# Biology 321 Spring 2013 Assignment Set #3 *Pedigree Analysis*

➔ *You are responsible for working through on your own, the general rules of thumb for analyzing pedigree data to differentiate autosomal and sex-linked traits – see pedigree analysis guidelines in lecture material and Chapter 2 of text*

***Chapter 2 Reread Section 2. 6: Human Pedigree Analysis***
***Examine solved problems 2 & 3. Work problems 13, 14, 45, 51, 52, 57, 58, 64, 74, 79***

***Chapter 3*** ***Optional:*** *Read very interesting section on Organelle genes and look at striking pedigree on pg 109.*

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***Required Problem Assignments in 9th edition of text***
http://fire.biol.wwu.edu/trent/trent/assignmentset3.9.pdf

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## *Set 3 Problems sorted by analytical and/or content type*

***Sorting through the complexities of real data or ambiguous data: see also ambiguous pedigrees***
This problem set: 2, 3, 5

***Sorting through small data sets where progeny count will not necessarily match predicted probabilities for each phenotypic/genotypic class:*** see most pedigrees
This problem set: 2, 3, 11

***Basic Probability Product and Sum rules (see also combining pedigrees and probability)***
This problem set: 1

***Conditional probability (limiting the possible outcomes) --see also combining pedigrees and probability***
Text Chapter 2: Solved problem 2,
This problem set: 1

***Simple pedigree analysis***
This problem set: 4, 5

***Ambiguous pedigrees***
Text Chapter 2: 74,
This problem set: 4, 5, 6, 7, 8, 9, 10

***Factoring allele frequencies into pedigree analysis***
Text Chapter 2: 58, 74
This problem set: 3c&d, 4, 7, 8, 10

***Pedigrees and genotype assignment***
Text Chapter 2: 51, 52, 64, 79
This problem set: You should define allele symbols and assign genotypes while working through most of these problems --independent of whether they are specifically requested.

***Combining pedigrees and probability***
Text Chapter 2: solved problems 2 & 3; 51, 58, 79
This problem set: 8

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## Basic Pedigree Problems

Online Pedigree practice problems:
http://www.mansfield.ohio-state.edu/~sabedon/biol1128.htm

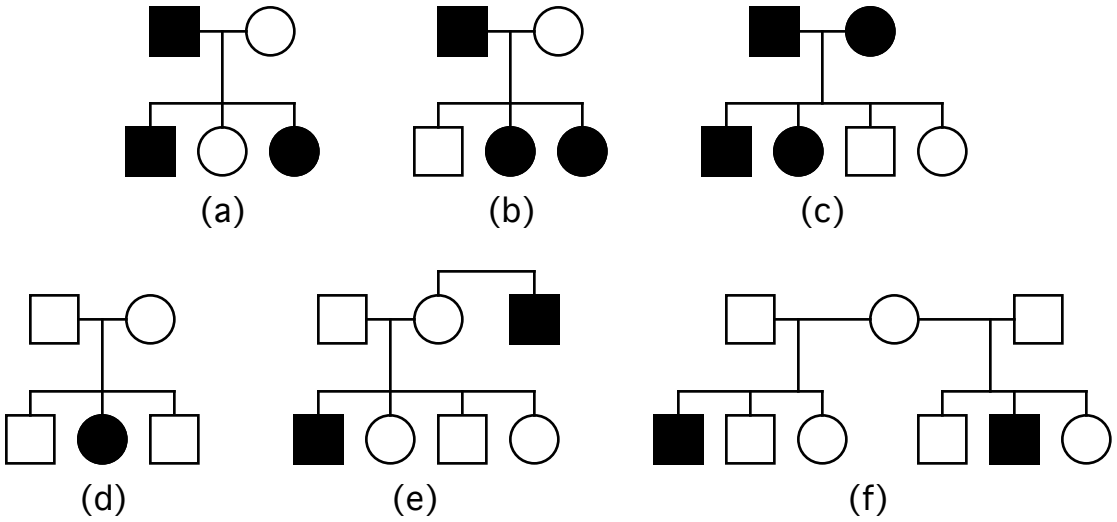
❖ **Problem 1** Two individuals are heterozygous for an autosomal recessive allele.
a. If they produce 3 offspring, what is the probability that all three progeny have the dominant phenotype? Show your work.
b. Three offspring are produced from this mating and all three have the dominant phenotype. *Given this outcome*, what is the probability that all three are homozygous for the dominant allele. Show your work.
c. If they produce 3 offspring, what is the probability that they have both types of progeny (dominant and recessive). NOTE: there is an easy way to work this (by extending your calculation f rom part a) Show your logic and work.

