

Rare Diseases and Scientific Inquiry

developed under a contract from the
National Institutes of Health

Office of Rare Diseases Research



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This material is based on work supported by the
National Institutes of Health under Contract No.
HHSN263200800031C. Any opinions, findings,
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Foreword

Rare Diseases and Scientific Inquiry is the most recent addition to the National Institutes of Health (NIH) Curriculum Supplement Series. This series brings the latest medical science and research discoveries from NIH into the K–12 classroom. NIH plays a vital role in the health of all Americans and seeks to foster interest in research, science, and medicine-related careers for future generations. The NIH Office of Science Education is dedicated to promoting scientific literacy and the knowledge and skills we need to secure a healthy future for all.

Rare Diseases and Scientific Inquiry gives students an opportunity to grapple with some of the most challenging and engaging medical issues that confront our society. We designed *Rare Diseases and Scientific Inquiry* to complement existing life science curricula and to be consistent with *National Science Education Standards*. Middle school science teachers, medical experts, education specialists, scientists, representatives from the NIH Office of Rare Diseases Research (ORDR), and curriculum-design experts from Biological Sciences Curriculum Study (BSCS) created the activities. The collaborative development process includes geographically dispersed field tests by teachers and students.

The curriculum supplements enable teachers to facilitate learning and stimulate student interest by applying scientific concepts to real-life scenarios. Design elements emphasize key biology concepts and analytic methods, cutting-edge science content, and built-in assessment tools. Activities promote active and collaborative learning to help students develop problem-solving strategies and critical-thinking skills.

Each of our curriculum supplements comes with a complete set of printed materials for teachers, including extensive background and resource information, detailed lesson plans, and masters for student worksheets. The Web site accompanying *Rare Diseases and Scientific Inquiry* has interactive materials to support the lessons. The supplements are distributed for free to educators across the United States upon request. They may be copied for classroom use and educational purposes but may not be sold.

We welcome your feedback. For a complete list of curriculum supplements and ordering information, or to submit feedback, visit <http://science.education.nih.gov> or write to
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We appreciate the valuable contributions from the talented staff at BSCS. We are also grateful to the NIH scientists, advisors, and all other participating professionals for their work and dedication. Finally, we thank the teachers and students who participated in focus groups and field tests to ensure that these supplements are both engaging and effective. I hope you find our series a valuable addition to your classroom, and I wish you a productive school year.

Bruce A. Fuchs, Ph.D.
Director
Office of Science Education
National Institutes of Health

About the National Institutes of Health

Founded in 1887, NIH is the federal focal point for health research in the United States. Today, it is one of the agencies in the Department of Health and Human Services. Its mission is science in pursuit of fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to extend healthy life and reduce the burdens of illness and disability. NIH works toward meeting the mission by providing leadership, direction, and grant support to programs designed to improve the health of the nation through research.

NIH's education programs contribute to ensuring the continued supply of well-trained

basic research and clinical investigators, as well as the myriad professionals in many allied disciplines who support the research enterprise. These efforts also help educate people about scientific results so that they can make informed decisions about their own—and the public's—health.

This curriculum supplement is one such education effort. It is a collaboration among the Office of Rare Diseases Research, the NIH Office of Science Education, and Biological Sciences Curriculum Study.

For more about NIH, visit <http://www.nih.gov>.

About the Office of Rare Diseases Research

The Office of Rare Diseases (ORD) was established in 1993 at the National Institutes of Health. Later, the ORD's focus on research prompted a name change to the Office of Rare Diseases Research (ORDR). The ORDR provides information on rare diseases and rare disease research; supports scientific conferences; cosponsors, with the National Human Genome Research Institute, the Genetic and Rare Diseases Information Center; and coordinates and supports research on the diagnosis and treatment of rare diseases both intramurally and extramurally. The Office also funds the Rare Diseases Clinical Research Network (RDCRN), a group of clinical research sites in the United

States and several foreign countries working on about 100 different rare diseases, and is working to harmonize community efforts on patient registries and biospecimen repositories. A rare disease (also called an “orphan disease”) is a condition affecting fewer than 200,000 people in the United States (about 1 in 1,500) or one affecting more people but “for which no reasonable expectation exists that the costs of developing or distributing a drug can be recovered from the sale of the drug in the United States” (Orphan Drug Act of 1983).

For more about the ORDR, visit <http://rarediseases.info.nih.gov>.

About Biological Sciences Curriculum Study

Headquartered in Colorado Springs, Colorado, BSCS was founded in 1958 as a curriculum study committed to an evidence- and inquiry-based approach to science education. BSCS instructional materials and professional development services are based on current research about teaching and learning for all science classrooms, kindergarten through college.

BSCS's materials are extensively field-tested in diverse settings across the country and evaluated for proven effectiveness. The BSCS 5E

Instructional Model and inquiry are hallmarks of its materials, placing students at the center of their learning.

The BSCS mission is to transform science teaching and learning through research and development that strengthens learning environments and inspires a global community of scientifically literate citizens. BSCS is a 501(c)(3) nonprofit organization.

For more information, please visit <http://www.bscs.org>.

Introduction to *Rare Diseases and Scientific Inquiry*

Calling a disease “rare” raises questions. What does it mean to say that a disease is rare? Why should rare diseases be singled out for special attention? In the United States, a disease is considered rare if it affects fewer than 200,000 people. Approximately 7,000 rare diseases are recognized, and researchers continue to describe new ones. Taken together, rare diseases represent a significant health concern affecting over 25 million Americans. Like more-common diseases, rare diseases may be caused by gene mutations, infection from pathogens, and exposure to harmful substances in the environment.

Because rare diseases affect fewer people than common diseases do, they have traditionally been allocated fewer research resources. This has made it more difficult for people with rare diseases to obtain accurate diagnoses of their conditions. Even with an accurate diagnosis, patients may find that there are no existing medications or other treatments to help them. People with rare diseases may feel isolated and even stigmatized. Fortunately, during the past 25 years, increased attention has been devoted to the study of rare diseases, and new treatments are being developed to help patients.

What Are the Objectives of the Supplement?

Rare Diseases and Scientific Inquiry has two main objectives: to help students in grades 6–8 understand

1. that studying rare diseases is not only important to the people affected by the diseases, but it also contributes to understandings that researchers can apply to other, more-common diseases or, more generally, to how the body works and

2. the process of scientific inquiry through studying rare diseases.

The lessons in this supplement help students sharpen their skills in observation, critical thinking, experimental design, and data analysis. They also make connections to other disciplines such as English, mathematics, and social science.

As the supplement achieves its objectives, it helps convey to students the purpose of scientific research. Students experience how science provides evidence that can be used to understand and treat human disease. Ongoing research affects how we understand the world around us and gives us the foundation for improving choices about our personal health and the health of our community.

The lessons in this supplement encourage students to think about the relationships among knowledge, choice, behavior, and human health in this way:

**Knowledge (what is known and not known)
+ Choice = Power**

Power + Behavior = Enhanced Human Health

The final objective of this supplement is to encourage students to think in terms of these relationships now and as they grow older.

Why Teach the Supplement?

Middle school life science classes offer an ideal setting for integrating many areas of student interest. In this supplement, students participate in activities that integrate inquiry, science, human health, mathematics, and

science-technology-society relationships. The real-life context of the supplement's classroom lessons is engaging for students, and they can immediately apply what they learn to their lives.

What's in It for the Teacher?

Rare Diseases and Scientific Inquiry meets many of the needs of teachers in modern classrooms:

- The supplement meets science content, teaching, and assessment standards in the *National Science Education Standards*

(National Research Council (NRC), 1996). It pays particular attention to the standards on scientific inquiry.

- It is integrated with other subjects, drawing most heavily from science, social science, mathematics, and health.
- It has a Web-based technology component that includes interactive activities and simulations.
- Finally, the supplement includes built-in assessment tools, which we note with an assessment icon in each lesson.

Table 1. Correlation of *Rare Diseases and Scientific Inquiry* to Middle School Biology Topics

Topics	Lesson 1	Lesson 2	Lesson 3	Lesson 4	Lesson 5
Important levels of biological organization include cells, organs, tissues, organ systems, whole organisms, and ecosystems.		✓	✓	✓	
Specialized cells carry out specialized functions.	✓	✓	✓	✓	✓
Humans have various body systems including those for digestion, reproduction, circulation, excretion, movement, control and coordination, and protection from disease.	✓	✓	✓	✓	✓
Body systems interact with each other.			✓	✓	✓
Every organism requires a set of instructions for specifying traits. Heredity is the passage of these instructions from one generation to another.		✓	✓	✓	✓
Hereditary information is contained in genes. An inherited trait of an individual can be determined by one or by many genes. A single gene can influence more than one trait.			✓	✓	✓
The characteristics of an organism can be described in terms of a combination of traits. Some traits are inherited, and others result from interactions with the environment.			✓	✓	✓
Natural environments may contain substances and microbes that are harmful to human beings.	✓	✓	✓	✓	✓

In addition, the supplement provides a means for professional development. Teachers can engage in new and different teaching practices like those described in this supplement without completely overhauling their entire program. In *Designing Professional Development for Teachers of Science and Mathematics*, S. Loucks-Horsley and coauthors (1998) write that supplements such as *Rare Diseases and Scientific Inquiry* can “offer a window through which teachers can get a glimpse of what new teaching strategies look like in action.” By experiencing a short-term supplement like this one, teachers can “change how they think about teaching and embrace new approaches that stimulate students to

problem solve, reason, investigate, and construct their own meaning for the content.” The use of supplemental material like *Rare Diseases and Scientific Inquiry* can encourage reflection and discussion and stimulate teachers to improve their practices by focusing on student learning through inquiry.

A correlation of the supplement’s major concepts with the biology and scientific inquiry topics often included in the middle school life science curricula follows (Tables 1 and 2). We hope this information helps teachers make decisions about incorporating this material into the curriculum.

Table 2. Correlation of *Rare Diseases and Scientific Inquiry* to Middle School Scientific Inquiry Topics

Topics	Lesson 1	Lesson 2	Lesson 3	Lesson 4	Lesson 5
Testable questions can be answered through scientific investigations.		✓	✓	✓	✓
Scientific investigations use appropriate tools to gather, analyze, and interpret data.		✓	✓	✓	✓
Evidence is used to develop explanations and make predictions.		✓	✓	✓	✓
Critical thinking is used to relate evidence to explanations.	✓	✓	✓	✓	✓
Alternative explanations are recognized and analyzed.	✓	✓	✓	✓	✓
Mathematics is important to scientific inquiry.		✓	✓	✓	✓

Implementing the Supplement

We designed the five lessons in this supplement to be taught in sequence for approximately 10 days, assuming class periods of about 50 minutes. The following pages offer general suggestions about using these materials in the classroom; you will find specific suggestions in the procedures of each lesson.

What Are the Goals of the Supplement?

Rare Diseases and Scientific Inquiry is designed to help students attain these major goals associated with scientific literacy:

- to understand a set of basic scientific principles related to the study of rare diseases and the relationships of rare diseases to common diseases and human health,
- to experience the process of scientific inquiry and develop an enhanced understanding of the nature and methods of science, and
- to recognize the role of science in society and the relationship between basic research and human health.

What Are the Science Concepts and How Are They Connected?

The lessons are organized into a conceptual framework that allows students to start with what they already know about disease and scientific inquiry, some of which may be incorrect. They then gain a scientific perspective

on rare diseases and the importance of these diseases to medicine and to their lives.

Students begin by considering their initial thoughts about disease, its causes, what makes a disease rare, and what it might be like to cope with a rare disease (Lesson 1). Students then explore the three major causes of disease (genetics, environmental exposure, and infectious agents). They focus on the case of an infectious bacterium that can cause both a common and a rare disease (Lesson 2). We use a case study to explain how a rare disease is identified and to illustrate the sometimes difficult problem of obtaining an accurate diagnosis (Lesson 3). In Lesson 4, students investigate how medical research and clinical trials have affected the treatment of a rare disease.

Lesson 5, the final lesson, gives students an opportunity to consider what they have learned in the previous lessons. The creation of an informational poster has students reconsider what they learned about rare diseases: how the diseases are investigated, how medical research can affect their treatment, and what it is like to cope with one. The following chart (Table 3) illustrates the science content and conceptual flow of the classroom lessons and activities.

Table 3. Science Content and Conceptual Flow of the Lessons

Lesson	Learning Focus, from BSCS 5E Instructional Model	Major Concepts
Lesson 1— What Is a Rare Disease?	Engage	Students may have different ideas about the definition of “disease.” They may also have naïve preconceptions about what makes a disease rare and how rare diseases are treated, and they may have attitudes about people with rare diseases.
Lesson 2— What Causes Rare Diseases?	Explore	Diseases have three main causes: genetics, environmental exposure, and infectious agents. These three influences sometimes interact with each other. An infectious agent may be able to cause a common disease in one case and a rare disease in another case. Doctors must ask testable questions and collect evidence to answer such questions when coming to a diagnosis.
Lesson 3— The Difficulty of Diagnosis	Explain	Some rare diseases are inherited. A rare disease may affect multiple body systems. Rare diseases sometimes share symptoms with more-common diseases, which can make getting a proper diagnosis difficult. People with a rare disease must sometimes cope with a stigma associated with being different from others.
Lesson 4— The Importance of Medical Research	Elaborate	A karyotype can provide evidence that a disease has a genetic cause. Some genetic diseases are inherited, while others are not. Much medical information is available online, but not all of it is useful or reliable. Clinical trials are an application of the scientific method to medicine. They have helped improve treatments for many rare diseases.
Lesson 5— Communicating about Rare Diseases	Evaluate	Patient support groups, government agencies, and other organizations exist to provide reliable information about rare diseases to the public. Knowledge about rare diseases and their impacts on people’s lives may reduce the stigma sometimes associated with having a rare disease.

How Does the Supplement Correlate to the *National Science Education Standards*?

Rare Diseases and Scientific Inquiry supports teachers in their efforts to reform science education in the spirit of the National

Research Council’s 1996 *National Science Education Standards (NSES)*. The content of the supplement is explicitly standards based. The following chart (Table 4) lists the specific content standards that this supplement addresses.

Table 4. Alignment of Rare Diseases and Scientific Inquiry Lessons with National Science Education Standards for Content, Grades 5–8

Table 4a. NSES Standard A, Science as Inquiry

As a result of activities in grades 5–8, all students should develop	Correlation to <i>Rare Diseases and Scientific Inquiry Lessons</i>
Abilities necessary to do scientific inquiry	1, 2, 3, 4
<ul style="list-style-type: none"> Identify questions that can be answered through scientific investigations. 	1, 2, 3, 4
<ul style="list-style-type: none"> Design and conduct a scientific investigation. Students should develop general abilities, such as systematic observation, making accurate measurements, and identifying and controlling variables. 	4
<ul style="list-style-type: none"> Use appropriate tools and techniques to gather, analyze, and interpret data. 	2, 3, 4
<ul style="list-style-type: none"> Develop descriptions, explanations, predictions, and models using evidence. Students should base their explanations on what they observed, and as they develop cognitive skills, they should be able to differentiate explanation from description—providing causes for effects and establishing relationships based on evidence and logical argument. 	1, 2, 3, 4
<ul style="list-style-type: none"> Think critically and logically to make the relationships between evidence and explanations. 	2, 3, 4
<ul style="list-style-type: none"> Recognize and analyze alternative explanations and predictions. 	2, 3, 4
<ul style="list-style-type: none"> Communicate scientific procedures and explanations. 	2, 3, 4
<ul style="list-style-type: none"> Use mathematics in all aspects of scientific inquiry. 	3, 4
Understandings about scientific inquiry	2, 3, 4, 5
<ul style="list-style-type: none"> Different kinds of questions suggest different kinds of scientific investigations. Some investigations involve observing and describing objects, organisms, or events; some involve collecting specimens; some involve experiments; some involve seeking more information; some involve discovery of new objects and phenomena; and some involve making models. 	2, 3, 4
<ul style="list-style-type: none"> Mathematics is important in all aspects of scientific inquiry. 	3, 4
<ul style="list-style-type: none"> Scientific explanations emphasize evidence, have logically consistent arguments, and use scientific principles, models, and theories. 	2, 3, 4, 5
<ul style="list-style-type: none"> ... Asking questions and querying other scientists' explanations is part of scientific inquiry. 	2, 3, 4, 5

Table 4b. NSES Standards C, F, and G, Life Science, Science in Personal and Social Perspectives, and History and Nature of Science

As a result of activities in grades 5–8, all students should develop understanding of	Correlation to <i>Rare Diseases and Scientific Inquiry</i> Lessons
Standard C. Structure and Function in Living Systems	All
<ul style="list-style-type: none"> • ... Different tissues are ... grouped together to form larger functional units, called organs. Each type of cell, tissue, and organ has a distinct structure and set of functions that serve the organism as a whole. 	2, 3, 4
<ul style="list-style-type: none"> • The human organism has systems for digestion, respiration, reproduction, circulation, excretion, movement, control, and coordination, and for protection from disease. These systems interact with each other. 	2, 3, 4
<ul style="list-style-type: none"> • Disease is a breakdown in structures or functions of an organism. 	All
Standard C. Reproduction and Heredity	2, 3, 4
<ul style="list-style-type: none"> • Every organism requires a set of instructions for specifying its traits. Heredity is the passage of these instructions from one generation to another. 	2, 3, 4
<ul style="list-style-type: none"> • The characteristics of an organism can be described in terms of a combination of traits. Some are inherited, and others result from interactions with the environment. 	3, 4
<ul style="list-style-type: none"> • Hereditary information is contained in genes, located in the chromosomes of each cell. Each gene carries a single unit of information. An inherited trait of an individual can be determined by one or by many genes, and a single gene can influence more than one trait. A human cell contains many thousands of different genes. 	4
Standard F. Personal Health	1, 2, 4
<ul style="list-style-type: none"> • Natural environments may contain substances (for example, radon and lead) that are harmful to human beings. 	1, 2, 4
Standard F. Risks and Benefits	1, 2, 3, 4
<ul style="list-style-type: none"> • Students should understand the risks associated with natural hazards (fires, floods, tornadoes, hurricanes, earthquakes, and volcanic eruptions), with chemical hazards (pollutants in air, water, soil, and food), biological hazards (pollen, viruses, bacterial, and parasites), social hazards (occupational safety and transportation), and personal hazards (smoking, dieting, and drinking). 	1, 2, 4
<ul style="list-style-type: none"> • Individuals can use a systematic approach to thinking critically about risks and benefits. 	3, 4
Standard G. Nature of Science	
<ul style="list-style-type: none"> • Scientists formulate and test their explanations of nature using observation, experiments, and theoretical and mathematical models. 	2, 3, 4
<ul style="list-style-type: none"> • It is part of scientific inquiry to evaluate the results of scientific investigations, experiments, observations, theoretical models, and the explanations proposed by other scientists. Evaluation includes reviewing the experimental procedures, examining the evidence, identifying faulty reasoning, pointing out statements that go beyond the evidence, and suggesting alternative explanations for the same observations. 	2, 3, 4, 5

Teaching Standards

The suggested teaching strategies in all the lessons support educators as they work to meet the teaching standards outlined in the *National Science Education Standards* (NRC, 1996).

This supplement helps science teachers plan an inquiry-based program by providing short-term objectives for students. It also includes planning tools such as the Science Content and Conceptual Flow of the Lessons chart (Table 3) and a suggested timeline for teaching the supplement (page 18). Teachers can use the supplement to update their curriculum in response to their students' interest in this topic. The focus on active, collaborative, and inquiry-based learning helps teachers support the development of student understandings and nurture a community of science learners.

The structure of the lessons enables teachers to guide and facilitate learning. All the activities encourage and support student inquiry, promote discourse among students, and challenge students to accept and share responsibility for their learning. Using the BSCS 5E Instructional Model, combined with active, collaborative learning, allows teachers to respond effectively to the diversity of student backgrounds and learning styles. The supplement is fully annotated, with suggestions for how teachers can encourage and model the skills of scientific inquiry, as well as foster the curiosity, skepticism, and openness to new ideas and data that characterize the successful study of science.

Assessment Standards

Teachers can engage in ongoing assessment of their teaching and of student learning by using the assessment components embedded in each lesson. The assessment tasks are authentic; they are similar in form to tasks that students will engage in outside the classroom or that scientists do. Annotations guide teachers to these opportunities for assessment and provide answers to questions that can help teachers analyze students' feedback.

How Does the BSCS 5E Instructional Model Promote Active, Collaborative, Inquiry-Based Learning?

The lessons in this supplement use a research-based pedagogical approach called the BSCS 5E Instructional Model, or the BSCS 5Es. The BSCS 5Es are based on a **constructivist** theory of learning. A key premise of this theory is that students are active thinkers who build (or construct) their own understanding of concepts out of interactions with phenomena, the environment, and other individuals.

A constructivist view of science learning recognizes that students need time to

- express their current thinking;
- interact with objects, organisms, substances, and equipment to develop a range of experiences on which to base their thinking;
- reflect on their thinking by writing and expressing themselves and comparing what they think with what others think; and
- make connections between their learning experiences and the real world.

The three key findings related to student learning identified in *How People Learn* (Bransford et al., 2000), a comprehensive review of research on learning, support the pedagogical strategies promoted by implementing the BSCS 5Es:

- Students enter class with a variety of preconceptions that may later significantly interfere with learning if those preconceptions are not engaged and addressed.
- To develop competence in a given subject, students must build a strong foundation of factual knowledge within the context of a coherent conceptual framework.
- Students benefit from a metacognitive approach to learning that emphasizes goal setting and self-monitoring.

