Lecture Handout 3-Hedrick ch2 (continued)

Review of topics

Approach to problem sets

Review of topics

- **Dominant allele**: the allele (upper case) responsible for the phenotype in an individual with a heterozygous genotype

- **Recessive allele:** the allele that is present but with no effect on phenotype in an individual with a heterozygous genotype (allele written in lower case)

- **Simple or complete dominance**: phenotype of a heterozygote is that of the dominant allele

- **Incomplete or partial dominance**: heterozygote has an intermediate phenotype

- **Codominance**: heterozygotes express **both** phenotypes, eg MN blood cell locus

MN blood cell locus (codominance)

- Discovered in 1927 by Landsteiner and Levine
- M+N+ are common antigens on the protein, detected by specific antibodies. Sometimes associated with adverse events following transfusion
- Codes for glycophorin (membrane spanning protein with sugar molecules) in red blood cells
- Confined to humans and related hominoids; Chrom. 4
- Three phenotypes M, MN, N, coded by three genotypes, MM, MN and NN respectively.

Hedrick Table 2.8 allele frequency estimates, where N number of individuals for one or both sexes as appropriate; p + q = 1

(1) Haploid, organelle, and Y chromosome	$\hat{q} = \frac{N_2}{N}$
(2) Codominance	$\hat{q} = \frac{\frac{1}{2}N_{12} + N_{22}}{N}$
(3) Dominance	$\hat{q} = \left(\frac{N_{22}}{N}\right)^{1/2}$
(4) Codominance, X-linked or haplo-diploid AND	$\hat{q}_f = \frac{\frac{1}{2}N_{12} + N_{22}}{N_f}$
	$\hat{q}_m = \frac{N_2}{N_m}$

ABO blood cell locus

- Discovered in 1900, critical for safe blood transfusion, determined by recipient antibodies and donor antigens

- Four phenotypes: A, B, AB, O.

- Three alleles: A, B and O (often represented as I^A, I^B and i, respectively). A and B are codominant, O is recessive to both A or B.

recipient	donor
A	A or O
B	B or O
AB	A, B, AB, or O
O	O

Hedrick Table 2.9, like 2.8 but for multiple alleles--draw unit squares with 3 alleles to see how these make sense.

(1) Haploid, n alleles	$\hat{p}_i = \frac{N_i}{N}$
(2) Codominance, n alleles	$\hat{p}_i = \frac{N_{ii} + \frac{1}{2}\sum_{j=1}^{n} N_{ij}}{N}$
(3) Dominant series, three alleles	$\hat{p}_1 = 1 - \left(\frac{N_{22} + N_{23} + N_{33}}{N}\right)^{1/2}$
	$\hat{p}_2 = \left(\frac{N_{22} + N_{23} + N_{33}}{N}\right)^{1/2} - \left(\frac{N_{33}}{N}\right)^{1/2}$
	$\hat{p}_3 = \left(\frac{N_{33}}{N}\right)^{1/2}$
(4) Two alleles codominant, one recessive	$\hat{p}_1 = 1 - \left(\frac{N_{22} + N_{23} + N_{33}}{N}\right)^{1/2}$
	$\hat{p}_2 = 1 - \left(\frac{N_{11} + N_{13} + N_{33}}{N}\right)^{1/2}$
	$\hat{p}_3 = \left(\frac{N_{33}}{N}\right)^{1/2}$

For (3), see coat color in horses (below)

Always keep in mind ploidy and dominance. In this example, the locus is DIPLOID (autosomal), but there is a sex difference in the frequency of alleles...