❖ **Problem 2** The guidelines given to you in class were designed to help you learn how to interpret pedigrees. Do not memorize these guidelines -- you should be able to generate each rule from the basic genetic principles of Mendelian and sex-linked inheritance. Look at each "rule" carefully. For a pedigree to be consistent with a specific mode of inheritance, which rules must be met? Which rules might apply, but are not absolutely required? Under which circumstances would the latter apply or not apply?

❖ **Problem 3**
**a.** Does a study of pedigrees always permit a person to determine whether an allele is dominant or recessive?
**b.** Why is it much easier to analyse human pedigrees for autosomal dominant traits than for autosomal recessive ones?
**c.** Why are parents of individuals homozygous for rare recessive alleles likely to be related?
**d.** Briefly discuss the conditions under which a recessive trait may appear to be inherited as a dominant one and vice versa and the precautions necessary in drawing conclusions from pedigree analysis.

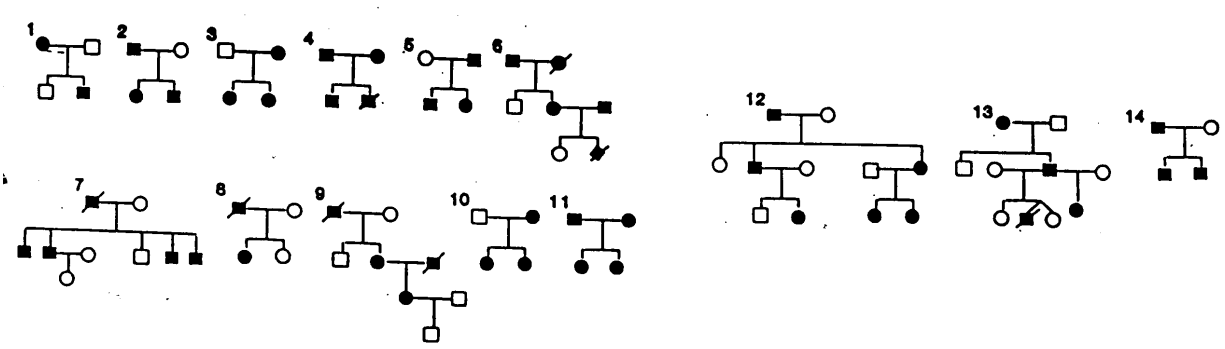
❖ **Problem 4**

What pattern(s) of inheritance can be ruled out for the following pedigrees? What is the most likely mode of inheritance in each case assuming that the trait is very rare?



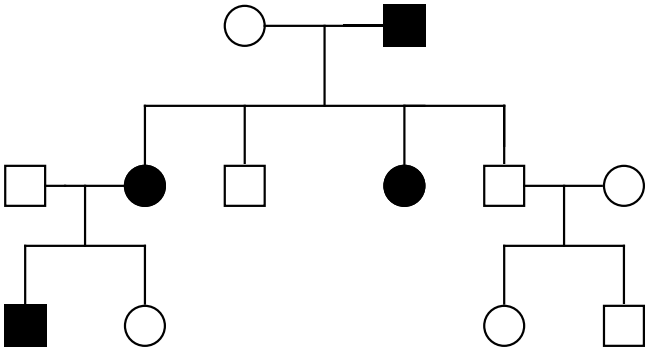

❖ **Problem 5** (i) Examine the pedigrees shown below. Pedigree #4 is:
a. consistent with autosomal recessive, autosomal dominant, X-linked dominant and X-linked recessive inheritance.
b. consistent only with autosomal recessive inheritance
c. eliminates autosomal dominant inheritance only because both progeny are affected
d. I don't agree with any of these statements

(ii) If all of the pedigrees are taken together and assuming no complications, the mode of inheritance of this disease state must be:
a. autosomal recessive
b. autosomal dominant
c. X-linked dominant d. X-linked recessive
e. more than one mode of inheritance is consistent with all of these pedigrees




## ❖ Problem 6

One day a man comes into the office of a genetic counselor. He is suffering from a very rare genetic disease. The genetic counselor puts together the following pedigree of the man's family. The genetic counselor then tells the man that he cannot pass the trait onto his sons, but that, even if he marries a normal woman, all of his daughters are out of luck: they will all have the genetic disease.