The BSCS 5Es sequence the learning experiences so that students can construct their own understanding of a science concept

over time. The model leads students through five phases of active learning that are easily described using five words that begin with the letter *E*: Engage, Explore, Explain, Elaborate, and Evaluate. Rather than just listening and reading, students are also analyzing and evaluating evidence, experiencing, and talking with their peers in ways that promote the development and understanding of key science concepts. These inquiry-based experiences include both direct experimentation and development of explanations through critical and logical thinking. Students often use technology to gather evidence, and mathematics to develop models or explanations.

The BSCS 5Es emphasize student-centered teaching practices. Students participate in their learning in ways that are different from those seen in a traditional classroom. The following charts exemplify what teachers do (Table 5) and what students do (Table 6) in the BSCS 5E Instructional Model.

The following paragraphs illustrate how we implemented the BSCS 5Es in *Rare Diseases and Scientific Inquiry*.

Engage

Students come to learning situations with prior knowledge. The Engage lesson gives you the chance to find out what students already know or think they know about the topic and concepts to be developed.

The Engage phase of this supplement (in Lesson 1) is designed to

- pique students' curiosity and generate interest;
- determine students' current understandings about disease, the scientific study of disease, and their attitudes toward disease;
- encourage students to compare their ideas with those of others; and
- give you a chance to hear or read students' current conceptions, which you can address in the later lessons.

Explore

In the Explore phase of the supplement (Lesson 2), students investigate a variety of medical problems and consider possible causes for each. Students interact with medical reports, assess which problems pose the biggest risks, and act accordingly. The lesson allows students to express their developing understanding of rare diseases and scientific inquiry through analyzing and comparing data, analyzing hypothetical situations, and answering questions.

Explain

The Explain phase provides opportunities for students to connect their previous experiences and begin to make conceptual sense of the main ideas of the supplement. It also allows you to introduce formal language, scientific terms, and content information that might make students' previous experiences easier to describe and explain.

In the Explain phase (Lesson 3), students investigate a case study dealing with **Marfan syndrome**. Students

- explain, in their own words, concepts and ideas about the causes of rare diseases;
- listen to and compare others' explanations of the results with their own;
- become involved in student-to-student discourse in which they explain their thinking to others and debate their ideas;
- record their ideas and current understandings; and
- revise their ideas.

Elaborate

In the Elaborate lesson (Lesson 4), students make conceptual connections between new and previous experiences. They draw on their knowledge about rare diseases and scientific inquiry to investigate how medical research can help doctors diagnose and improve treatments for a rare disease. In this lesson, students

- connect ideas and apply their understandings of rare diseases and scientific inquiry to the treatment of childhood **leukemia**,

Table 5. Understanding the BSCS 5E Instructional Model: What the Teacher Does

Phase	<i>Consistent with the BSCS 5E Instructional Model</i>	<i>Inconsistent with the BSCS 5E Instructional Model</i>
Engage	<ul style="list-style-type: none"> • Piques students’ curiosity and generates interest • Determines students’ current understanding (prior knowledge) of a concept or idea • Invites students to express what they think • Invites students to raise their own questions 	<ul style="list-style-type: none"> • Introduces vocabulary • Explains concepts • Provides definitions and answers • Provides closure • Discourages students’ ideas and questions
Explore	<ul style="list-style-type: none"> • Encourages student-to-student interaction • Observes and listens to the students as they interact • Asks probing questions to help students make sense of their experiences • Provides time for students to puzzle through problems 	<ul style="list-style-type: none"> • Provides answers • Proceeds too rapidly for students to make sense of their experiences • Provides closure • Tells the students that they are wrong • Gives information and facts that solve the problem • Leads the students step-by-step to a solution
Explain	<ul style="list-style-type: none"> • Encourages students to use their common experiences and data from the Engage and Explore lessons to develop explanations • Asks questions that help students express understanding and explanations • Requests justification (evidence) for students’ explanations • Provides time for students to compare their ideas with those of others and perhaps to revise their thinking • Introduces terminology and alternative explanations after students express their ideas 	<ul style="list-style-type: none"> • Neglects to solicit students’ explanations • Ignores data and information students gathered from previous lessons • Dismisses students’ ideas • Accepts explanations that are not supported by evidence • Introduces unrelated concepts or skills
Elaborate	<ul style="list-style-type: none"> • Focuses students’ attention on conceptual connections between new and former experiences • Encourages students to use what they have learned to explain a new event or idea • Reinforces students’ use of scientific terms and descriptions previously introduced • Asks questions that help students draw reasonable conclusions from evidence and data 	<ul style="list-style-type: none"> • Neglects to help students connect new and former experiences • Provides definitive answers • Tells students that they are wrong • Leads students step-by-step to a solution
Evaluate	<ul style="list-style-type: none"> • Observes and records as students demonstrate their understanding of concept(s) and performance of skills • Provides time for students to compare their ideas with those of others and perhaps to revise their thinking • Interviews students as a means of assessing their developing understanding • Encourages students to assess their own progress 	<ul style="list-style-type: none"> • Tests vocabulary words, terms, and isolated facts • Introduces new ideas or concepts • Creates ambiguity • Promotes open-ended discussion unrelated to the concept or skill

Table 6. Understanding the BSCS 5E Instructional Model: What the Students Do

Phase	<i>Consistent with the BSCS 5E Instructional Model</i>	<i>Inconsistent with the BSCS 5E Instructional Model</i>
Engage	<ul style="list-style-type: none"> • Become interested in and curious about the concept/topic • Express current understanding of a concept or idea • Raise questions such as, What do I already know about this? What do I want to know about this? How could I find out? 	<ul style="list-style-type: none"> • Ask for the “right” answer • Offer the “right” answer • Insist on answers or explanations • Seek closure
Explore	<ul style="list-style-type: none"> • Use materials and ideas • Conduct investigations in which they observe, describe, and record data • Try different ways to solve a problem or answer a question • Acquire a common set of experiences so they can compare results and ideas • Compare their ideas with those of others 	<ul style="list-style-type: none"> • Let others do the thinking and exploring (passive involvement) • Work quietly with little or no interaction with others (only appropriate when exploring ideas or feelings) • Stop with one solution • Demand or seek closure
Explain	<ul style="list-style-type: none"> • Explain concepts and ideas in their own words • Base their explanations on evidence acquired during previous investigations • Record their ideas and current understanding • Reflect on and perhaps revise their ideas • Express their ideas using appropriate scientific language • Compare their ideas with what scientists know and understand 	<ul style="list-style-type: none"> • Propose explanations from “thin air” with no relationship to previous experiences • Bring up irrelevant experiences and examples • Accept explanations without justification • Ignore or dismiss other plausible explanations • Propose explanations without evidence to support their ideas
Elaborate	<ul style="list-style-type: none"> • Make conceptual connections between new and former experiences • Use what they have learned to explain a new object, event, organism, or idea • Use scientific terms and descriptions • Draw reasonable conclusions from evidence and data • Communicate their understanding to others • Demonstrate what they understand about the concept(s) and how well they can implement a skill 	<ul style="list-style-type: none"> • Ignore previous information or evidence • Draw conclusions from “thin air” • Use terminology inappropriately and without understanding
Evaluate	<ul style="list-style-type: none"> • Compare their current thinking with that of others and perhaps revise their ideas • Assess their own progress by comparing their current understanding with their prior knowledge • Ask new questions that take them deeper into a concept or topic area 	<ul style="list-style-type: none"> • Disregard evidence or previously accepted explanations in drawing conclusions • Offer only yes-or-no answers or memorized definitions or explanations as answers • Fail to express satisfactory explanations in their own words • Introduce new, irrelevant topics

- use and understand scientific terms and descriptions accurately and in context,
- draw reasonable conclusions from evidence and data,
- add depth to their understandings of rare diseases and scientific inquiry, and
- communicate their understandings to others.

Evaluate

The Evaluate lesson is the final phase of the instructional model, but it only provides a “snapshot” of what the students understand and how far they have come. In reality, the assessment of students’ conceptual understanding and ability to use skills begins with the Engage lesson and continues through each of the other phases. Combined with the students’ written work and performance of tasks throughout the supplement, however, the Evaluate lesson can serve as a summative assessment of what students know and can do.

The Evaluate lesson (Lesson 5) gives students a chance to

- demonstrate their understandings of rare diseases and scientific inquiry,
- share their current thinking with others,
- assess their own progress by comparing their current understandings with their initial ideas, and
- ask questions that take them deeper into a concept.

What’s the Evidence for the Effectiveness of the BSCS 5E Instructional Model?

Support from educational research studies for teaching science as inquiry is growing (for example, Geier et al., 2008; Hickey et al., 1999; Lynch et al., 2005; and Minner et al., 2009). A 2007 study, published in the *Journal of Research in Science Teaching* (Wilson et al., 2010), is particularly relevant to the *Rare Diseases and Scientific Inquiry* supplement.

In 2007, with funding from NIH, BSCS conducted a randomized, controlled trial to assess the effectiveness of the BSCS 5Es. The study used an adaptation of the NIH

supplement *Sleep, Sleep Disorders, and Biological Rhythms*, developed by BSCS in 2003 (NIH and BSCS, 2003). Sixty high school students and one teacher participated. The students were randomly assigned to either the experimental or the control group. In the experimental group, the teacher used a version of the sleep supplement that was closely aligned with the theoretical underpinnings of the BSCS 5Es. For the control group, the teacher used a set of lessons based on the science content of the sleep supplement but aligned with the most commonplace instructional strategies found in U.S. science classrooms (as documented by Weiss et al., 2003). Both groups had the same master teacher.

Students taught with the BSCS 5Es and an inquiry-based approach demonstrated significantly higher achievement for a range of important learning goals, especially when the results were adjusted for variance in pretest scores. The results were also consistent across time (both immediately after instruction and four weeks later). Improvements in student learning were particularly strong for measures of student reasoning and argumentation. The following chart (Table 7) highlights some of the study’s key findings. The results of the experiment strongly support the effectiveness of teaching with the BSCS 5Es.

Evidence also suggests that the BSCS 5Es are effective in changing students’ attitudes on important issues. In a research study conducted during the field test for the NIH curriculum supplement *The Science of Mental Illness* (NIH and BSCS, 2005), BSCS partnered with researchers at the University of Chicago and the National Institute of Mental Health. The study investigated whether a short-term educational experience would change students’ attitudes about mental illness. The results showed that after completing the curriculum supplement, students stigmatized mental illness less than they had beforehand. The decrease in stigmatizing attitudes was statistically significant (Corrigan et al., 2007; Watson et al., 2004).

Table 7. Differences in Performance of Students Receiving Inquiry-Based and Commonplace Instructional Approaches

Measure	Mean for Students Receiving Commonplace Teaching	Mean for Students Receiving Inquiry-Based Teaching	Effect Size
Total test score pretest (out of 74)	31.11	29.23	Not applicable
Total test score posttest	42.87	47.12	0.47
Reasoning pretest (fraction of responses at the highest level)	0.04	0.03	Not applicable
Reasoning posttest (fraction of responses at the highest level)	0.14	0.27	0.68
Score for articulating a claim (out of 3)	1.58	1.84	0.58
Score for using evidence in an explanation (out of 3)	1.67	2.01	0.74
Score for using reasoning in an explanation (out of 3)	1.57	1.89	0.59

Source: C.D. Wilson et al. 2010. The relative effects and equity of inquiry-based and commonplace science teaching on students' knowledge, reasoning, and argumentation. *Journal of Research in Science and Teaching*, 47(3), 276–301.

Note: Effect size is a convenient way of quantifying the amount of difference between two treatments. This study used the standardized mean difference (the difference in the means divided by the standard deviation, also known as Cohen's *d*). The posttest scores controlled for the variance in students' pretest scores. The reasoning posttest scores controlled for variance in students' reasoning pretest scores at the highest level.

How Does the Supplement Support Ongoing Assessment?

Teachers will use this supplement in a variety of ways and at different points in their curriculum. The most appropriate way to assess student learning occurs informally at various points within the five lessons, rather than just once, formally, at the end. We integrated assessment components within the lessons. These “embedded” assessment opportunities include one or more of the following strategies:

- performance-based activities, such as developing graphs or participating in a discussion of health effects or social policies;
- oral presentations to the class, such as reporting experimental results; and
- written assignments, such as answering questions or writing about demonstrations

These strategies allow you to assess a variety of aspects of the learning process, such as students' prior knowledge and current understandings, problem-solving and critical-thinking skills, level of understanding of new information, communication skills, and ability to synthesize ideas and apply understanding to a new situation.

How Can Controversial Topics Be Handled in the Classroom?

Teachers sometimes feel that the discussion of values is inappropriate in the science classroom or that it detracts from the learning of “real” science. The lessons in this supplement, however, are based on the conviction that much can be gained by involving students in analyzing issues of science, behavior, health,

and society. Society expects all citizens to participate in the democratic process, and our educational system must give students opportunities to learn to deal with contentious issues with civility, objectivity, and fairness. Likewise, students need to learn that science intersects with life in many ways.

In this supplement, students discuss, interpret, and evaluate basic science and health issues, some in light of their values and ethics. As students encounter issues they feel strongly about, some discussions might become controversial. The degree of controversy will depend on many factors, such as how similar the students are with respect to socioeconomic status, perspectives, value systems, and religious preferences. In addition, the language and attitude of the teacher factor into the flow of ideas and the quality of exchange among the students.

The following guidelines may help you facilitate discussions that balance factual information with feelings:

- Remain neutral. Neutrality may be the single, most important characteristic of a successful discussion facilitator.
- Encourage students to discover as much information about the issue as possible.
- Keep the discussion relevant and moving forward by questioning or posing appropriate problems or hypothetical situations. Encourage everyone to contribute, but do not force reluctant students into the discussion.
- Emphasize that everyone must be open to hearing and considering diverse views.
- Use unbiased questioning to help students critically examine all views presented.
- Allow for the discussion of all feelings and opinions.
- Avoid seeking consensus on all issues. The multifaceted issues that students discuss result in the presentation of divergent views, and students should learn that this is acceptable.
- Acknowledge all contributions in the same evenhanded manner. If a student seems to be saying something for its shock value, see whether other students recognize the inappropriate comment, and then invite them to respond.
- Create a sense of freedom in the classroom. Remind students, however, that freedom implies the responsibility to exercise that freedom in ways that generate positive results for all.
- Insist on a nonhostile environment in the classroom. Remind students to respond to ideas instead of to the individuals presenting those ideas.
- Respect silence. Reflective discussions are often slow. If a teacher breaks the silence, students may allow the teacher to dominate the discussion.
- At the end of the discussion, ask students to summarize the points that they and their classmates have made. Respect students regardless of their opinions about any controversial issue.

Using the Student Lessons

The heart of *Rare Diseases and Scientific Inquiry* is a set of five classroom lessons that allow students to discover important concepts related to rare diseases and scientific inquiry. To review these concepts in detail, refer to the Science Content and Conceptual Flow of the Lessons chart (Table 3), found on page 6.

Format of the Lessons

As you review the lessons, you will find that each contains several major features.

At a Glance summarizes the lessons with these sections:

- **Overview:** Provides a short summary of student activities.
- **Major Concepts:** Lists the central ideas the lesson is designed to convey.
- **Objectives:** Lists specific understandings or abilities students should have after completing the lesson.
- **Teacher Background:** Specifies which portions of the background section, Information about Rare Diseases and Scientific Inquiry, relate directly to the lesson. We do *not* intend for this reading material to form the basis of lectures to students, nor do we intend it to be a direct resource for students. Rather, it enhances your understanding of the content so that you can facilitate class discussions, answer student questions, and provide additional examples.

In Advance provides lists of items and preparations needed for the activities:

- **Web-Based Activities:** Tells you which of the lesson's activities use the *Rare Diseases and Scientific Inquiry* Web site as the basis for instruction.
- **Photocopies:** Lists the paper copies and overhead transparencies that you need to make from the masters provided at the end of the supplement.

- **Materials:** Lists all the materials other than photocopies that you need for each activity in the lesson.
- **Preparation:** Outlines what you need to do to be ready to teach the activities.

Procedure outlines the steps in each activity and provides implementation hints and answers to discussion questions.

The **Lesson Organizer** briefly summarizes the lesson. It outlines procedural steps for each activity and includes icons that notify you when masters, transparencies, and the Web site are used. You should use the lesson organizer only after you become familiar with the detailed procedures for the activities. It can be a handy resource during lesson preparation as well as during classroom instruction.

The **Masters** to be photocopied (student worksheets and reference materials) are found at the back of the supplement.

Icons appear throughout the lessons. They alert you to teaching aids that can help you implement the activities and enrich student learning.



Indicates steps that you can use as assessments, including informal indicators of student understanding, and the final assessment at the end of each lesson.



Identifies the teaching strategies that address specific science content standards as defined by the *National Science Education Standards* (NRC, 1996).



Shows when to use the Web site as part of the teaching strategy. A print-based alternative to each Web-based activity is provided for classrooms that don't have Internet access.



Identifies suggestions from field-test teachers for teaching strategies, classroom management, and supplement implementation.



Identifies a print-based alternative to a Web-based activity.

Timeline for Teaching the Supplement

The timeline below (Table 8) outlines the optimal plan for completing the five lessons. It assumes you will teach the activities on consecutive days of 50-minute class periods. If your class requires more time for discussing issues raised in this supplement or for completing activities, adjust your timeline accordingly.

Table 8. Suggested Timeline

Timeline	Activity
3 weeks ahead	Reserve computers. Check performance of Web site.
7 days ahead	Make photocopies and transparencies. Gather materials.
School day 1	Lesson 1 Activity 1: What Is a Rare Disease?
School day 2	Lesson 2 Activity 1: Causes of Disease Activity 2: Is a Rare Disease Present?
School day 3	Lesson 2 Activity 2: Is a Rare Disease Present? Activity 3: How Rare Is Rare?
School day 4	Lesson 3 Activity 1: A Parent's Dilemma Activity 2: Connective Tissue
School day 5	Lesson 3 Activity 3: A Common Thread
School day 6	Lesson 4 Activity 1: An Unwelcome Diagnosis
School day 7	Lesson 4 Activity 1: An Unwelcome Diagnosis (conclude)
School day 8	Lesson 4 Activity 2: Clinical Trials
School day 9	Lesson 5 Activity 1: Creating an Informational Poster
School day 10	Lesson 5 Activity 2: Reflecting on Rare Diseases

Using the Web Site

The Web site for *Rare Diseases and Scientific Inquiry* can help you organize your use of the supplement, engage student interest in learning, and orchestrate and individualize instruction as learning is taking place. Lessons 2, 3, 4, and 5 have activities on the Web site for classrooms with online access. To access the site, go to <http://science.education.nih.gov/supplements/rarediseases/>.

Under “Web Portion of Student Activities,” click on the link to a specific lesson. (If your classes don’t have access to the site, you can use the print alternatives included with the lessons.)

Hardware and Software Requirements

The Web site can be accessed with any computer browser. To experience full functionality of the site, Adobe Flash Player must be installed on the hard drive of each computer that will access the site (available for free at <http://get.adobe.com/flashplayer/>).

Collaborative Groups

We designed all the activities in this supplement to be completed by teams of students working together. Although individual students working alone can complete many of the steps, this strategy will not stimulate the types of student-student interactions that are part of active, collaborative, inquiry-based learning. Therefore, we recommend that you organize collaborative groups of two to four students each, depending on the number of computers available. Students in groups larger than this will have difficulty organizing student-computer interactions equitably. This can lead to one or two students assuming the primary responsibility for the computer-based work. Although large groups can be efficient, they do not allow all students to experience the in-depth discovery

and analysis that the Web site was designed to stimulate. Group members not involved directly may become bored or lose interest.

We recommend that you keep students in the same collaborative groups for all the activities in the lessons. This will allow each group to develop a shared experience with the Web site and with the ideas and issues the activities present. A shared experience will also enhance your students’ perceptions of the lesson as a conceptual whole.

If your student-to-computer ratio is greater than four to one, you will need to change the way you teach the supplement from the instructions in the lessons.

Web Materials for People with Disabilities

The Office of Science Education (OSE) provides access to the Curriculum Supplement Series for people with disabilities. The online versions of this series comply with Section 508 of the Rehabilitation Act. If you use assistive technology (such as a Braille or screen reader) and have trouble accessing any materials on our Web site, please let us know. We will need a description of the problem, the format in which you would like to receive the material, the URL of the requested material, and your contact information.

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Information about Rare Diseases and Scientific Inquiry

1.0 A History of Rare Diseases in the United States

An axiom taught in medical schools around the world goes like this: When you hear hoofbeats, think horses, not zebras. We don't want future physicians thinking about the most fanciful possibilities when they see a patient. We want them to start with the most obvious diagnosis. Many potential diagnoses are so rare that most doctors will never see a patient with any of them. Rare diseases (that is, the zebras) do occur, though, and physicians must keep them in the back of their minds as they try to determine what is actually wrong with their patients. This is why the Office of Rare Diseases Research has unofficially adopted the zebra as its mascot.

In the United States, a disease is considered rare if it affects fewer than 200,000 Americans (Institute of Medicine (IOM), 2010). Some rare diseases, such as cystic fibrosis and Tourette's syndrome, are relatively well known to the public, but most are not. About 7,000 rare diseases have been identified, and researchers continue to describe new ones. Many affect fewer than 1,000 people in the United States, but taken together, they represent a significant health concern affecting an estimated 25 million (ORDR, 2009). The majority of rare diseases are caused by gene mutations, but they can also be caused by infection from pathogens and exposure to environmental toxins.

