

CHAPTER 3

How Genes and the Environment Influence Our Health

CHAPTER 3

How Genes and the Environment Influence Our Health

SECTION A	
How Stable and How Powerful Is DNA?	S161
1. DNA Paradoxes	S162
SECTION B	
How Do Heritable Changes in Genes Occur?	S163
1. Inducing Mutations with Ultraviolet Light	S164
SECTION C	
Is It Nature, or Is It Nurture?	S171
1. Albino Plants: A Model Gene-Environment Interaction	S172
2. Heart Disease: A Personal Gene-Environment Interaction	S178
SECTION D	
What Are Some of the Features of “Simple” Genetic Diseases?	S183
1. Some “Simple” Heritable Defects	S184
2. Phenylketonuria (PKU) Illustrates the Complexities of Some “Simple” Genetic Diseases	S186
3. The Special Inheritance Patterns of Sex-Linked Mutations	S188
4. Investigating Human Genetic Diseases	S190
SECTION E	
How Does a Genetic Counselor Detect Mutant Genes?	S193
1. Detecting the Duchenne Muscular Dystrophy (DMD) Mutation	S194
SECTION F	
How Can I Become a Genetic Counselor?	S203
1. How Can I Become a Genetic Counselor?	S204



CHAPTER 3

**How Genes
and the
Environment
Influence
Our Health**

SECTION A

**How
Stable
and How
Powerful
is DNA?**

DNA Paradoxes

DNA IS A MOLECULE of many apparent contradictions.

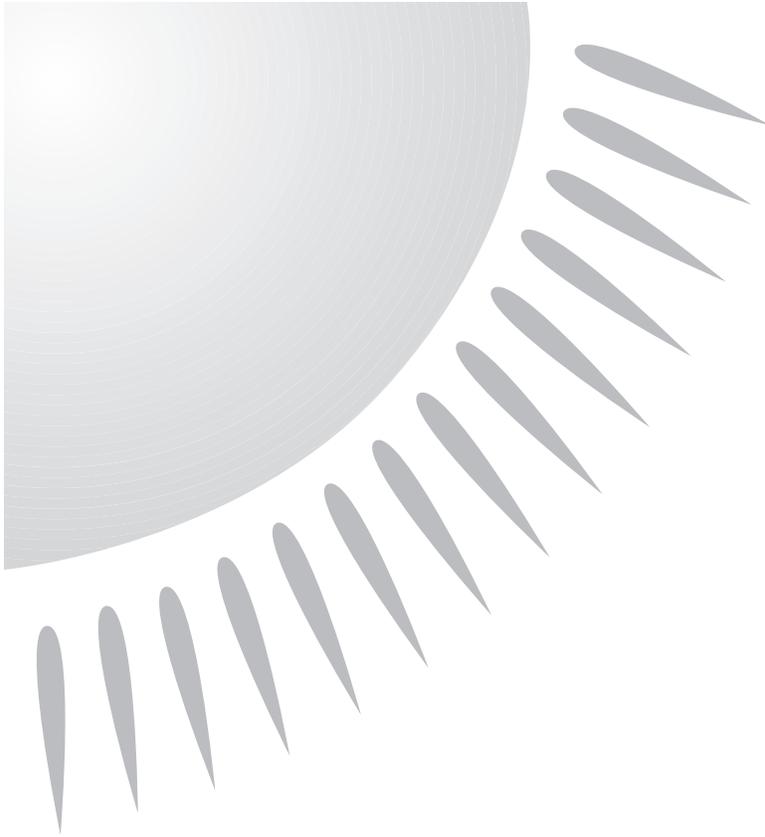
The continuity of life from generation to generation depends upon the fact that DNA molecules are usually extremely stable and are passed on unchanged from one generation to the next. But at the same time, the ability of life to change and adapt to new circumstances depends on the ability of DNA to undergo rapid changes from one stable state to a new stable state. The constancy of most of our DNA accounts for the fact that we and other people around the world are recognizable as members of the same species. Yet stable variations in human DNA that have accumulated through the ages account for the fact that we all have recognizable differences. Extending this concept to other organisms, DNA is the source of both the striking similarities and the amazing differences among the many life forms that populate our planet.

We may tend to think of DNA as being all powerful, because it can store instructions for making all the parts of all the organisms on earth. Yet in a very real sense DNA is totally powerless. A slave to its environment, DNA is unable to mediate any of the important reactions of life. It is even dependent on many other kinds of molecules that are present with it inside a cell for one of the most important reactions of life, its own replication.

Furthermore, it is the environment inside and around the cell in which a gene exists, and not the gene itself, that determines whether any of the information that the gene carries will ever be used, and if so, when, how, and with what effects.

It takes thousands and thousands of gene products all working together smoothly to keep us in good health. But a single gene product that is unable to function properly can be enough to destroy our health.

In this chapter, you will deal with some of these apparently contradictory aspects and complexities of DNA biology. First, you will perform experiments to study how different aspects of the environment interact to determine whether or not DNA will undergo a permanent change, or **mutation**. Then, you will take two different approaches to examining how certain aspects of the environment can determine whether or not particular genes that are part of an individual's genotype will be expressed to the extent that they will significantly influence the individual's phenotype. This will lead into an extended study of the roles that particular gene mutations play in human health. The culmination of this section will come when you prepare a brochure designed to help a genetic counselor provide an affected family with useful information about a genetic disease that affects one or more members of that family. Then, in the last exercise of this section, you will use a technique called **gel electrophoresis** to simulate the process by which a genetic counselor would determine which members of the family might be likely to suffer symptoms of the heritable disease in question.



CHAPTER 3

**How Genes
and the
Environment
Influence
Our Health**

SECTION B

**How Do
Heritable
Changes
in Genes
Occur?**

Inducing Mutations with Ultraviolet Light

INTRODUCTION

LIFE DEPENDS ON THE stability of DNA molecules and the ability of the cell to replicate them accurately generation after generation. But occasionally a DNA molecule is damaged by something in the environment. And occasionally mistakes occur during DNA replication. Either type of accident can result in a mutation, a heritable change in a gene. A DNA molecule that has been changed by mutation is normally just as stable and just as capable of faithful replication as it was before the mutation. Therefore, mutations can be passed on. The human genetic diseases you will study later in this chapter all involve mutations.

Some mutations cause no detectable change in the organism in which they occur, and some cause only unimportant changes. But many mutations cause serious abnormalities or death. Occasionally, however, a mutation occurs that improves the adaptation of an organism to its environment. It has been the slow accumulation of such rare, beneficial mutations in different kinds of organisms that has resulted in the diversity of the living world. When a mutation occurs in the absence of any human intervention, it is said to be **spontaneous** (even though it may have been the result of some external influence). But when it occurs as a result of a deliberate act of a biologist (usually as part of a genetic study), it is called an **induced mutation**. In this exercise, you will attempt to induce mutations that cause bacteria to change color.

You will use **ultraviolet light** (UV) to induce mutations in your bacteria. UV is present in sunlight as radiation that (as the name suggests) is just beyond the violet end of the visible spectrum. UV is absorbed by, and damages, DNA, and therefore it is a powerful **mutagen** (mutation-causing agent) and **carcinogen** (cancer-causing agent). Fortunately, however, the ozone layer of earth's upper atmosphere filters out most of the UV that streams toward earth from the sun. If the ozone layer were to disappear, the surface of the earth would become uninhabitable. Indeed, some scientists believe that the drastic decline in frog and salamander populations that has been observed around the world in the past ten years is probably a result of the thinning of the ozone layer. It is also believed that this thinning has been caused by chlorofluorocarbons (CFCs), such as Freon, which were once used as refrigerants and propellants in hair-spray cans.

Even at present ozone levels, the ability of organisms to live at the surface of the earth is due to their remarkable ability to repair DNA damage that has been caused by UV. The importance of DNA repair is highlighted by a genetic disease called xeroderma pigmentosum (XP) in which a critical enzyme required for DNA repair is nonfunctional. People with XP characteristically have many skin abnormalities, and most of them die of skin cancer before age 20.

As important as they are, however, our DNA repair systems are inadequate to fully protect us against the carcinogenic effects of the UV rays in sunlight or tanning salons. It is now recognized that a single sunburn as a child or teenager can increase the risk of skin cancer many years later. Those who deliberately expose themselves to UV by sun-bathing or visiting tanning salons are playing a dangerous game of chance somewhat similar to Russian roulette.

Because UV is absorbed by the top few layers of skin cells in humans, however, UV radiation cannot penetrate to our ovaries or testes, where our germ cells are stored. Thus, UV damage in humans is largely restricted to cells in the skin and eyes. Although it is the principal cause of human skin cancer, UV does not cause heritable mutations that can be passed on to our offspring.

In contrast, small one-cell organisms, such as bacteria, do not have the benefit of a protective layer of skin, and any nonfatal UV-induced mutations that they experience are invariably passed on to their progeny. We will take advantage of that fact in this exercise to study the mutagenic effects of UV on bacteria. We will also study the effects of visible light on bacteria that have been exposed to UV.