**(i)** What mode of inheritance did the genetic counselor imply with his advice to the man?

a. X-linked recessive b. autosomal recessive c. X-linked dominant
d. autosomal domiant e. Y-linked

**(ii)** Do you agree with the conclusions of the counselor and the advice that he gave?

a. Yes, since the trait is very rare, recessive inheritance is eliminated and the counselor's advice is sound.

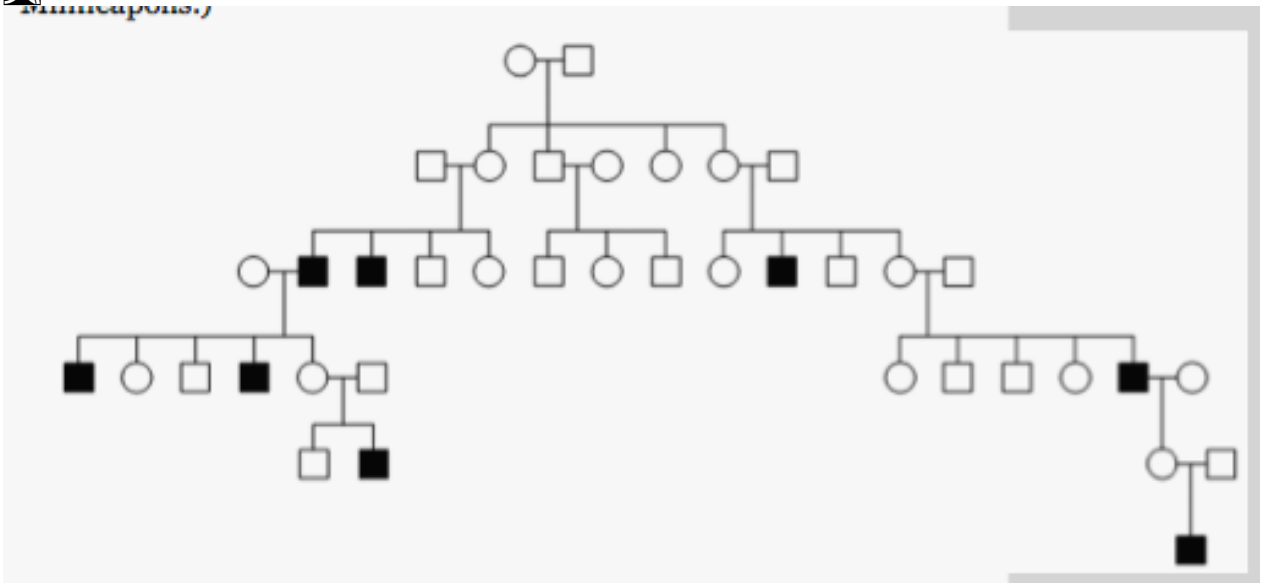
b. No. Recessive inheritance is still a likely possibility and the man should have been informed of that.

c. No. Autosomal dominant inheritance is clearly indicated. In that case, if the man marries a phenotypically normal woman, there is a 50:50 chance that any child would be affected.

d. Yes and no. The counselor has good reason to suspect X-linked dominant inheritance, but he should have also considered another mode of inheritance as a possibility.

e. Yes and no. The counselor was correct in his conclusion about the mode of inheritance, but incorrect in his predictions about the possible progeny of the man.

## Problem 7

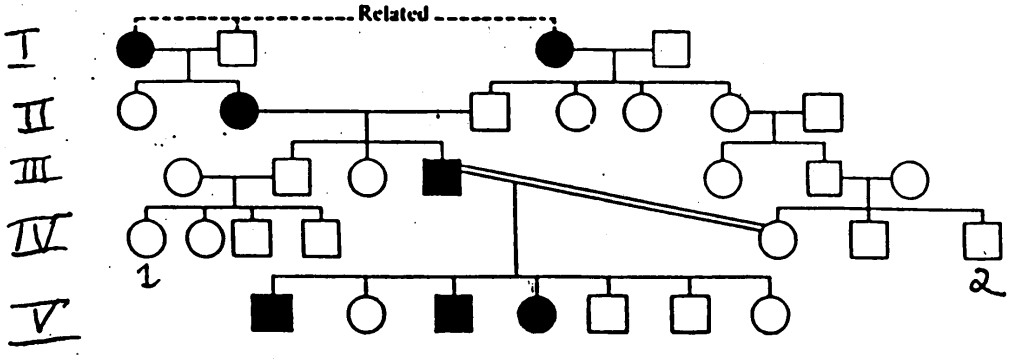


Examine the pedigree shown above. For each mode of inheritance listed below indicated: E = this mode of inheritance is excluded by the data
C = this mode of inheritance is consistent with the data