A smaller number of diseases are called "neglected diseases." This term is often applied to tropical infections that are overwhelmingly

concentrated in the world's poorest countries. Examples of neglected diseases include the following:

- Leishmaniasis, a parasitic disease affecting about 12 million people worldwide and found, rarely, in the United States among people who have been traveling (World Health Organization, 2009).
- Dengue fever, a disease caused by a virus transmitted through a mosquito bite. It affects about 50 million to 100 million people worldwide but is very rare in the United States (Centers for Disease Control and Prevention (CDC), 2009).
- Schistosomiasis, a parasitic disease affecting multiple organs. It affects an estimated 200 million people worldwide and is not found in the United States (CDC, 2008).

A disease is sometimes described as having a trajectory, meaning that the number of people affected by the disease changes through time. This means that a rare disease may become common, and a common disease may become rare. For example, AIDS was once a rare disease, but as HIV infection spread around the world, it became a common disease. Effective disease prevention programs can turn a once-common disease into a rare one. This has happened to diseases such as measles and mumps through childhood vaccination programs. Healthcare professionals are concerned that some currently rare diseases may become common due to the spread of drug-resistant pathogens and public opposition to childhood vaccinations (IOM, 2010).

Patients and their families dealing with rare diseases face obstacles beyond coping with the diseases themselves (Rados, 2003):

- Many patients experience the frustration of not being able to obtain an accurate diagnosis. For approximately one-third of patients with a rare disease, correct diagnosis takes between one and five years. In Europe, researchers analyzed surveys from over 6,000 patients involving eight rare diseases, including Marfan syndrome, cystic fibrosis, and Duchenne’s muscular dystrophy. Over 40 percent of the respondents indicated that their first diagnosis was wrong, and 25 percent reported that it took between 5 and 30 years to obtain a correct diagnosis (Faurisson, 2004).
- Patients often feel isolated and don’t know anyone else who is dealing with the same disease.
- Many patients must travel long distances to reach appropriate medical care.
- The cost of diagnosis and treatment can be very expensive.
- There may be no medications or other treatments for the disease.

Until the mid-1980s or so, the study of rare diseases was a low priority for the medical community. Since then, however, researchers have focused more attention on rare diseases for reasons we explain below. The increased

visibility of rare diseases and resources devoted to them gave us the opportunity to develop a curriculum supplement that allows students to gain an understanding of the concept of rare diseases and how they are studied. To appreciate the advances made in the area of rare diseases since 1980, it’s helpful to look at a brief history of the field.

Because each rare disease affects so few people, pharmaceutical companies reasoned that it was not cost effective to develop drugs to treat them. Because those companies were not interested in “adopting” the research needed to develop drugs, the lack of attention to rare diseases led to the terms “orphan diseases” and, for the drugs needed to treat them, “orphan drugs.” In the United States, this situation began to change in the 1980s. The Food and Drug Administration (FDA) established the Office of Orphan Products Development (OOPD). Its aim is to identify and support the development of orphan drugs and biologic products needed to treat rare diseases. To carry out its mission, the OOPD works in collaboration with other stakeholders such as the research community, academia, rare disease organizations, and pharmaceutical companies.

Congress passed the Orphan Drug Act (ODA) in 1983. The ODA helps foster the development of orphan drugs by providing financial incentives

Figure 1. Congress stimulated research on rare diseases by passing the Orphan Drug Act.



to pharmaceutical companies. A medication that has orphan drug status must meet the same safety and efficacy standards as other drugs. A company working on an orphan drug receives tax credits and a seven-year period to exclusively market the drug when it's ready. In the 10 years before the ODA, only 10 drugs aimed at rare diseases were privately developed. Since then, the FDA has approved more than 350 orphan drug applications. Drugs aimed at rare diseases accounted for over 30 percent of the innovative drug applications approved by the FDA from 2004 to 2008 (Coté, 2009).

Medical devices intended to treat patients with rare diseases are not clearly addressed by the ODA. In 1996, the FDA created the Humanitarian Device Exemption (HDE) provision of the Safe Medical Devices Act of 1990. It allows the expedited approval of a medical device for treating a rare disease provided that the device is safe and is likely to benefit patients. This approval can be granted without costly clinical studies. From 1996 to 2003, the OOPD gave out 32 HDEs (Rados, 2003). One example of where the provision has had an impact is in the rare placental disorder twin-to-twin transfusion syndrome. Blood vessels often connect the circulation of developing twins, and sometimes this leads to one twin receiving more blood flow than the other. A device approved through the HDE provision allows physicians to identify blood vessels that connect the twins in utero and then normalize the blood flow in those vessels (National Organization for Rare Disorders, 2011).

The Rare Diseases Act of 2002 established the Office of Rare Diseases (ORD) at NIH to provide information on rare diseases, including their diagnosis and treatment, and help establish links among investigators, patients, and research subjects. The Office's focus on research soon prompted a name change to the Office of Rare Diseases Research (ORDR). ORDR staff work to identify rare diseases where research is lacking and to support research in those areas. In 2003,

ORDR helped fund the Rare Diseases Clinical Research Network (RDCRN). It consisted originally of 10 research consortia and a Data and Technology Coordinating Center; by 2009, the Network had grown to 19 consortia plus a Data Management and Coordination Center. The network has conducted or is conducting about 100 studies across the United States and several other countries. Each consortium focuses on a group of medically related rare diseases.

Although many rare diseases have no effective treatment options, medical research is producing tangible benefits for many patients and their families. During the 1960s, people with cystic fibrosis had a life expectancy of fewer than 10 years. Today, people with the disease can expect to live to nearly 40 years (Cystic Fibrosis Foundation, 2008). A 2008 review of treatments for 65 rare diseases revealed that between 1983 and 2008,

- the number of diseases with no treatment options decreased from 31 to 17 and
- the number of diseases that fully responded to treatment increased from 8 to 20 (Campeau et al.).

Attention to rare diseases has grown since the 1980s through the efforts of nonprofit organizations and foundations, some of which were created by people affected by rare diseases (Rados, 2003). For example, Brad and Vicki Margus had two boys with ataxia-telangiectasia (A-T), a fatal genetic disorder that involves the loss of motor control, among other symptoms. Brad left his business to start the A-T Children's Project, a nonprofit organization aimed at isolating the gene responsible for A-T and providing support for affected families. His efforts were rewarded in 1995, when a scientist supported by funds from the A-T Children's Project identified the gene (called *ATM*) associated with the disease (Savitsky et al., 1995). It turned out that the *ATM* gene codes for a protein that helps mediate a cell's response to DNA damage by regulating its progression through the cell cycle. The isolation of the *ATM* gene not only helped researchers better

understand the cause of this rare disease, but it shed light on a mechanism of cancer.

Research on a rare disease often produces findings that provide insight into more-common diseases. For example, Wilms' tumor (a rare pediatric cancer) research has been cited as a model for understanding the genetics and molecular biology of pediatric cancers in general (Feinberg and Williams, 2003). Research into Tangier disease (a very rare disease associated with improper cholesterol processing) identified a target for therapy to lower the risk for heart disease and provided insight into Alzheimer's disease (Delude, 2009). In other cases, research findings have helped prevent a rare disease. For example, women can follow simple nutritional measures to reduce the incidence of birth defects such as spina bifida in their children.

Many of the same patients and families who lobbied for the passage of the Orphan Drug Act worked to create a nonprofit organization that would address their needs. Founded in 1983, the National Organization for Rare Disorders (NORD) provides information about diseases, referrals to patient organizations, research grants, and advocacy for the rare diseases community.

2.0 The Impact of Genomics on Rare Diseases

Most rare diseases are caused by genetic mutations or variations. In fact, we now think that 80 percent or more of rare diseases have a genetic cause (NIH, 2010; NORD, 2007). This means that we can use genetics and rare diseases in a curriculum supplement to address concepts such as these:

- Some rare diseases are more prevalent in certain groups.
- Inherited and environmental factors affect the function of an organism and may contribute to the occurrence of rare diseases.
- People affected by inherited rare diseases should not be stigmatized.
- People affected by inherited rare diseases can lead meaningful lives.

To help provide information on genetics and rare diseases, the National Human Genome Research

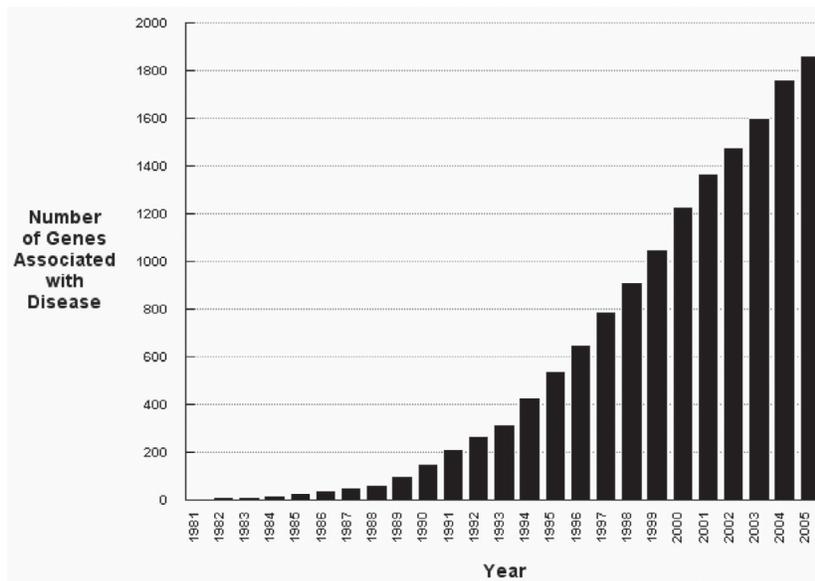
Institute and ORDR established the Genetic and Rare Diseases Information Center in 2002. The next year, the completion of the Human Genome Project (HGP) opened the floodgates on a torrent of human genetic data. Once the reference sequence was finished, it became clear that the human genome contained fewer genes than originally expected—about 25,000 total. After scientists had established the approximate number of human genes, they turned their attention to assessing the amount of genetic variation among human populations. The aim is to associate specific genetic variations with diseases, both common and rare. As seen in the following graph (Figure 2), the pace of disease-gene discovery shows no sign of leveling off (McKusick-Nathans Institute et al., 2005).

Soon after scientists began to explore genes related to disease through the HGP, NIH began researching human genetic variation through the International HapMap Project. Data from the HGP indicated that the genomes of any two humans are, amazingly, more than 99 percent the same. This observation also means that any two individuals have several million differences in their genomes.

The most common type of genetic variation is called a single nucleotide polymorphism (SNP, pronounced “snip”). A SNP is a place in the genome where individuals may vary by a single base pair. The human genome contains more than 10 million different SNPs (International HapMap Consortium, 2007). SNPs that are clustered close together on the chromosome are inherited together as a single unit, or haplotype. The International HapMap Project used DNA samples from people of diverse ethnic backgrounds to assemble a map of these haplotype blocks.

The International HapMap Project, completed in 2005, produced a map containing data on more than 1.3 million SNPs (International HapMap Consortium, 2005). Scientists immediately used HapMap data to conduct genome-wide association studies, in which genomes from many people are rapidly scanned to identify

Figure 2. Cumulative pace of disease-gene discovery in humans, 1981–2005.



Source: Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD). World Wide Web URL: <http://www.ncbi.nlm.nih.gov/omim/>

SNPs associated with diseases. Once the scientists characterize the disease-associated SNPs, they can use the data to help prevent, diagnose, and treat diseases. Within two years, HapMap data helped identify more than 50 genes associated with diseases, including type 2 diabetes, Crohn's disease, elevated cholesterol, rheumatoid arthritis, multiple sclerosis, and prostate cancer (Massachusetts General Hospital, 2007).

The completion of the International HapMap Project did not stop the exploration of human genetic variation. In 2007, a second-generation human haplotype map was assembled containing data on over 3.1 million SNPs (International HapMap Consortium, 2007). This second map, with its increased density of SNPs, allows researchers to identify recently inherited chromosomal segments that may hold a key to understanding rare disease-associated variations that until now have been very difficult to detect.

The single base variations associated with the HapMap Project are not the only types of genetic variation associated with disease. Structural

variations involving thousands of bases of DNA sequence are also being investigated. Such structural variations are associated with variation in gene expression (Stranger et al., 2007), female infertility (Stefansson et al., 2005), susceptibility to HIV infection (Gonzalez et al., 2005), systemic autoimmunity (Fanciulli et al., 2007), and genetic disorders such as Williams-Beuren syndrome and velocardiofacial syndrome (Freeman et al., 2006; Lupski and Stankiewicz, 2005).

Some rare diseases are caused by simple genetic mutations or variations and can serve as good examples for middle school students learning about a disease and its biological functions as well as the fundamentals of genetics. The inheritance of single-gene diseases is relatively simple. The more-common single-gene disorders include the following:

- sickle cell disease: A recessive disorder in which affected people produce abnormal hemoglobin.
- cystic fibrosis: A recessive disorder in which the body produces thick, sticky mucus that clogs the lungs and leads to infections. It is the most common fatal genetic disease in the United States.

Figure 3. Data from the International HapMap Project are being used to identify genes associated with rare diseases.



Source: <http://hapmap.ncbi.nlm.nih.gov>

- Tay-Sachs disease: A recessive disorder that results in the progressive destruction of the nervous system in children. After genetic testing and community counseling programs became available in 1970, the incidence of Tay-Sachs disease in the United States and Canada decreased by 90 percent in the Jewish population most at risk for the disease (Kaback et al., 1993).
- Huntington's disease: An autosomal dominant disorder that usually appears during middle age and leads to progressive loss of control over movement and intellectual faculties.

Today, about 1,500 different tests are available to detect mutations associated with genetic diseases. This number may seem large, but it falls well short of the number of rare diseases thought to have genetic causes (National Center for Biotechnology Information, 2009). Many of these genetic tests are offered by just a few laboratories across the country. Furthermore, the tests may be expensive and may not be covered by medical insurance.

3.0 Rare Infectious Diseases

Some rare diseases are caused by infection with a pathogen. Rare diseases spread by pathogens have the potential to become common diseases, provided that conditions promoting transmission are present. The spread of AIDS illustrates how a once rare disease (because it was new) can become common in a relatively short time.

One class of rare diseases is associated with an unusual type of infectious agent called prions, which are thought to consist entirely of protein

and to lack the DNA or RNA genome found in viruses. The term prion was coined by Stanley Prusiner in 1982 to describe proteinaceous infectious particles associated with diseases such as scrapie in sheep, bovine spongiform encephalopathy (mad cow disease) in cattle, and Creutzfeldt-Jakob disease in humans.

The infectious nature of prions in humans was first observed among the Fore people living in the highlands of New Guinea in the 1950s. Women and children were dying from a progressive brain disease called kuru by the local people. Research by Carleton Gajdusek established that the infectious agent, then thought to be a conventional virus, was being transmitted through the practice of cannibalism (Gajdusek et al., 1967).

All prion diseases characterized so far affect the structure of the brain or other neural tissues and are untreatable and fatal. The prion particle is derived from a protein that is a normal part of the **central nervous system**. For reasons unknown, the normal protein, PrP, sometimes misfolds, and in its new conformational state is able to induce other PrP molecules to do the same. This wave of PrP molecules turning into prions becomes an assault on the brain, thus producing the disease symptoms.

There are many unanswered questions about prions, including, what's the role of the PrP protein in the cell? Two recent studies suggest a possibility to explore (Steele et al., 2006; Zhang et al., 2006). We know that although prion diseases exclusively affect the nervous system, the PrP protein is found throughout the body. The two studies show that the PrP protein is expressed on the surface of **stem cells** in the **bone marrow** and on cells that become neurons. In both cases, PrP seems to support the ability of the cells to mature and divide. Establishing the normal role for PrP should open new avenues for understanding and, ultimately, treating this rare but devastating class of diseases. As research into infectious diseases continues, the goal is to make the common diseases rare and the rare diseases extinct.

4.0 Rare Diseases Caused by Environmental Toxins

Some rare diseases result not from faulty genes or infection by pathogens, but from exposure to toxins or other extrinsic factors in the environment. As with infectious diseases, those caused by exposure to environmental toxins may be either common or rare, and the rare ones have the potential to become common.

Harmful extrinsic factors may be of natural or human origin. Natural factors include ionizing radiation (from sunlight or elements such as radon), heavy metals (such as lead and mercury), and chemicals produced by organisms. Many plants produce chemicals that function as pesticides. Other plant toxins are produced in response to stresses caused by severe weather, ultraviolet light, and infection by microbes.

Some of the most potent naturally occurring toxins are produced by microorganisms. Botulinum, for example, is produced by the bacterium *Clostridium botulinum* and causes the rare disease botulism. Most cases of botulism involve eating food contaminated with preformed botulinum neurotoxin. In rare cases, called colonization botulism, a person eats food containing spores of *C. botulinum*. The spores germinate inside the body, resulting in a colony of bacteria that then produce the toxin. The appearance of colonization botulism is associated with certain risk factors, most commonly the digestive disorder Crohn's disease (Health Canada, 2007).

Other rare diseases are caused by exposure to industrial chemicals. This can happen as a result of lifestyle choices (such as smoking) or living or working in a harmful environment. Some industrial chemicals are strongly associated with specific diseases. For example, virtually all cases of mesothelioma are attributed to exposure to asbestos. Table 9 lists several harmful industrial chemicals and the diseases that result from exposure to them.

Although the causes of rare diseases can be classified as genetic or environmental, many of

Table 9. Industrial Chemicals and Their Associated Diseases

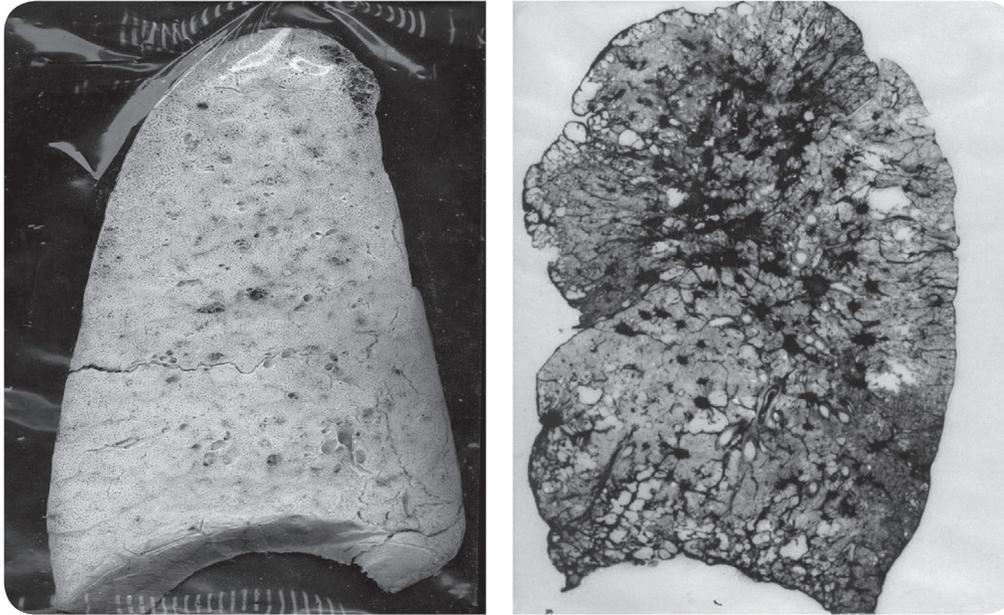
Chemical	Disease(s)
Asbestos	Asbestosis; mesothelioma
Beryllium	Chronic beryllium disease
Coal dust	Pneumoconiosis
Cotton dust	Byssinosis
Dioxins, polychlorinated biphenyls (PCBs)	Chloracne
Nylon flocking	Flock worker's lung
Silica	Silicosis
Vinyl chloride	Angiosarcoma
Welding fumes	Metal fume fever

Source: Adapted from G.M. Solomon. 2005. Rare and common diseases in environmental health. San Francisco Medical Society Web site. Retrieved August 10, 2008: <http://www.sfms.org/AM/Template.cfm?Section=Home&template=/CM/HTMLDisplay.cfm&ContentID=1644>.

the diseases are, in fact, multifactorial, meaning that they result from interactions between genetic and environmental factors. Since the HGP was completed in 2003, researchers have been working to establish the genes' functions and relationships to both health and disease.

Some scientists are exploring how the interaction of genes and environmental factors produces disease. For example, Michael Borchers has been investigating a receptor protein called NKG2D found on the surface of lung cells (Borchers et al., 2006). Normally, the NKG2D protein helps the immune system attack and destroy lung tissue damage caused by infection from a pathogen. However, when the lungs experience chronic low-level damage from environmental toxins through smoking or exposure in the workplace, the amount of tissue damage may exceed the body's ability to repair it. In such cases, the activity of NKG2D is unwanted because it stimulates the immune system to attack the affected tissue—and contributes to chronic lung disease instead providing

Figure 4. Long-term exposure to coal dust causes the illness known as black lung. Normal lung (left) and affected lung (right).



Source: www.cdc.gov/niosh, National Institute for Occupational Safety and Health (NIOSH), Division of Respiratory Disease Studies

protection from it. Borchers believes that by blocking the activity of NKG2D, he can stop this immune response and minimize damage to the lungs (University of Cincinnati, 2006).

