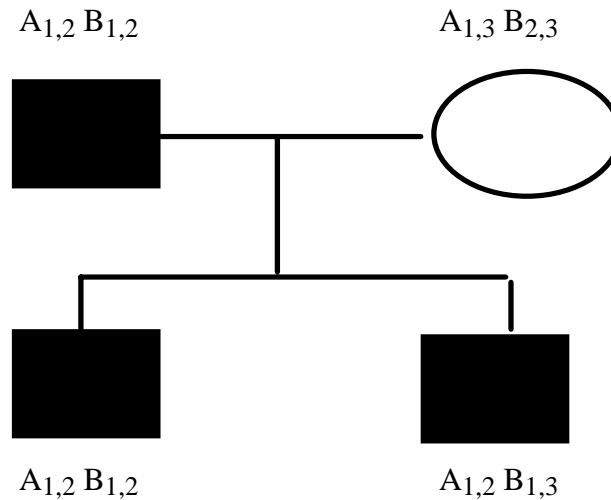


**Homework questions.** Please provide your answers on a separate sheet. These questions are mostly from lectures 15 and 16. Each question is worth one point unless stated otherwise.

1. (two points) Examine the following pedigree.



The  $A_1$  alleles in the two brothers are identical by state (this just means that they are both  $A_1$ ). The same is true of  $B_1$ . In either case can you infer that they are identical by descent? In other words, which alleles are identical by descent (neither,  $A_1$ ,  $B_1$ , or both)?

(Questions 2-8, one point each): Consider two populations, 1 and 2, that differ at two unlinked loci, A and B. In each population a specific allele is fixed at each locus (all individuals in population 1 have the genotype  $A_{1,1} B_{1,1}$  while all individuals in population 2 have the genotype  $A_{2,2} B_{2,2}$ ).

First, you cross a single male from population 1 with a single female in population 2.

2. What is the expected frequency of **each** of the nine possible genotypes in the F1 progeny?

The possible genotypes are

$A_{1,1} B_{1,1}$  ;  $A_{1,1} B_{1,2}$  ;  $A_{1,1} B_{2,2}$  ;  
 $A_{1,2} B_{1,1}$  ;  $A_{1,2} B_{1,2}$  ;  $A_{1,2} B_{2,2}$  ;  
 $A_{2,2} B_{1,1}$  ;  $A_{2,2} B_{1,2}$  and  $A_{2,2} B_{2,2}$

3. Is locus A at Hardy-Weinberg equilibrium in the F1 generation (your answer would be the same for locus B)?

4. Do the two alleles  $A_1$  and  $B_1$  show linkage disequilibrium (association) in this F1 generation? (consider the haplotypes that are transmitted by this F1 generation to the F2 generation).

5. What is the expected frequency of each of the nine possible genotypes in the F2 progeny (assuming random mating among the F1)?

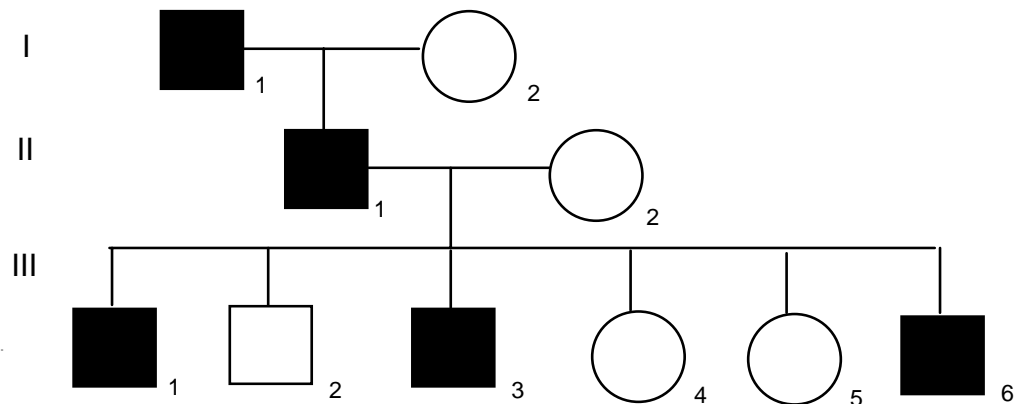
6. Is locus A at Hardy-Weinberg equilibrium in the F2 generation?
7. What is the frequency of each of the four possible haplotypes ( $A_1B_1$ ,  $A_1B_2$ ,  $A_2B_1$ , and  $A_2B_2$ ) in gametes transmitted from the F2 generation to the F3 generation?
8. Do the two alleles  $A_1$  and  $B_1$  show linkage disequilibrium in this F2 generation? (again, consider haplotypes transmitted to the next generation, the F3).