_____ Autosomal recessive inheritance of the trait; recessive allele is **common** in the population **ARC**
____ Autosomal Recessive inheritance (recessive allele is **very rare**) **ARR**
____ X-linked recessive inheritance (recessive allele is **common**) **XRC**
____ X-linked dominant inheritance **XD**
____ Autosomal Dominant **AD**
____ X-linked dominant; *only males show the trait; dominant allele is very rare* **XDM**
____ Autosomal Dominant and *only males show the trait* **ADM**
___ Y-linked -- the gene specifying the trait is on the Y chromosome **Y**

- For each mode of inheritance that you excluded, *circle* the portion of the pedigree that **excluded** this inheritance pattern and *label* with the appropriate acronym (indicated by letters in bold).
- Note, you *do not need to explain* why the region of the pedigree excludes the mode of inheritance-- just circle and label it.
- If more than one region of the pedigree excludes a particular mode of inheritance, just indicate one region.
- Be as *precise as possible* when indicating the portion of the pedigree that is relevant.

**Problem 8** Many generations after a French orphan named Martin Fugate settled on the banks of eastern Kentucky's Troublesome Creek, his genetic legacy is still evident in many of the Fugate descendants and their kin: they are born with dark blue skin. The blue tint is lost within a few weeks, leaving dark blue lips and fingernails as evidence of the trait. The phenotype of this trait is due to an enzymatic defect that results in the abnormal accumulation of a nonfunctional form of hemoglobin, which is the same color as the oxygen-depleted blood in the veins of a normal individual. **EXTRA COPIES OF THIS PEDIGREE ARE ON THE NEXT PAGE.**




**a. (7 pts.)** Which modes of inheritance are **definitely EXCLUDED** by this pedigree? For each excluded mode, *circle a portion of the pedigree that is inconsistent with the mode of inheritance and indicate which mode it excludes*.

***For each mode of inheritance listed below indicate:***

E = this mode of inheritance is excluded by the data

C = this mode of inheritance is consistent with the data

_____ Autosomal recessive inheritance of the trait; recessive allele is **rare** in the general population **ARR**

_____ Autosomal recessive inheritance of the trait; recessive allele is **common** in the general population **ARC**

____ X-linked recessive inheritance; recessive allele is **common** in the general population **XRC**

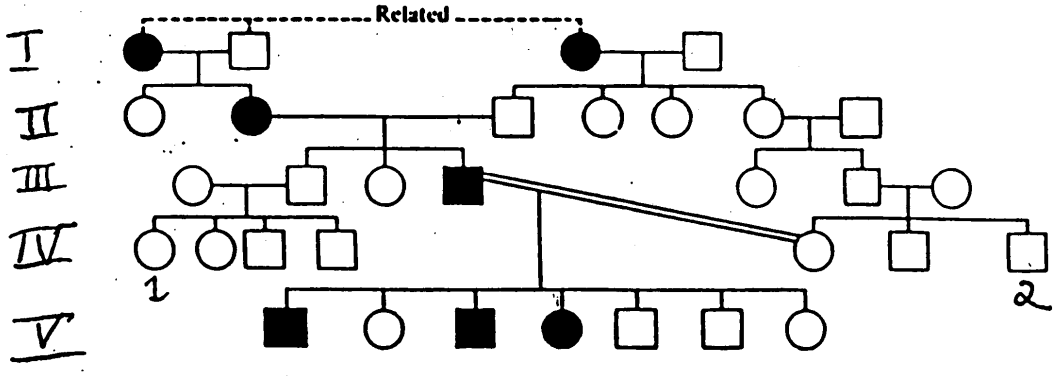
____ X-linked dominant inheritance **XD**