Other causes of rare diseases include

- nutritional deficiency: for example, beriberi results from a lack of thiamine;
- injury: for example, commotion cordis is associated with ventricular fibrillation and sudden death, which result from a nonpenetrating blow to the chest; and
- a treatment for another disease: for example, radiation is often used as a cancer treatment, but it may also cause radiation-induced meningioma (a rare central nervous system tumor).

5.0 Rare Diseases Featured in This Curriculum Supplement

5.1 Necrotizing Fasciitis

Necrotizing fasciitis (NF) is a bacterial infection. The bacteria attack the soft tissue and the fascia, a sheath of tissue that covers muscles. Most commonly, the infection is from Group A

Streptococcus bacteria strains. This is the same kind of bacteria responsible for causing strep throat. Most strep strains are easily killed by **antibiotics**. Some are not, though, and, under the right set of conditions, can cause NF. These conditions include the following:

- An opening in the skin through which the bacteria enter the body. The opening can be large, as a result of trauma or surgery, or very small, as from a pinprick or paper cut.
- Contact with the bacteria, either from inside the person or from another infected person.
- Infection by an invasive strain of the Group A *Streptococcus* bacteria.

After the bacteria enter the body, they reproduce quickly and release toxins and enzymes that destroy soft tissue and fascia. The dead tissue must be removed to save the patient's life.

The bacteria are able to elude the body's immune system and spread through different tissue layers. In addition to the tissue damage, the infection can result in toxic shock, which is characterized by a drop in blood pressure; a weak, rapid pulse; fever; dizziness and confusion; and difficulty breathing.

Fortunately, NF is rare, although accurate statistics are hard to find. In 1996, the CDC estimated that there were between 500 and 1,500 cases of NF in the United States and that 20 percent of these resulted in death (National Necrotizing Fasciitis Foundation (NNFF), 2009).

Symptoms of NF: NF produces flu-like symptoms, so people initially believe that they simply have the flu. Misdiagnosis is common, which can have devastating consequences because the bacterial infection advances so fast. The symptoms of NF progress as follows (NNFF, 2009):

Early symptoms (usually within the first 24 hours)

- An opening in the skin (from even a slight trauma) has appeared, allowing the bacteria to enter the body.
- The patient feels discomfort in the general area of the trauma.
- The pain increases out of proportion to the injury.
- Flu-like symptoms appear such as vomiting, diarrhea, dehydration, fatigue, weakness, muscle pain, and fever.
- Intense thirst develops as the body dehydrates.

Advanced symptoms (usually within three to four days)

- The painful area of the body begins to swell and may show a purplish rash.
- The painful area may develop large, dark blisters.
- The wound may take on a bluish, white, or dark, mottled, flaky appearance.

Critical symptoms (usually within four to five days)

- Blood pressure drops severely.
- Heartbeat increases.
- A rash may appear over the body, caused by toxins released by the bacteria.
- Toxic shock causes the body's organs to shut down.
- Unconsciousness results as the body becomes too weak to fight the infection.

Figure 5. An invasive strain of the Group A *Streptococcus* bacteria can enter the body through a foot blister.



Source: NTECH HEALTH AND WELLNESS

Treatment of NF: NF requires treatment at a hospital. The patient is given intravenous antibiotics, and the infected tissue is removed. Depending on the severity of symptoms, other treatments may be needed, such as blood transfusions and medications to raise blood pressure and boost the immune system.

Surviving NF: Patients surviving NF may be left with minimal to severe scarring. Almost all patients need to have at least some skin removed. As a result, they may have to undergo a series of skin grafts. In some cases, amputation of an affected limb is necessary.

5.2 Marfan Syndrome

Marfan syndrome is a genetic disease of the connective tissue. It's caused by mutations in the gene that codes for the connective tissue protein fibrillin-1. As a result of the mutated *fibrillin-1* gene, another protein called "transforming growth factor beta" (TGF β) increases in concentration, causing certain connective tissue problems. The Marfan syndrome phenotype is inherited as an autosomal dominant trait. This means that a single copy of the mutated gene is enough to cause the disorder. It also means that an affected person has a 50 percent chance of passing on the disorder to each child. The syndrome is mostly an inherited condition, but in about 25 percent of cases, it's caused by a spontaneous mutation in a sperm or egg

cell of an unaffected parent (Dietz, 2009). The National Marfan Foundation estimates that about 200,000 people in the United States are living with Marfan syndrome or a related connective tissue disorder (National Marfan Foundation, 2011).

Features of Marfan Syndrome: People with Marfan syndrome have the genetic mutation in all their cells. This means that the disorder affects the connective tissue in many different body systems. The medical features associated with Marfan syndrome appear at all ages, including in infants and small children. Some of the most common features of Marfan syndrome are listed below (Table 10). With early diagnosis, proper treatment, and careful

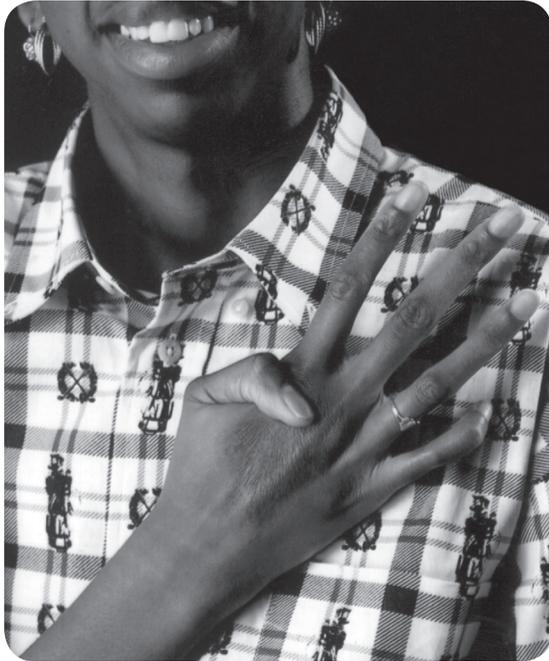
management, it's possible for people with Marfan syndrome to live a normal life span.

Diagnosis of Marfan Syndrome: The connective tissue problems associated with Marfan syndrome can affect multiple body systems. This can complicate diagnosis of the disorder. Doctors may treat patients with the syndrome for several medical problems at once without realizing that they stem from a single cause. Although we know that Marfan syndrome is caused by mutations in the *fibrillin-1* gene on chromosome 15, there's no simple blood test that can diagnose the disorder. Instead, doctors have established a set of diagnostic criteria to use. These criteria span various body systems and are classified as either major or minor.

Table 10. Features of Marfan Syndrome

Cardiovascular System
The aorta (main blood vessel that carries blood from the heart) may be enlarged and weakened.
The layers of the aorta may be separated, causing it to tear more easily.
The mitral valve that separates the upper and lower halves of the left side of the heart may be enlarged and may not work properly.
Skeletal System
Tall and thin body type
Scoliosis (curvature of the spine)
Chest sinks in or sticks out
Flexible joints
Flat feet
Teeth very crowded together
Ocular System
Severe myopia (nearsightedness)
Dislocated eye lens
Detached retina
Early glaucoma or cataracts
Other Body Systems
Stretch marks on skin, not from pregnancy or weight gain
Sudden lung collapse
Swelling of the sac that surrounds the spinal column

Figure 6. Marfan syndrome is associated with flexible joints.



Source: National Marfan Foundation

To make a diagnosis of Marfan syndrome, the doctor compares the patient's medical history, results of a physical examination, and results from laboratory tests with the set of diagnostic criteria. If no one in the patient's family has Marfan syndrome, the doctor makes the diagnosis if the patient has major criteria in two different body systems and minor criteria in a third body system. If the patient has a parent or sibling with Marfan syndrome, the doctor makes the diagnosis if the patient has major criteria in one body system and minor criteria in a second body system. A person may have many features associated with Marfan syndrome in a single body system but still not be diagnosed with the disorder.

Treatment of Marfan Syndrome: Although there's no cure for Marfan syndrome, certain treatments can minimize or, in some cases, prevent complications. Depending on which body systems are affected, an appropriate team of specialists create an individualized treatment

program. Table 11 lists some of the available disease-management options.

5.3 Childhood Leukemia

Leukemias are cancers of the blood or bone marrow that usually result in the overproduction of **white blood cells** and that are classified by how long it takes for the disease to appear and worsen (acute and chronic) and by the type of blood cell affected (lymphocytic or myeloid):

- Acute leukemia is characterized by the rapid appearance of immature blood cells, called blasts, produced in the bone marrow. This overcrowding of cells prevents the bone marrow from making healthy blood cells. The lack of healthy white blood cells (which help fight infection) leaves the patient vulnerable to repeated bouts of colds and flu. The lack of healthy **red blood cells** leads to anemia and fatigue. Acute forms of leukemia may occur in people of all ages, but they are often the forms seen in children.
- Chronic leukemia is characterized by a more gradual accumulation of relatively mature blood cells. It may take months or years to progress. This form of leukemia can also be found in people of all ages but is more common among older people.
- Lymphocytic leukemia is a cancer of the B cells, a kind of lymphocyte (or white blood cell) that plays a role in the immune system.
- Myeloid leukemia is a cancer of other cells, such as red blood cells, **platelets**, and other types of white blood cells.

This supplement is concerned with acute lymphoblastic leukemia (ALL), which is the most common form of leukemia in children. The Leukemia and Lymphoma Society estimates that in 2009, there were 5,760 new cases of ALL in children in the United States.

Symptoms of ALL: The most common symptoms appearing in children with ALL are fever; recurring infections; easy bruising or bleeding; lumps in the neck, underarms, stomach, or groin; pain or a feeling of fullness below the ribs; fatigue; and the loss of appetite.

Table 11. Disease-Management Options for Marfan Syndrome

<p>Cardiovascular System</p> <ul style="list-style-type: none"> • Echocardiograms to assess the size of the aorta • Medications to relieve stress on the aorta • Corrective surgery
<p>Skeletal System</p> <ul style="list-style-type: none"> • Annual examinations to look for changes in the spine and breastbone • Orthopedic braces • Corrective surgery
<p>Ocular System</p> <ul style="list-style-type: none"> • Early, regular eye exams • Eyeglasses or contact lenses • Corrective surgery
<p>Nervous System</p> <ul style="list-style-type: none"> • Medication for pain
<p>Pulmonary System</p> <ul style="list-style-type: none"> • Avoidance of smoking • Examination to detect breathing problems during sleep • Medical attention for collapsed lung
<p>Physical Activity</p> <ul style="list-style-type: none"> • Avoidance of collision and contact sports • Individualized exercise plan

Diagnosis of ALL: In addition to a physical exam and patient history, blood tests are used to diagnose ALL. The different types of blood cells are counted to determine whether they are present in abnormal ratios. A **biopsy** of the bone marrow allows cells from the bone, blood, and bone marrow to be examined for an abnormal appearance. A cytogenetic analysis also may be carried out, because some forms of ALL are associated with the appearance of trisomies (having three instead of the normal two copies of a chromosome) in the affected cells. Trisomies can be detected in a kind of photograph of the chromosomes called a **karyotype**. To make the karyotype easier to analyze, the individual chromosomes are cut out from the original photograph and rearranged in pairs. A trisomy involving one or more

chromosomes may be seen in the leukemia cells but not in unaffected cells taken from other parts of the body.

Treatment of ALL: The treatment of ALL has made continual progress since the 1960s, mostly thanks to the results of clinical trials on children with the disease. During clinical trials, one group of children receives the so-called standard treatment, which is the best care known at the time. Researchers compare the health of this group of children with one or more additional groups of children who receive a modified form of the standard care that is designed to test some new treatment, such as a different dose or a new drug. The success of a treatment is described in terms of its five-year survival rate, which refers to the percentage of patients who live at least five years after cancer was diagnosed. Today, the five-year survival rate for children with ALL in the United States is over 80 percent (American Cancer Society, 2009).

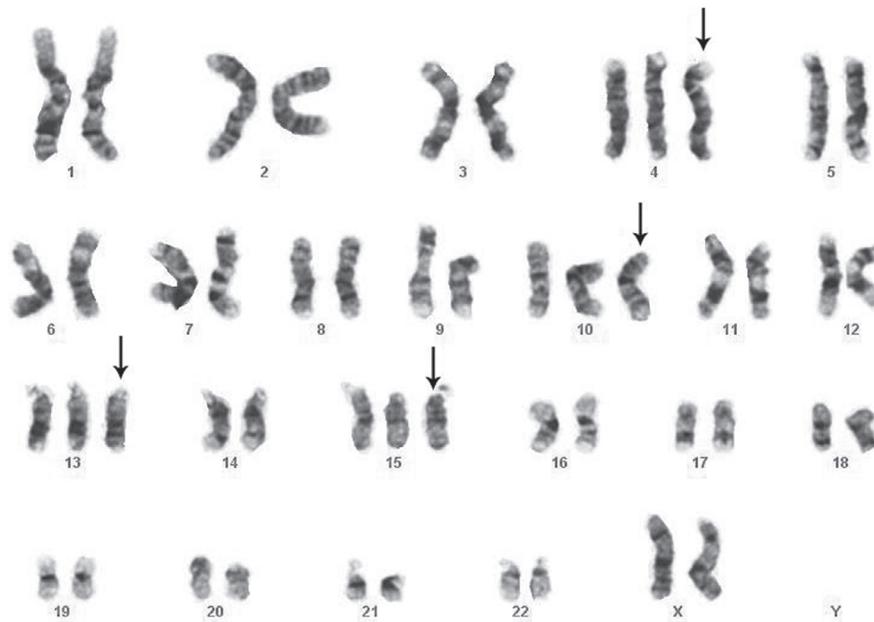
Current treatment for ALL consists of several phases:

- *Induction Chemotherapy:* This initial phase uses a combination of drugs such as **prednisone** and **vincristine** to kill most of the cancer cells.
- *Consolidation Therapy:* In this phase, a different combination of drugs is used to target any remaining cancer cells.
- *Preventive Therapy:* The aim of this phase is to prevent the spread of the disease to the central nervous system. It may involve irradiation of the head and the injection of drugs directly into the spine.
- *Maintenance Therapy:* In this final phase of treatment, lower doses of the drugs are administered for up to three years in an attempt to keep the disease from reappearing.

Some high-risk ALL patients may also receive a bone marrow transplant.

Causes of ALL: ALL has no single cause. Ultimately, ALL is a genetic disease in the sense that it results from genetic damage (mutation)

Figure 7. A karyotype from a leukemia patient may show abnormal numbers of chromosomes.



Source: Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine

to a single cell that then spreads to progeny cells. The DNA damage may result from natural or medical radiation (that is, from the sun or medical X-rays) or from environmental exposure to toxic substances such as the solvent benzene. ALL is sometimes linked to infection, as from the human T-lymphotropic virus. Most cases of ALL are spontaneous, meaning that the mutations occurred spontaneously in that individual patient and were not inherited. ALL can, however, sometimes run in families.

6.0 Rare Diseases as a Topic for the Middle School Science Classroom

The topic of rare diseases provides an excellent context for teaching core life science content in the middle school classroom (see Tables 3 and 4). According to the *National Science Education Standards (NSES)*, middle school students should develop a basic understanding of heredity and genetics (NRC, 1996). Since the majority of rare diseases have a genetic basis, we can use them as real-life examples of the relationship between genes and health. Many rare diseases are linked to single genes, making

them appropriate for study by middle school students who have only basic knowledge of the relationship between genotype and phenotype. In addition, single-gene disorders allow for the study of the fundamentals of inheritance.

Middle school students are often introduced to the concept of disease as the breakdown of structures or functions of an organism. Rare diseases offer opportunities to expand on that concept by exploring how diseases are linked, not just to genetics, but also to the environment and infection by pathogens. Infectious diseases are an important example of an interrelationship between organisms, since we can use them to illustrate structural similarities and differences between the cells of the host and the pathogen. Furthermore, students can examine the structure-function relationship of systems in the body by studying the differences between diseased and unaffected states.

Rare diseases offer an engaging context for exploring body systems, which are often treated as a vocabulary-laden series of diagrams.

Investigating how a rare disease affects a body system can help students understand how that system normally works. The wide variety of rare diseases ensures that we can select examples that focus primarily on individual body systems. We can use other rare diseases to illustrate functional interactions between body systems.

Furthermore, this curriculum supplement gives students a chance to address any misconceptions they may have about rare diseases. Most students know very little about rare diseases. They usually haven't experienced one themselves or in their immediate family. This lack of familiarity can promote misconceptions about rare diseases and the healthcare system's responses to them. An informal survey of Web sites for support groups for patients with rare diseases suggests several misconceptions that the curriculum supplement should address, including the following:

- *All Rare Diseases Are Being Actively Researched:* Many people, especially those with health insurance and good health, may not be aware of the limitations of the healthcare system in terms of the resources available to treat patients and the state of medical knowledge available to develop drugs and treatments for rare diseases. Despite the efforts of the government, pharmaceutical companies, and patient support organizations, many rare diseases are underfunded and not actively researched.
- *A Disease Must Not Be Rare If It Is Well Known:* Students often assume that if they have heard of a disease, it must not be rare. Examples of well-known rare diseases are cystic fibrosis, sickle cell anemia, and mumps. By addressing this misconception, this curriculum supplement can help students understand the statistical definition of rare diseases.
- *Very Little Is Known about Rare Diseases:* Although limited research has been done on some rare diseases, others have been researched extensively. Especially after the passage of the Orphan Drug Act in 1983, increased funds from the U.S. government have been available to study rare diseases.
- *Family Doctors Are Well Equipped to Diagnose Rare Diseases:* Despite technologies such as the Internet that make information about rare diseases available at a moment's notice, most family doctors are ill equipped to diagnose a rare disease. In many instances, a patient with a rare disease will be the first one ever encountered by the doctor. Furthermore, many rare diseases share symptoms with more-common diseases, and doctors naturally think of common diseases first when considering the diagnosis. This knowledge may help students understand why many patients with rare diseases will visit a number of different doctors over a one-to-five-year period before obtaining a correct diagnosis.
- *Rare Diseases Are Fatal:* Since, by definition, most people have not encountered rare diseases firsthand, their impressions about these diseases come from print and television media. Stories about patients with rare diseases tend to emphasize children and gravely ill people. Rare diseases display the same variations as more-common diseases. Some rare diseases are, in fact, fatal and strike their victims during childhood. Others are less serious and can be cured or effectively managed.

Figure 8. Some rare diseases have been extensively studied, while others have not.



Source: PhotoDisc

7.0 Scientific Inquiry

Scientific inquiry refers to the diverse ways in which scientists study the natural world and propose explanations based on the evidence derived from their work. Inquiry also refers to the activities of students in which they develop knowledge and understanding of scientific ideas, as well as an understanding of how scientists study the natural world.

—NRC, 1996

7.1 Scientific Inquiry as a Topic for the Middle School Science Classroom

Scientific inquiry is a topic well suited to the middle school classroom. The *NSES* stress both abilities and understandings about inquiry (NRC, 1996; see Section 7.2 in *Inquiry in the National Science Education Standards* (NRC, 2000)). As discussed in the *NSES*, students are naturally curious about the world. Inquiry-based instruction offers an opportunity to

- engage student interest in and knowledge about scientific investigation,
- sharpen critical-thinking skills,
- distinguish science from nonscience,
- make students aware of the importance of basic research, and
- humanize the image of scientists.

7.2 Scientific Inquiry in the National Science Education Standards

Inquiry is a multifaceted activity that involves making observations; posing questions; examining books and other sources of information to see what is already known; planning investigations; reviewing what is already known in light of experimental evidence; using tools to gather, analyze, and interpret data; proposing answers, explanations, and predictions; and communicating the results. Inquiry requires identification of assumptions, use of critical and logical thinking, and consideration of alternative explanations.

—NRC, 1996

The *National Science Education Standards* recognize inquiry as both a learning goal and a

Figure 9. *In the classroom, scientific inquiry can be both a learning goal and a teaching method.*



Source: Corbis

teaching method (NRC, 1996). To that end, the content standards for scientific inquiry include both abilities and understandings about inquiry. The *NSES* identify five essential elements of inquiry teaching and learning that apply across all grade levels:

1. Learners are engaged by scientifically oriented questions.
Strategies to improve students' ability to ask scientific questions include providing examples and modeling the formation of testable questions (Krajcik et al., 1998), providing materials that stimulate questions (Chin and Brown, 2002; Harlen, 2001), and encouraging students to formulate their own questions (Harlen, 2001).
2. Learners give priority to evidence, which allows them to develop and evaluate explanations that address scientifically oriented questions.
Scientists obtain evidence in the form of scientific data by recording observations and making measurements. They can check the accuracy of the data by repeating the observations or making new measurements. In the classroom, students use such data to construct explanations for scientific phenomena. Unfortunately, students have difficulty both using appropriate evidence (Sandoval and Reiser, 1997) and including it in their written explanations (Bell and Linn, 2000).

3. Learners formulate explanations from evidence to address scientifically oriented questions.
Scientific explanations are consistent with the available evidence and are subject to criticism and revision. Furthermore, scientific explanations extend beyond current knowledge and propose new understandings that extend the knowledge base. The same is true for students who generate new ideas by building on their personal knowledge base. Explanations are rarely a part of classroom practice, and students need to be explicitly taught how to formulate scientific explanations (Kuhn et al., 2006; McNeill and Krajcik, 2007).
4. Learners evaluate their explanations in light of alternative explanations, particularly those reflecting scientific understanding.
Scientific inquiry differs from other forms of inquiry in that proposed explanations may be revised or thrown out altogether in light of new information. As students compare their results with those of others, they may consider alternative explanations.

They should also compare their results with current scientific knowledge.