Serratia marcescens, the bacterium you will use for this experiment, normally produces a red pigment. Synthesis of the pigment involves many different enzyme-catalyzed steps and can be blocked by a mutation in any one of the genes encoding the numerous enzymes required for pigment synthesis. Therefore, pigment synthesis by *Serratia* provides a sensitive test for the presence of mutagenic agents. It is important to note that bacteria normally are haploid (have only one copy of each gene); therefore there are no recessive mutations in bacteria, and every mutation normally exerts its full effect right away. In this exercise, we will subject *Serratia* to **UV mutagenesis**, the induction of mutations with UV.

As a way of studying the effects of visible light on UV-exposed bacteria, your teacher will divide your class into two sets of groups. One group will incubate its UV-irradiated bacteria in the dark, and the other group will incubate its UV-irradiated bacteria in the light.

MATERIALS

For each group of four students:

- 1 marking pen
- 4 petri dishes containing agar
- 1 tube containing *Serratia* bacteria
- 1 1000 μ l micropipettor
- 1 sterile pipette tip
- 1 sterile inoculating loop
- 1 UV light source
- 1 watch with second hand
- plastic wrap (light-incubated groups only)
- aluminum foil (dark-incubated groups only)
- 1 spray bottle of disinfectant

PROCEDURE

Day 1: Irradiating the Bacteria

1. With the marking pen, label the bottom of each dish with your group name, either *light* or *dark* (depending on which group you have been assigned to) and one of the UV exposure times: 0, 30, 60, or 90 seconds (Fig. 1).

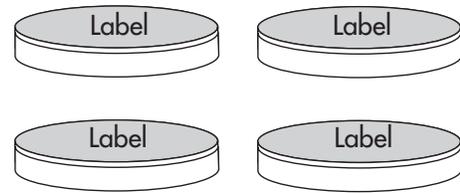


Figure 1

2. Swirl the tube of bacteria to suspend them evenly. Use the micropipettor to add 100 μ l of bacteria to the middle of each dish (Fig. 2). Measure carefully so that each dish will have the same number of bacteria.

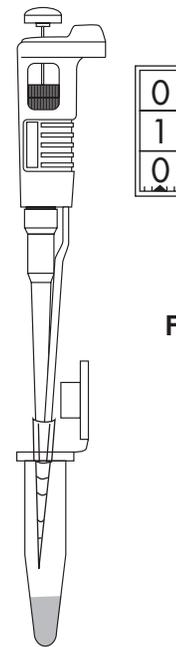


Figure 2

3. Use a sterile inoculating loop to spread the bacteria over the entire surface of each dish (Fig. 3). Avoid rubbing hard enough to damage the agar, but spread the bacterial culture as uniformly as possible. Place the inoculating loop in the waste beaker after use.

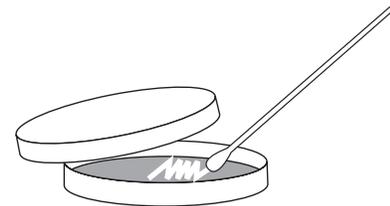


Figure 3

4. Take your plates to the UV light when directed by your teacher. **WARNING:** UV light can damage your eyes! Do not look into the light when it is turned on.
5. Place all four dishes with their lids on directly below the UV light. (UV light does not pass through the lids of petri dishes, so the bacteria will only be UV irradiated when the lids are off the plates.)

Make one member of your group responsible for timing the UV exposures. When that person gives the signal, remove the lids from all three dishes that are to be irradiated. (Do NOT remove the lid from the 0 sec. control dish.) When the person doing the timing says, “30 seconds,” cover the dish marked *30 sec.* Continue until the other two dishes have been exposed for 60 and 90 seconds.

6. If you are in a “light” group, wrap your dishes in plastic wrap. Then take all four dishes to the well-lit area indicated by your teacher and leave them there to incubate.

If you are in a “dark” group, stack all four dishes, wrap them tightly in aluminum foil, and label the foil with your group name. Place the stack where your teacher indicates.

7. Wipe your work area with disinfectant. Wash your hands.
8. Allow the bacteria to grow at room temperature for 3-4 days.

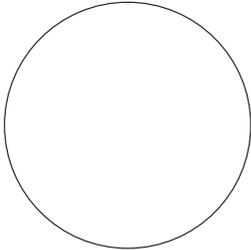
Day 4 or 5: Here Come the Mutants!

1. If yours is a “light” group, team up with a “dark” group, and vice versa. Unwrap the dark-incubated dishes and lay out the light- and dark-incubated dishes side by side.
2. Observe the number, size, and colors of the bacterial colonies on each dish. Make a representative drawing of the dish on the UV Mutagenesis work sheet. You do not need to count the exact number of colonies on each dish, but summarize your observations in the spaces provided.
3. When you have finished describing your observations, open each dish, spray the agar surface with disinfectant, tape the dishes shut and dispose of them as your teacher instructs you to do. Wipe your work area with disinfectant. Wash your hands.
4. Answer the questions on the work sheet.

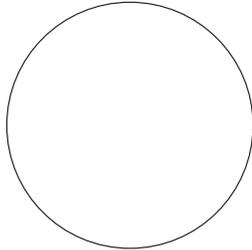
UV MUTAGENESIS WORK SHEET

1. Draw pictures of what you observe on your dishes:

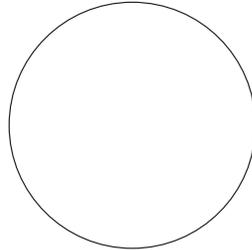
Dark-incubated dishes



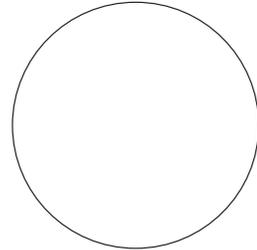
0 Seconds



30 Seconds

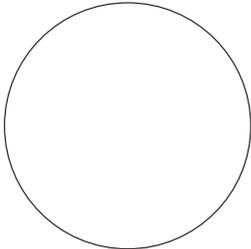


60 Seconds

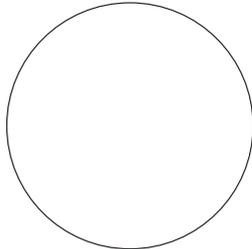


90 Seconds

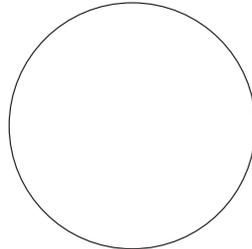
Light-incubated dishes



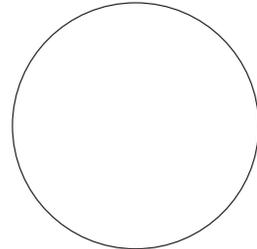
0 Seconds



30 Seconds



60 Seconds



90 Seconds

2. Describe the bacterial colonies on your dark-incubated control dish (0 seconds of UV). Then list and describe the differences among the bacterial colonies seen on each of the dark-incubated experimental dishes relative to those on the dark control dishes.

Dark-incubated control (0 sec.) dish: _____

Dark-incubated 30 sec. dish _____

Dark-incubated 60 sec. dish _____

Dark-incubated 90 sec. dish _____

3. Based on these observations, summarize the effects that UV irradiation has on *Serratia* bacteria.



Name _____

Date _____ Hour _____

4. Now describe any differences among the bacterial colonies on each of the light-incubated dishes relative to those on the corresponding dark-incubated dish. (That is, compare the light-incubated control dish to the dark-incubated control dish, the light-incubated 30 sec. dish to the dark-incubated 30 sec. dish, and so forth.)

Control (0 sec.) dishes: _____

30 sec. dishes: _____

60 sec. dishes: _____

90 sec. dishes: _____

5. Based on the above observations, summarize the effects that cultivation in visible light has on UV-exposed *Serratia* bacteria.

6. Can you formulate a hypothesis to account for such an effect of visible light?

7. Do all of the bacteria on a dish appear to respond to UV and visible light in the same way? Why?

8. Do all of the mutations that you observe in *Serratia* after UV irradiation appear to be harmful? Explain.

9. Is it possible that a mutation could be beneficial? Explain.



CHAPTER 3

**How Genes
and the
Environment
Influence
Our Health**

SECTION C

**Is it
Nature,
or Is it
Nurture?**

Albino Plants: A Model Gene-Environment Interaction

INTRODUCTION

WHETHER THE TOPIC HAS been bird migration, human intelligence, cancer, or any one of countless other biological phenomena, nonscientists – and occasionally some scientists – have often argued endlessly about whether the explanation for the phenomenon should be sought in **nature** (genetic differences) or **nurture** (environmental influences). To most biologists such arguments constitute just so much wasted breath. This is because they recognize one overriding generalization about the living world to which there are no known exceptions. And if you remember nothing else from your study of genetics, this is the generalization that you should remember: **Every phenotypic trait of every living being is the result of some set of gene-environment interactions.** If one wants to understand any particular trait of any individual organism, human or otherwise, the question to be answered is not whether that trait has a genetic or an environmental basis. The question to be answered is what genes and what environmental factors have interacted to shape that trait.

In this section, we will take two approaches to exploring this concept. The first will involve a lab experiment, in which we will examine the way in which genes and environment interact during plant development to control the production of **chlorophyll**, the green pigment required for photosynthesis. The second will involve a simulation, in which we will explore how genetic and environmental factors interact to determine one's prospects of developing heart disease, the principle cause of death in the United States and most other industrialized countries.

