

CASE TEACHING NOTES for "Sometimes it *is* All in the Genes"

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OVERVIEW / BACKGROUND

In this story, a pregnant woman receives a routine genetic test indicating that she carries the mutation for cystic fibrosis, a devastating disease that causes excess mucus formation in organs such as the lungs, usually resulting in death by the mid-30s. She convinces her husband to get tested and discovers that he too is a carrier. After wrestling with the prospects of the 25 percent chance that their unborn child has this disease, the couple decides to have amniocentesis done so that their child can also be tested. The results indicate that their son will have cystic fibrosis. By this time, the woman is five months pregnant. They have their son and deal with the daily routine of treatments and therapies to keep him as well as possible. Finally, they hear of a gene therapy trial and have to decide whether to enter their son into a research study to see if he can be cured of his disease.

The overall goal of this case is to allow students to become acquainted with both the scientific and the ethical issues surrounding a simple Mendelian recessive genetic disorder, cystic fibrosis. With the completion of the sequencing of the human genome rapidly approaching, estimated to occur sometime in 2003 (<http://genome.ucsc.edu/>), the issues that are described in this case will most certainly become commonplace. Already the genes for many other fatal genetic disorders like Huntington, Duchenne muscular dystrophy (DMD), and Tay Sachs have been discovered and genetic screens have been done. However, like CF these diseases cannot be cured at this time. Huntington and DMD are highly similar to CF in that people with these afflictions can live rich lives for many years. However, at some point, as with CF, quality of life changes and the life spans of afflicted individuals are shortened. Students must understand the basics of genetics because it is highly likely that those who decide to become parents will be faced with some of the very choices presented here.

This case was designed for a health and wellness general education course that is entirely case based. Students enrolled in the course range in background from first year non-science majors to senior science majors. This case has been successfully received by students from all points of this spectrum of backgrounds and is often one of the favorite cases of many of the students in the course. As explained under "Classroom Management" below, the case could easily be adapted for other teaching purposes.

Objectives:

This case allows the introduction and discussion of various ideas at the instructor's discretion, but the following list includes concepts that the authors intended to be emphasized during the presentation of this case. Upon completion of the case students should be able to:

- Explain and use relevant terminology: *dominant, recessive, carrier, gene, mutation, disorder, allele*.
- Calculate the probabilities of inheriting recessive traits and passing them on to offspring.
- Discuss the symptoms of and treatments for cystic fibrosis.
- Describe amniocentesis as a technique for in utero testing and discuss the ethics of having it done.
- Discuss the purpose of in utero testing for genetic disorders for which there is no current cure.
- Discuss clinical trials, gene therapy techniques, and the ethics of "playing God."

BLOCKS OF ANALYSIS

Part I—The Genetic Test

Specific Objectives:

- Introduce inheritance and the consequences of inheriting or passing on a genetic disorder.
- Relate the term "inheritance" to the terms "genes" and "genetics".
- Introduce the concepts of recessive genes and two alleles for each gene.
- Distinguish between an inherited "genetic disorder" and an infectious "disease".
- Introduce the concept of genetic screening.

Additional Background for Part I

In the U.S., CF occurs in 1 out of every 2,500 people of European descent and 1 out of every 17,000 African Americans; it is less common in Asian Americans.

Although the use of the term "disease" for inherited illnesses is common even among the medical community, a better term is "disorder," and the two terms are not always interchangeable. As the text of the case states, infectious illnesses are correctly referred to as diseases. However, because genetic defects are often pleiotropic, causing many and varied symptoms, the term "disorder" better encompasses the full suite of manifestations of a problem stemming from a defective gene.

For suggested answers to the questions in this part of the case, see the [answer key](#).

Part II—Sharing the Bad News

Specific Objectives:

- Introduce basic genetics and patterns of inheritance.
- Building on Part I, explain the term "recessive" and the concept of being diploid in more detail.
- Introduce the concept of a mutant allele.
- Teach students how to determine the probabilities involved in the inheritance of a recessive trait.

Before handing out Part II, use the information from Part I to segue into a mini-lecture in which you can lead the students into defining some terminology and to explain some basic information about genes. For example, Dr. Kwin calls cystic fibrosis a "recessive" disorder and says that Nancy could be a "carrier of the gene." Ask the students to explain what the following terms mean:

gene

A piece of DNA that contains the information for a protein that will have some function/role/job in the cell.

mutation

A change in the DNA of a gene that causes the protein to be defective.

genetic disorder

Sometimes a mutation in a gene causes a disease or genetic disorder.

allele

A form of a gene; usually we think of two alleles with genetic disorders: the normal allele and the mutant allele that causes the disorder.

dominant

An allele that is expressed/shows its presence when there is at least one copy of it in a cell.

recessive

An allele that is expressed/shows its presence only when there are two copies of it in a cell.

carrier

A person who has one normal allele of a gene and one mutant allele that can cause the genetic disorder.

Then ask them how many copies of a gene there are in each cell [people normally have two copies of each gene]. This is sufficient knowledge for this case although the instructor should be aware that there are NOT two copies of the genes on the X and Y chromosomes, in case this comes up. Normal XY males have only one of each gene found on these two chromosomes. Normal XX females have two of each X chromosome gene but one X chromosome is turned "off" in each cell so that they effectively have only one copy of the X genes, just like males. The genes on the X chromosome that are "off" are still there, they just cannot be used. The CF gene is on chromosome 7 so people normally have two copies of it, one that they received from their father and the other that they received from their mother.