5. Learners communicate and justify their proposed explanations.
Scientists communicate their results in such detail that other scientists can reproduce their work. This gives science an important quality-control mechanism. Other scientists can use the results to investigate new but related questions. Students also benefit by sharing their results with their classmates. This gives them a chance to ask questions, examine evidence, identify faulty reasoning, consider whether conclusions go beyond the data, and suggest alternative explanations.

The following chart (Table 12) lists the abilities and understandings about inquiry appropriate for middle school, taken from the *NSES content standards for scientific inquiry* (NRC, 1996). These abilities and understandings are consistent with student performance expectations in the National Assessment of Educational Progress (NCES, 2011).

Table 12. NSES Content Standards for Scientific Inquiry, Grades 5–8

Fundamental Abilities Necessary to Do Scientific Inquiry
<ul style="list-style-type: none"> • Identify questions that can be answered through scientific investigations. • Design and conduct a scientific investigation. • Use appropriate tools and techniques to gather, analyze, and interpret data. • Develop descriptions, explanations, predictions, and models using evidence. • Think critically and logically to make the relationships between evidence and explanations. • Recognize and analyze alternative explanations and predictions. • Communicate scientific procedures and explanations. • Use mathematics in all aspects of scientific inquiry.
Fundamental Understandings about Scientific Inquiry
<ul style="list-style-type: none"> • Different kinds of questions suggest different kinds of scientific investigations. • Current scientific knowledge and understanding guide scientific investigations. • Mathematics is important in all aspects of scientific inquiry. • Technology used to gather data enhances accuracy and allows scientists to analyze and quantify results of investigations. • Scientific explanations emphasize evidence, have logically consistent arguments, and use scientific principles, models, and theories. • Science advances through legitimate skepticism. • Scientific investigations sometimes result in new ideas and phenomena for study, generate new methods or procedures for an investigation, or develop new technologies to improve the collection of data.

Glossary

antibiotic: A drug that can kill or inhibit the growth of bacteria. Antibiotics are not effective against viruses.

aorta: The largest artery in the human body. It originates in the left ventricle of the heart and extends down into the abdomen.

asthma: A chronic inflammatory disease of the airways. Its symptoms include wheezing, coughing, and shortness of breath.

biopsy: A medical procedure that involves removing of a small amount of tissue for examination. The tissue sample is often analyzed by a pathologist to determine the presence or extent of a disease.

bone marrow: Spongy tissue found in the hollow interiors of some large bones. Bone marrow contains stem cells that produce various types of blood cells.

cardiologist: A doctor with specialized training in the prevention, diagnosis, and treatment of diseases associated with the heart and circulatory system.

central nervous system: That part of the nervous system consisting of the brain and spinal cord.

chromosome: An organized package of DNA found in the nucleus of the cell. Humans have 23 pairs of chromosomes—22 pairs of numbered chromosomes, called autosomes, and one pair of sex chromosomes, X and Y.

clinical trial: A controlled study designed to measure the safety or effectiveness of a new drug or medical procedure.

common disease: A disease that affects a relatively large population. In contrast, a rare disease is defined as one affecting fewer than 200,000 people in the United States.

conjunctivitis: An inflammation of the outermost layer of the eye (also called pinkeye). The inflammation may be caused by a virus, a bacterium, or an allergic reaction.

connective tissue: A type of tissue that functions to connect other tissues to each other and hold organs in place. The protein collagen is an important structural component of connective tissues.

disease: A condition characterized by the improper functioning of one or more body parts or systems. The most common causes of diseases are genetic mutation, infection by a pathogen, and exposure to a harmful substance in the environment.

echocardiogram: A medical procedure that uses sound waves to create a moving picture of the heart. An echocardiogram provides a more detailed view of the heart than an X-ray does, and it doesn't involve exposure to radiation.

Ehlers-Danlos syndrome: A group of inherited diseases of the connective tissue. The syndrome is caused by defects in the collagen protein that result in a variety of symptoms affecting multiple body systems. The condition may be mild or life threatening.

genetics: The study of the inheritance patterns of traits. Genetic information is coded in the molecule DNA. Changes to DNA, called mutations, can cause disease.

heart murmur: An extra or unusual sound in the heartbeat. Some heart murmurs are harmless, while others indicate heart problems.

infectious agent: Usually a microscopic agent, such as a virus or bacterium, that can cause an infection and be spread from person to person.

institutional review board: A committee established to approve, monitor, and review medical research involving human subjects.

karyotype: A photograph showing the number and shape of an individual's chromosomes.

leukemia: A cancer of the blood-forming tissues in the bone marrow. Leukemia is often characterized by the production of large numbers of unhealthy white blood cells.

lumbar puncture: A medical procedure also known as a spinal tap. It involves obtaining a small sample of cerebrospinal fluid for analysis. It can be used to look for the presence of an infectious disease such as meningitis or for cancer cells.

Lyme disease: A disease transmitted by a tick bite. Caused by a bacterial infection, Lyme disease is characterized by headaches, fever, depression, and a circular skin rash.

lymph node: A small, spherical organ of the immune system. Lymph nodes are distributed throughout the body and are connected by lymph vessels. They trap bacteria and foreign particles.

Marfan syndrome: A genetic disorder of the connective tissue. Because connective tissue is found throughout the body, features of Marfan syndrome are observed in many different body systems.

medical geneticist: A doctor with specialized training in the diagnosis and treatment of genetic diseases.

methotrexate: A drug used to treat various forms of cancer as well as other diseases. It works against rapidly dividing cells by interfering with the synthesis of DNA, RNA, and protein molecules.

mitral valve prolapse: A heart problem resulting from a faulty valve that separates the upper and lower chambers of the left side of the heart. Symptoms of the condition include chest pain, fatigue, heart palpitations, cough, and shortness of breath after activity.

mutation: A change to the sequence of a DNA molecule. Mutations may be caused by radiation, chemicals, viruses, and mistakes that occur during DNA replication.

myopia: A condition in which the eye focuses incorrectly, making distant objects appear blurred (also called nearsightedness).

necrotizing fasciitis: A rare but very serious bacterial infection that can destroy skin, muscle, and underlying tissues (also called flesh-eating disease). If not treated immediately, it can be fatal.

ophthalmologist: A doctor with specialized training in the diagnosis and treatment of eye problems.

Orphan Drug Act: A piece of federal legislation passed in 1983. It gives pharmaceutical and healthcare companies financial incentives to develop drugs and other products aimed at the treatment of rare diseases.

orthopedist: A doctor with specialized surgical training in the treatment of disorders of the skeletal system.

osteogenesis imperfecta: A genetic disease characterized by brittle bones that easily break.

platelet: A type of blood cell produced by the bone marrow. Platelets help blood coagulate in response to damage to the blood vessels.

prednisone: A drug used to treat inflammatory diseases and some forms of cancer. In the treatment of leukemia, prednisone induces cancer cells to commit suicide.

pulmonologist: A doctor with specialized training in the diagnosis and treatment of respiratory diseases.

rare disease: In the United States, a rare disease is one that affects fewer than 200,000 people.

red blood cell: A type of blood cell produced in the bone marrow. Red blood cells are responsible for transporting oxygen to the cells of the body.

Rocky Mountain spotted fever: A disease transmitted by a tick bite. Caused by a bacterial infection, Rocky Mountain spotted fever is characterized by headaches, fever, muscle pain, and skin rash.

scleroderma: A disease of the connective tissue that involves an excessive accumulation of the protein collagen. Because connective tissue is found throughout the body, features of scleroderma are observed in many different body systems.

scoliosis: A medical condition in which a person's spine shows a curve from side to side. Scoliosis may be associated with other diseases, and its symptoms range from mild to severe.

stem cell: A cell with the potential to form many of the different cell types found in the body. When stem cells divide, they can form more stem cells or other cells that perform specialized functions.

stigma: In a social setting, a public disapproval of some personal characteristic or belief that is at odds with the cultural norms.

vincristine: A drug used to treat some forms of cancer. It targets rapidly dividing cells by interfering with the action of a protein needed for cell division.

white blood cell: A type of blood cell produced by the bone marrow. White blood cells are part of the immune system and help protect the body against foreign material and infection by pathogens.

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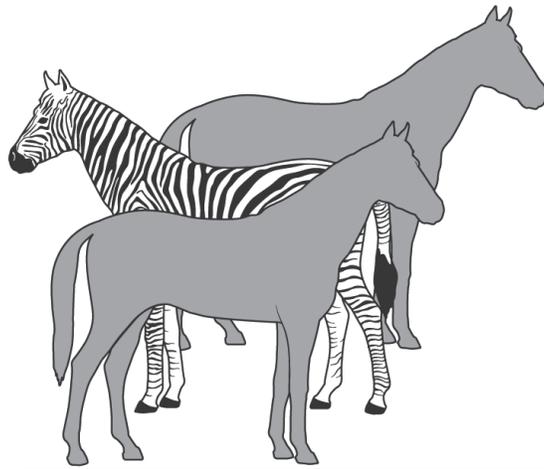
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Lesson 1

What Is a Rare Disease?



Engage

At a Glance

Overview

Lesson 1 asks students to consider their feelings about rare diseases and their attitudes toward people affected by a rare disease. Students are presented with a fictional scenario in which a reality TV show is thinking about filming a student with a rare disease joining the class. A short list of questions elicits students' preconceptions about disease and its causes. Students distinguish between diseases that can be cured and those that can be controlled.

Major Concepts

- Diseases have three main causes:
 - genetics,
 - environmental exposure, and
 - infectious agents.
- Rare diseases may become common, and common diseases may become rare.
- Some rare diseases can be cured, while many others can be managed through treatment.
- People with a rare disease sometimes must cope with the stigma associated with their condition.

Objectives

After completing this lesson, students will have

- recorded their preconceptions about the nature of disease and
- considered their feelings about people who are affected by rare diseases.

Teacher Background

Consult the following sections in Information about Rare Diseases and Scientific Inquiry:

1.0 A History of Rare Diseases in the United States (pages 21–24)

2.0 The Impact of Genomics on Rare Diseases (pages 24–26)

3.0 Rare Infectious Diseases (page 26)

4.0 Rare Diseases Caused by Environmental Toxins (pages 27–28)

In Advance

Web-Based Activities

Activity	Web Component?
1	No

Photocopies, Transparencies, Equipment, and Materials

Photocopies and Transparencies
1 transparency of Master 1.1
1 copy of Master 1.2 for each student
Equipment and Materials
None

Preparation

Each student will need to maintain a notebook or folder dedicated to this supplement. Most lessons involve handouts and ask students

to record information in their notebooks. The lessons also include opportunities for students to record their initial ideas and answers to questions about rare diseases and scientific inquiry. To help them monitor their own understandings and track how their thinking has changed, students will frequently refer back to their previous work and their initial understandings. Decide what format will work best for your students. If your students normally use bound composition books, they can continue to use these and tape or staple handouts into the book. Alternatively, students can use notebook paper for their writing, and then keep their notes and their handouts in binders or folders.

Procedure

Activity 1: What Is a Rare Disease?

Estimated time: 50 minutes

Note: During this lesson, students have an opportunity to express their initial ideas about rare diseases and consider their feelings toward people who are coping with rare diseases. The lesson begins with a reality TV show scenario where a student with a rare disease is about to join the class. The aim of this scenario is to bring the idea of rare diseases into students' lives. The intent of the lesson is not to teach content about rare diseases and their causes and management, but rather to elicit students' prior knowledge about rare diseases. Responses to the questions posed during the lesson can help you assess students' relative familiarity with the concepts and identify misconceptions. Intended to be brief, this initial assessment of preconceptions can help you adjust your teaching of Lessons 2 through 5.

1. **Begin the lesson by explaining that you have received a letter from a television producer asking for help with a new reality TV show his production company is developing.**
2. **Display Master 1.1, *Letter from a Producer*. Ask for a volunteer to read the letter aloud to the class.**

The letter explains that a proposed reality TV show will take place in a middle school and involve a class that includes one student who has a rare disease. The show will give viewers an idea of how this student interacts with teachers and other students. The specific nature of the disease has not yet been decided.

3. **Further explain that the principal has asked your class to help with the producer's request. Ask,**
 - "How would you feel about having such a student join the class?"
 - "What questions would you want to ask before the student arrives?"
 - "What questions would you want to ask the student who has the rare disease?"

Write these three questions on the board.

4. **Instruct students to record these questions and their answers to them in their notebooks. They should also record any feelings they have about the student joining their class.**

This step is intended to have students briefly record their initial feelings about people with rare diseases and to elicit any questions



Students' responses to these questions will help you assess their initial attitudes toward rare diseases and those affected by them.

or concerns they might have. Give students about five minutes to complete this task.

5. **After students have recorded their thoughts and questions, ask for one or two volunteers to share something they wrote in their notebooks.**

At this time, accept all answers. Do not attempt to answer the students' questions or make judgments about their feelings.

6. **Comment that the feelings expressed and the questions asked are understandable and that students will be learning about rare diseases during the remainder of this lesson and in the four lessons that follow.**
7. **Explain that you will begin by exploring what the word "disease" means to them. Give each student a copy of Master 1.2, *Thinking about Disease*. Instruct students to answer the questions and carry out the task described on the handout.**

Explain that this handout is not meant to be a test. Instead, it is designed to help students organize their thinking about disease. Students' responses to the handout will identify their preconceptions about disease. Give students about 10 minutes to complete the handout.

Note: Students may ask questions that, although good, address issues that interrupt the flow of the lesson. One strategy for honoring such questions is to establish a "parking lot" on a piece of chart paper or the board. One half of the parking lot is labeled "unanswered" and the other half is labeled "answered." Questions that are best answered at a later time are written on sticky notes and placed in the "unanswered" column. As questions are addressed in the activities, move the sticky notes to the answered side of the parking lot.

8. **After students have completed Master 1.2, ask for volunteers to share their responses to Questions 1–3.**

Answer key for questions on Master 1.2, *Thinking about Disease*

1. What is a disease?

Many students will respond that a disease is a sickness that results from an infectious agent such as a germ, bacterium, or virus. If other causes such as genetics or exposure to environmental toxins are not mentioned, do not be concerned. These other disease causes will be brought out in Question 3 and in the next lesson.

2. How do doctors tell whether someone has a disease?

Students will likely think of blood or other types of laboratory tests. This question also provides an opportunity to discuss different types of disease symptoms such as fever, pain, and skin rashes.



Content Standard C:

Disease is a breakdown in structures or functions of an organism. Some diseases are the result of intrinsic failures of the system. Others are the result of damage by infection by other organisms.

Ask students to describe how the doctor can observe or measure these symptoms.

3. What do you think causes disease?

Again, students likely will mention infectious agents. If they don't mention other causes, challenge them to think of a disease caused by something other than an infectious agent. If necessary, ask guiding questions to bring out the ideas that heredity and exposure to toxic substances in the environment are also causes.

9. **Ask students to report some of the diseases they listed for Question 4 on the handout. As they respond, record and display for the class a list of about 20 diseases. After the list is assembled, ask students to think about the causes of these diseases and whether there are ways to group these diseases based on their causes. Instruct students to organize the 20 diseases in their notebooks in a way that illustrates the different causes.**

Students may elect to make a table with the columns corresponding to different causes and the rows corresponding to disease examples. Some students may be concerned that a given disease could have or be influenced by more than one cause. Ask these students to consider using a graphical representation such a Venn diagram to illustrate these interactions.

Students may have listed diseases for which they don't know the causes. This is understandable. The important part of this exercise is not to compile a lengthy list of diseases and their causes but rather to give students a chance to express their preconceptions about diseases and their causes. If students ask you what causes a particular disease and you know the cause, tell them so they can classify it. If you don't know the cause of the disease, instruct the student to put a question mark next to the disease and not to worry about classifying it by its cause.

Note: You may want to assign Step 9 (causes-of-disease organizer) as homework.

10. **After students have completed the task, ask for volunteers to describe how they organized the diseases in their notebooks. Ask each volunteer to explain the general causes of the diseases and to list an example for each. Ask whether any of the diseases have more than one cause or whether any of the listed causes interact with each other.**

Ask questions to clarify students' thinking, but do not correct misconceptions at this time. The three main causes of disease (infectious agents, heredity or genetics, and exposure to environmental toxins) will be addressed in the subsequent lessons.



The manner in which individual students organize the list of diseases will help you assess the student's initial ideas about diseases and their causes and to identify misconceptions the student may have.

Environmental exposure may be somewhat confusing. One can argue that a disease brought about by exposure to a pathogen is environmental since the pathogen is found in the environment. For our purpose, a disease caused by environmental exposure refers to a nonliving agent such as radiation, heavy metals, or a toxin produced by another organism.

11. Ask for volunteers to share their responses to Question 5.

5. What does it mean to call a disease “rare”?

Students’ responses will vary. If students struggle with this question, rephrase it by asking whether some diseases affect more people than others. You may mention that in this country, a disease is considered to be rare if 200,000 people or fewer have it. To help students make some sense of this number, you can mention that the U.S. population was about 311 million people in 2011.

12. Ask, “Do you think that a disease that is rare always remains rare? Can a rare disease become a common disease?”

Students’ responses will vary. If students don’t bring it up, ask guiding questions to bring out the idea of a new infectious disease such as swine flu that begins as a rare disease and then becomes common as it spreads.

13. Ask, “Can a common disease become a rare disease?”

If a student doesn’t mention this, direct the discussion to medicine’s ability to control or even eradicate some diseases. You may mention polio as an example of a disease that was once common but is now rare. Smallpox has actually been extinguished.

14. Ask for volunteers to share their responses to Question 6 (whether the diseases they listed are curable, controllable, or not controllable).

For many diseases on their lists, students will not be able to say whether they are curable, controllable, or not controllable. Bring out in the discussion examples of diseases that are curable, such as many bacterial infections, and others that are controllable, such as diabetes.

15. Explain that some diseases are relatively easy to treat and others are more difficult. Ask, “What are some reasons that one disease might be more difficult to treat than another?”

Students may focus on specific diseases. Try to get them to speak in general terms to address issues such as the amount of information

known about the disease, the ease of diagnosis, and the amount of resources that society devotes to the study and treatment of the disease.

Remind students to return Master 1.2 to their notebooks. They will revisit the ideas they recorded on the handout in a later lesson.

- 16. Conclude the lesson by remarking that the lessons that follow will give students opportunities to reflect on the ideas brought out during this lesson and to modify their thinking if necessary.**

Lesson 1 Organizer

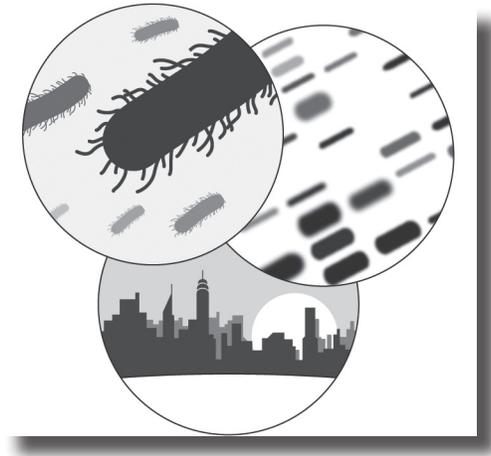
Activity 1: What Is a Rare Disease? Estimated time: 50 minutes	Page and Step
Explain that a TV producer wants to film a reality show about a student with a rare disease joining the class. Display Master 1.1 , and have someone read it aloud.	Page 47 Steps 1 and 2 
Write these questions on the board as you ask them: <ul style="list-style-type: none"> • “How would you feel about having such a student join the class?” • “What questions would you ask before the student arrives?” • “What questions would you ask the student who has the rare disease?” 	Page 47 Step 3
Instruct students to write the answers in their notebooks.	Page 47 Step 4
Ask one or two volunteers to share their answers with the class.	Page 48 Step 5
Explain that students will be learning about rare diseases in the lessons that follow. To begin, they will explore the nature of disease. <ul style="list-style-type: none"> • Hand out a copy of Master 1.2 to each student. • Instruct students to follow the directions on the handout. 	Page 48 Steps 6 and 7 
Ask volunteers to share their responses to Questions 1–3.	Page 48 Step 8
Ask volunteers to report diseases they listed for Question 4. <ul style="list-style-type: none"> • Record and display a list of about 20 diseases students mentioned. • Ask students whether they can group these diseases by cause. 	Page 49 Step 9
Ask volunteers to explain how they grouped the diseases.	Page 49 Step 10
Ask volunteers to share their responses to Question 5.	Page 50 Step 11
Ask students, <ul style="list-style-type: none"> • “Do you think a disease that is rare always remains rare?” • “Can a rare disease become a common disease?” • “Can a common disease become a rare disease?” 	Page 50 Steps 12 and 13
Ask volunteers to share their responses to Question 6.	Page 50 Step 14
Explain that diseases vary in how easy they are to treat. Ask, “What are some reasons that one disease might be more difficult to treat than another?”	Page 50 Step 15
Explain that students will be reflecting on these ideas and changing their thinking if necessary.	Page 51 Step 16

 = Involves making a transparency.

 = Involves copying a master.

Lesson 2

What Causes Rare Diseases?



Explore

At a Glance

Overview

In this lesson, students assume the roles of medical officers working to protect the health of soldiers at an army post. In the course of their duties, they must consider the major causes of disease and pay special attention to infectious diseases that have the potential to spread throughout the post. One soldier becomes infected with a common bacterial species that leads to the development of a serious rare disease.

Major Concepts

- Diseases have three main causes:
 - genetics,
 - environmental exposure, and
 - infectious agents.
- A bacterial species that causes a common disease can sometimes cause a rare disease.
- Disease causes sometimes interact.

