assortment, you can work with the blood-type gene and the hemoglobin gene separately. Set up two monohybrid crosses with the following parents: Mom is heterozygous for type B blood and has the sickle cell trait, while Dad has type AB blood and also has the sickle cell trait.

   a. What are the chances that a child of this couple will have type B blood and have the sickle cell trait? (show work)

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   b. What are the chances that a child will have type AB blood and will not have the sickle cell disease? (show work)

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   c. What are the chances that a child will have type B blood and have the sickle cell disease? (show work)

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   d. What are the chances that a child will have type B blood and at least some normal hemoglobin? (show work)

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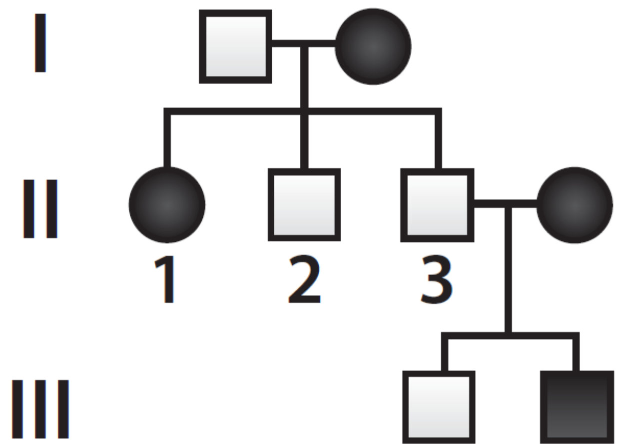
PEDIGREES

6. The following pedigree traces sickle cell disease through three generations of a family. Use the pedigree to answer the following questions.



a. What is the genotype of the father in the first generation? ____________________

b. What is the genotype of the daughter in the second generation? ____________________

c. What is the genotype of individual 3 in the second generation? How do you know?

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d. If the couple in the second generation has another child, what are the chances the child will have sickle cell disease? __________ Have the sickle cell trait? __________ Have completely normal hemoglobin? __________

e. If the entire family moves to the lowlands of East Africa, four of the five males in the pedigree will have two genetic advantages over the other individuals in the family. Explain the two advantages.

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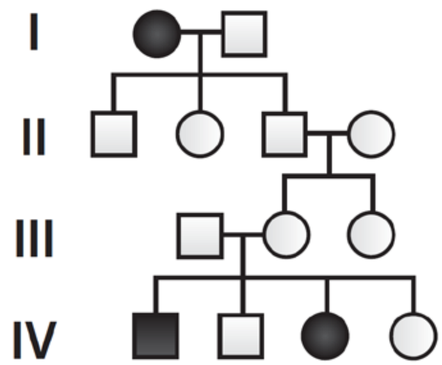
7. The following pedigree traces sickle cell disease through four generations of a family living in New York City. Use the pedigree to answer the following questions.



a. What is the genotype of the mother in the first generation? ___________

b. What are the possible genotypes of the father in the first generation? ___________

c. What can you say about the genotype of all the children of the couple in the first generation? Explain your answer.

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d. Regarding the answer to part c, based on where the family resides, why would this genotype be considered a disadvantage? ____

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e. What are the genotypes of the parents in the third generation?

Mother: _________ Father: _________ Explain how you know.

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f. What is/are the possible genotype(s) of the mother in the second generation? ___________

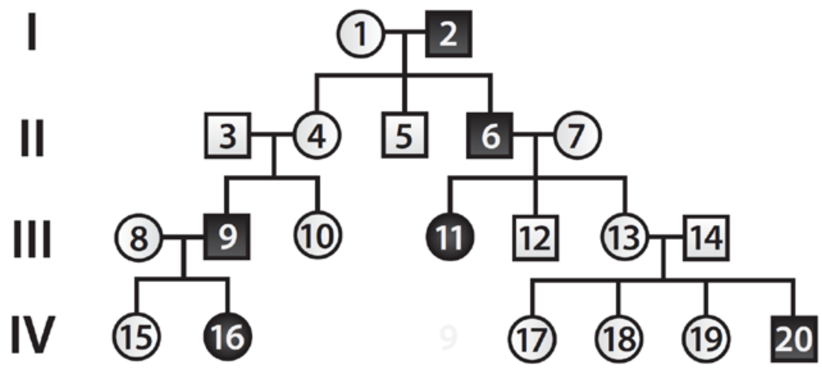
g. If the couple in the third generation has another child, what are the chances the child will have sickle cell disease? ___________

Have the sickle cell trait? ___________

Be homozygous for normal red blood cells? ___________

Be resistant to malaria and not have sickle cell disease? ___________

8. The following pedigree traces sickle cell disease through four generations of a family living in the highlands of eastern Africa. Use the pedigree to answer the following questions.



a. What are the genotypes of the following individuals? (If more than one genotype pertains, include all possibilities.)

Individual #1:	___________	Individual #10:	___________
Individual #2:	___________	Individual #13:	___________
Individual #7:	___________	Individual #17:	___________

b. If individuals 13 and 14 have another child, what are the chances that he or she will have sickle cell disease? _______________

c. If the same couple has 3 more children, what are the chances that the 3 kids will have the sickle cell trait? (show work) ____

d. Based on where this family lives, is the sickle cell trait genotype a genetic advantage? Explain.

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e. If individuals 8 and 9 have 4 more children, what are the chances two of them will be homozygous for normal red blood cells? Explain why.

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9. Imagine that you are a genetic counselor, and a couple planning to start a family comes to you for information. Jerome was married before, and he and his first wife had a daughter with sickle cell disease. The brother of his current wife, Michaela, died of complications from sickle cell disease, but neither of her parents has the disease.

    a. Draw a pedigree representing this family. Be sure to clearly label Jerome and Michaela.

    b. What is the probability that Jerome and Michaela will have a baby with sickle cell disease? (Note that neither Jerome nor Michaela have sickle cell disease.) Show your work.

10. Natasha and Demarcus are planning on having children. Each has a sister with sickle cell disease. Neither Natasha nor Demarcus nor any of their parents have the disease, and none of them has been tested to see if they have the sickle cell trait.

    a. Draw a pedigree representing this family. Be sure to clearly label Natasha and Demarcus.

    b. Based on this incomplete information, calculate the probability that if this couple has a child, the child will have sickle cell disease.