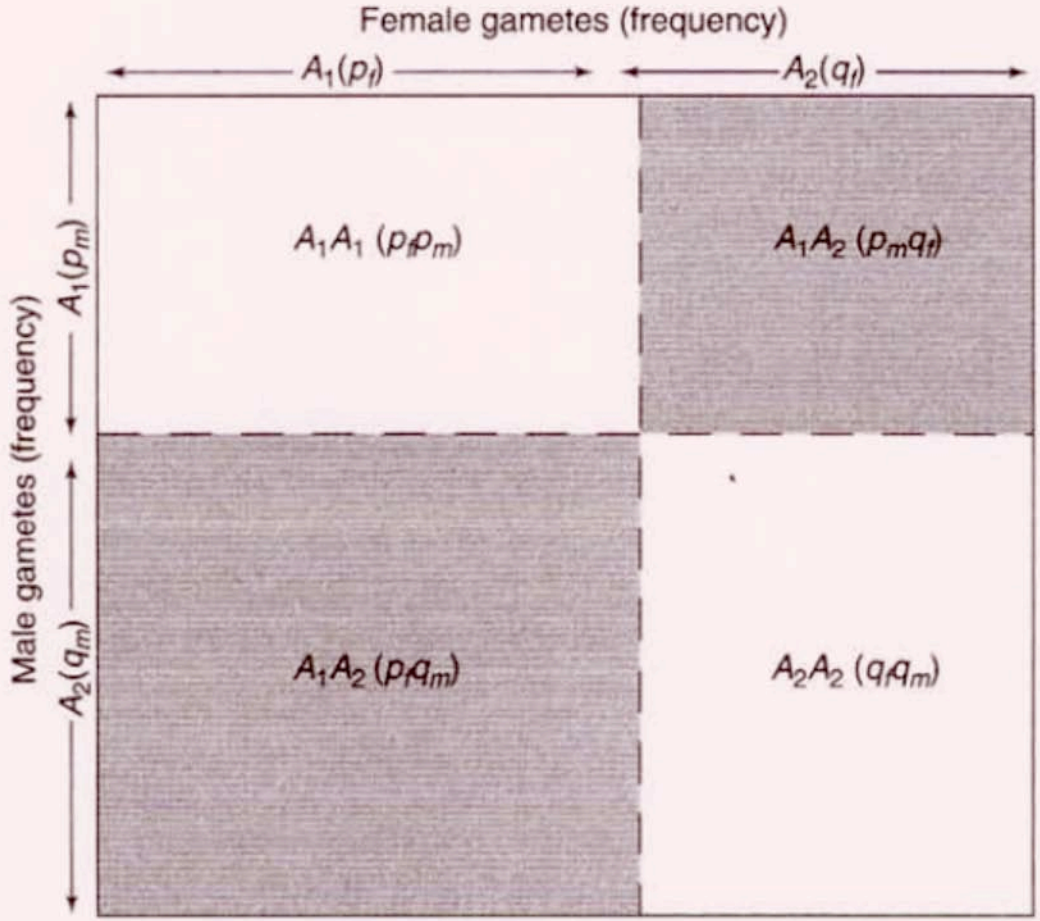


Figure 2.3. The proportions of zygotes formed from random union of gametes where female and male gametes differ in allele frequency and the heterozygotes area is shaded.

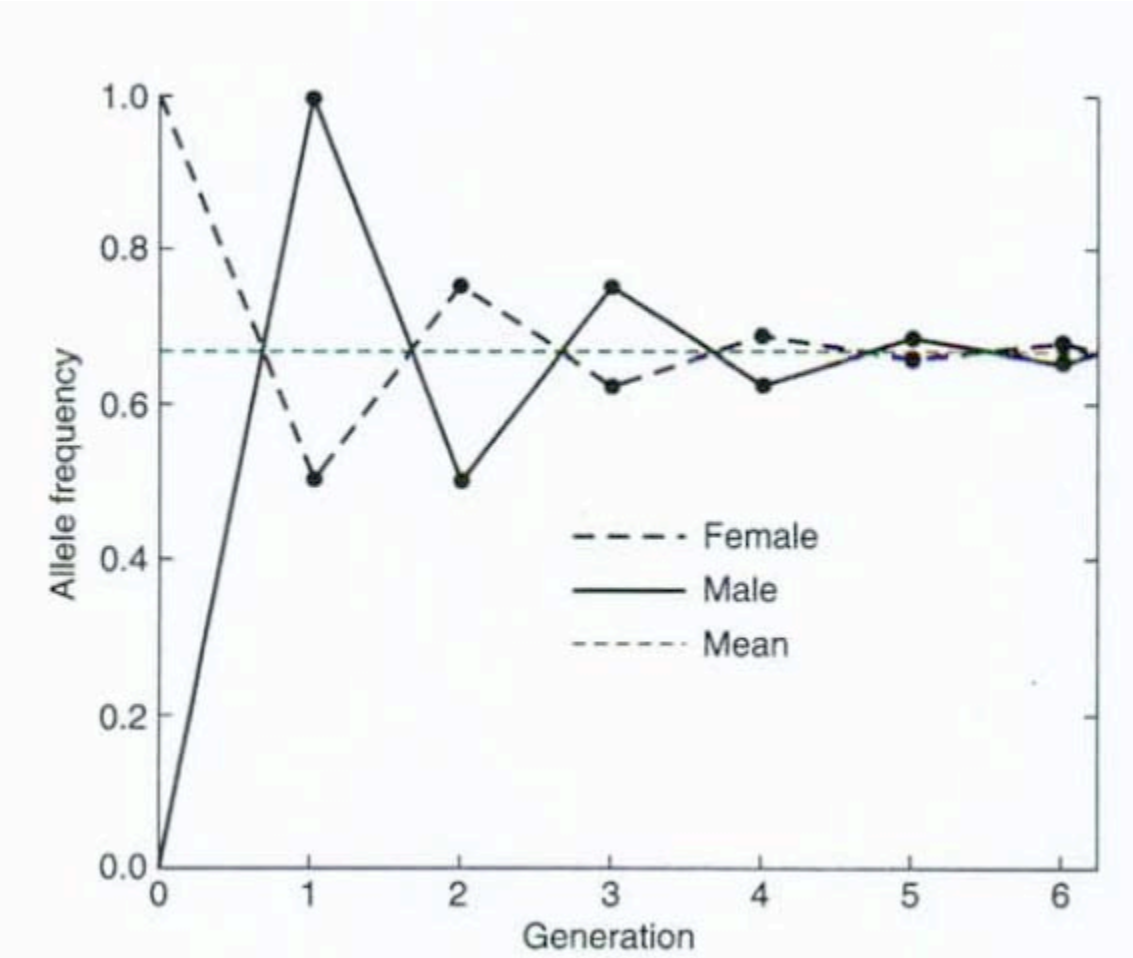
…while in this example the locus is HAPLO-DIPLOID (sex-linked or X-linked), and the difference is in the number of chromosomes per sex, and not necessarily a sex difference in allele frequency…