Objectives

After completing this lesson, students will have

- considered the different causes of disease,
- recognized that a single species of pathogen can cause two different diseases depending on the route of infection, and
- discussed an example of how two different disease causes (infection and genetics) can interact to produce a rare disease.

Teacher Background

Consult the following sections in Information about Rare Diseases and Scientific Inquiry:

2.0 The Impact of Genomics on Rare Diseases (pages 24–26)

3.0 Rare Infectious Diseases (page 26)

4.0 Rare Diseases Caused by Environmental Toxins (Pages 27–28)

5.1 Necrotizing Fasciitis (pages 28–29)

6.0 Rare Diseases as a Topic for the Middle School Classroom (pages 33–34)

In Advance

Web-Based Activities

Activity	Web Component?
1	Yes
2	Yes
3	No

Photocopies, Transparencies, Equipment, and Materials

Photocopies and Transparencies
<p>Activity 1: Causes of Disease</p> <p>For Classes Using Web-Based Activity: 1 transparency and 1 copy for each pair of students of Master 2.1</p> <p>For Classes Using Print-Based Activity: 1 transparency and 1 copy for each pair of students of Master 2.1 1 copy of Masters 2.2 and 2.3 for each pair of students</p>
<p>Activity 2: Is a Rare Disease Present?</p> <p>For Classes Using Web-Based Activity: 1 copy of Master 2.7 for each pair of students</p> <p>For Classes Using Print-Based Activity: 1 copy of Masters 2.4, 2.5, 2.6, and 2.7 for each pair of students (Optional: For Master 2.6, block out the photos before copying; see Note on page 62.)</p>
<p>Activity 3: How Rare Is Rare?</p> <p>None</p>

Continued

Equipment and Materials

For Activities 1 and 2, Web-based versions, students will need computers with Internet access.

For Activity 3, you will need baby lima beans for each group of four students:

- 1 small container with 9 beans and 1 bean colored red and
- 1 large container with 99 beans and 1 bean colored red.

Preparation

Activity 1

Make photocopies and a transparency.

For classes using the Web version, verify that the computer lab is reserved for your classes or that the classroom computers are set up for the activities. Refer to Using the Web Site for details about the Web site. Check that the Internet connection is working properly.



Log on to the Web Portion of Student Activities section of the site at

<http://science.education.nih.gov/supplements/rarediseases/student>

Select “Lesson 2: What Causes Rare Diseases?” so students can begin the activity right away.

Activity 2

Review the photos of the necrotizing fasciitis (NF) patient on Master 2.6, *Medical Reference Manual: Necrotizing Fasciitis*. **If the photo of the late-stage infection is too graphic for your students, block it out before copying.** Make photocopies.

Activity 3

Each group of four students will need

- 1 small container with 9 baby lima beans and 1 bean colored red (use a marking pen) and
- 1 large container with 99 baby lima beans and 1 bean colored red (use a marking pen).

It will save time if you weigh the beans rather than count them. There are approximately 100 baby lima beans per 1.33 ounces (37.7 grams).

Procedure

Note: This is an Explore lesson. It is designed to give students a common experience they can use to begin constructing understandings about rare diseases and their causes. In this lesson, students assume the roles of medical officers at an army post. This scenario gives students a real-life context in which to consider genetics, infectious agents, and environmental exposure as the major causes of disease. The lesson focuses on the rare disease necrotizing fasciitis (NF), more commonly known as flesh-eating disease. The serious nature of this disease may be disturbing to some students. The lesson stresses that although NF is caused by a commonly encountered bacterium, the immune system normally stops the infection before it becomes dangerous. In rare cases (about 1 in 100,000 people), the bacteria elude the immune system and the infection can lead to organ failure and death. The hands-on probability activity is included to help make the rarity of the disease more understandable and thus reduce any student anxiety.

Activity 1: Causes of Disease

Estimated time: 30 minutes

- 1. Explain that in this lesson, you will be concerned with this question: What causes rare diseases?**

Display this question for the class. Students should recall some causes of disease from the first lesson. In Step 8, you may need to remind students that there are three general causes of disease: infectious agents, heredity (genetics), and exposure to toxins in the environment.

- 2. Open the activity by explaining that students will assume the roles of medical officers who are in charge of looking after the health of soldiers at an army post. The post is where new recruits are trained.**

If necessary, explain to students that an army post is where soldiers are stationed. The soldiers live and sleep in close quarters called barracks, which are like dormitories. When they are sick or injured, soldiers visit a clinic called an infirmary.

- 3. Arrange the students in pairs. Explain that their task as medical officers is to examine the list of all visits to the infirmary during the previous week. They are looking for any patterns that would indicate a health concern on the post.**

For example, students should be on the lookout for any clusters of illness or accidents that may represent a larger threat to the soldiers and limit the ability of the army post to meet its responsibilities.

(For print version, skip to Step 4-p below.)



In classrooms using the Web version of this activity:

4a-w. Give each student pair a copy of Master 2.1, *Medical Officer Report Form*. Explain that students will add information to the form by accessing medical information on the post's Web site.

4b-w. Instruct student pairs to proceed to

<http://science.education.nih.gov/supplements/rarediseases/student>

Students should click on “Lesson 2: What Causes Rare Diseases?” and then “Activity 1: Infirmary Visits, Week 1.”

5a-w. Instruct students to look over the reasons that each soldier went to the infirmary and to think about the nature of the causes of the soldiers' complaints.

Students can sort the patients by their patient number, location (the barracks they live in), and medical complaint. This step should take no more than about five minutes.

5b-w. After students have had a chance to look over the information on the New Visits to the Infirmary, Week 1, table ask, “What are two general reasons why soldiers reported to the infirmary?”

Students may want to respond by citing specific complaints. At this point, simply direct the discussion to bring out the fact that soldiers reporting to the infirmary were either sick or injured.

Continue with Step 6 on page 58.

In classrooms using the print version of this activity:



4-p. Give each student pair one copy each of Master 2.1, *Medical Officer Report Form*, and Master 2.2, *Visits to the Infirmary, Week 1*. Instruct students to look over the reasons that each soldier went to the infirmary and to think about the nature of the causes of the soldiers' complaints.

This step should take no more than about five minutes.

5-p. After students have had a chance to look over the information in Master 2.2, ask, “What are two general reasons why soldiers reported to the infirmary?”



Content Standard C:

Disease is a breakdown in structures or functions of an organism. Some diseases are the result of intrinsic failures of the system. Others are the result of damage by infection by other organisms.

Content Standard F:

Natural environments may contain substances (for example, radon and lead) that are harmful to human beings.

Students may want to respond by citing specific complaints listed on the handout. At this point, simply direct the discussion to bring out the fact that soldiers reporting to the infirmary were either sick or injured.

- 6. Acknowledge that soldiers may become injured for many different reasons. Ask, “What about sickness?” Remind the students that in Lesson 1, they came up with three general causes of disease: infectious agents, heredity (genetics), and exposure to environmental toxins. Ask, “Which of these three causes is most likely to be responsible for a health problem that can spread throughout the post?”**

Students should recognize that a disease caused by an infectious agent is the most likely to spread throughout the post.

- 7. Display Master 2.1. Ask for a volunteer to summarize the reasons that soldiers came to the infirmary.**

Display the responses as you list them. Guide the discussion to focus on the following:

- Barracks A has a cluster of six soldiers complaining of sore, itchy eyes.
- Barracks G has a cluster of six soldiers complaining of sore throat.
- Barracks E has two soldiers with a skin rash.
- Four soldiers from three different barracks have sore toes from wearing new boots.
- One soldier has a cut on the leg.
- One soldier complains of shortness of breath.
- One soldier twisted his ankle.

- 8. Remind students that they need to look for potential health threats to the post. Ask, “Do you see any patterns or cases that worry you?”**

Students should respond that the clusters of sore, itchy eyes; sore throats; and skin rashes could each potentially spread to other soldiers on the post. Students may also mention the soldier in Barracks I who complained of shortness of breath. The other soldiers visiting the infirmary have problems that probably won't spread.

- 9. Mention that it is possible that one or more types of infectious disease may be present on the post. Ask, “How can we tell whether or not a soldier has a bacterial infection?”**

Students' responses will vary. They may mention other symptoms such as mucous discharge or running a fever. If not mentioned by

a student, turn the discussion to laboratory tests. Students may first think of a blood test. Explain that doctors can obtain a swab from a patient's throat or other part of the body and test it for the presence of infectious bacteria.

10. **Explain that as medical officers, they have the ability to test for the presence of different species of bacteria that had previously infected soldiers on the post. Two different tests can be ordered:**
- **Test 1: Looks for infection by bacterial species A, B, and C. These species are associated with common infections for pinkeye and sore throats as well as infections resulting from cuts and abrasions.**
 - **Test 2: Looks for bacterial infections associated with skin rashes caused by Rocky Mountain spotted fever or Lyme disease. Test 2 also looks for exposure to poison ivy (not caused by bacteria).**

Note: While it is true that medical tests sometimes look for multiple causes at the same time, the tests described in this activity were created to make the test-ordering procedure easy for students to carry out.

(For print version, skip to Step 11-p on page 60.)



In classrooms using the Web version of this activity:

11-w. Instruct students to return to the Web site in their pairs and select the lab tests (if any) to perform on the soldiers. After making their selections, students should summarize on Master 2.1 which tests they ordered, which soldiers were tested, and why they ordered each test. Conduct a brief discussion to reach a consensus about which tests (if any) should be ordered and for whom.

Since the exact causes of the soldiers' illnesses are not known, students should decide to test the soldiers with eye redness and sore throats with Test 1, which looks for infection by bacterial species A, B, and C.

Soldiers with skin rashes should be tested using Test 2, which looks for infection by the bacteria associated with Rocky Mountain spotted fever and Lyme disease as well as exposure to poison ivy. Students may decide not to perform tests on the soldiers complaining of sore toes. Explain that such foot blisters can become infected and suggest that they, too, be tested for possible infection using Test 1 (infection by bacterial species A, B, and C).

Some students may want to play it safe and order both tests for each soldier. Make it clear that tests come with costs, and the

infirmary must perform efficiently. Therefore, only needed tests should be ordered.

Note: Pinkeye (conjunctivitis) can either be contagious or not. The contagious form of the disease is caused by a bacterial or a viral infection. A number of different bacterial species can cause a pinkeye infection.

12-w. Instruct student pairs to return to the Web site and click on “Activity 1: Lab Test Results.”

The table that appears contains the same information about soldiers visiting the infirmary that is in “Activity 1: Infirmary Visits, Week 1.” It also lists which lab tests were ordered, the lab test results, the patient diagnosis, and the patient treatment.

13-w. Instruct students to briefly summarize in their notebooks those cases with the potential to spread throughout the army post. Also ask them to describe how the cases were treated.

Students need not list information about each soldier. Instead, they can describe groups of soldiers with similar complaints and test results.

End of Web-based activity.

In classrooms using the print version of this activity:



11-p. Instruct student pairs to decide which lab tests (if any) to perform on which soldiers. Groups should summarize on Master 2.1 which tests they ordered, which soldiers were tested, and why they ordered each test. Conduct a brief discussion to reach a consensus about which tests (if any) should be ordered and for whom.

Since the exact causes of the soldiers' illnesses are not known, students should decide to test the soldiers with eye redness and sore throats with Test 1, which looks for infection by bacterial species A, B, and C.

Soldiers with skin rashes should be tested using Test 2, which looks for infection by the bacteria associated with Rocky Mountain spotted fever and Lyme disease as well as exposure to poison ivy. Students may decide not to perform tests on the soldiers complaining of sore toes. Explain that such foot blisters can become infected and suggest that they, too, be tested for possible infection using Test 1 (infection by bacterial species A, B, and C).

Some students may want to play it safe and order all tests for each soldier. Make it clear that tests come with costs, and the infirmary must perform efficiently. Therefore, only needed tests should be ordered.

Note: Pinkeye (conjunctivitis) can either be contagious or not. The contagious form of the disease is caused by a bacterial or a viral infection. A number of different bacterial species can cause a pinkeye infection.

12-p. Give each student pair one copy of Master 2.3, *Test Results, Week 1*.

This handout contains the same information about soldiers visiting the infirmary that was found on Master 2.2. It also lists which lab tests were ordered, the lab test results, the patient diagnosis, and the patient treatment.

13-p. Instruct students to briefly summarize in their notebooks those cases with the potential to spread throughout the army post and to describe how they were treated.

Students need not list information about each soldier. Instead, they can describe groups of soldiers with similar complaints and test results.

Activity 2: Is a Rare Disease Present?

Estimated time: 40 minutes

(For print version, skip to Step 1-p on page 62.)



In classrooms using the Web version of this activity:

Note: In Step 9 of this activity, students access a medical reference manual that contains two images of a patient with flesh-eating disease. One of the images is rather graphic and may be disturbing to some students. We recommend that you view the images before class and decide whether you want students to see them. If you decide not to let students see them, instead of using the Web site for this step, give each student pair one copy of Master 2.6, *Medical Reference Manual*, on which you have blocked out the photos.

1-w. Keep the students in pairs. Explain that one week has gone by, and you are ready to discuss the patient outcomes from that week. You are also going to present a list of new visits to the post's infirmary.

2-w. Instruct students to proceed to

<http://science.education.nih.gov/supplements/rarediseases/student>

Students should click on “Lesson 2: What Causes Rare Diseases?” and then “Activity 2: Follow-up on Week 1 Visits.”

After students have had a chance to look over the information in the table, ask for volunteers to summarize what they learned about the treatment outcomes of the Week 1 infirmary visits.

The cases of pinkeye, sore throat, skin rash, and asthma have responded (or are responding) to treatment. Cases of sore toes and injuries were treated, but it is too soon to describe outcomes.

3-w. Ask, “Did you learn anything that causes you to be concerned?”

Many students will probably note that the treatments are working and will, therefore, express no particular concerns. Some students may be concerned that two of the six soldiers being treated for sore throats returned to the infirmary. Others may note that three of the four soldiers who developed blisters on their feet tested positive for infection by bacterial species A.

4-w. Instruct students to click on “Activity 2: Infirmary Visits, Week 2.” As before, instruct students to reflect on the information and summarize in their notebooks the soldiers’ reasons for coming to the infirmary.

This step should take no more than about five minutes.

Continue with Step 5 on page 63.

In classrooms using the print version of the activity:



Note: In Step 9-p, student pairs get a copy of Master 2.6, which contains two images of a patient with flesh-eating disease. One of the images is rather graphic and may be disturbing to some students. We recommend that you view the images before class and decide whether you want students to see them. If not, block out the images on Master 2.6 before making copies.

1-p. Keep the students in their pairs. Explain that one week has gone by and you are ready to discuss the patient outcomes from that week. You are also going to present a list of new visits to the post’s infirmary.

2-p. Give each student pair one copy of Master 2.4, *Follow-up on Week 1 Infirmary Visits*.

- 3-p. After groups have had a chance to look over Master 2.4, ask, “Did you learn anything that causes you to be concerned?”**

Many students will probably note that the treatments are working and will, therefore, express no particular concerns. Some students may be concerned that two of the six soldiers being treated for sore throat returned to the infirmary. Others may note that three of the four soldiers who developed blisters on their feet tested positive for infection by bacterial species A.

- 4-p. Give each pair one copy of Master 2.5, *Visits to the Infirmary, Week 2*. As before, instruct students to reflect on the information on the handout and to summarize, in their notebooks, the soldiers’ reasons for coming to the infirmary.**

This step should take no more than about five minutes.

- 5. Ask for volunteers to summarize the information they recorded in their notebooks.**

Display students’ responses as you list them. Guide the discussion to focus on the following:

Some soldiers who visited the infirmary during Week 1 returned.

- Two soldiers from Barracks G who reported to the infirmary during the first week complaining of sore throat returned with similar complaints.
- One of the soldiers with a sore toe has developed a severe infection from bacterial species A.

Most soldiers who visited the infirmary were first-time patients.

- Four soldiers from Barracks G appeared complaining of sore throat.
- Two soldiers from Barracks A appeared complaining of sore throat.
- Two soldiers (from Barracks B and F) appeared complaining of skin rashes.
- One soldier appeared with a cut on the head.
- One soldier appeared with an injured ankle.
- One soldier appeared with a sore toe.

- 6. Remind students that you are concerned about infectious diseases that might spread to the rest of the post. Ask, “Is there any evidence of a bacterial infection spreading throughout the post?”**

Students may observe that the infection with bacterial species C that caused the pinkeye is under control and not cause for concern. They should also observe that new cases of infection by bacterial species

A are sending soldiers from other barracks to the infirmary with sore throats. Some will likely report that this is a cause for concern. Finally, some students may note that bacterial species A is also responsible for a severe foot infection in one soldier who developed a blister from wearing new boots.

7. **Explain that you are concerned about the foot infection that has quickly become serious. Observe that bacterial species A seems to be responsible for two different diseases: the inflammation of the throat seen in many soldiers and the severe foot infection in one soldier. Ask, “Can the same bacterial species be responsible for causing two different diseases?”**

Students will probably not be able to give a knowledgeable answer to this question. Guide the discussion to bring out the possibility that the same bacteria infecting different parts of the body might produce different symptoms.

8. **Acknowledge that it is difficult to know whether bacterial species A can cause two very different-looking diseases. Explain that the severe foot infection could be due to flesh-eating disease, which is very rare though very serious. Suggest that some research may help discover whether there is a possible link between bacterial species A and flesh-eating disease. Explain that students can look up flesh-eating disease in the Medical Reference Manual, which has a section on microbiology and disease.**

- 9-w. Give each pair one copy of Master 2.7, *Questions about a Rare Disease*. Instruct students to read the information about flesh-eating disease in the Medical Reference Manual and use it to answer the questions on Master 2.7. (To get to the Web version of the manual, students should follow Step 2-w above but click on “Activity 2: Medical Reference Manual.”)

Give students about 10 minutes to complete the tasks.

In classrooms using the print version of the activity:

- 9-p. Give each pair one copy of Master 2.6, *Medical Reference Manual: Necrotizing Fasciitis*, and Master 2.7, *Questions about a Rare Disease*. Instruct students to read Master 2.6 and use it to answer the questions on Master 2.7.

Give students about 10 minutes to complete the tasks.



Content Standard A:

Scientific explanations emphasize evidence, have logically consistent arguments, and use scientific principles, models, and theories.



Students' answers to the questions will help you assess how well they can use multiple forms of evidence to support a scientific explanation.



10. After students have completed the tasks, ask for volunteers to report answers to each question on Master 2.7.

Answer key for Master 2.7, *Questions about a Rare Disease*

1. What evidence suggests that bacterial species A causes both sore throat and foot infection?
 - *Bacterial species A was cultured from throat swabs of soldiers with sore throats and from toe swabs of three out of four soldiers who developed blisters from wearing new boots.*
 - *The Medical Reference Manual mentions that flesh-eating disease can be caused by different species of bacteria, including the one that causes strep throat.*
2. What evidence suggests that the soldier with the foot infection has flesh-eating disease?
 - *A toe swab tested positive for bacterial species A.*
 - *The symptoms (redness, swelling, and nausea) are consistent with flesh-eating disease, as is the timeline (symptoms progressing quickly).*
3. Why are there many cases of sore throat but only one case of flesh-eating disease?
 - *Sore throats can spread among soldiers living together.*
 - *Flesh-eating disease generally doesn't spread because it requires contact with an open wound.*
4. What evidence is there that flesh-eating disease is a rare disease?
 - *The Medical Reference Manual states that it is rare disease. The odds of getting it are about 1 in 100,000.*
 - *Three soldiers with foot blisters tested positive for bacterial species A, but only one soldier developed flesh-eating disease.*
5. What should be the next step in treating the soldier with the foot infection? Explain your reasoning.
 - *The soldier should be sent immediately to a hospital with the resources needed to treat flesh-eating disease. The disease is very serious. According to the Medical Reference Manual, 2 out of 10 patients die from it.*

Activity 3: How Rare Is Rare?

Estimated time: 30 minutes

Note: The purpose of this activity is to make the 1 in 100,000 probability of coming down with flesh-eating disease more real to the class. It is not important that the students understand how the probability calculation is performed.



Content Standard A:
Mathematics is important in all aspects of scientific inquiry.

1. Observe that we all come into contact with bacterial species A and that it causes the common disease of strep throat. As this lesson shows, sometimes a bacterium associated with a common disease can also cause a rare disease. Explain that although this lesson dealt with a person who developed flesh-eating disease, the rate of this infection is actually quite low. The odds of coming down with flesh-eating disease are about 1 in 100,000.
2. Explain that you will finish the lesson by performing a brief demonstration of the rarity of coming down with flesh-eating disease. Arrange the class in groups of four students. Give each group
 - 1 small container containing 9 baby lima beans and 1 baby lima bean that has been colored red and
 - 1 large container containing 99 baby lima beans and 1 baby lima bean that has been colored red.

3. Display this statement: “The odds of coming down with flesh-eating disease this year are 1 in 100,000.”
4. Explain that you will now explore that statement. Explain that a bean colored red represents a person who *may* come down with flesh-eating disease. Instruct one student from each group to close his or her eyes and select 1 bean from the small container of 10 beans.
 - Ask, “Did anyone get a red bean?”

Selecting the red bean means that the student *may* come down with flesh-eating disease.