When we look around a country hillside or a city park in late spring, we see such a lush abundance of green trees, green grass – yes, and green weeds – that we tend to take for granted the chlorophyll molecule that paints our surroundings green. We may reflect on the fact that our own life, and the life of all other organisms around us, depends on chlorophyll, the wonder molecule that captures the energy of sunlight and makes photosynthesis, and this life, possible. But probably no one but a plant biologist ever spends much time worrying about how the synthesis of this “green” molecule is controlled. Leaves are green, and that's that, right?

In this exercise, however, we will get vivid evidence that chlorophyll synthesis is a clear example of the generalization that all traits of all organisms are a result of gene-environment interactions. To be more specific, we will germinate seeds produced by tobacco plants that were heterozygous for a gene that has a dramatic effect on chlorophyll synthesis. Half of the class will allow their seeds to germinate in the light, while the other half will place their seeds in a dark place to germinate. This will permit your class to determine how an environmental factor, light, interacts with the genotype of the seedlings to regulate chlorophyll production.

MATERIALS

For each group of students:

- 1 petri dish containing black agar
- 1 marking pen
- 30 tobacco seeds

PROCEDURE

Your teacher will divide the class into two sets of groups, designated “light” and “dark,” and will also indicate which “light” and “dark” groups will pair up for the data analysis.

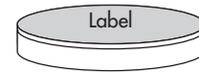


Figure 1

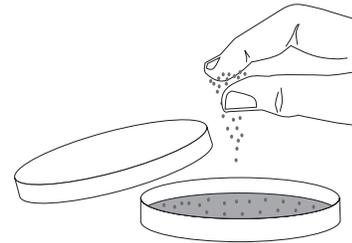


Figure 2

1. With the marking pen, label the bottom of your Petri dish with your group name, hour, and either light or dark, depending on which team you were assigned to by your teacher (fig 1).
2. Count out 30 tobacco seeds. Make a small pile with the seeds and press your index finger down onto them. The seeds should stick to your finger. Raise the lid of your petri dish and use your thumb to gently rub the seeds from your finger; sprinkle the seeds evenly over the surface of the agar (fig. 2). Do not touch the agar or leave the dish uncovered any longer than necessary.
3. If you are in a “light” group, place your petri dish under the lights. If you are in a “dark” group, wrap your petri dish in foil before placing it under the lights. Write the name of your group on the foil.
4. When your teacher says it is time to do so (which will probably be 7-10 days later), observe your seedlings. Count and record the number of green seedlings and the number of white seedlings on your plate. Record the numbers on your Albino Plant work sheet. If you are in a “dark” group, share your data with your partner “light” group and vice versa. Record the data collected by your partner group on your work sheet.
5. Whether you are in a “light” or a “dark” group, place your petri dish under the lights for further growth. (Do not wrap the “dark” dishes in foil this time.)
6. When your teacher says it is time to do so (which will probably be 2-3 days after the first observation), observe your seedlings and the seedlings of the other group with which you are paired. Count and record the number of green seedlings and the number of white seedlings on both dishes and record the numbers on your Albino Plant work sheet.
7. Record the data obtained by your two groups on the class data table. When the numbers for the whole class have been totaled up, record these totals on your work sheet.
8. Complete the Data Analysis work sheet.

Name _____

Date _____ Hour _____

ALBINO PLANT WORK SHEET

Data from your own pair of groups:

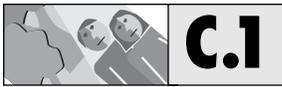
Number of plants on "light" plate		
Color	Observation #1 Light incubated	Observation #2 Light incubated
Green		
White		

Number of plants on "dark" plate		
Color	Observation #1 Dark incubated	Observation #2 Light incubated
Green		
White		

Data from the whole class:

Number of plants on "light" plates				
Group	Observation #1 Light incubated		Observation #2 Light incubated	
	Green	White	Green	White
Totals				

Number of plants on "dark" plates				
Group	Observation #1 Dark incubated		Observation #2 Light incubated	
	Green	White	Green	White
Totals				



Name _____

Date _____ Hour _____

DATA ANALYSIS

Use the data collected by the class as a whole to answer the following questions.

1. What ratio of green seedlings to white seedlings was present in the light-incubated seedlings on the first day of observation?

First express this as a ratio of the total numbers of green seedlings and white seedlings observed. (For example, 461:119)

Now divide the larger by the smaller number to express it as an exact ratio. (For example, $461:119 = 3.87:1$)

Now convert this exact ratio to the nearest integral ratio. (For example, $3.87:1 \approx 4:1$)

2. What did you expect the ratio of green seedlings to white seedlings to be, given that this difference in color has a simple genetic basis? Explain.

3. Do you think that the difference between the exact ratio that you calculated for Question 1 and the expected ratio that you gave for Question 2 is significant? Explain.



Name _____

Date _____ Hour _____

4. What ratio of green plants to white plants was present in the dark-incubated seedlings on the first day of observation?

5. Is this significantly different than the ratio of green plants to white plants that was present in the light-incubated seedlings on the first day of observation?

6. Formulate a hypothesis to explain this difference between the light-incubated and dark-incubated seedlings.

7. How could your hypothesis be tested?

8. Compare the ratios of green seedlings to white seedlings that were observed in the dark-incubated seedlings on the first observation and the second observation.

First observation: _____

Second observation: _____

9. How do you account for any difference between these two ratios?

10. What overall conclusion can you draw from the data collected in this experiment?



Name _____

Date _____ Hour _____

AN OPTIONAL STEP: A CHI-SQUARE ANALYSIS OF THE ALBINO PLANT DATA

1. Following the instructions for How to Perform a Chi-Square Test on Any Data Set (see Chapter 2, Section E.3) and using the data collected by the class as a whole, calculate χ^2 and p for the light-incubated seedlings on the first day of observation.

χ^2 : _____ p: _____

2. Based on the value of p that you obtained, do you think that the class data for the light-incubated seedlings are consistent with the hypothesis that seedling color is determined by a pair of alleles that exhibit a simple dominant-recessive relationship? Explain.

3. Repeat the calculation of χ^2 and p for the light-incubated seedlings on the first day of observation, using only the data collected by your own group.

χ^2 : _____ p: _____

4. Based on the value of p that you obtained this time, do you think that your own data are consistent with the hypothesis that seedling color is determined by a pair of alleles that exhibit a simple dominant-recessive relationship? Explain.

5. Which data set gave you the higher p value, the class data or your own data? Explain.

6. Do you think you need to perform a χ^2 test to determine whether the data that your class collected with respect to the dark-incubated plants during the first observation are consistent with the proposed hypothesis? Explain.

Heart Disease: A Personal Gene-Environment Interaction

INTRODUCTION

THE IDEA THAT GENES and environment interact to determine phenotype is not just an abstract concept that applies only to test organisms in laboratory experiments. It is an inescapable reality that affects each of us throughout our lives. Moreover, the environment with which our genes must interact to influence our health is largely the environment that we generate by our own lifestyle choices.

Nothing illustrates these principles more clearly than human heart disease. Heart disease remains the principal cause of death in the United States. It is a clear example of what is called a **multifactorial disease**, a disease that is caused not by any one factor but by the interplay of several factors, including genes and lifestyle. Although heart disease is being used as the example in this exercise, it is not an isolated example; most serious human diseases are multifactorial. Before going on, we should point out one common misconception about the environmental risk factors involved in heart disease: namely, that they only matter when you get older. This leads to the attitude that “It’s OK to eat greasy junk food, smoke and drink while you’re young, because you can always clean up your act later on when it matters.” It is true that one’s health is likely to be improved by “cleaning up one’s act” at any age. Nevertheless, it is now very clear that the clogging of the arteries that eventually leads to heart disease can begin in early childhood as a result of poor diet and lack of exercise.

The genetic factors contributing to heart disease are many and complex. There is no single heart disease gene that will cause heart disease if you have one allele and prevent heart disease if you have a different allele. Instead, there appear to be many genetic loci at which particular alleles increase and other alleles decrease the probability that you will get heart disease.

Fortunately or unfortunately, there presently is no way to determine which alleles at most of these loci a particular individual possesses. But some clues come from family history. If many members of your family have had heart disease in the past, it is fairly likely that you have inherited one or more alleles that increase your **heritable predisposition** (genetic risk) of developing heart disease. However, a complete absence of heart disease from your family history provides no assurance that you are free of genetic risk factors.



Whatever the level of one's genetic risk for heart disease, lifestyle choices play a terribly important role in determining whether or not heart disease will actually strike, and if so, at how young an age and how severely. Among the most important environmental risk factors are diet, exercise, smoking, alcohol or drug abuse, high blood pressure, and stress. The way in which these factors interact with various genetic factors is quite complex and poorly understood. But one thing is certain: The more genetic and environmental risk factors that you possess, the more likely it is that you will eventually develop heart disease.

In this exercise, we will run a simulation that should permit you to understand how genetic and environmental risk factors interact to determine the probability that one will experience a multifactorial disease like heart disease. For practical reasons, the assumptions that have gone into setting up this simulation have been simplified greatly relative to conditions in the real world. For example, only three genes will be considered in the simulation, and it will be assumed that the various genetic and environmental risk factors are all strictly additive in their effects. In reality, it appears that many genes are involved, and that various genetic and environmental risk factors may interact in a multiplicative, rather than an additive, manner.