TABLE 2.6 The genotype frequencies after one generation of random mating for an X-linked locus or a gene in a haplo-diploid organism.

Mating type			*Female offspring*			*Male offspring*	
♀	♂	*Frequency*	A_1A_1	A_1A_2	A_2A_2	A_1	A_2
$A_1A_1 \times A_1$		P_fP_m	P_fP_m	—	—	P_fP_m	—
$A_1A_1 \times A_2$		P_fQ_m	—	P_fQ_m	—	P_fQ_m	—
$A_1A_2 \times A_1$		H_fP_m	$\frac{1}{2}H_fP_m$	$\frac{1}{2}H_fP_m$	—	$\frac{1}{2}H_fP_m$	$\frac{1}{2}H_fP_m$
$A_1A_2 \times A_2$		H_fQ_m	—	$\frac{1}{2}H_fQ_m$	$\frac{1}{2}H_fQ_m$	$\frac{1}{2}H_fQ_m$	$\frac{1}{2}H_fQ_m$
$A_2A_2 \times A_1$		Q_fP_m	—	Q_fP_m	—	—	Q_fP_m
$A_2A_2 \times A_2$		Q_fQ_m	—	—	Q_fQ_m	—	Q_fQ_m
Total		1	p_fp_m	$p_fq_m + p_mq_f$	q_fq_m	p_f	q_f

How many fewer mating types (genotype x haplotype) are there than for an autosomal locus (genotype x genotype) with 2 alleles?

…finally for this locus BOTH ploidy AND allele frequencies must be considered: the locus is HAPLO-DIPLOID (sex-linked or X-linked), AND there is also an INITIAL sex difference in allele frequency in the first generation. But male and female allele frequencies quickly become identical.



1. A population of flies includes 400 females, with 250 wild-type and 150 recessive mutants, and 600 males, with 375 wild-type and 225 mutants.

   a. If a single fly is sampled from this population, what is the probability that it is wild-type?

   …

   e. If a single fly is sampled from this population, what is the probability that it is wild-type female?

   …

   h. If one male fly and one female fly were sampled from this population and mated, what is the probability that their first offspring would be a mutant?

