Case Teaching Notes

for

"In Sickness and in Health: A Trip to the Genetic Counselor"

by

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Introduction / Background

This interrupted case study was originally developed for use in a non-science major general biology course and has also been used in a non-science major human genetics course. In both instances, the students had already received a very brief introduction to Mendelian genetics, but little else.

The case centers on a discussion between a young couple planning a family and a genetic counselor they're seeing because of a family history of genetic disease. The case allows students to see how Mendel's rules apply to more than just pea plants, and the narrative provides several jumping off points where expansion of the topic at hand can be encouraged. Depending on the personality of the class, I have spent as little as a single 90-minute period or as long as three periods working on the case.

After the initial introduction, students are required to construct a pedigree from somewhat disjointed information before the genetic analysis can begin. While the case explicitly deals with the inheritance of single gene dominant, recessive, and sex-linked disorders, the opportunity exists to introduce the concepts of lethality, epistasis, multifactorial disorders, etc., again depending on the personality and sophistication of the class. Lastly, the case provides an introduction to Hardy-Weinberg equilibria. Most students have trouble with both the theory and application of Hardy-Weinberg and I tend to use this as an introduction that I can revisit later during a discussion of population genetics, helping to solidify student understanding of the topic.

Objectives

At the conclusion of the case, students should be able to successfully:

- Construct a pedigree from a written narrative.
- Be able to determine, from a pedigree, carriers of recessive genetic diseases and the probability that they will pass those diseases on to their offspring.
- Understand the rules governing the inheritance of single gene dominant, recessive, and sex-linked disorders and be able to apply them to analyze simple genetics problems.
- Be able to determine the carrier frequency of a trait given the prevalence of the trait in the population, as well as understand the significance of carrier frequency.

Classroom Management

Students are divided into small groups. Ten to 15 minutes should be devoted to the first part of the case, much of which is generally spent clarifying terminology that may be unfamiliar to the average non-science major. A few minutes should also be spent explaining the symbols and conventions seen in a typical pedigree.

Student groups will generally find five to 10 minutes adequate for constructing a pedigree; more time may be needed if the students are expected to access the references listed in the case on the Internet. When enough time has passed, reassemble the students and construct a consensus pedigree on the front board. Verify that this pedigree is correct and that each group agrees with it before going further. Place the pedigree off to one side of the board so that it may stay up as a visual reference throughout the remainder of the period.

Five to 10 minutes can be spent lecturing on the basic concepts of dominant genetic traits. Have the students return to their groups for 10 minutes to read and then answer the questions at the end of Part II. Reconvene to go over the answers and modify the pedigree so that it indicates the genotypes of each individual affected with myotonic dystrophy.

Spend 10 to 15 minutes lecturing on recessive genetic traits, emphasizing the role of carriers in their transmission. Allow students five minutes to read and then answer the questions at the end of Part III. Tell them you are especially interested in their answer to Question 3—why would factor VIII deficiency not be an autosomal recessive trait?

Use five to 10 minutes to discuss sex linkage. Allow student groups an equal amount of time to read and answer the questions at the end of Part IV. Spend a few minutes going over the answers to Part IV and an additional 10 to 15 minutes ascertaining that the major concepts presented to this point are understood.

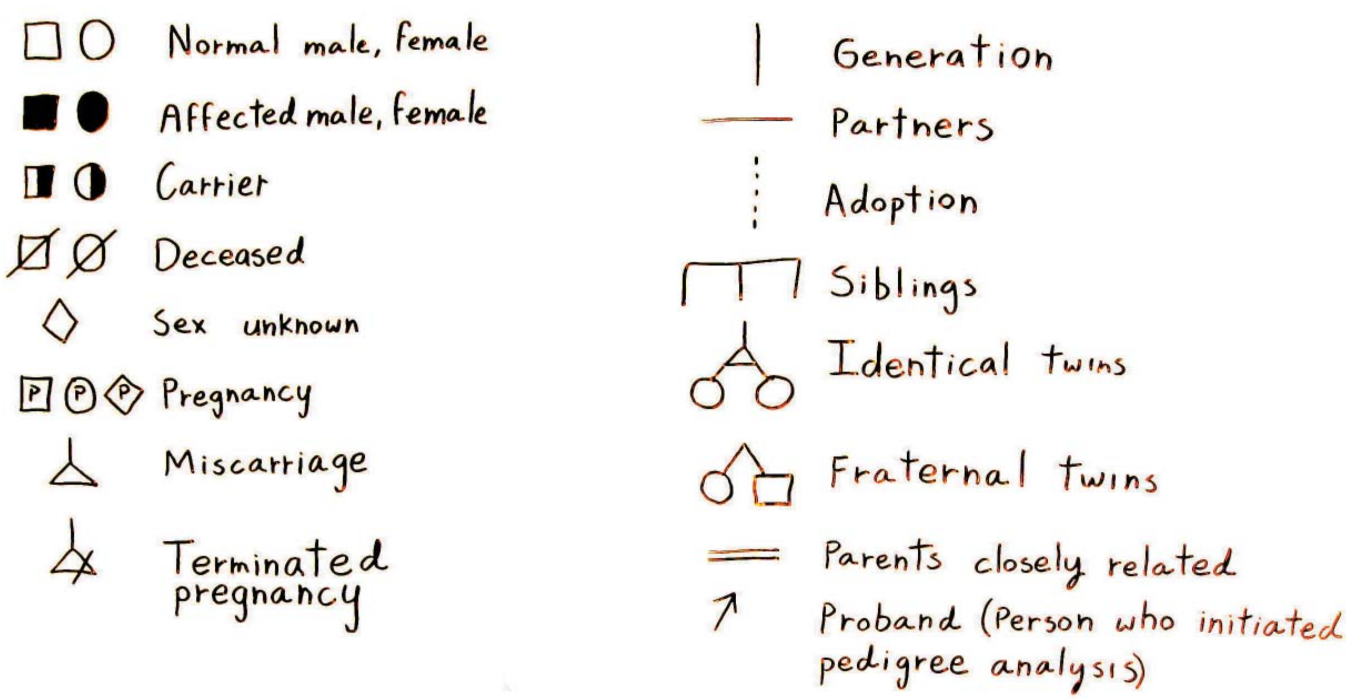
If Internet access is readily available, allow students 15 to 20 minutes to complete Part V on their own. If that is not practical, spend five to 10 minutes discussing Hardy-Weinberg and allow students an additional 10 minutes to complete the questions. After reconvening, use five minutes or so to go over the answers to the questions.

