How to Solve Genetics Problems

Remember—the most important thing to do is to begin organized and remain organized all through the problem. Genetics problems are solved entirely by logic and careful procedure.

I. How to start
   A. Begin by writing out all of the information you have about the gene(s) and alleles in question. If you aren't given symbols to use, make up your own, being sure to follow the rules and conventions applicable.
      1. All alleles of the same gene must be given some version of the same symbol
      2. If you have complete dominance, one convention is to assign a capital letter to the dominant allele and a lower case letter to any recessive allele(s). Note that many genes have multiple letter symbols. (For example, the cinnabar gene in fruit flies uses the two-letter symbol "cn.")
      3. If you have incomplete dominance, it is probably a good idea to use superscripts, etc., rather than upper and lower case letters, since the latter encourage you to think in terms of complete dominance.
      4. If you are dealing with an X-linked gene, make sure that the symbols you choose help you remember all through the problem solution that your gene is on the X chromosome. In other words, choose symbolism which won't ignore the Y.
      5. ****Ignore this if your class didn't learn this method of symbolism**** If you are dealing with a gene with a clear wild type allele, the general convention is to assign a lower case or upper cast letter to the <u>mutant</u> allele (depending upon whether it is a dominant or recessive mutant), then assign the same symbol with a superscripted + for the wild type allele. Example: In fruit flies, cinnabar eye is a recessive mutant for the normal (wild type) dull red eye color. The symbol used for the cinnabar allele is "cn." The symbol for the wild type allele is "cn^+." Note that even though the wild type allele is dominant, the "cn" is still lower case. You should interpret "cn^+" as meaning "the dominant wild type allele of the recessive cinnabar mutation." A second example: In humans the genetic disorder Huntington's disease is caused by a dominant mutation. So the normal, wild type allele for this gene is recessive. The symbol for the Huntington's gene is "H" (representing the mutant variant). The letter is a capital letter because the mutation is dominant. The wild type allele of this gene is represented as H^+ (meaning "the recessive wild type allele of the dominant Huntington's Disease mutation".
      6. ****Ignore this if your class didn't learn this method of symbolism**** Sometimes this final method of symbolism is simplified by omitting the letter symbol for the wild type allele altogether, and simply representing the wild type as a "+." Obviously, this symbolism can become confusing if you are working with more than one gene, and should thus be used carefully.
   B. Before you can begin to figure out what kinds of offspring a couple of parents will have, you must figure out the genotypes of the parents. If you are not given this information, than apply those five rules of pedigree analysis to figure it out.
   C. Rule #1 will enable you to perform the next step. You must be able to figure out the kinds of gametes produced by your two parents. Remember that no gamete will contain two alleles for any gene; also remember that sex linkage will affect the gametes produced by a male.

II. How to solve a single-gene cross
   A. Getting the genotypic ratio using the Punnett's square method:
      1. Follow the instructions above.
      2. Once you have figured out the gametes for your two parents, construct a table with one column for each of the mother's gametes and one row for each of the father's gametes.

3. The small boxes inside the table represent the possible types of fertilization events which these two parents can produce. Fill in each square with a combination of the mother's alleles from the top of the column and the father's allele from the left of the row. By convention, in a heterozygous genotype the symbol for the dominant allele is written first. Be consistent.
4. Once the boxes are all filled in, determine all the different kinds of genotypes contained in these inside boxes. Copy those genotypes out.
5. Because for each parent, each of the possible different kinds of gametes will be produced in equal numbers, each square within your Punnett's square represents the same fraction of the offspring. Count how many times each different genotype occurs in the table and write those numbers beside each of the genotypes you listed in step four.. This will give you the genotypic ratio. *Caution* a ratio never consists of just numbers. It must also include the descriptions which go with the numbers.
6. To get the phenotypic ratio, ask yourself, "How many of these genotypes produce the same phenotype?" The answer to this question will depend upon the dominance relationships between the alleles in question. Add together the numbers for the genotypic classes which will give the same phenotype. This will lead you to the phenotypic ratio.

B. Getting the Phenotypic Ratio
1. Complete dominance: If you have complete dominance, your homozygous dominant genotype and your heterozygous genotype will produce the same phenotype. Therefore, you add those two classes together. The homozygous recessive remains by itself.
2. Incomplete or Codominance: If you have incomplete of Codominance, no two of your genotypic classes will produce the same phenotype, so the numbers in your phenotypic ratio will be the same as those in your genotypic ratio.
3. Pseudodominance: The most common type of pseudodominance occurs when one of your genotypes is lethal. In this case, for instance, all of one of your genotypes will die, and thus will not be counted in the living offspring (and are therefore not included in the phenotypic ratio). Your phenotypic ratio will thus consist simply of the numbers of the surviving classes. Careful: If you are asked a question like, "What fraction of the offspring will have will have curly wings?" be sure that your fraction is adjusted so that your classes will add up to 100% of the living offspring. After all, you never count the dead ones.
4. Multiple alleles: If your gene has more than two alleles, remember all the way through the problem that no one individual can have more than two of the alleles at a time, and that no gamete can have more than one. It doesn't matter how many alleles the gene has. Keeping this in mind, interpreting your phenotypes simply becomes a matter of referring carefully to the information you originally recorded about your gene. The dominance relationships may very will be different for each pair of alleles.