MATERIALS

For each group of four or five students:

- 4 labeled envelopes containing Environmental Risk Cards
- 2 containers each containing 12 poker chips or other objects in three colors



Name _____

Date _____ Hour _____

HEART DISEASE WORK SHEET

1. Determine your environmental (lifestyle) risk. Draw one slip (without looking) from each of the envelopes (A, B, C, and D) that your teacher will pass around. Record the information on that slip in the table below. Add the numbers to get your total environmental risk score.

Envelope	Characteristic	Personal attribute	Score
A	Weight		
B	Diet		
C	Smoking		
D	Exercise		

My total environmental (lifestyle) risk = _____

2. Determine your genetic risk. Two cups containing poker chips or other objects of different colors will now be passed around. The different colored chips will represent alleles with different risk values. One cup will be labeled “Mother’s Genes,” and the other will be labeled “Father’s genes.” When one of these cups reaches you, close your eyes, stir the chips, and pick three chips with your eyes still closed. Open your eyes, record the colors of the chips in the spaces below, and then return the chips to the cup and pass the cup on to the next person. After all students have selected and recorded the colors of their three chips, your teacher will announce the risk score associated with each color of allele. Record these scores below, add up your genetic risk, and then add up your total heart disease risk.

Colors of “Mother’s Genes:” 1. _____ 2. _____ 3. _____

Points for “Mother’s Genes:” 1. _____ 2. _____ 3. _____

Colors of “Father’s Genes:” 1. _____ 2. _____ 3. _____

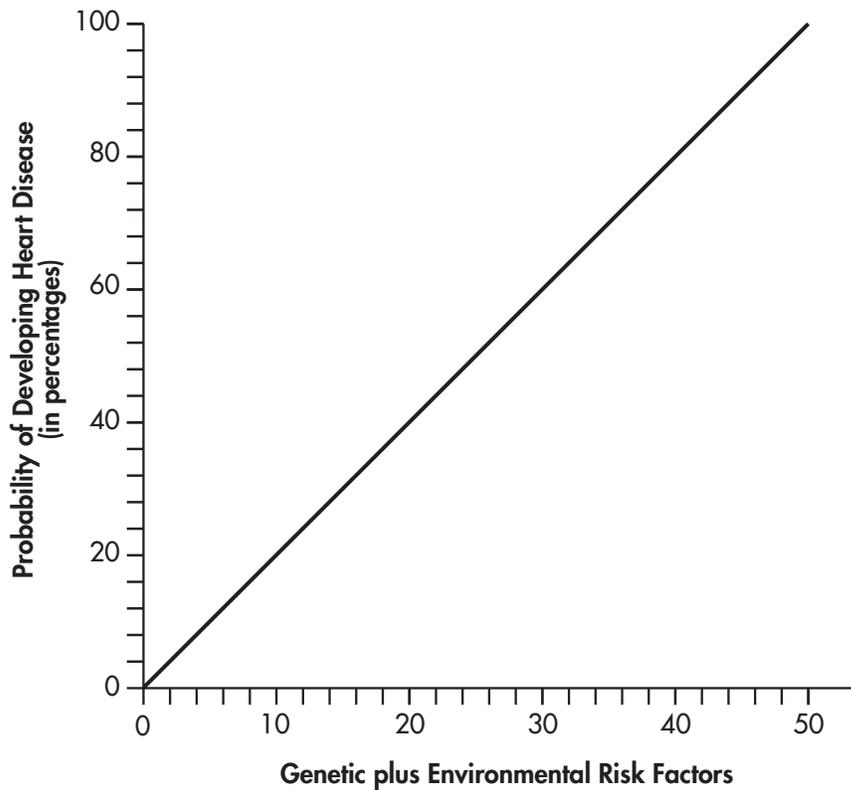
Points for “Father’s Genes:” 1. _____ 2. _____ 3. _____

My total genetic risk = _____

3. Determine your total risk.

My total risk of contracting heart disease = lifestyle risk + genetic risk = _____

4. Using the graph below, determine your probability of developing heart disease.



5. If this were my actual risk score (as opposed to my simulated risk score),

my probability of contracting heart disease would be about _____%.

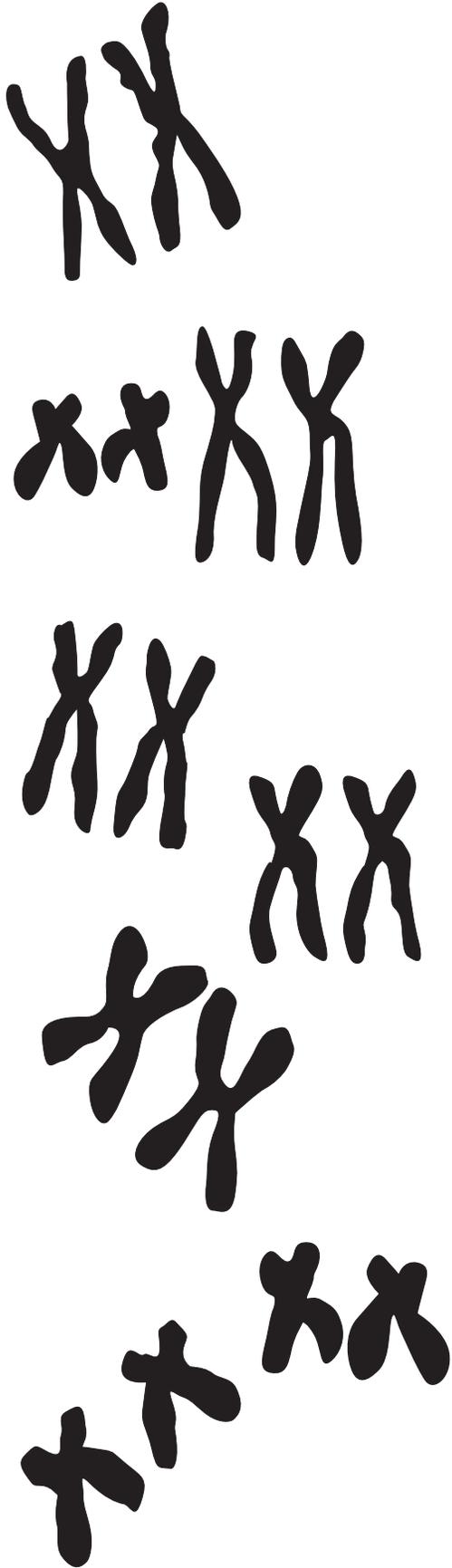
6. My calculated risk of getting heart disease is _____% due to my environmental

(lifestyle) factors and _____% due to genetic factors.

7. Indicate the most important changes you could make in your lifestyle changes to lower your risk of heart disease if your simulated risk scores were your actual risk scores.

8. By doing the above, I could lower my probability of developing heart disease to about

_____%.



CHAPTER 3

**How Genes
and the
Environment
Influence
Our Health**

SECTION D

**What Are
Some of the
Features of
“Simple”
Genetic
Diseases?**

Some “Simple” Heritable Defects

INTRODUCTION

GENES AND THE PROTEINS that they encode are the source of our life and health. Our well-being depends on the proper functioning of thousands of proteins, each of which is encoded by its own gene.

Occasionally, however, one of these genes undergoes a mutation that seriously impairs the function of the corresponding protein. In any individual unfortunate enough to inherit two copies of the mutant gene, any cells that are dependent on the proper functioning of the corresponding protein are in danger. That, in turn, places the whole individual in danger.

More than 4,000 human diseases are now known in which the disease symptoms are primarily a consequence of functional abnormalities of a single mutant protein. The table in Section D.1 lists just a few of the more well-known diseases of this type. Fortunately, even the most common of these diseases are quite rare.

Diseases of the sort listed in the table are commonly called **single-gene diseases** to distinguish them from a disease like heart disease, which (as we saw in the last exercise) has a multigene, multifactorial basis. However, it is now realized that such a distinction is not as meaningful as it might first appear to be. In Section D.2, PKU, one of the most well-known of the single-gene diseases, will be used to illustrate this.