By this point the issue of privacy will most likely have been raised by one or more students. If it hasn't, use Part VI to focus the discussion in that direction. The length and intensity of this discussion depends almost entirely on the personality of the class. Don't force the issue. If your particular group of 19-year-olds is not excited about discussing job discrimination, retirement planning, and medical insurance, let it be. It often takes a few students with personal experience in this area to reach the critical mass needed for a discussion.

Blocks of Analysis

Part I—Pedigree Construction

This section introduces the major players in the case, Greg and Olga, and sets the stage for a discussion of their family history. Students must construct a pedigree using information provided by Greg and Olga. Common pedigree symbols are shown below in Figure 1.



Part I also provides the instructor with an opportunity to point out that persons with recessive genetic diseases (or serious diseases of any kind for that matter) often meet one another in waiting rooms, support groups, etc. Because of this the chances of one carrier marrying another is actually far greater than it would at first appear.

A pedigree of Greg and Olga's family is shown in the Answer Key to this case.

Part II—Autosomal Dominant Traits

Part II introduces autosomal dominant traits using myotonic dystrophy as an example. The first step here is to define both autosomal and dominant. The former is easy—autosomal traits are those that are equally likely to affect men and women. Greg's family has two female and two male members affected with myotonic dystrophy. Defining dominant requires that the concepts of genotype, phenotype, diploid, haploid, homozygous, heterozygous and allele be introduced, in at least a limited way, if this hasn't already been done. From here it is easy to understand that a dominant disease is one in which only one copy of the disease causing allele need be present for the disease to occur. The reference for myotonic dystrophy given in the case provides background information on the disease itself.

Part III—Autosomal Recessive Traits

Part III is concerned with the inheritance of autosomal recessive traits and should flow easily from Part II. Because there is no direct example of an autosomal trait in the case, the instructor should take a few minutes to provide an example of what such a trait looks like and reinforce the fact that two carriers can give rise to an affected offspring. Any of the recessive traits mentioned in the case (albinism, sickle cell, cystic fibrosis) will do. The references provided at the end of this part present background information on several of these diseases.

Part IV—Sex-Linked Inheritance

Part IV covers sex-linked inheritance, using factor VIII deficiency as an example. Students need to be reminded (or taught outright, depending on their level) that females inherit an X chromosome from each parent while males inherit an X from their mother and a Y chromosome from their father. Because men are hemizygous (have only a single copy) for X-linked genes, recessive traits will be expressed, as they have no alternate allele to dominate them. The references provided in the case present background information on hemophilia A as well as red-green color blindness. Other relatively common X-linked traits include Duchenne muscular dystrophy, which causes progressive weakening of the muscles, and Ichthyosis (literally fish disease), which results in dark, scaly skin due to an inability to remove cholesterol from skin cells. All of these traits are recessive in nature. Although X-linked dominant traits do exist, they are exceedingly rare.

Part V—Population Genetics

Part V introduces population genetics and Hardy-Weinberg equilibria. I usually use this as a brief introduction to the topic and return for a more thorough look at population genetics a little later in the course. The two equations central to population genetics are of course $P + q = 1$, and $P2 + 2Pq + q2 = 1$. The former equation simply states that the sum of the frequencies of the dominant alleles (P) and recessive alleles (q) in the population must equal 1. The latter equation is a binomial expansion relating the probability of genotypes for a gene with two alleles. This equation can be defined for students using a Punnett square to cross two persons who are heterozygous for a gene in which the dominant allele is represented by P and the recessive allele by q (i.e., $Pq \times Pq$). The results of the cross, PP, Pq, Pq, qq, display the relationship $P2 + 2Pq + q2 = 1$.

The example in this case is the most accessible, dealing with an autosomal recessive trait. Here, homozygous recessive individuals can be easily identified in the population as being q2 and the frequency of the recessive allele in the population can be found by taking the square root of q2. Once q is known, simple algebra can be used to determine the frequency of the dominant allele ($P + q = 1$) as well as the frequency of heterozygotes in the population ($P2 + 2Pq + q2 = 1$). As in the instance seen in this case, if the number of affected persons in a population is known then the carrier frequency for the trait can be determined. The reference provided in the case provides examples and several problems (with accompanying answers) for students.

Part VI—Unsettled Issues

The last part of the case is open-ended and raises issues related to privacy, ethics, and the law. I like to remind my students that in a democracy they can assist in deciding these issues and it always helps to come to the table intellectually prepared. The references in the case provide a good starting point for any discussion.

Answer Key

Answers to the questions posed in the case study are provided in a separate answer key to the case. Those answers are password-protected. To access the answers for this case, go to the key. You will be prompted for a username and password. If you have not yet registered with us, you can see whether you are eligible for an account by reviewing our password policy and then apply online or write to answerkey@sciencecases.org.

References / Resources

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