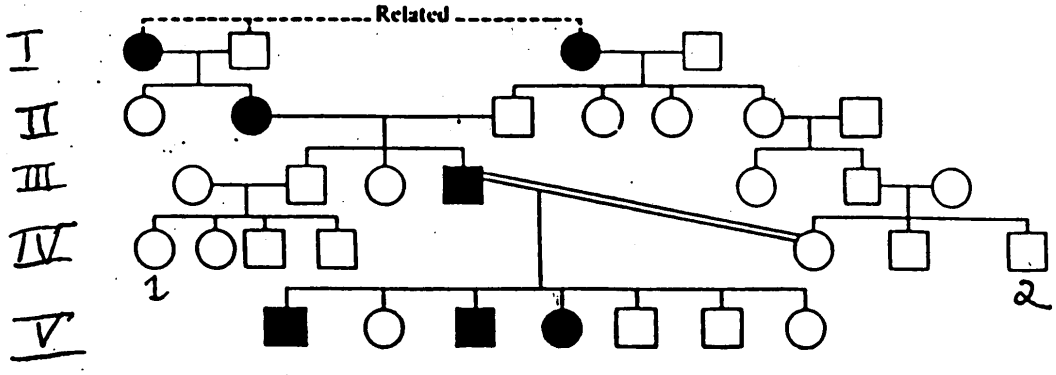
____ Autosomal Dominant **AD**

- For each mode of inheritance that you **excluded**, *circle* the portion of the pedigree that **excluded** this inheritance pattern and *label* with the appropriate acronym (indicated by letters in bold).
- Note, you *do not need to explain* why the region of the pedigree excludes the mode of inheritance-- just circle and label it.
- If more than one region of the pedigree excludes a particular mode of inheritance, just indicate one region. Be as *precise as possible* when indicating the portion of the pedigree that is relevant.

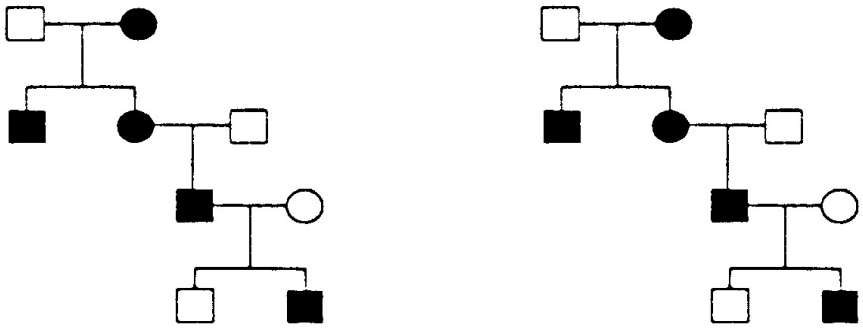
**b.** Individuals IV 1 and IV 2 want to marry. They visit a genetic counselor who assesses the pedigree. He agree with your general assessment of the pedigree from part a, but advises the couple that they have a zero probability of having a blue child. What mode of inheritance is implied by the counselor's conclusion? Very briefly explain.

**c.** Do you agree with the counselor's advise? What is the alternative way to assess the pedigree that would result in a different conclusion? Use a copy of the pedigree to defend/ illustrate your answer.



**Problem 9** ASSUME NO COMPLICATIONS



duplicate copies of the same pedigree

Examine the pedigree shown above. For each mode of inheritance listed below indicated:
E = this mode of inheritance is excluded by the data
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_____ Autosomal recessive inheritance of the trait; recessive allele is **common** in the population **ARC**
____ Autosomal Recessive inheritance (recessive allele is **very rare**) **ARR**
____ X-linked recessive inheritance (recessive allele is **common**) **XRC**
____ X-linked recessive inheritance (recessive allele is **very rare**) **XRR**
____ X-linked dominant inheritance **XD**
____ Autosomal dominant inheritance **AD**

- For each mode of inheritance that you excluded, *circle* the portion of the pedigree that **excluded** this inheritance pattern and *label* with the appropriate acronym (indicated by letters in bold).
- Note, you *do not need to explain* why the region of the pedigree excludes the mode of inheritance-- just circle and label it.
- If more than one region of the pedigree excludes a particular mode of inheritance, just indicate one region.