5. Display this below the statement about probability: “1/10.” Explain that the odds of picking a red bean from the small container were 1 in 10.
 - If a student has selected the red bean, explain that it doesn’t mean the student will get flesh-eating disease but rather that the possibility still exists.
 - If no one selected a red bean, produce one yourself and explain that this represents the possibility that an individual will come down with flesh-eating disease.
6. Instruct another student from each group to select a bean from the large container without looking.
 - Ask, “Did anyone get a red bean?”

Most likely, no one will have picked a red bean.

7. Display this next to the “1/10”: “× 1/100.” Explain that the odds of picking a red bean from the large container were 1 in 100.

- If a student has selected the red bean, explain that, as before, it doesn't mean that the student will get flesh-eating disease but rather that the possibility still exists.
 - If no one selected a red bean, produce one yourself and explain that this represents the possibility that an individual will come down with flesh-eating disease.
8. Instruct students to put the bean they selected back into the large container and remix the beans.
 9. One last time, instruct another student from each group to select a bean from the large container without looking.
 - Ask, "Did anyone get a red bean?"

As before, it is unlikely that a student will have picked a red bean.

10. Display this next to the "1/100": "× 1/100." Explain that, just as last time, the odds of picking a red bean from the large container were 1 in 100.
11. Explain that this activity modeled the 1 in 100,000 probability of coming down with flesh-eating disease. Display the answer to the probability calculation:

$$1/10 \times 1/100 \times 1/100 = 1/100,000$$

12. Summarize by explaining that to reach the 1/100,000 odds of coming down with flesh-eating disease, a group would have had to pick the red bean from the small container and pick it again both times from the large container.

Note: Some students may wonder what it would look like to pick one red baby lima bean out of a pile of 100,000 beans. You may explain that 100,000 baby lima beans would weigh about 83 pounds and fill a large wheelbarrow.

13. Conclude the lesson by asking,
 - "What are two reasons why flesh-eating disease is so rare?"
 - "Which two general causes of disease interacted to allow flesh-eating disease to develop?"

Students should comment that the bacteria responsible for flesh-eating disease are normally found in the throat and airways, but in the case of flesh-eating disease, the bacteria enter another part of the body through an open wound.

If not brought up by a student, mention that the vast majority of people don't develop flesh-eating disease even when infected through an open wound. Most people's immune systems stop the infection; but in rare cases, a person has an immune system that (because of genetics) allows the infection to become established. Also, people with weakened immune systems are at higher risk for infection.

Lesson 2 Organizer: Web Version



Activity 1: Causes of Disease Estimated time: 30 minutes	Page and Step
Explain that students will explore what causes rare diseases and assume the roles of medical officers in charge of the health of soldiers at an army post.	Page 56 Steps 1 and 2
Arrange the class into pairs. Explain that they will look at a list of infirmary visits for the previous week and look for patterns that suggest a health concern.	Page 56 Step 3
Give each pair a copy of Master 2.1 , and instruct pairs to go to the Web site for the curriculum.	Page 57 Step 4-w 
Instruct students to click on "Activity 1: Infirmary Visits, Week 1" and to think about the reasons why soldiers went to the infirmary.	Page 57 Step 5a-w 
Ask, "What are two general reasons why soldiers reported to the infirmary?"	Page 57 Step 5b-w
Remind students about the three general causes of disease: <ul style="list-style-type: none"> • infectious agents, • heredity (genetics), and • environmental toxins. Ask, "Which of these three causes is most likely to be responsible for a health problem that can spread throughout the post?"	Page 58 Step 6
Display Master 2.1 . <ul style="list-style-type: none"> • Ask for a volunteer to summarize the reasons that soldiers came to the infirmary. • Record and display these reasons. • Ask, "Do any patterns or cases worry you?" 	Page 58 Steps 7 and 8 
Mention that one or more types of infectious disease may be present on the post. Ask, "How can we tell whether or not a soldier has a bacterial infection?"	Page 58 Step 9
Explain that they can order tests for bacterial infections. <ul style="list-style-type: none"> • Test 1 looks for infections by bacterial species associated with pinkeye, sore throats, and infected cuts and abrasions. • Test 2 looks for infections associated with skin rashes caused by Rocky Mountain spotted fever or Lyme disease bacteria and for exposure to poison ivy. 	Page 59 Step 10
Instruct pairs to return to the Web site, order the needed tests, and record on Master 2.1 which tests they ordered and why.	Page 59 Step 11-w 
Ask students to click on "Activity 1: Lab Test Results." Tell students to summarize in their notebooks those cases that could spread throughout the post and to describe how they were treated.	Page 60 Steps 12-w and 13-w 

1

2

3

4

5

Activity 2: Is a Rare Disease Present? Estimated time: 40 minutes	Page and Step
Explain that one week has gone by, and you are ready to discuss patient outcomes from Week 1. <ul style="list-style-type: none"> • Instruct pairs to go the Web site and click on "Activity 2: Follow-up on Week 1 Visits." • Ask volunteers to summarize the outcomes described there. 	Page 61 Steps 1-w and 2-w 
Ask, "Did you learn anything that causes you to be concerned?"	Page 62 Step 3-w
Instruct pairs to click on "Activity 2: Infirmary Visits, Week 2" and then to summarize in their notebooks the reasons soldiers came to the infirmary.	Page 62 Step 4-w 
Ask volunteers to report what they wrote in their notebooks, display their responses, and discuss.	Page 63 Step 5
Ask, "Is there any evidence of a bacterial infection spreading throughout the post?"	Page 63 Step 6
Explain that you are concerned about the serious foot infection. <ul style="list-style-type: none"> • Observe that bacterial species A seems to cause both sore throats and the foot infection. • Ask, "Can the same bacterial species be responsible for causing two different diseases?" 	Page 64 Step 7
Explain that the foot infection could be caused by flesh-eating disease. Instruct students to look up the disease in the Medical Reference Manual.	Page 64 Step 8
Give each pair a copy of Master 2.7 . Instruct students to go to the Web site, click on "Activity 2: Medical Reference Manual," and use the information there to answer the questions on Master 2.7 .	Page 64 Step 9-w  
Ask volunteers to report their answers to the questions on Master 2.7 .	Page 65 Step 10

Activity 3: How Rare Is Rare? Estimated time: 30 minutes	Page and Step
Observe that bacterial species A is common and causes strep throat. It can also cause the rare flesh-eating disease. Explain that the odds of getting flesh-eating disease are 1 in 100,000.	Page 66 Step 1
Arrange the class in groups of four. Give each group <ul style="list-style-type: none"> • 1 small container with 9 baby lima beans and 1 baby lima bean colored red and • 1 large container with 99 baby lima beans and 1 baby lima bean colored red. 	Page 66 Step 2
Display this statement: "The odds of coming down with flesh-eating disease this year are 1 in 100,000."	Page 66 Step 3
Explain that the red bean represents a person who <i>may</i> come down with flesh-eating disease. <ul style="list-style-type: none"> • Have one student from each group pick a bean from the small container without looking. • Ask, "Did anyone get a red bean?" 	Page 66 Step 4
Display this: "1/10." Explain that the odds of picking a red bean were 1 in 10.	Page 66 Step 5
Have another student from each group pick a bean from the large container. Ask, "Did anyone get a red bean?"	Page 66 Step 6
Display this next to 1/10: " $\times 1/100$." Explain that the odds of picking a red bean were 1 in 100.	Page 66 Step 7
Tell students to place the selected beans back into the large container and mix. Have another student once again pick a bean from the large container. Ask, "Did anyone get a red bean?"	Page 67 Steps 8 and 9
Display next to 1/100, " $\times 1/100$." Explain that, as before, the odds of picking a red bean were 1 in 100.	Page 67 Step 10
Explain that this activity modeled the 1 in 100,000 probability of coming down with flesh-eating disease. <ul style="list-style-type: none"> • Display the answer to the probability calculation: "$1/10 \times 1/100 \times 1/100 = 1/100,000$." • Explain that to get flesh-eating disease, a group would have had to pick the red bean from the small container and pick it again both times from the large container. 	Page 67 Steps 11 and 12
Conclude the lesson by asking, <ul style="list-style-type: none"> • "What are two reasons why flesh-eating disease is so rare?" • "Which two general causes of disease interacted to allow flesh-eating disease to develop?" 	Page 67 Step 13

M = Involves copying a master.  = Involves using the Internet.

T = Involves making a transparency.

Lesson 2 Organizer: Print Version



Activity 1: Causes of Disease Estimated time: 30 minutes	Page and Step
Explain that students will <ul style="list-style-type: none"> • explore what causes rare diseases and • assume the roles of medical officers in charge of the health of soldiers at an army post. 	Page 56 Steps 1 and 2
Arrange the class into pairs. Explain that they will look at a list of infirmary visits for the previous week and look for patterns that suggest a health concern.	Page 56 Step 3
Give each pair a copy of Masters 2.1 and 2.2 , and ask students to read over the reasons for the visits.	Page 57 Step 4-p 
Ask, "What are two general reasons why soldiers reported to the infirmary?"	Page 57 Step 5-p
Remind students about the three general causes of disease: <ul style="list-style-type: none"> • infectious agents, • heredity (genetics), and • environmental toxins. Ask, "Which of these three causes is most likely to be responsible for a health problem that can spread throughout the post?"	Page 58 Step 6
Display Master 2.1 . <ul style="list-style-type: none"> • Ask a volunteer to summarize the reasons that soldiers came to the infirmary. • Record and display these reasons. • Ask, "Do any patterns or cases worry you?" 	Page 58 Steps 7 and 8 
Mention that one or more types of infectious disease may be present on the post. Ask, "How can we tell whether or not a soldier has a bacterial infection?"	Page 58 Step 9
Explain that people can order tests for bacterial infections. <ul style="list-style-type: none"> • Test 1 looks for infections by bacterial species associated with pinkeye, sore throats, and infected cuts and abrasions. • Test 2 looks for infections associated with skin rashes caused by Rocky Mountain spotted fever or Lyme disease bacteria and for exposure to poison ivy. 	Page 59 Step 10
Instruct pairs to decide and then record on Master 2.1 which lab tests (if any) to order for which soldiers and why.	Page 60 Step 11-p
Give each pair a copy of Master 2.3 . Ask students to summarize in their notebooks the cases that could spread throughout the post and to describe how they were treated.	Page 61 Steps 12-p and 13-p 

Activity 2: Is a Rare Disease Present? Estimated time: 40 minutes	Page and Step
Explain that one week has gone by, and you are ready to discuss patient outcomes from Week 1 and to present a list of new infirmary visits. Give each student pair a copy of Master 2.4 , and ask students to look it over.	Page 62 Steps 1-p and 2-p 
Ask, "Did you learn anything that causes you to be concerned?"	Page 63 Step 3-p
Give each pair a copy of Master 2.5 , and ask students to look it over. Instruct pairs to summarize in their notebooks the reasons soldiers came to the infirmary.	Page 63 Step 4-p 
Ask volunteers to report what they wrote in their notebooks, display their responses, and discuss.	Page 63 Step 5
Ask, "Is there any evidence of a bacterial infection spreading throughout the post?"	Page 63 Step 6
Explain that you are concerned about the serious foot infection. <ul style="list-style-type: none"> • Observe that bacterial species A seems to cause both sore throats and the foot infection. • Ask, "Can the same bacterial species be responsible for causing two different diseases?" 	Page 64 Step 7
Explain that the foot infection could be caused by flesh-eating disease. Instruct students to look up the disease in the Medical Reference Manual.	Page 64 Step 8
Give each pairs a copy of Masters 2.6 and 2.7 . Instruct students to use Master 2.6 to answer the questions on Master 2.7.	Page 64 Step 9-p 
Ask volunteers to report their answers to the questions on Master 2.7 .	Page 65 Step 10

Activity 3: How Rare Is Rare? Estimated time: 30 minutes	Page and Step
Observe that bacterial species A is common and causes strep throat. It can also cause the rare flesh-eating disease. Explain that the odds of getting flesh-eating disease are 1 in 100,000.	Page 66 Step 1
Arrange the class in groups of four. Give each group <ul style="list-style-type: none"> • 1 small container with 9 baby lima beans and 1 baby lima bean colored red and • 1 large container with 99 baby lima beans and 1 baby lima bean colored red. 	Page 66 Step 2
Display this statement: "The odds of coming down with flesh-eating disease this year are 1 in 100,000."	Page 66 Step 3
Explain that the red bean represents a person who <i>may</i> come down with flesh-eating disease. <ul style="list-style-type: none"> • Have one student from each group pick a bean from the small container without looking. • Ask, "Did anyone get a red bean?" 	Page 66 Step 4
Display this: "1/10." Explain that the odds of picking a red bean were 1 in 10.	Page 66 Step 5
Have another student from each group pick a bean from the large container. Ask, "Did anyone get a red bean?"	Page 66 Step 6
Display this next to 1/10: " $\times 1/100$." Explain that the odds of picking a red bean were 1 in 100.	Page 66 Step 7
Tell students to place the selected beans back into the large container and mix. Have another student once again pick a bean from the large container. Ask, "Did anyone get a red bean?"	Page 67 Steps 8 and 9
Display next to $1/100$, " $\times 1/100$." Explain that, as before, the odds of picking a red bean were 1 in 100.	Page 67 Step 10
Explain that this activity modeled the 1 in 100,000 probability of coming down with flesh-eating disease. <ul style="list-style-type: none"> • Display the answer to the probability calculation: "$1/10 \times 1/100 \times 1/100 = 1/100,000$." • Explain that to get flesh-eating disease, a group would have had to pick the red bean from the small container and pick it again both times from the large container. 	Page 67 Steps 11 and 12
Conclude the lesson by asking, <ul style="list-style-type: none"> • "What are two reasons why flesh-eating disease is so rare?" • "Which two general causes of disease interacted to allow flesh-eating disease to develop?" 	Page 67 Step 13

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Lesson 3

The Difficulty of Diagnosis



Explain

At a Glance

Overview

Some people who have a rare disease struggle to obtain a proper diagnosis. In Lesson 3, students become involved with a case study of a boy with the rare genetic disease Marfan syndrome. Because Marfan syndrome shares symptoms with other, more-common diseases, it can take a long time for patients to receive the correct diagnosis. Students observe how problems with a single gene can affect many different body systems. The lesson concludes with students considering comments made by young people with Marfan syndrome.

Major Concepts

- Because some rare diseases have symptoms similar to more-common diseases, obtaining a correct diagnosis can be difficult.
- A rare disease may have a genetic cause.
- A rare disease, like some common diseases, may affect many different body systems at the same time.
- People with rare diseases may sometimes be viewed as being “different” by their peers and other members of society.

Objectives

After completing this lesson, students will have

- observed how problems in a single gene can affect many different body systems,

- encountered the difficulty often associated with diagnosing a rare disease, and
- recognized that people affected by Marfan syndrome face challenges in their lives, and despite these challenges, they have the same hopes and dreams as others and perhaps a unique view about the value of health.

Teacher Background

Consult the following sections in Information about Rare Diseases and Scientific Inquiry:

2.0 The Impact of Genomics on Rare Diseases (pages 24–26)

5.2 Marfan Syndrome (pages 29–31)

In Advance

Web-Based Activities

Activity	Web Component?
1	Yes
2	No
3	Yes

Photocopies, Transparencies, Equipment, and Materials

Photocopies and Transparencies
<p>Activity 1: A Parent’s Dilemma For Classes Using the Web-Based Version: 1 transparency of Master 3.1 1 copy of Master 3.2 for each student</p> <p>For Classes Using the Print-Based Version: 1 transparency of Master 3.1 1 copy of Master 3.2 for each student 1 copy of Masters 3.3, 3.4, 3.5, and 3.6 for each group of 4 students (each group member gets a different master)</p>
<p>Activity 2: Connective Tissue 1 transparency of Master 3.7</p>
<p>Activity 3: A Common Thread For Classes Using the Web-Based Version: 1 copy of Master 3.8 for each pair of students</p>

For Classes Using the Print-Based Version:

1 copy of Masters 3.8, 3.9, and 3.10 **for each pair of students**

1 transparency of Master 3.11

Equipment and Materials

For Activities 1 and 3, the Web-based versions, you'll need computers with Internet access.

For Activity 2, you'll need, **per student pair:**

- 1 new (never-before-stretched) rubber band from a dish labeled "A"
- 1 previously stretched rubber band from a dish labeled "B"
- 1 paper clip
- 1 soda can containing about 2 ounces of water*
- 1 meter stick

*Any weight of 2–3 ounces (55–85 grams) that can be easily attached to the paper clip will work.

Preparation

Activity 1

For classes using the Web version, verify that the computer lab is reserved for your class or that classroom computers are set up for the activities. Refer to Using the Web Site for details about hardware and software requirements for the Web site. Check that the Internet connection is working properly.



Log on to the Web Portion of Student Activities section of the Web site:

<http://science.education.nih.gov/supplements/rarediseases/student>

Select "Lesson 3: The Difficulty of Diagnosis."

Activity 2

Each pair of students will need a meter stick, a rubber band that has been repeatedly stretched (about 25 times), and a rubber band that hasn't been stretched. Use the same color rubber band for both stretched and nonstretched rubber bands so they look identical. Place the nonstretched rubber bands into a dish labeled "A" and the stretched rubber bands into a dish labeled "B."

Activity 3

For classes using the Web version, verify that the computer lab is reserved for your class or that classroom computers are set up for the activities. Set the computers to the opening screen for Activity 3, as you did for Activity 1.



Procedure

Note: This is an Explain lesson. It is designed to build on students' common experience learning about the causes of rare diseases. Students assume the roles of staff working for a medical geneticist. The scenario gives students a chance to apply their understandings about disease and scientific inquiry to explain the underlying cause of diverse symptoms displayed by a patient. In this lesson, students will use what they learned in the first two lessons about diagnosing disease. At this point, students should be able to construct more strongly supported explanations. They should focus on scientific principles as opposed to simply expressing their ideas and offering preliminary explanations.

We chose Marfan syndrome for this lesson because it is a rare disease caused by mutations in a single gene. It affects different body systems and can be difficult to diagnose. Patrick, the fictional patient, is a teenager who wants to play sports but has medical problems that cause his parents to worry about his participation. This realistic scenario is designed to be engaging to middle school students.

The mutations associated Marfan syndrome affect connective tissue. Realizing that students have little knowledge about connective tissue and its functions, we designed Activity 2 to give students a simple model that illustrates how the connective tissue of people with Marfan syndrome differs from that of healthy people.

Activity 1: A Parent's Dilemma

Estimated time: 25 minutes

- 1. Begin the lesson by explaining that you will investigate a case study of a child who has a rare disease. In addition to the difficulty of obtaining a correct diagnosis, students will see how patients and their families cope with this particular rare disease.**
- 2. Display Master 3.1, *To Play or Not to Play?* Ask for different volunteers to read each paragraph aloud to the class.**
- 3. Ask students to place themselves in the position of Patrick's parents and then ask, "Would you allow Patrick to try out for the basketball team?"**

Students' responses will vary. Many students will conclude that Patrick should be allowed to play basketball since none of the doctors said that he shouldn't play. Some students may know of a friend or family member with one of the conditions described and base their opinion on that example. At this time, don't express an

opinion yourself about whether Patrick should be allowed to play basketball.



Tip from the field test: Consider taking a poll of the students in the class. Ask how many would allow Patrick to play basketball. Later, at the end of the lesson, poll students again and discuss why their opinions have changed or stayed the same.

- 4. Comment that this discussion about playing basketball and health prompted Patrick's parents to look into the family's medical history. Especially on his father's side of the family, some relatives have had medical problems similar to Patrick's. Several have had serious heart problems. The parents are worried that an inherited disease might run in the family.**

If necessary for your students, relate the idea of inherited disease to genes and mutations. You may need to explain that some diseases that run in families are caused by mutations to a single gene and that by looking at a family tree, doctors can sometimes see evidence for a genetic cause for the disease. This connection will be important later in the lesson.

- 5. Explain that Patrick and his parents next visited a medical geneticist, a doctor who specializes in diagnosing people with genetic diseases. A medical geneticist works with other doctors when it appears that a patient's disease may have a genetic cause.**

Again, if necessary, you may want to explain that many (though not all) genetic diseases are rare. This means that a family doctor may never have seen a patient with the rare disease and not think of it when making a diagnosis.

- 6. Explain that for the rest of Activity 1, students will work in groups of four. They will assume the roles of medical specialists assisting the medical geneticist in diagnosing Patrick. Because Patrick has medical problems that affect different body systems, each member of the group will be responsible for a different body system. The four specialties (and their body systems) are**
 - orthopedist (skeletal system),
 - ophthalmologist (visual system),
 - cardiologist (heart and circulation system), and
 - pulmonologist (respiratory system).



Content Standard C:

Every organism requires a set of instructions for specifying its traits. Heredity is the passage of these instructions from one generation to another.



Content Standard C:

The human organism has systems for digestion, respiration, reproduction, circulation, excretion, movement, control, and coordination, and for protection from disease. These systems interact with each other.

Note: During Lesson 5, students will create an informational poster about either Marfan syndrome or childhood leukemia. With this in mind, you might want to stress the need to take good notes during Lessons 3 and 4.

(For print version, skip to Step 7-p on page 81.)



In classrooms using the Web version of the activity:

7-w. Give each student one copy of Master 3.2, *Medical Specialty Report Form*. Direct students to their computer stations.

Web browsers should be at

<http://science.education.nih.gov/supplements/rarediseases/student>

This is a menu page that contains a link for this activity.

