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

INTRODUCTION

Hemoglobin is a protein found in red blood cells (RBCs) 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 RBC after releasing its oxygen. This clumping causes the RBC 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 RBCs. 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 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 RBCs are normal. However, due to having one copy of the sickle cell allele, these individuals do manifest some sickling of their RBCs 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 RBCs in these people block blood flow in blood vessels, causing pain, serious infections, and organ damage.

MATERIALS

critical values table (see page 12)

PROCEDURE

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

what is hemoglobin?
what causes sickle cell anemia?
what does HBA stand for?
People who have the AA genotype have which phenotype?
what does HBS stand for?
People w/ genotype AS display which phenotype?
People w/ genotype SS display which phenotype?
List the alleles involved w/ SC disease.