III. How to solve problems with X-linkage
A. The basic approach to this problem is the same as to the single gene cross above, except that you must be careful devising the gametes from the male parent, you must keep track of that Y chromosome at every step of the process, and you must report offspring by gender. Don't simply lump the male and female offspring together. In sex linkage problems, gender is frequently a very important part of the phenotype.
B. There are two common forms of symbolism used for X-linked genes. The more complete is to represent the X-linked alleles by using a capital letter X with a superscript which represents the gene in question, and simply using the capital letter Y to represent the Y chromosome. For example, in humans red/green colorblindness is caused by an X-linked recessive allele. Using this symbolism, we'd represent the dominant allele as X^C, the recessive as X^c and the Y as… Y. So a heterozygous female would be X^CX^c and a colorblind male would be X^cY. A rather simpler method is to simply use C, c, and Y, and leave the X out completely. If this simpler method is

chosen, it's important to be careful to remember that the gene is X-linked, so the Y chromosome doesn't get forgotten. Using this system, our heterozygous female would be Cc and our colorblind male would be cY. Note that the male still only gets one copy of that X-linked gene—either the C or the c, but never both.

C. You will construct your Punnett's square exactly as above, except that you will use the Y as the male's second gamete. If you fail to do this, your parents will have no male offspring.

D. Report your phenotypic ratio by gender—males separate from females. This won't always matter, but it is often a vital part of the phenotypic results of your mating.

E. Finally, remember that there are some special oddities about X-linked traits.
   1. In order to show an X-linked recessive trait, a female must inherit the recessive allele from both parents; a male must inherit it only from one parent. For this reason, X-linked traits are much more common in males than in females.
   2. Since a male always inherits his Y chromosome from his father, all of his X-linked traits come from his mother.
   3. ****Ignore this if your class didn't learn about sex in birds**** In birds, sex works backward from in humans and fruit flies. In birds the male is homogametic (designated ZZ) while the female is heterogametic (ZW).
   4. ****Ignore this if your class didn't learn about sex limited and sex influenced traits**** Some traits are affected by gender, but are not carried on the X or Y chromosome. Sex limited traits are autosomal, but can be expressed in only one gender. Sex influenced traits are also autosomal, and have different expressions in the different genders.

F. Y-linked (holandric) traits are the easiest of all traits to follow. Every male passes his Y chromosome to all of his male offspring and to none of his female offspring. Every male inherits his father's entire Y chromosome. Therefore, as long as you have an unbroken male line of descent, all males thus connected will have copies of the same Y chromosome. If Dad's got it, so do all of his sons; so does his father and his father's father. Unfortunately, there are very few Y-linked traits known.

IV. Solving problems with two (or more) genes. ****Ignore this if your class didn't learn about two-gene problems****

A. These problems are approached exactly the same way as problems with one gene. The only significant trap is in figuring out the proper gamete contents. Remember that every gamete will contain exactly one allele for every gene. Thus, if your parent has a genotype of AaBb, he or she can produce four different kinds of gametes: AB, Ab, aB and ab. He or she cannot produce AA, BB, A, b, etc.

B. Some gene interactions become important in problems involving more than one gene.
   1. Epistasis is a situation in which one gene interferes with the expression of another gene. The most famous of these conditions is albinism, which is homozygous recessive condition which prevents the expression of all other genes which affect color. The effect of epistasis becomes important only at the point where you are figuring out the phenotypes of the offspring. At that point, just be very sure that you pay attention to that original information you wrote out about your genes. Note that epistasis is not the same thing as dominance. Dominance relationships are the interactions between alleles for the same gene. Epistasis is the influence of one gene on a completely different gene. Albino caused by a recessive allele, yet it overcomes the influence of many other genes.
   2. Dominance Modification occurs when the dominance relationship between two alleles is affected the other genes in the organism. For example, in gerbils, the albino allele is usually completely recessive to its normal partner allele. However, if a gerbil is homozygous for a different recessive condition called dilute, the albino allele and its normal partner show incomplete dominance.

V. How to solve genetics problems using statistics.

A. A Punnett's square is actually a statistical table—a device which allows you to "do" statistics without doing the calculations. But genetics is a statistical science, and problems can also be solved using statistics.

B. When solving a genetics problem, you are calculating probabilities. The probability of a particular event is the "chance" that event will occur. It's a prediction.