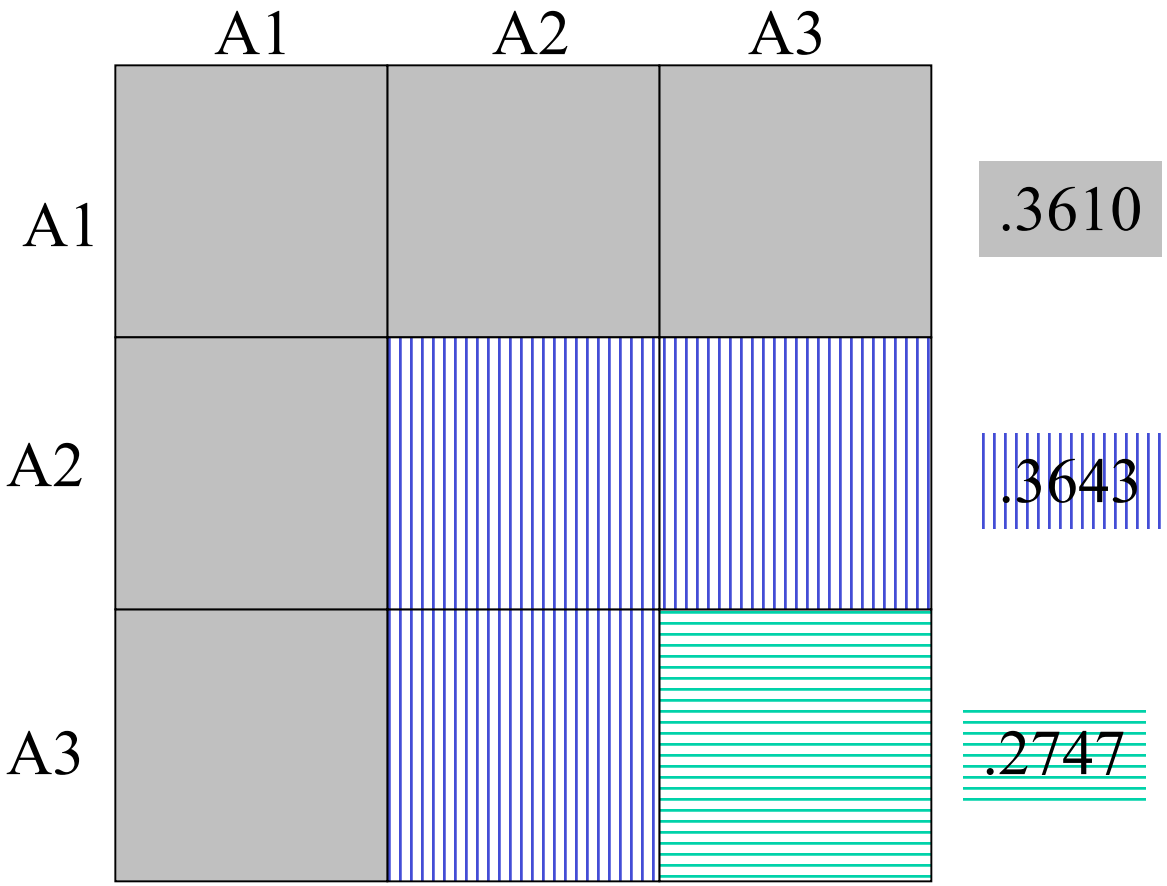
Problem set guideline:
When in doubt, generate a table for the data

	Wild Types	Mutants	Total
Females	250	150	400
Males	375	225	600
Total	625	375	1000

6. Coat Color in horses is determined by multiple alleles. A complete black horse (C1 black horse with black mane and tail) is dominant to a bay horse (C2 brown horse with black legs, mane and tail) and a mahogany bay. A Bay is dominant to a mahogany bay (C3 brown horse with black roots, legs, mane, and tail). Given a sample of 7000 horses (Black, bay, and mahogany bay), what is the allele frequencies of the three phenotypes.

Color	Observed Number	Observed Frequency
Black	2527	.3610
Bay	2550	.3643
Mahogany Bay	1923	.2747

Problem set guideline:
When in doubt, generate a unit square



Frequentist probability

- Proportion of times that an event occurs in a large number of trials.

- e.g., coin toss, Mendelian genetics, Punnett Square, HWE, lottery tickets etc.

Bayes' theorem

- Is in contradistinction to frequentist probability
- Published (posthumously) by Reverend Thomas Bayes, died 1761
- Used to compute the posterior probability
- The posterior probability is the conditional probability that is assigned after relevant evidence is taken into account.