A FEW HUMAN CONDITIONS CAUSED PRIMARILY BY A HERITABLE DEFECT IN A SINGLE PROTEIN

Condition	Protein Affected
Albinism (lack of pigment in skin, hair and eyes)	tyrosinase, an enzyme required to produce melanin from the amino acid tyrosine
Bubble-baby syndrome (failure to make antibodies; the heritable equivalent of AIDS)	adenosine deaminase, an important blood-cell enzyme
Cretinism (severe deficiencies of physical and mental development)	an enzyme required to make the hormone thyroxin from tyrosine
Cystic fibrosis (thick mucus in lungs and many other abnormalities, leading to early death)	a membrane protein required for normal ion balance and secretory activity of cells
Emphysema (loss of elasticity of air sacs in lung)	α 1-antitrypsin, an inhibitor of the protein-digesting enzyme, trypsin (symptoms are aggravated by smoking)
Gout (arthritis-like inflammation of joints)	hyperactivity of an enzyme required for metabolism of ribonucleotides (symptoms strongly affected by diet)
Hemolytic anemia (breakdown of red blood cells)	any one of at least 14 different red blood cell enzymes
Hemophilia (severe hemorrhaging from minor injuries)	any one of 12 different enzymes required for normal blood clotting
Huntingtons disease (progressive mental and physical deterioration, usually beginning after age 40)	a brain protein called <i>huntingtin</i> , the normal function of which is uncertain and the mutant form of which accumulates in the nuclei of brain cells, leading to progressive loss of brain functions
PKU, or phenylketonuria (severe brain damage unless dietary intake of the amino acid phenylalanine is restricted)	phenylalanine hydroxylase, an enzyme required to dispose of excess dietary phenylalanine
Sickle-cell anemia (red blood cells deform and block capillaries, causing severe pain and tissue damage)	the β -globin part of the hemoglobin molecule (symptoms intensified by vigorous exercise and high altitudes)
Tay-Sachs disease (blindness, seizures, mental deterioration, early death)	hexosaminidase, an enzyme required for the breakdown of certain sugar-lipid compounds in brain cells
Xeroderma pigmentosum (mottled, thick, scaly skin condition, usually terminating with fatal skin cancer)	a DNA endonuclease required for repairing DNA that has been damaged by ultraviolet light and has not been cured via photo repair

Phenylketonuria (PKU) Illustrates the Complexities of Some “Simple” Genetic Diseases

PHENYLALANINE IS ONE OF the 20 amino acids present in nearly every protein molecule of every living creature. Humans cannot synthesize the phenylalanine that they need to make their proteins, so none of us could survive without phenylalanine in our diet. However, since phenylalanine is present in nearly every protein molecule in every kind of food we eat, most of us get more phenylalanine from our food than we actually need. Aspartame, the artificial sweetener that is also known as *NutraSweet* and used to sweeten many diet foods, now serves as important source of phenylalanine in some diets, because aspartame is about 50% phenylalanine. Getting extra phenylalanine is no problem for most of us, because we have an enzyme called phenylalanine hydroxylase that converts any extra phenylalanine into tyrosine, another amino acid that we need for making proteins.

However, some people have a mutant gene that encodes a nonfunctional phenylalanine hydroxylase. As a result they are unable to convert phenylalanine to tyrosine. Instead, their body converts any extra phenylalanine that they eat into toxic substances called **phenylketones**, which eventually show up in their urine. Such people are said to have **phenylketonuria**, or **PKU**. Phenyl ketones can cause serious brain damage, especially in babies. Therefore, unless PKU is diagnosed and treated at birth, children with it can quickly develop brain abnormalities and very severe mental handicaps. In most developed countries, however, all babies are tested for PKU immediately after birth, and those with it are immediately placed on a low-phenylalanine diet that includes artificial milk. Such a diet permits normal brain development.

PKU seems like a clear-cut example of a “simple” single-gene disease. It occurs only in people who are homozygous for the mutant allele that encodes a defective phenylalanine hydroxylase enzyme. Heterozygous individuals are symptom-free. However, PKU is also a clear example of the concept implied by the title of this section: namely, that even single-gene diseases can be surprisingly complex.

Although PKU is always thought of as a genetic disease, it clearly illustrates the principle that all aspects of the phenotype are a result of a gene-environment interaction. The symptoms of PKU can be almost completely prevented by simply modifying the environment – specifically, by removing phenylalanine-rich foods from the diet from early childhood on.

Another complication is that PKU is actually a set of closely related diseases, rather than a single disease. More than half of all individuals with PKU are homozygous for the most common mutant allele of the gene encoding phenylalanine hydroxylase. However, most of the remaining PKU individuals have one copy of that most-common mutation in combination with one of many other less-common mutant alleles. These different less-common mutations cause different degrees of phenylalanine hydroxylase deficiency, and thus result in different degrees of mental retardation in untreated children.

PKU is a single-gene disease in the sense that it only occurs in individuals who have two mutant alleles of the gene encoding phenylalanine hydroxylase. However, in another sense it is a multigene disease. This is because many other genes determine how severe the symptoms of PKU will be in untreated babies. Children who are from different families but have the same mutant alleles and similar diets, can have very different degrees of mental retardation. And a few such children are nearly symptom free. The nature of these other interacting genes is largely unknown, but it is thought that some of them probably control factors regulating how sensitive the cells in the developing brain are to phenyl ketones present in the blood.

In short, it is appropriate to consider the mutant genes encoding phenylalanine hydroxylase as the principal cause, but not the sole cause, of PKU. The disease is clearly multifactorial.

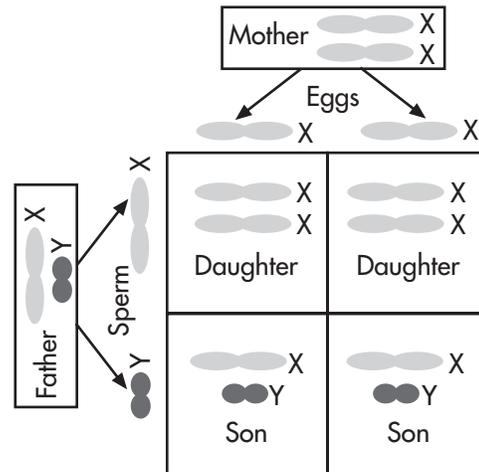
A further complication of PKU has been discovered recently. Women who are homozygous for the mutant PKU allele but have been on a low-phenylalanine diet all of their lives can be free of any PKU symptoms. But sometimes these women have babies who are born with PKU-like brain defects. Such brain defects occur even in babies who are not homozygous for the mutant PKU allele themselves. Apparently a low-phenylalanine diet is adequate to protect the mother – but sometimes not her unborn baby – from the adverse effects of PKU.

It is known that many other so-called single-gene diseases exhibit similar complexities. Probably most of them do. However, hundreds of diseases in this category are so rare that they have never been studied in any detail.

The Special Inheritance Patterns of Sex-Linked Mutations

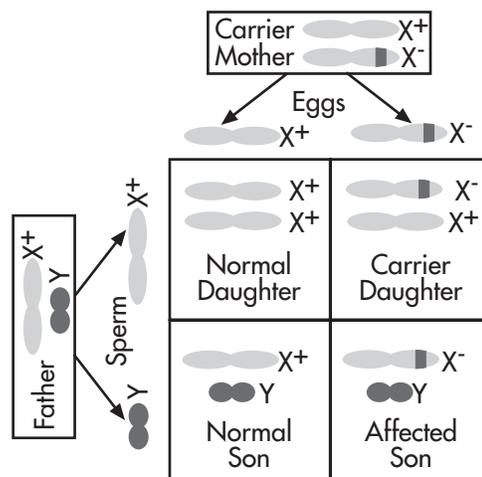
IN HUMANS AND ALL other mammals, gender is determined by the X and Y chromosomes, which are known as the **sex chromosomes**.

Whereas females possess two X chromosomes, males possess one X and one Y chromosome. This results in very specific chromosome inheritance patterns. Children of both sexes inherit an X chromosome from their mother. But whereas girls also inherit an X chromosome from their father, boys never do. They always inherit a Y chromosome from their father, as shown in the Punnett square to the right.



Most genetic disorders occur in males and females with about the same frequency. But certain disorders occur much more frequently in males than in females, and most frequently in men whose mother's father had the same condition. Some examples are red-green color blindness, hemophilia, and Duchenne muscular dystrophy.

These conditions are known as **sex-linked disorders**, because they are a result of mutations of genes that are located on the X chromosome. Thus, they show an inheritance pattern just like the inheritance pattern for the X chromosomes. If a boy develops a sex-linked disorder such as hemophilia (in which blood fails to clot normally), there is a very high probability that his mother is a **carrier** for the disease. That is, that she is heterozygous for the hemophilia mutation, which is recessive. (In rare cases, the boy's hemophilia could be due to a new mutation that occurred in the nucleus of the egg from which he was derived.) We can see how such diseases are transmitted in the Punnett square to the right, in which the mother's normal chromosome is labeled X⁺ and the one carrying the mutant allele is labeled X⁻. The father's X chromosome is also labeled X⁺.





Name _____

Date _____ Hour _____

SEX-LINKED MUTATION WORK SHEET

1. If a woman is a carrier for a mutation causing a sex-linked disorder, what is the chance that one of her sons will have the disorder? Explain.

2. If a woman who is a carrier for a sex-linked disorder already has one son who has the disorder, what is the chance that if she has a second son he will also have the disorder? Explain.

3. If a man has a sex-linked disorder, what is the chance that he will pass it on to one of his sons? Explain.

4. If a man has a sex-linked disorder, what is the chance that one of his daughters will be a carrier for that disorder? Explain.

5. If a man has a sex-linked disorder, what are the chances that one of his grandsons will inherit that disorder? Explain.

6. It has been postulated that a condition known as “hairy ears” is caused by a mutation of a gene on the Y chromosome. Assuming that this is true, what is the chance that one of the sons of a man with hairy ears will inherit the “hairy-ear mutation?” Explain.

7. What is the chance that one of the daughters of the man referred to above will pass the “hairy-ear mutation” on to one of her sons? Explain.

Investigating Human Genetic Diseases

INTRODUCTION

HUMAN DNA CONTAINS ABOUT six billion base pairs packed into 46 chromosomes in each of the approximately four trillion cells in a human body. So it's not too surprising that there are many different things that can go wrong with human genes. Indeed, the most surprising fact may be that we do not all suffer from some serious genetic defect.

The only feature shared by all genetic diseases is that they involve some kind of mutation affecting one or more genes. However, there are several different kinds of mutations that can be present, and they differ with respect to their origins and their heritability patterns.