1. Probabilities are expressed as decimals.
   a. A probability of 1.0 is a certainty. It's equivalent to a chance of 100%. The probability that, if you toss a coin into the air, it will come back down (given that we are on the surface of the Earth and that there are no obstacles to prevent its descent) would be 1.0.
   b. A probability of zero means the event will never happen. The probability of tossing a penny into the air and have it come down magically changed into a quarter is zero.
   c. The probabilities of all possible outcomes for an event must add up to 1.0. For example, if you have a bag full of marbles, some of which are red and some of which are blue, the probability that you will randomly pull out a red marble and the probability that you will randomly pull out a blue marble must add up to 1.0. Those are the only possible outcomes, so they have to add up to 100% of the possible outcomes.
2. The mathematically formal way to express probabilities uses the letter "P" to mean probability. For our two examples above, the formal expressions would be:
   a. P (tossed coin will fall) = 1.0
   b. P (tossed penny will turn to quarter) = 0.0
3. To calculate the probability that two independent events will occur at the same time, we multiply their individual probabilities. If the probability of Arthur P. Farkenparker actually coming to class on a test day is 0.25, and the probability that he will pass any exam is 0.1, then the probability that he will come to class and pass a test is (0.25)x(0.1) = 0.025. Poor Arthur. Note the word "and" in the previous sentence. If your description of the occurrence of two events includes the word "and," chances are you need to multiply probabilities. We'd express this as P (APF comes to class **and** APF passes exam) = 0.25 x 0.1 = 0.025.
4. If more than one event will satisfy the conditions of our prediction, we add their probabilities. For example, Suzie Que's parents have promised her a trip to Hawaii if she earns a grade higher than a C in her biology class. The probability that she will earn a B is 0.4. The probability that she will earn an A is 0.1. She wins the deal if she earns an A **or** a B, so P (A or B) = 0.4 + 0.1 = 0.5. Suzie has a 50% chance to earn herself a trip to Hawaii. Note the word "or" in the description. "Or" generally means you add probabilities.

C. Gamete probabilities

1. We know that, at least in animals, gametes are produced from the products of meiosis. For every chromosome in an organism, each gamete will carry a single chromatid.
2. There are two chromatids of each kind (because the sister chromatids of a chromosome are identical), so for a heterozygote (eg, Bb), we know that the probability that a gamete will carry a particular allele for that gene is 0.5. P(B) = 0.5 and P (b) = 0.5
3. For a homozygote (eg. BB), of course, all gametes will carry the same allele. P(B) = 1.0 and P(b) = 0.
4. If we are following more than one gene, we figure out the probabilities for each individual gene and use our "and" rule above to figure out the full gametes. For example, suppose we have an individual with the genotype AaBbCc. How do we figure out the probabilities of each kind of gamete?
   a. First step: how many kinds of gametes can this parent produce, and what are they?

i. The first part of this question can be calculated statistically. There are three genes, and for each of the three, this parent offers two possible alleles. So the total number of gametes will have to take into account the possibilities for all three genes. You calculate it like this: 2 (possibilities for the A gene) x 2 (possibilities for the B gene) x 2 (possibilities for the C gene) = 8 total possible combinations of these alleles.

ii. For the second part, just figure all the possible ways these alleles can combine, remembering that every gamete will have exactly one allele for each kind of gene.

ABC	aBC
ABc	aBc
AbC	abC
Abc	abc

b. Now for each of these possibilities, we do our probability calculations. For example, what is the probability that we'll get the gamete ABC? We already know that P(A) = 05, P(B) = 0.5 and P(C) = 0.5. So what is P(A and B and C)? We simply multiply probabilities: p=P(A and B and C) = 0.5 x 0.5 x 0.5 = 0.125.

c. All of these possible gametes will end up having the same probability. And note that 8 x 0.125 = 1.0.

5. Calculating genotypes.

a. Precisely the same kinds of rules apply when calculating the probabilities for the possible genotypes of offspring. Suppose we are mating Bb x Bb. For each parent, the probabilities for the gametes are P(B) = 0.5 and P(b) = 0.5. The possible genotypes for offspring are BB, Bb and bb.

b. Apply the same rules used above to calculate the probabilities of these three different outcomes. Note, however, that there are two different ways to get the Bb outcome, depending upon which parent donates which allele. So we need to calculate the probability of getting "B from mother **and** b from father" **or** "b from mother **and** B from father."

P(B and B) = 0.5 x 0.5 = 0.25

P([B and b] or [b and B]) = (0.5 x 0.5) + (0.5 x 0.5) = 0.5

P(b and b) = 0.5 x 0.5 = 0.25

6. Calculating phenotypes

a. This is even easier. Of course, if you have incomplete or codominance, your phenotypic ratio will be identical to your genotypic ratio.

b. If you have complete dominance, of course, some of your genotypes produce the same phenotype. Suppose this problem involved our gerbil gene for brown and black fur color. B is the symbol for the brown allele, b is the symbol for the black allele. B is completely dominant to b. Among the offspring of the cross above, we would expect only two phenotypic results: brown and black. A brown baby can be either BB **or** Bb, so the total probability of getting a brown result will include both of these genotypes.

P(Brown) = P(BB or Bb) = 0.25 + 0.5 = 0.75

P(Black) = P(bb) = 0.25