Later (questions 9-11), you allow a large and equivalent number of individuals from the two populations -- for example, 500 males and 500 females from population 1 and 500 males and 500 females from population 2 -- to mate at random (and they do mate at random).

9. Is locus A at Hardy-Weinberg equilibrium in the "F1" generation?
10. Do the two alleles  $A_1$  and  $B_1$  show linkage disequilibrium in this F1 generation?
11. If the "F1" generation again mates randomly, do  $A_1$  and  $B_1$  show linkage disequilibrium in the resulting F2 generation?

This pedigree shows a family affected by an autosomal dominant genetic disease.

Genotypes for three linked markers, A, B and C, are shown



Homework due at the **beginning** of class on **Tuesday, Nov. 14, 2006.**

**The exam will be Nov. 21. Homework will be returned on Nov. 16 at 11:10.**

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The genotypes are:

I-1        A<sub>1,2</sub> B<sub>1,2</sub> C<sub>1,2</sub>

I-2        A<sub>3,3</sub> B<sub>3,3</sub> C<sub>3,3</sub>

II-1       A<sub>1,3</sub> B<sub>1,3</sub> C<sub>1,3</sub>

II-2       A<sub>4,4</sub> B<sub>4,4</sub> C<sub>4,4</sub>

III-1      A<sub>1,4</sub> B<sub>1,4</sub> C<sub>1,4</sub>

III-2      A<sub>3,4</sub> B<sub>3,4</sub> C<sub>3,4</sub>

III-3      A<sub>1,4</sub> B<sub>1,4</sub> C<sub>3,4</sub>

III-4      A<sub>1,4</sub> B<sub>3,4</sub> C<sub>1,4</sub>

III-5      A<sub>3,4</sub> B<sub>3,4</sub> C<sub>3,4</sub>

III-6      A<sub>1,4</sub> B<sub>1,4</sub> C<sub>1,4</sub>

12. Indicate the phase of alleles in individual II-1 by showing his haplotypes. There are four possibilities. They are

a) A<sub>1</sub> B<sub>1</sub> C<sub>1</sub> / A<sub>3</sub> B<sub>3</sub> C<sub>3</sub>

b) A<sub>1</sub> B<sub>1</sub> C<sub>3</sub> / A<sub>3</sub> B<sub>3</sub> C<sub>1</sub>

c) A<sub>1</sub> B<sub>3</sub> C<sub>3</sub> / A<sub>3</sub> B<sub>1</sub> C<sub>1</sub>

d) A<sub>1</sub> B<sub>3</sub> C<sub>1</sub> / A<sub>3</sub> B<sub>1</sub> C<sub>3</sub>

13. (3 points; one point per pair of markers) For each individual in the third generation (III-1, III-2, III-3, III-4, III-5 and III-6) indicate whether they are recombinant, nonrecombinant or indeterminate for each pair of **markers** in this pedigree (e.g. draw a 6 by 3 table with six individuals on one axis and the three pairs markers (A and B, B and C and A and C) on the other. Fill in all 18 squares with yes or no..

14. Ignoring all of the other loci, calculate a lod score for linkage to of the disease to A with  $\theta = 0$

15. Now, assume that this disease is only 80% penetrant. What is the lod score for linkage to A with  $\theta = 0$  under this revised model?

16. Now, assume that the penetrance is 100%, but there is a probability of 5% of phenocopy (i.e. 5% of people who are not at genetic risk show the trait).

Now, what is the lod score for linkage to A with  $\theta = 0$

17. Ignoring all other loci, what value of  $\theta$  would give the highest lod score for linkage of the disease to B?