Genetics 6

- **Answer to iClicker 6A**
- **Solving Pedigrees**
  - **example and tips for exam**
- **Pedigrees and Risk**
  - **Intro**
  - **Rules**
  - **Example**
- **Answer to iClicker 6B**
- **Due in Lab next week**
  - **Pre-Lab 3**
  - **LEGO Mitosis lab report**

Marfan syndrome update →

de novo event in 25% of cases

Solving Pedigree Problems

find mode of inheritance
- autosomal rec.
- autosomal dom.
- sex-linked rec.

} on the exam

Tips ① be careful about small #'s of offspring
→ can't depend on the ratio
→ can use ratios to rule out possibilities

② assume disease is rare
→ unrelated people w/ the disease are rare

③ start w/ the people you know for sure

ex. 

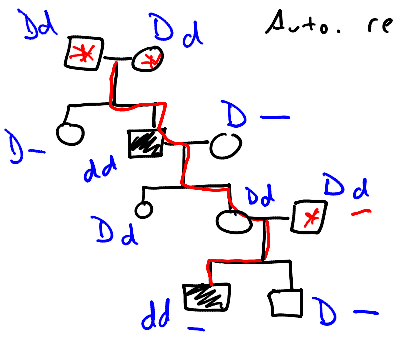
parents unaffected, offspring are affected

→ NOT autosomal dom.

leaves us w/ auto. rec. or sex-link.

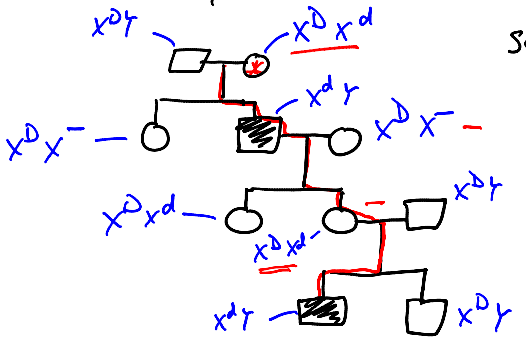
Autosomal rec.

allele	contr. phen.
D	normal (dom)
d	disease (rec)



Sex-link.

allele	contr. to phenotype
X^D	normal (dom)
X^d	disease (rec)
Y	none



which mode is more likely

Probability & Risk

probability (P) → liklihood that an event will happen

$P = 0$ → won't happen

$P = 1$ → defintely will happen

if $P = 3/4$ → in a large # trials

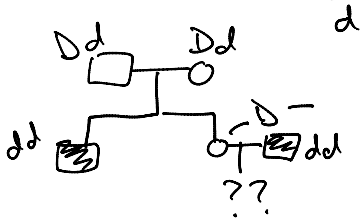
it will happen 3 out of 4 times

Rule: P of (A and B) = $p(A) \times p(B)$

ex. Autosomal rec.

D = dom. normal

d = rec. disease



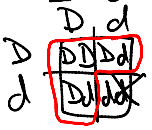
to have a child w/ dd

mom must be Dd (A)

and she must give d

to the child (B)

P_A = what are the chances of mom being a carrier



3 ways to be un affected
→ 2 way she can be a carrier (Dd)

$P(A) = 2/3$

if she's a carrier Dd

$P(B) = 1/2$

$P_{child\ w/\ disease}$ is $P_A \times P_B = \frac{2}{3} \times \frac{1}{2} =$

$1/3$

Bio 111 Counting "Unrelated Carriers"

In lecture, I talked about "counting unrelated carriers" - finding out how many people had to bring in a disease allele to explain a particular pedigree. This was useful in the case where more than one mode of inheritance was *possible* but you were asked to determine which was *more likely*. There are many ways to figure this out; this handout describes one possible way. Thanks to Silas for suggesting this.

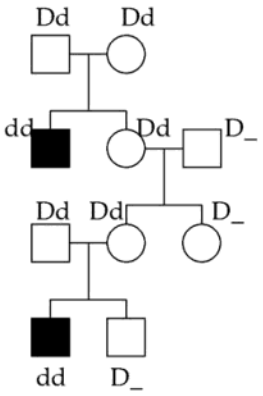
More precisely, we are counting the number of people who had to bring a disease allele into the family. Why is this important? Because, since any given genetic disease is usually quite rare, individuals with a disease allele must also be rare. Therefore, a mode of inheritance that requires more of these rare individuals is less likely than one that requires fewer.

Put another way, we are trying to account for each of the disease alleles found in individuals in the pedigree and to count the number of individuals who brought these alleles into the family.

Here is one way to do it:

1. Work out the pedigree and find out the *possible* mode(s) of inheritance. If only one is possible, this technique is not necessary. If more than one is possible, continue.
2. Fill in the genotypes of all individuals in the pedigree.
3. Starting with the affected individual at the lowest part of the pedigree, star all the individual(s) that gave this individual a disease allele.
4. Work your way up the pedigree from each starred individual. If their disease allele can be traced to another person in the pedigree, erase their star and move it to the source of the disease allele.
5. When you have reached the top of the pedigree, you will have accounted for all the disease alleles. The number of starred individuals is the number of 'unrelated carriers'.