One important distinction is between **germline mutations**, which are mutations that are passed on in eggs and/or sperm and thus end up in every cell of the offspring, and **somatic mutations**, which originate within a single body cell, and thus are present in only that cell and its direct descendants. Germline mutations can be passed on from generation to generation and are the basis for most heritable diseases such as sickle-cell anemia and PKU. Somatic mutations cannot be passed on to one's offspring, but can cause serious diseases, such as cancer. Although a cancer can damage essential organs, and therefore the entire body, it always starts out as a genetic change within a single cell of the body, most often a change in one of the genes that controls cell division.

Another important distinction is between **point mutations**, which involve DNA sequence changes at one point within a single gene, and **chromosomal mutations**, which involve abnormalities affecting large chromosomal regions or even whole chromosomes. In most cases the diseases listed in Table D.1 and many others are the result of point mutations. But some serious diseases, for example Down syndrome, are the result of having one extra chromosome. Such a problem indicates that the chromosomes did not separate properly at the meiotic division that was involved in formation of either the sperm or the egg.

Other distinctions involve differences of the sort that you have already encountered – such as the distinction between dominant and recessive mutations and between single-gene and multigene diseases.

A final distinction to be made is between sex-linked mutations, which are mutations of genes that are located on the X (or occasionally the Y) chromosome, and **autosomal mutations**, which are mutations of genes that are located on any other chromosome.

PRODUCING A PAMPHLET FOR A GENETIC COUNSELOR

In this exercise, you are to produce a pamphlet about some particular genetic disorder. The intent is to produce a pamphlet of the sort that could be displayed in a genetic counselor's waiting room for parents and family members to pick up and read. You should supply information regarding the following topics:

1. Title of the disorder. (You may want to create an interesting title for your brochure, but avoid being too cute. Remember that for an affected family seeking help, a genetic disease can be very serious business.)
2. Symptoms of the condition. (Find as many as you can, list them, and describe them clearly and concisely.)
3. The type of genetic change that causes this condition (select one).
 - a. A point mutation involving a base substitution, deletion, or addition; autosomal or sex-linked; dominant or recessive. Explain how this kind of mutation occurs and is transmitted from generation to generation.
 - b. A chromosomal mutation involving a deletion, duplication, translocation, or inversion of a piece of a chromosome. Explain how this kind of chromosomal mutation occurs.
 - c. A missing or extra chromosome. Explain how this kind of chromosomal abnormality occurs.
4. The frequency with which this condition occurs in the population. Does it occur more frequently in certain human populations than in others?
5. Environmental factors (such as diet, exercise, exposure to sunlight) that may be known (or even thought) to affect the severity of the disease.
6. Treatments, if any, for this condition.
7. Facilities that offer treatments for individuals suffering from this condition and/or emotional support for members of the family. (Hospitals, genetic counselors, support groups, websites, Yellow Pages) Be specific.

To investigate these questions, you may use library reference books, medical and general encyclopedias, genetics textbooks, and the Internet. Websites have been created to provide information about many such genetic disorders.



The topics listed above should be the basis for sections of your pamphlet. As you are writing, remember that your audience is made up of individuals whose understanding of genetic terms and concepts may be quite limited. At the end of your pamphlet, list two references in acceptable bibliographic style. You may use clip art or your own artwork to enhance your pamphlet.

The grading of your pamphlet will be based on:

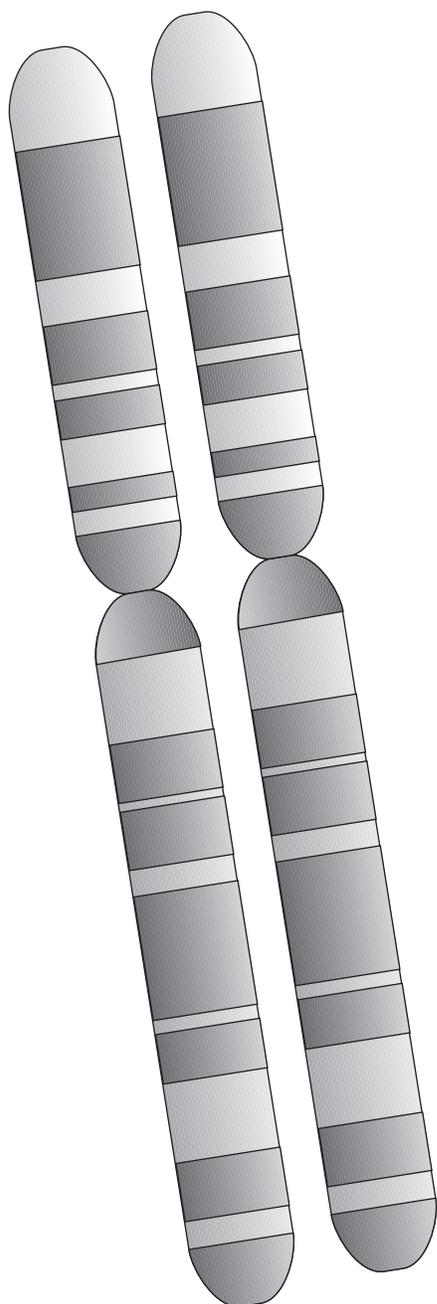
1. Evidence that you accessed, analyzed, and synthesized the relevant information.
2. The completeness and accuracy of the information that you presented.
3. The clarity with which you expressed this information.
4. The overall appearance of your finished pamphlet.

Below is a sampling of genetic diseases that you might investigate and produce a pamphlet about.

achondroplasia
breast cancer
club foot
color blindness
coronary artery disease
cystic fibrosis
Down syndrome
fragile X syndrome
Huntingtons disease
Klinefelter syndrome
Marfan syndrome
phenylketonuria
Prader-Willi syndrome
retinoblastoma
spina bifida
trisomy 13 syndrome
Wolf-Hirschhorn syndrome

beta-thalassemia
cleft palate
colon cancer
congenital hip dysplasia
cri-du-chat syndrome
diabetes, non-insulin dependent
Duchenne muscular dystrophy
hemophilia
hypertension
Lesch-Nyhan syndrome
neurofibromatosis
polycystic kidney disease
pyloric stenosis
sickle-cell anemia
Tay-Sachs disease
Turner syndrome

There are many other possibilities. If you have come across a disease in your reading that interests you as a possible research topic, but is not included in the above list, discuss it with your teacher.

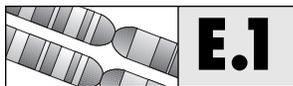


CHAPTER 3

**How Genes
and the
Environment
Influence
Our Health**

SECTION E

**How Does
a Genetic
Counselor
Detect
Mutant
Genes?**



Detecting the Duchenne Muscular Dystrophy (DMD) Mutation

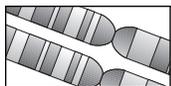
IN THIS EXERCISE WE will pretend that you are a technician in a genetic counselor's laboratory. You will perform a DNA screening test that is similar to the one used by real genetic counselors, and then you will interpret the results and decide how to present this genetic information to the family that is involved.

The situation you will be dealing with is the following: Mary and John Smith have three children: Daniel, age 5; Alice, age 4; and Michael, age 1. Mary is two months pregnant. Recently Mary and John noticed that Daniel was having trouble climbing the stairs. He also complained several times that he was really tired after playing tag with his sister. Daniel's doctor suggested some medical tests, which brought the family some bad news: Daniel has a disease called Duchenne muscular dystrophy (DMD).

Mary and John had never heard of DMD before, so they asked the doctor a lot of questions and went to the library for more information. They learned that DMD is a sex-linked genetic disease, which means that it results from damage to a gene on the X chromosome. That is why almost everyone with DMD is male. A girl may inherit an X chromosome with a defective copy of the DMD gene from her mother and like her mother, she will be a carrier for DMD. But the girl most likely will be protected from developing DMD by the normal X chromosome she gets from her father. In contrast, a boy does not get an X chromosome from his father, and if the X chromosome he gets from his mother carries a defective copy of the DMD gene, he will develop DMD.

Usually boys with DMD are healthy until the age of 4 or 5, at which time their muscles start to weaken. The doctor told the Smiths that Daniel would probably need a wheelchair in a few years, and that he would probably die before the age of 21. Although scientists are working to find a cure for this disease, there is no effective treatment for DMD now.

Obviously, Mary and John were very upset by this news about Daniel. Then they began to worry about their other children. Because Mary was a carrier for DMD, it was possible that Michael would develop DMD also, although he was too young to show any symptoms yet. They also worried about their unborn child and whether he or she might be at risk for DMD. Finally, even though Alice would not develop DMD, the Smiths wanted to find out whether she was a carrier like her mother. When the doctor explained that there is a genetic test that could determine whether each family member had the defective gene for DMD, Mary and John decided that they wanted this information. So the doctor sent them to a genetic counseling center where the tests could be done.