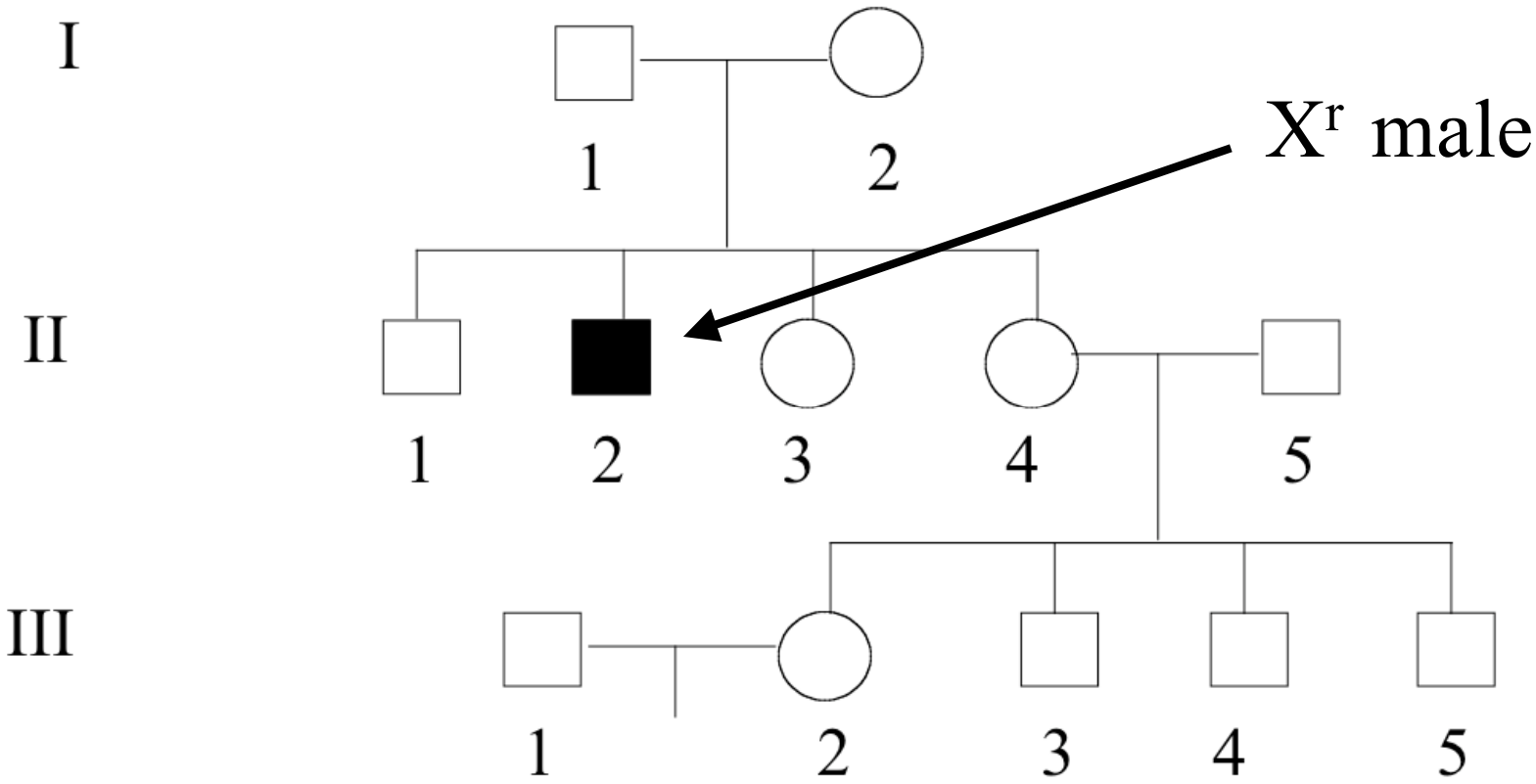
Bayes' theorem example

What is the probability of A, given that one has evidence about the outcome B:

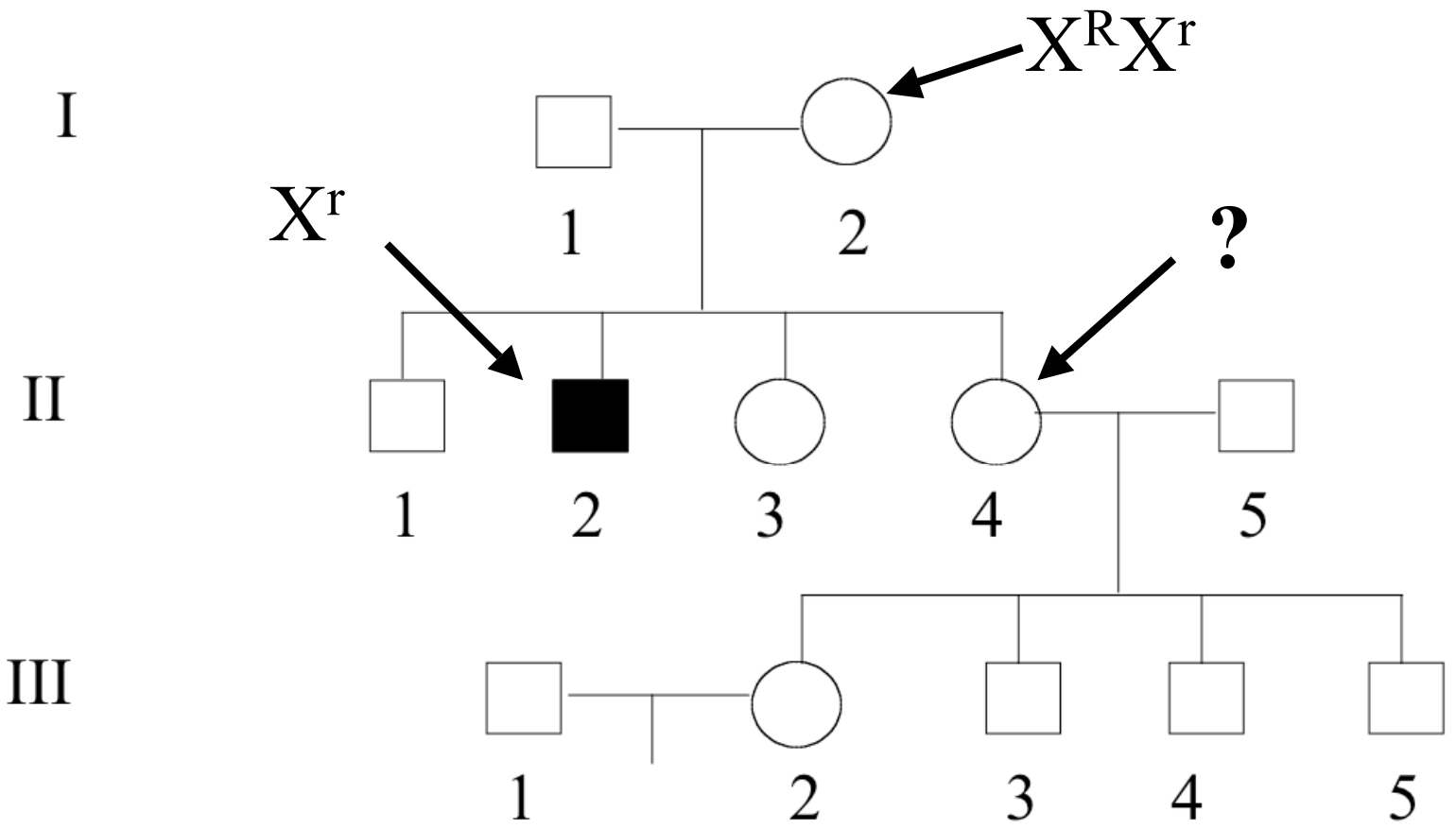
$$P(A|B) = \frac{P(B|A)\,P(A)}{P(B|A)P(A) + P(B|A^C)P(A^C)}.$$

In this equation, B means the outcome, and A^c means the complement of A ("not A")

Sex linked trait: phenotype related to the chromosomal sex of the individual; alleles are carried on the **haplo-diploid** X chromosome, for which males are **hemizygous**, eg red-green color blindness



Using ancestors and descendants, what is the probability that II-4 is heterozygous?



Since the question says to use evidence about the outcome, Bayes' theorem applies

What is the "posterior" probability of A, given that one has data about the outcome B

$$P(A|B) = \frac{P(B|A)\,P(A)}{P(B|A)P(A) + P(B|A^C)P(A^C)}.$$

P(A) and P(not A) are frequentist calculations (prior probability in the absence of evidence)

P(B given A) and P (B given not A) are conditional

Red-green colorblind question using Bayes' theorem

$$P(A|B) = \frac{P(B|A)\,P(A)}{P(B|A)P(A) + P(B|A^C)P(A^C)}.$$

Pr 3 wild type sons if mother is heterozygote vs.

Pr 3 wild type sons if mother is homozygote

Multiply each by prior probability of the given genotype (.5 for both in this case)

The sum of the two probabilities is the denominator.