Here is an example; suppose you saw the following pedigree:



This pedigree is not consistent with Autosomal Dominant inheritance.

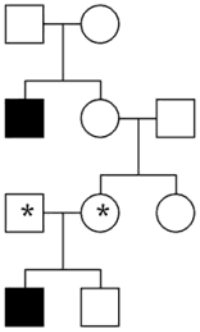
It is consistent with Autosomal Recessive and Sex-Linked Recessive.

Start with Autosomal Recessive:

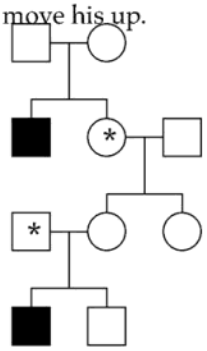
allele	contribution to phenotype
D	normal (dominant)
d	diseased (recessive)

The genotypes of individuals in the pedigree are shown at the left.

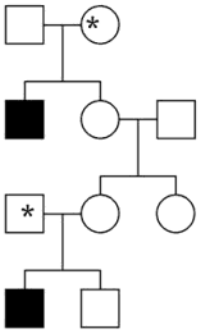
a) Step (3). Start with the son at the bottom of the pedigree. He got his d's from his parents. Star them.



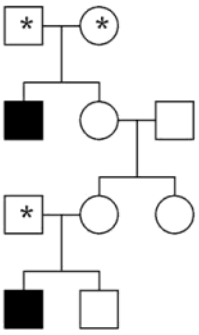
b) Step (4). Where did the *ed mother get her d? From her mother. To show this, move her star up. We don't know where the father got his *, so don't move his up.



c) Step (4) again. Where did the mother from (b) get her d? From her mother or father. So, you should star one or the other of the parents at the top of the pedigree. Because we don't know anything about the parents of the top generation, it doesn't matter which one we star, so star the mother for now (we may revise this later).



d) Step (3). Now you must account for the disease alleles in the other affected male. They came from his parents. Note that you have already *ed his mother; there is no need to * her twice. Since you have no information about the parents of the *ed individuals, you can't move their start. Therefore, you are done.



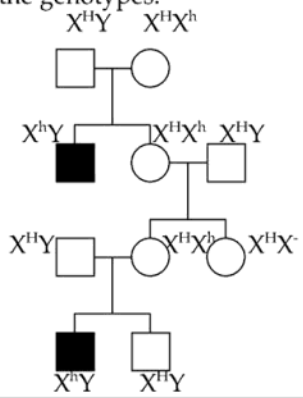
Now you have accounted for all of the d's in the pedigree. Three unrelated carriers are required to explain this pedigree as autosomal recessive.

On the next page, we work it through for Sex-Linked Recessive:

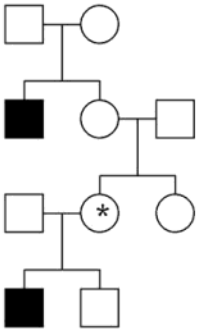
allele	contribution to phenotype
X^H	normal (dominant)
X^h	disease (recessive)
Y	none

Genetics 6-3

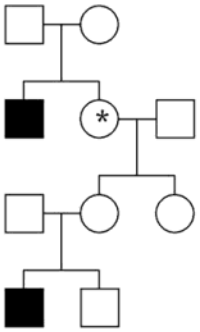
Here are the genotypes:



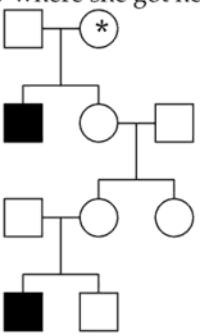
e) Step (3). Start with the affected son at the bottom of the pedigree. He got his X^h from his mother. Star her.



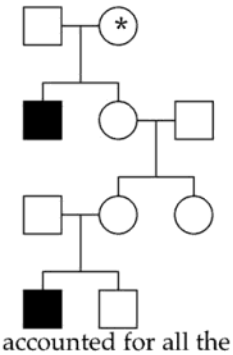
f) Step (4). The *ed mother in (e) got her X^h from her mother. Move the * up to her.



g) Step (4) again. The *ed female from (f) got her X^h from her mother. Move the * up to her. Because we don't know where she got her X^h, we cannot move her *.



h) Step (3). Start from the other affected son. He got his X^h from his mother. She is already *ed. There is no more information in the pedigree, so you are done.



You have accounted for all the X^h's. There is only one unrelated carrier required to explain this pedigree as sex-linked recessive.

Since an autosomal recessive explanation of **this pedigree** requires 3 unrelated carriers and a sex-linked recessive explanation of **this pedigree** requires only one of these rare individuals, sex-linked recessive is the *most likely mode of inheritance.*