E.1

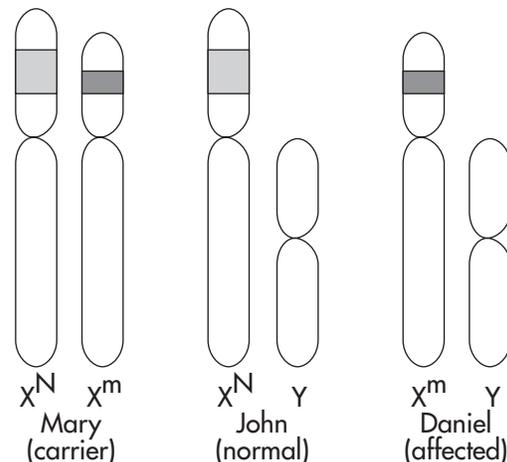
First the genetic counselor met with Mary and John and reviewed with them all of the information about DMD that they had received earlier. She tried to make sure that they understood the nature of the test that was to be performed, what kinds of information it could provide them, and how they might choose to use that information once they had it. When the Smiths assured their counselor that they understood, and that they did want to have the test performed, you, as lab technician, took a small drop of blood from a finger of each family member. Mary also went through a process of fetal blood sampling, so that the DNA from her unborn child could also be tested. The genetic counselor told Mary and John to come back in a week to find out the test results.

You took the Smith's blood samples and isolated DNA from the white blood cells in each of them. But the DMD gene that the Smith family wished you to analyze was only one of many thousand genes in each of the resulting DNA samples. So, to get enough of this particular gene to study, you used a procedure called **PCR** (short for **polymerase chain reaction**) to amplify (make many copies of) the tiny section of DNA that contained the DMD gene.

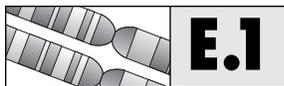
PCR uses **DNA polymerase** (the same enzyme that cells use to replicate their DNA before they divide) to replicate, over and over again, a particular DNA region of interest. A single round of replication takes only about two minutes. Then both the copies made in that first round can be replicated again, and so on. At this rate of doubling, PCR can produce over a billion copies of a piece of DNA in about an hour. With so many copies of that gene in each tube, it becomes much easier to compare genes from different individuals and see if they are the same or different

You have used PCR to make billions of copies of the DMD genes from the DNA sample taken from each member of the Smith family. Now your next job is to analyze the samples and determine which ones contain only copies of the wild-type DMD allele, which ones contain only copies of the mutant DMD allele, and which ones contain copies of both DMD alleles. As an expert, you know that most mutations that cause this disease involve a deletion of part of the DNA from the DMD gene, so that the mutant alleles will be shorter than the wild-type alleles. As illustrated in

the diagram, this implies that Mary, who is a carrier for DMD, has one normal and one short (mutant) allele at the DMD locus. Since John, being a male, has only one X chromosome and does not have DMD, his DMD allele must be of normal length. Daniel has the DMD disorder, so he must have received the X chromosome with the defective DMD gene from his mother.



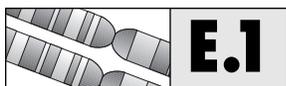
Now the question is, Which DMD alleles do the other family members have? That's what you will try to determine.



DNA molecules that differ in length can be separated and analyzed by a process known as **agarose gel electrophoresis**. This method uses an electric current to push DNA molecules through a gel-like substance called **agarose**. Small DNA molecules move through the gel faster than large ones.

You will use agarose gel electrophoresis to simulate the procedure that the genetic counseling lab would use to determine the genotypes of a set of family members with respect to a gene of interest – such as the DMD gene. In a real diagnostic test, PCR-amplified DNA samples derived from the blood cells of the various members would be subjected to gel electrophoresis, and then the gel would be stained to make the DNA fragments visible. Each family member's DNA sample would then be seen to contain one or both of two different sizes of DNA fragments: small or large. From this information, the counselor would then determine whether each individual had only the normal allele, only the mutant allele, or one of each (and therefore was a carrier).

Because we do not have a real Smith family, a real PCR machine, or a real PCR technician available in our classroom, we will use two dyes of slightly different color to represent the mutant and normal DNA fragments of interest. Each sample you receive for electrophoresis will contain one or both of these dyes. The dyes are ones that (like DNA molecules of different lengths) move through a gel at different rates when subjected to an electric field. The faster-moving dye will represent the mutant DMD allele, and the slower moving one will represent the wild-type allele. Your job will be to determine which allele(s) each member of the Smith family possesses, by inspecting the gel at the end of the electrophoresis.



MATERIALS

For each group of students (group size to be determined by equipment availability):

- 1 precast agarose gel, or 1 gel-casting tray plus masking tape, 1 or 2 gel-casting combs and 50 ml of 0.8% agarose in water
- a gel electrophoresis chamber and power supply
- a small container of tap water
- 1 20 μ l micropipettor
- a weighing boat or piece of white paper
- 6 dye samples labeled A-F
- 6 pipette tips

PROCEDURE

If your teacher provides you with a pre-poured agarose gel, you will begin at step e. below.

1. To prepare the agarose gel:
 - a. Seal the ends of the gel-casting tray with masking tape. Insert the comb near one end of the casting tray. If your teacher instructs you to put two combs in your tray, so that two groups of students can run their samples at the same time, the second comb should be placed just beyond the center of the tray. Place the tray on a level surface where it will not be disturbed while the gel solidifies.
 - b. Carefully obtain a flask with melted agarose solution from the water bath or hot plate.
 - c. Carefully pour about 50 ml of the agarose solution into the casting tray, to fill it to a depth of about 4 mm. The gel should cover only about one-third of the height of the comb teeth.
 - d. Do not move or jar the casting tray while the agarose solidifies. As it becomes solid (10-15 minutes), the agarose will change from clear to cloudy.
 - e. When the agarose is solid, carefully remove the tape from the casting tray to expose the ends of the gel.
 - f. Take the gel to the area where the gel electrophoresis chamber has been set up next to the power supply. Place the gel in the electrophoresis chamber so that the end containing the comb is toward the black electrode. Fill the chamber with tap water to a level that just covers the entire surface of the gel.
 - g. Slowly and gently remove the comb, taking care not to rip the gel. The water will lubricate the comb so it pulls out more easily.
 - h. Make certain that the wells (holes) left in the gel by the comb are completely covered with a layer of water. If you notice “dimples” around the wells, slowly add water until they disappear.

2. To load the samples:

- a. Use a micropipettor to load 5 μl of each sample into separate wells as shown in the diagram below. Leave one well empty at each end (fig. 1).
- b. Using two hands, steady the micropipettor over a well.
- c. Carefully dip the pipette tip through the surface of the water, center it over the well, and then gently depress the pipette plunger to slowly expel the sample into the appropriate well. If the tip is centered over the well, the DNA will sink to the bottom of the well. Do not release the plunger until the tip is out of the buffer.
- d. As one person adds the samples to the wells, another member of the group should label the diagram on the DMD Diagnosis Work Sheet to indicate which sample went in which well.

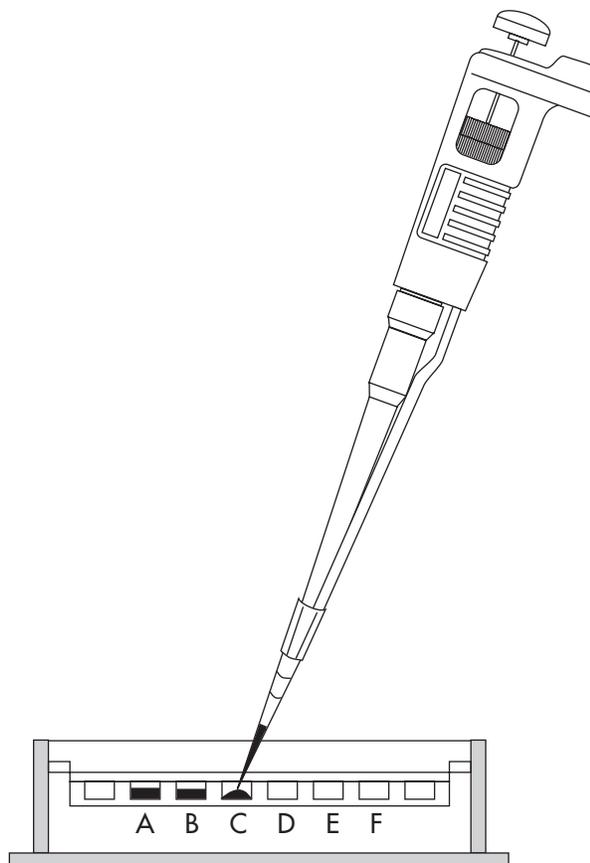
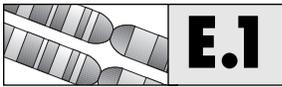


Figure 1

- e. If two groups of students are to run their samples in the same gel, one group of students should finish putting their samples in one set of wells before the second group begins to add their samples to the other set of wells.



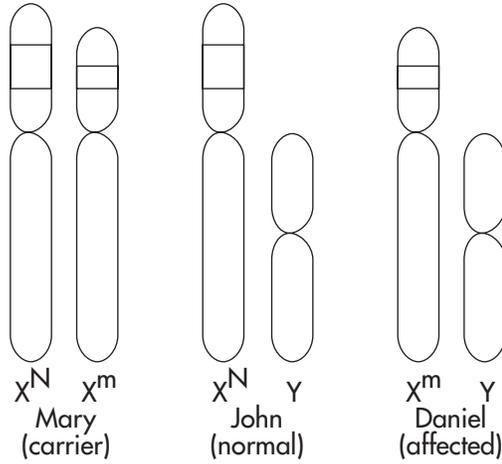
3. To separate DNA through electrophoresis:
 - a. Avoid moving or bumping the electrophoresis chamber as you do the following:
Close the top of the electrophoresis chamber and connect the electrical leads to the power supply, red to red and black to black. Make sure both electrodes are connected to one channel of the power supply.
 - b. Notify your teacher that you are ready to run your gel.
 - c. As soon as you get your teacher's approval, set the power source to 130 volts and turn on the unit.
 - d. The dial should now register approximately 50-100 milliamps. This confirms that current is flowing through the gel. If you do not detect a current, turn off the power supply, check the connections, and try again.