For suggested answers to the questions in this part of the case, see the [answer key](#).

Additional Question to Pose:

For more advanced students, ask them how Jake has misused the word "gene" and what term he should really use. Jake misuses the word "gene" in paragraph 13. Everyone has two copies of the CFTR gene, which when mutated can cause CF. Therefore, everyone passes one copy of this "gene" onto their offspring. The word he really means to use is "allele," which refers to different versions of the same gene.

Part III—The Decisions Become Tougher**Specific Objectives:**

- Introduce the concept that a mutated gene results in a defective protein.
- Describe how the defective protein causes CF, and how this molecular problem creates the gross symptoms of CF.
- Explain the symptoms of CF in more detail, demonstrating the serious nature of CF.
- Explain that for this (and most) genetic disorders, nothing can be done prior to birth to help the child.
- Introduce the procedure and purpose of amniocentesis.

For suggested answers and additional background for the questions in this part of the case, see the [answer key](#).

Part IV—New Hope or a False Hope?

Specific Objectives:

- Introduce symptoms of and current treatments available for cystic fibrosis.
- Introduce the concept of clinical trials and the ethics of enrolling children.
- Explain the problems and potentials of gene therapy.

Important Note About the Questions: Question 2 in this part could prove to be challenging for non-science students and can be considered optional. The inclusion of both Questions 1 and 2 make the case scientifically accurate. However, the authors of the case have taught the case numerous times without Question 2 and the students learned the essential concepts. The major point for health or introductory courses is made in Question 1. Since gene therapy corrects the root cause by inserting a functional gene, the disorder is truly cured. Diseases in cells that are frequently replaced during the life span of an individual (e.g., epithelial, epidermal, blood cells) are an exception because the cure would not be expected to be permanent. In these types of cells, the cure would only be permanent if the gene is replaced in the stem cells that give rise to those cells.

For suggested answers to the questions in this part of the case, see the [answer key](#).

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](#).

CLASSROOM MANAGEMENT

The class typically has 30 students divided into six groups. However, the case could easily be used in larger classes. These groups are assigned by the instructor at the beginning of the semester and are maintained throughout the entire course. The case developers, who have together taught this case over a dozen times in the past two years, have presented the material using two different approaches, either of which works well:

- We handed out Parts I and II sequentially, taking time to discuss the answers to the questions for those parts during a 55-minute class period. Part III was then given to the students as a take-home exercise along with some of the appropriate website references to use as resources. Students worked on the questions either independently or in groups outside of class, and then discussed their answers at the beginning of the next class period. Students then received Part IV and discussed the answers to those questions.
- We handed out each part sequentially and discussed the answers to the questions during a 2-hour class period.

We believe that this case could be easily modified to emphasize specific learning outcomes. For example, an instructor could focus on the genetics in a genetics course, on the molecular biology of the CFTR protein in a biochemistry, cell biology, or chemistry course, on the symptoms and treatments in a physiology course, or on the ethics of genetic testing/gene therapy in a genetics, sociology, or philosophy course. In fact, one of the authors has successfully used this case as part of a 12-week bioethics course for high school- through senior citizen-aged members of her church.

EDITOR'S NOTE

Teachers interested in this case may also be interested in another case on cystic fibrosis on our website entitled Woe to That Child and its accompanying teaching notes.

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WEBSITE REFERENCES

- <http://www.cff.org/> (CF Foundation) (especially the page on CF clinical trials: http://www.cff.org/research/clinical_trials.cfm?ID=116)
- <http://www.cfcare.com/> (CF Research, Inc.)
- <http://users.ox.ac.uk/~genemed> (at the bottom is a link to CF with more information about the disorder, molecular mechanisms, incidence, etc.)
- <http://www.genetics.med.ed.ac.uk/cysfib/background.shtml> (gene therapy and research on CF)
- http://clinicaltrials.gov/ct/gui/c/w1b/info/resources?JServSessionIdzone_ct=q5tir5y462 (a very complete government site explaining clinical trials)
- <http://www.fda.gov/fdac/special/newdrug/benefits.html> (a description of how the FDA weighs benefits versus risk)
- <http://www.fda.gov/cder> (everything you always wanted to about the process of drug and therapy development and approval)
- http://www.pbs.org/gene/resource/7_resource.html (a link to a PBS special which took a very human view of a couple who found out via genetic testing that their unborn twins would have CF. The site has additional resources. In addition, the videotape can be purchased and provides a quite powerful view of the problems surrounding these issues)
- <http://www.geocities.com/HotSprings/Villa/4210/> (personal web page of Lisa, a 20-year-old college student from Wisconsin who has CF; great links off here for more information as well)
- <http://vmsb.csd.mu.edu/~5418lukasr/cystic.html> ("Cystic Fibrosis Index of On-Line Resources; there are numerous links on this site for CF, children's illnesses, genetic disorders, and research)
- <http://www.pslgroup.com/dg/ee7fa.htm> (gene therapy for CF)

- http://www.thescientist.com/yr2002/jun/roberts_p12_020624.html (gene therapy review that mentions CF and recent developments—requires free registration)
- http://consensus.nih.gov/cons/106/106_statement.htm#2_1_What (incidence of CF in tabular form)

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***Note:** Both authors contributed equally to this case and its teaching notes.

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