Be as *precise as possible* when indicating the portion of the pedigree that is relev

**Problem 10** Two individuals heterozygous for the same recessive mutant allele mate and produce 4 offspring. Assume the gene in question is autosomal. ***Calculate the probability of the following outcomes:***

- all 4 kids show the dominant phenotype
- all 4 show the recessive phenotype
- 3 dominant and one recessive
- 1 dominant and three recessive
- 2 dominant and 2 recessive

Note: your probabilities should add up to 1

**Problem 11 Review the collection of short cystinuria pedigrees discussed in lecture.** Presumably with a collection of pedigrees and a large enough set of data, the segregation patterns (ratios of affected and unaffected kids) will tend to approximate predicted probabilities.

a. Assess the outcome of all crosses between known heterozygotes. If all these data are combined, is the ratio of normal to affected (wildtype to mutant) about 3:1?
b. If not, speculate as to why the data might still be skewed even when a relatively large pool of data are assessed.

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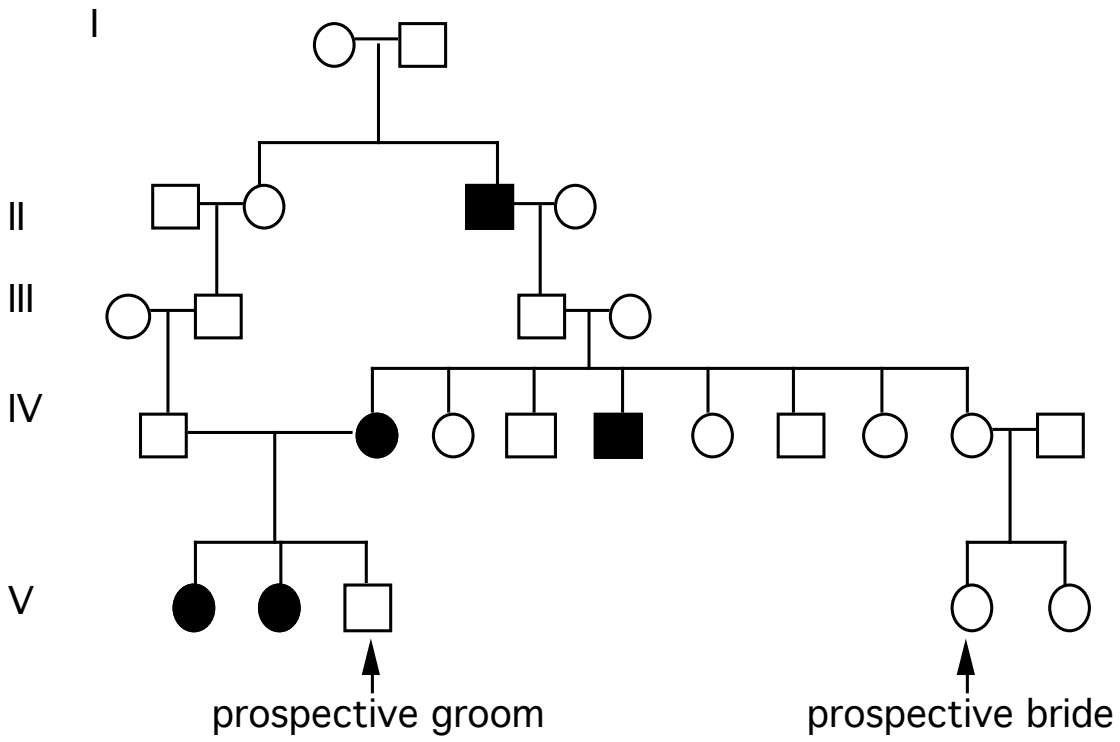
**Problem 12** This pedigree on the next page shows the inheritance in an extended family group of an ***autosomal recessive trait.*** *For each of these calculations, show your work and circle your answer. To get full credit, you must show how you arrived at your answer. You must tell me the identity of each fraction. I will also look at how you have assigned genotypes on pedigree.*

**a.** What is the probability that ***both*** the prospective groom ***and*** the prospective bride are heterozygous? In doing this calculation, assume that the bride's dad is homozygous for the dominant allele

**b.** What is the probability that neither are heterozygous? That one is het and the other homozygous for the normal allele?

**c.** The father of the prospective groom argues that the son should pick a mate from the population at large. If the frequency of heterozygotes in the population at large is 0.1%, what is the probability that the first child is affected if the prospective groom follows his father's advice? ***Just set up the answer.***


I
II
III
IV
V
prospective groom
prospective bride