CAUTION: Electric shock hazard! Do not put fingers or other objects into the box while power supply is on.

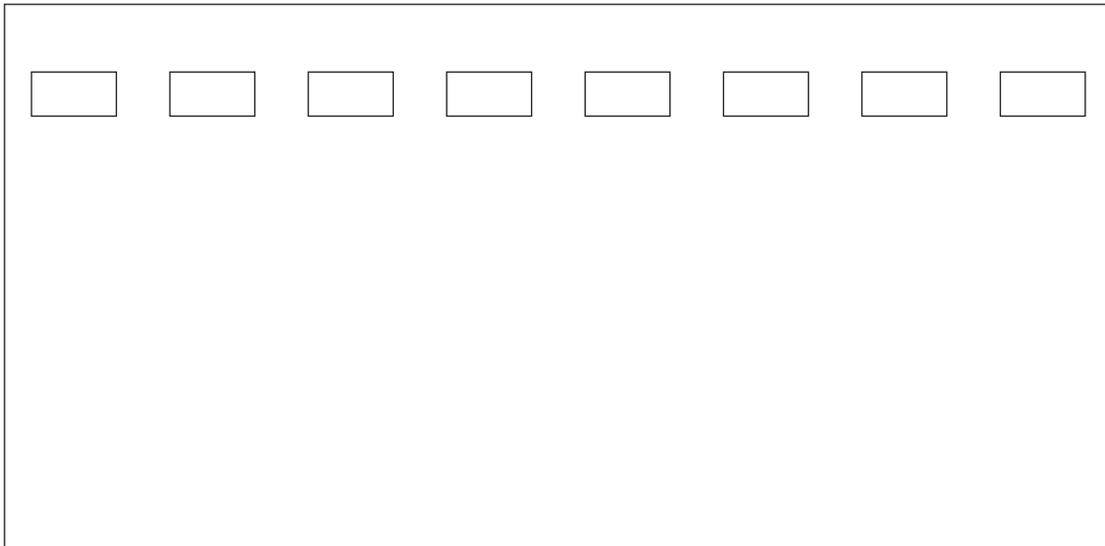
- e. Shortly after the current is applied, you should see the samples moving into the gel.
- f. Run the electrophoresis for approximately 15 minutes. Check to monitor the progress of the dye bands. (If you leave the gel running for too long, the dyes will run out the end of the gel and get lost in the water.)
- g. When the dyes have moved far enough to be clearly distinguishable, turn off the power supply. Then disconnect the leads.
- h. Carefully remove the gel from the electrophoresis chamber and place it in a weighing boat or on a piece of white paper for viewing. Then complete the DMD Diagnosis Work Sheet.

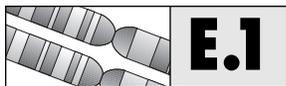
DMD DIAGNOSIS WORK SHEET

1. On the diagram below, color the defective alleles purple and the normal alleles blue.
 NOTE: Deletion not to scale.



2. On the diagram below, a) above each well, put the letter that was on the sample that was loaded into that well and b) using colored pencils, draw all the bands that you observed on your gel after electrophoresis.





Name _____

Date _____ Hour _____

3. Fill in each of the blanks in the data table below:

Sample	Family Member	# of DMD Alleles	Genotype	Status
Tube A	Mother Mary	2	$X^N X^m$	Carrier
Tube B	Father John	1	_____	Healthy
Tube C	Son Daniel	1	_____	Has DMD
Tube D	Daughter Alice	_____	_____	_____
Tube E	Son Michael	_____	_____	_____
Tube F	Fetus M or F (circle)	_____	_____	_____

4. Which allele moves further into the gel, the normal (X^N) or mutant (X^m) allele? Why?

5. Is the daughter, Alice, a carrier for DMD? How can you tell? _____

6. Does Michael have DMD? How can you tell? _____

7. What can you tell the Smith family about their unborn child? _____

8. Why are most patients with DMD male? _____

9. Can a boy be a carrier for DMD without having the disease? Why or why not?

10. If you were the genetic counselor in this case, what would you tell the Smiths about their test results?

Career

CHAPTER 3

How Genes and the Environment Influence Our Health

SECTION F

How Can I Become a Genetic Counselor ?

How Can I Become a Genetic Counselor?

A GENETIC COUNSELOR WORKS with individuals or families who are afflicted with a genetic disease or are concerned that they might be. As knowledge has increased, the list of genetic diseases has been extended to include such complex, multifactorial conditions as diabetes, heart disease, and Alzheimer's, in addition to the more classical single-gene diseases (PKU) and chromosomal diseases (Down syndrome).

In many cases families with a sick child will be referred to a genetic counselor by a family physician or pediatrician who suspects that the child's symptoms may be due to a particular disease that has a known genetic basis. In other cases a couple will seek the help of a genetic counselor much earlier, during early pregnancy, if their family histories suggest that their developing fetus may have some serious heritable disease. In yet other cases a couple may visit a genetic counselor even earlier, to determine whether they are carriers for a disease that runs in one or both of their families and to get advice about whether they should avoid pregnancy. But because the number and types of genetic abnormalities that can be detected by specific DNA tests is now increasing very rapidly (along with people's familiarity with genetics), a growing number of people seek the services of genetic counselors for more reasons every year.

The responsibilities of a genetic counselor may vary, but often include one or more of the following:

- helping to diagnose a disease suspected of being genetic by prescribing or performing appropriate DNA tests;
- providing the afflicted individual and/or other family members with information about the nature of the disease, its genetic basis, and the way that symptoms of the disease can be expected to change over time;
- working with the affected individual, other family members, and physicians to provide up-to-date information about various treatment options;
- informing relatives of the afflicted individual about their risks of being carriers for the disease, of being affected by it, and of passing it on to their children or grandchildren;
- prescribing or performing diagnostic tests designed to provide other family members with information that they request, regarding their own genetic status;
- providing a list of all possible options to a woman who is carrying a fetus that has been found to have a genetic liability.

It is generally agreed that one of the most important requirements for effective and ethical genetic counseling is being able to provide all of the relevant information to patients and family members in a value-neutral manner. That is to say, a genetic counselor should avoid trying to impose his or her own values on the decision making process of the patient or family. Rather, the job of the genetic counselor is to help those affected identify the course of action that they consider best in terms of their own values.

The first step toward a career in this area is to attend college and get a well-rounded education, with a strong background in the humanities and social sciences as well as an emphasis on chemistry and biology (and particularly genetics). Because genetic counseling often involves risk prediction and manipulation of probabilities, course work in statistics could prove very helpful. If it were possible to do a research project under the supervision of a faculty member who was interested in genetics, that could significantly enhance your preparation.

Such a college education would probably qualify you for a job as a technician in a genetic counseling laboratory, running diagnostic tests like the one that was simulated in the preceding exercise. However, in order to interact directly with patients and perform most of the responsibilities listed above, one must first become accredited as a genetic counselor by the American Board of Medical Genetics, and that requires studies beyond the undergraduate college level.

There are two principal routes one can follow after undergraduate studies to prepare for a position in genetic counseling. The first is to attend graduate school and study human genetics at either the MS or the PhD level. There are now several master of science programs in genetic counseling that lead to accreditation as a genetic counselor. Individuals who have followed this route generally provide patients and/or their families with information regarding the nature and possible progression of the disease that the patient is experiencing, assist family members with risk assessment, as well as ordering and interpreting diagnostic tests for other members of the family.

In order for you to be able to assume ultimate responsibility for genetic diagnosis, counseling, and treatment however, you would need to attend medical school and obtain an MD degree. Physicians with an interest in genetic counseling and treatment have traditionally specialized in pediatrics in the past, because most single-gene diseases and chromosomal diseases become apparent in infants. (Typically, about a third of all patients admitted to a pediatric hospital suffer such diseases.) However, this situation is changing, as genetics is increasingly being used to diagnose disease, assess patient risk, and select effective therapies for older individuals. Therefore, an increasing number of physicians are combining their interests and training in medical genetics with a specialization in internal medicine or family practice.

The three types of specialists discussed here (physicians specializing in genetic disease, accredited genetic counselors, and genetics lab technicians) will typically work together, often in conjunction with the patient's primary-care physician, on each case.

Additional information about preparing for such careers can be obtained from the following:

The National Society of Genetic Counselors, Executive Office
233 Canterbury Drive
Wallingford, PA 19086-6617
Telephone: (610) 872-7608
<http://www.kumc.edu/gec/prof/nsgc.html>

A World of Genetic Societies (links to various genetics-related sites)
<http://www.faseb.org/genetics>

Information about a broader range of careers in genetics is available at
<http://www.ornl.gov/hgmis/education/careers.html>