8-w. Instruct students to click on “Lesson 3: The Difficulty of Diagnosis,” and then “Activity 1: A Parent’s Dilemma.” Then they should click on one of the medical specialties (“Activity 1: Orthopedist,” “Activity 1: Ophthalmologist,” “Activity 1: Cardiologist,” or “Activity 1: Pulmonologist”).

Each group member must obtain information about Patrick that corresponds to the medical specialty the group is assigned. Each medical specialty contains a report from Patrick’s doctor. To help them make sense of this report, each medical specialty includes a link to a Medical Reference Manual: Disorders of Connective Tissue, which provides helpful background information. If you have enough computers for each student, then the process will move quickly.

9-w. Explain that information about Patrick’s medical history and physical exam is provided for each medical specialty. Instruct students to

- review their assigned medical specialty;
- record on Master 3.2 what they learn about Patrick’s medical history;
- record on Master 3.2 what they learn from Patrick’s physical exam; and
- use the Medical Reference Manual to learn about possible causes of Patrick’s medical problem, and then record them on Master 3.2.

Continue with Step 10 on page 81.

In classrooms using the print version of the activity:



7-p. Give each student one copy of Master 3.2, *Medical Specialty Report Form*.

8-p. Give each group one complete set (four masters total) of these masters about Patrick’s physical and medical history:

- **Master 3.3, *Heart and Circulatory System***
- **Master 3.4, *Visual System***
- **Master 3.5, *Respiratory System***
- **Master 3.6, *Skeletal System***

Each group member receives a set of handouts corresponding to that person’s assigned medical specialty. The information in the Medical Reference Manual section of each handout should help students make some sense of this information.

9-p. Instruct students to

- **read the information on the handouts,**
- **record on Master 3.2, the patient form, what they learn about Patrick’s medical history,**
- **record on Master 3.2 what they learn from Patrick’s physical exam, and**
- **use the Medical Reference Manual section from each handout to learn about possible causes for Patrick’s medical problem and record them on Master 3.2.**

10. Give students about 20 minutes to complete the task. Then, re-form the groups and instruct students in each group to

- **share their findings with each other and**
- **discuss whether they believe that Patrick’s various medical problems are connected and what evidence they have to support their conclusions.**

Students should be able to use specific information from the doctors’ reports and from the Medical Reference Manual to support their conclusions.

11. Ask for volunteers from each group to share their conclusions about whether Patrick’s various medical problems are connected.

Students should see a pattern: Patrick has problems with four different body systems. For each body system, the Medical Reference Manual mentions that the problem may be associated with connective tissue or, more specifically, with Marfan syndrome or Ehler-Danlos syndrome.

12. Congratulate the groups on their good work and agree that there might be a common cause for Patrick’s medical problems that involves connective tissue.



Content Standard A:

Students should base their explanations on what they observed, and as they develop cognitive skills, they should be able to differentiate explanation from description—providing causes for effects and establishing relationships based on evidence and logical argument.



Content Standard A:

Different kinds of questions suggest different kinds of scientific investigations. Some investigations involve observing and describing objects, organisms, or events; some involve collecting specimens; some involve experiments; some involve seeking more information; some involve discovery of new objects and phenomena; and some involve making models.

Activity 2: *Connective Tissue*

Estimated time: 25 minutes

1. Ask, “What is connective tissue?”

Students will probably not be able to answer this question. Since the name is descriptive, some students may venture guesses that connective tissue somehow holds parts of the body together. Accept all answers and explain that you will investigate the role of connective tissue in this and the next activity.

2. Explain that connective tissue is largely made of proteins. Further explain that it forms tissues that help hold organs in place, and it connect muscles to bones and bones to bones.

Note: You may point out to students that our skin is largely made of connective tissue and that this allows the skin to be elastic—capable of stretching. Also mention that as we age, the elasticity of skin decreases. You can simply demonstrate this by asking students to pinch some of the skin on the back of their hands and notice how long it takes the skin to return to its normal position. Then, repeat the demonstration using your own hand. Because you are older, the skin on your hand will take longer to return to its normal position.

3. Explain that for this demonstration, rubber bands will represent connective tissue. Each student pair will compare the elasticity (or looseness) of two rubber bands.

4. Display Master 3.7, *Measuring Elasticity*. Read the instructions aloud and make sure that students understand how to perform the elasticity measurements.

- 5. Arrange the students in pairs. Give each pair**
- 1 meter stick
 - 1 rubber band from dish A (nonstretched)
 - 1 paper clip
 - 1 soda can containing about 2 ounces of water (or other 2–3-ounce weight)

- 6. Instruct pairs to record in their notebooks**
- the question they are investigating and
 - how far down the meter stick the rubber band stretched.

Pairs should write in their notebooks a question such as, “Is one rubber band more elastic than the other?” Give students about five minutes to complete the measurements.

7. Collect the rubber bands from each pair and set them aside. Next, give each pair one rubber band from dish B (previously

stretched). Instruct students to make and record measurements as before.

8. After students have made and recorded their measurements, ask for volunteers to state their conclusions. Specifically, ask if the two rubber bands performed the same or differently—and if differently, how so.

Students should report that rubber band B (the previously stretched one) stretched further than rubber band A (the nonstretched one).

9. Explain that the rubber band from dish A (the nonstretched one) represents normal connective tissue. Ask, “What do think the rubber band from dish B represents?”

Students may have trouble answering this question. If so, guide the discussion to Patrick and the possible association of his symptoms to connective tissue. Before moving on, make sure students understand that rubber band B represents the connective tissue in a person whose cells contain DNA that has a mutation that causes the connective tissue to be looser than it should be.

10. Ask, “How might looser connective tissue affect the body? Think about Patrick and his medical problems.”

Mentioning Patrick may cause students to bring up mitral valve prolapse or a dislocated eye lens. If not described by a student, ask guiding questions to bring out the role of connective tissue. For example, the looser connective tissue causes the heart valve flaps to change shape and not make a tight seal, or the looser connective tissue can't hold the eye lens tightly in place.

11. Explain that in the final activity of the lesson, students will return to Patrick and his family and investigate whether he may have a rare disease affecting his connective tissue.

Activity 3: A Common Thread

Estimated time: 25 minutes

1. Remind students that in the previous analysis they found that Patrick's medical symptoms involve more than one body system and that these symptoms seem to be related to connective tissue. Explain that they will now investigate some disorders that affect connective tissue and try to decide whether one rare disorder is more likely than the others to be responsible for Patrick's medical condition.

In classrooms using the Web version of the activity:



2-w. Arrange the class into pairs. Give each pair one copy of Master 3.8, *Diagnosing a Connective Tissue Disorder*.

3-w. Direct the student pairs back to their computers. Instruct them to click on “Lesson 3: The Difficulty of Diagnosis,” then “Activity 3: A Common Thread,” and then “Activity 3: Medical Reference Manual.”

Students should follow the instructions on Master 3.8 to compare Patrick’s medical symptoms to those expected for four different disorders of connective tissue. Give students about 10 minutes to complete the tasks.

In classrooms using the print version of the activity:



2-p. Arrange the class into pairs. Give each pair one copy of Master 3.8, *Diagnosing a Connective Tissue Disorder*, and one copy of Master 3.9, *Medical Reference Manual: Disorders of the Connective Tissue*.

3-p. Instruct student pairs to follow the instructions on Master 3.8 to compare Patrick’s medical symptoms with those expected for four different disorders of connective tissue. Allow about 10 minutes for students to complete the tasks.

4. After students have finished, ask for volunteers to report their conclusions.

Students should report that, although some of Patrick’s symptoms fit more than one disorder, virtually all of his symptoms are consistent with Marfan syndrome.

Patrick’s medical history	Ehlers-Danlos syndrome	Marfan syndrome	Osteogenesis imperfecta	Scleroderma
Myopia		Yes		
Detached eye lens		Yes		
Asthma		Yes		
Collapsed lung		Yes		
Heart murmur		Yes		
Leaky heart valve	Yes	Yes		
Long arms and legs		Yes		
Curvature of spine		Yes	Yes	

5. **Agree that Marfan syndrome is the best explanation for Patrick's symptoms. Ask,**
- **“What is the cause of Marfan syndrome?”**
 - **“What evidence is there to suggest that Patrick may have Marfan syndrome?”**

Students should recall that Marfan syndrome runs in families and results from mutations in a gene that codes for a connective tissue protein.

Students should report that Patrick has many of the Marfan symptoms listed in the Medical Reference Manual.

In classrooms using the Web version of the activity:



- 6-w. **Explain that to complete Patrick's diagnosis, you want to see whether there is evidence of Marfan syndrome in Patrick's family. Direct the student pairs back to their computers and instruct them to click on “Lesson 3: The Difficulty of Diagnosis,” then “Activity 3: A Common Thread,” and then “Patrick's Family Tree.” Students should look at the information about Patrick's family and record in their notebooks any evidence they find that suggests a history of Marfan syndrome in the family.**

Students can roll over or tab through photos of each family member and read a brief description of the person's medical history. They will see a diagram of a family tree that shows only the father's side of the family. If students ask about the mother's side, explain that it is free of medical symptoms associated with connective tissue disorders and, therefore, not of interest.

Students also may notice that that Patrick has six uncles but no aunts. They may conclude that Marfan syndrome is sex-linked. This is a real family tree, and it's just by chance that the family tree has so many males.

In classrooms using the print version of the activity:



- 6-p. **Explain that to complete Patrick's diagnosis, you want to see if there is evidence of Marfan syndrome in Patrick's family. Give each student pair one copy of Master 3.10, *Patrick's Family Tree*. Instruct students to look at the information about Patrick's family and record in their notebooks any evidence they find that suggests a history of Marfan syndrome in the family.**

They will see a diagram of a family tree that shows only the father's side of the family. If students ask about the mother's side, explain that it is free of medical symptoms associated with connective tissue disorders and therefore not of interest.

Students also may notice that Patrick has six uncles but no aunts. They may conclude that Marfan syndrome is sex-linked. This is a real family tree, and it is just by chance that the family tree has so many males.

7. **After students have finished, remind them of the three major causes of disease: infectious agents, heredity (genetics), and exposure to environmental toxins. Ask,**
- **“Did you find any evidence of Marfan syndrome in Patrick’s family?”**
 - **“Is there evidence to suggest that Patrick’s symptoms may have a different cause?”**



The process of diagnosing Patrick with Marfan syndrome requires students to apply understandings about scientific inquiry. You can assess these understandings by noting how well students sift through various forms of evidence to find what is relevant to answering the question. Also note how well students evaluate alternative explanations for Patrick’s symptoms.

Give students 5–10 minutes to complete the task. Students should report that Patrick’s father, two uncles, and grandfather have had heart problems. Heart problems have many causes other than Marfan syndrome; however, students should also note that other Marfan-related symptoms are mentioned such as scoliosis, a detached eye lens, and a collapsed lung.

Some students may believe that Patrick’s symptoms come from another cause. As in Lesson 2, they may mention that people living in close quarters can pass on infections or may be exposed to the same environmental toxins. Acknowledge the truth of these observations, but point out that the members of Patrick’s extended family did not live together.

8. **Explain that today, an early diagnosis of Marfan syndrome allows people to take steps to protect their health and live long lives. Ask, “In what ways might having Marfan syndrome affect your life?”**

Students’ responses will vary. If necessary, remind students of the symptoms of Marfan syndrome and ask how these symptoms would affect their daily lives.

In classrooms using the Web version of the activity:



- 9-w. **Conclude the lesson by explaining that students will now watch a brief video of young people who have Marfan syndrome discussing their experiences. Instruct students to first write in their notebooks some questions they would like to ask a person with Marfan syndrome about what it is like to live with the condition.**

10-w. Direct students to their computers and instruct them to click on “Lesson 3: The Difficulty of Diagnosis,” then “Activity 3: A Common Thread,” and then “Activity 3: Patient Video.”

The video is brief, just 3.5 minutes long. If you have the ability to project the computer image, it may be simpler to watch the video as a class.

11-w. After students have watched the video, reconvene the class. Ask for volunteers to describe their reactions to the video and how it addressed (or did not address) the questions they wrote in their notebooks.

The video will not answer all of the questions asked by the students. Suggest that they perform a Web search to access information from foundations and patient support groups that can answer their questions.

Note: Students could also explore the Marfan syndrome section of the Positive Exposure site (www.positiveexposure.org/marfan.html). Fashion photographer, Rick Guidotti and Diane McLean, MD, PhD, MPH wanted to share the beauty of rare disease patients, so, in 1997, they founded Positive Exposure, starting with photos of some people with albinism. The site now features people with almost 30 diseases.



Tip from the field test: If you took a poll of the students in the class at the beginning of the lesson, take another now. Discuss why their opinions have changed or stayed the same.

End of Web-based activity.

In classrooms using the print version of the activity:



9-p. Conclude the lesson by explaining that students will now consider how Marfan syndrome affects the lives of those who have it. Ask students to take a moment to reflect on what they have learned about Marfan syndrome. Instruct them to write down in their notebooks

- **one question they would ask a doctor about having Marfan syndrome and**
- **one way they think having Marfan syndrome might affect their lives.**

10-p. After students have completed the tasks, ask for volunteers to report what they wrote in their notebooks.

Consider displaying a couple of questions and comments that students wrote in their notebooks.



Tip from the field test: If you took a poll of the students in the class at the beginning of the lesson, take another now. Discuss why their opinions have changed or stayed the same.

11-p. Display Master 3.11, *Living with Marfan Syndrome*. Explain that this master includes some comments from teenagers who have Marfan syndrome. Give students a couple of minutes to read the master.

Reveal the questions and comments on Master 3.11 one at a time, as you talk about them.

12-p. Instruct students to reflect on the questions and comments from the young people who have Marfan syndrome. Ask,

- “Were their questions and comments similar to or different from yours?”
- “How would you want to be treated by your classmates if you had Marfan syndrome?”

Answer key for questions on Master 3.11, *Living with Marfan Syndrome*

1. “Is there any possible way for the Marfan gene to be detected before a child is born and maybe find a way to prevent it from mutating itself?”

At present, prenatal testing is not available for Marfan syndrome. The mutated gene associated with Marfan syndrome is found in every cell of the body. Today’s technology cannot replace the mutated gene with a nonmutated gene.

2. “When they measured my heart with the echocardiogram, they told my mom they don’t think I should do marching band. I was wondering, if I don’t exert myself too much, if I take it at my own pace, do you think I will still be able to do it?”

The student asking the question was advised that she might be able to continue with marching band if after a practice or a performance, she didn’t feel exhausted and wasn’t short of breath and sweating.

Lesson 3 Organizer: Web Version



Activity 1: A Parent's Dilemma Estimated time: 25 minutes	Page and Step
Explain that you will explore a case study about a child who has a rare disease. Display Master 3.1 . Ask volunteers to read paragraphs aloud to the class.	Page 78 Steps 1 and 2 
Ask, "Would you allow Patrick to try out for the basketball team?"	Page 78 Step 3
Explain that Patrick's parents looked into their family history and found relatives on his father's side who have had medical problems similar to Patrick's.	Page 79 Step 4
Explain that the family visited a medical geneticist to see if Patrick's problems have a genetic cause.	Page 79 Step 5
Explain that students will assume the roles of medical specialists and work in groups of four. Each group member will be responsible for one of the following body systems: <ul style="list-style-type: none"> • orthopedist (skeletal system) • ophthalmologist (vision system) • cardiologist (heart and circulatory system) • pulmonologist (respiratory system) 	Page 79 Step 6
Direct the students to their computer stations in their groups. Give each student one copy of Master 3.2 .	Page 80 Step 7-w 
Instruct students to click on "Activity 1: A Parent's Dilemma" and then on one of the medical specialties.	Page 80 Step 8-w 
Instruct students to review their medical specialty and record on their handouts what they learn <ul style="list-style-type: none"> • about Patrick's medical history, • from Patrick's physical exam, and • about the possible causes of Patrick's medical problems, based on the information in the link to "Activity 3: Medical Reference Manual." 	Page 80 Step 9-w 
Instruct group members to share their findings and discuss whether Patrick's medical problems are connected to each other and the evidence to support their conclusion.	Page 81 Step 10
Ask volunteers from each group to share their conclusions about whether Patrick's medical problems are connected. Congratulate students on their good work and agree that there might be a common cause for Patrick's medical problems that involves connective tissue.	Page 81 Steps 11 and 12

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Activity 2: <i>Connective Tissue</i> Estimated time: 25 minutes	Page and Step
Ask, "What is connective tissue?" Explain that it's mostly made of proteins and forms tissues that help hold organs in place and that connect muscles to bones and bones to bones.	Page 82 Steps 1 and 2
Explain that students will use rubber bands to represent connective tissue and will compare the elasticity of two rubber bands.	Page 82 Step 3
Display Master 3.7 , read the instructions aloud, and make sure students understand how make the measurements.	Page 82 Step 4 
Arrange students in pairs. Give each pair <ul style="list-style-type: none"> • 1 meter stick • 1 rubber band from dish A (nonstretched) • 1 paper clip • 1 soda can containing about 2 ounces of water (or other 2–3-ounce weight) 	Page 82 Step 5
Instruct pairs to record in their notebooks <ul style="list-style-type: none"> • the question they are investigating and • how far down the meter stick the rubber band stretched. 	Page 82 Step 6
Collect the rubber bands. Give each pair a rubber band from dish B (previously stretched), and instruct pairs to make and record measurements as before.	Page 82 Step 7
Ask volunteers to report their conclusions. Did the two rubber bands perform differently and if so, how?	Page 83 Step 8
Explain that the rubber band from dish A (nonstretched) represents normal connective tissue. Ask, <ul style="list-style-type: none"> • "What do you think the rubber band from dish B represents?" • "How might looser connective tissue affect the body?" 	Page 83 Steps 9 and 10
Explain that now they will investigate whether Patrick has a rare disease affecting his connective tissue.	Page 83 Step 11

Activity 3: A Common Thread Estimated time: 50 minutes	Page and Step
Remind students that Patrick’s symptoms involve more than one body system and seem to have connective tissue in common. They will decide which, if any, rare disorder of connective tissue Patrick may have.	Page 83 Step 1
Arrange the class in pairs. Give each pair a copy of Master 3.8 .	Page 84 Step 2-w 
Direct the pairs to their computers to click on “Activity 3: A Common Thread” and then “Activity 3: Medical Reference Manual.”	Page 84 Step 3-w 
Ask volunteers to report their conclusions.	Page 84 Step 4
Agree that Marfan syndrome best explains for Patrick’s symptoms. Ask, <ul style="list-style-type: none"> • “What is the cause of Marfan syndrome?” • “What evidence is there to suggest that Patrick may have Marfan syndrome?” 	Page 85 Step 5
Explain that students will look for evidence of Marfan syndrome in Patrick’s family and record what they find in their notebooks. They should click on “Activity 3: A Common Thread” and then “Activity 3: Patrick’s Family Tree.”	Page 85 Step 6-w 
Remind students of the three major causes of disease. Ask, <ul style="list-style-type: none"> • “Did you find any evidence of Marfan syndrome in Patrick’s family?” • “Is there evidence to suggest that Patrick’s symptoms may have a different cause?” 	Page 86 Step 7
Explain that an early diagnosis of Marfan syndrome allows people to take steps to protect their health. Ask, “In what ways might having Marfan syndrome affect your life?”	Page 86 Step 8
Explain that the lesson concludes with a brief video about young people who have Marfan syndrome. Instruct students to first write in their notebooks questions they would like to ask a person with Marfan syndrome.	Page 86 Step 9-w 
Instruct pairs to watch the video: click on “Activity 3: A Common Thread” and then “Activity 3: Patient Video.”	Page 87 Step 10-w 
Ask volunteers to describe their reactions to the video and how the video related to their questions.	Page 87 Step 11-w 

 = Involves making a transparency.  = Involves using the Internet.

 = Involves copying a master.

Lesson 3 Organizer: Print Version



Activity 1: A Parent's Dilemma Estimated time: 25 minutes	Page and Step
Explain that you will explore a case study about a child who has a rare disease. <ul style="list-style-type: none"> • Display Master 3.1. • Ask volunteers to read paragraphs aloud to the class. 	Page 78 Steps 1 and 2 
Ask, "Would you allow Patrick to try out for the basketball team?"	Page 78 Step 3
Explain that Patrick's parents looked into their family history and found relatives on his father's side who have had medical problems similar to Patrick's.	Page 79 Step 4
Explain that the family visited a medical geneticist to see if Patrick's problems have a genetic cause.	Page 79 Step 5
Explain that students will assume the roles of medical specialists and work in groups of four. Each group member will be responsible for one of the following body systems: <ul style="list-style-type: none"> • orthopedist (skeletal system) • ophthalmologist (vision system) • cardiologist (heart and circulatory system) • pulmonologist (respiratory system) 	Page 79 Step 6
Give each student a copy of Master 3.2 .	Page 81 Step 7-p 
Give each group of four one complete set of masters of doctors' reports: Masters 3.3, 3.4, 3.5, and 3.6	Page 81 Step 8-p 
Instruct students to review their medical specialty and the information on the Medical Reference Manual section and record on Master 3.2 what they learn <ul style="list-style-type: none"> • about Patrick's medical history, • from Patrick's physical exam, and • about the possible causes of Patrick's medical problems, based on the information Master 3.9. 	Page 81 Step 9-p
Instruct group members to share their findings and discuss whether Patrick's medical problems are connected to each other and the evidence to support their conclusion.	Page 81 Step 10
Ask volunteers from each group to share their conclusions about whether Patrick's medical problems are connected. Congratulate students on their good work and agree that there might be a common cause for Patrick's medical problems that involves connective tissue.	Page 81 Steps 11 and 12

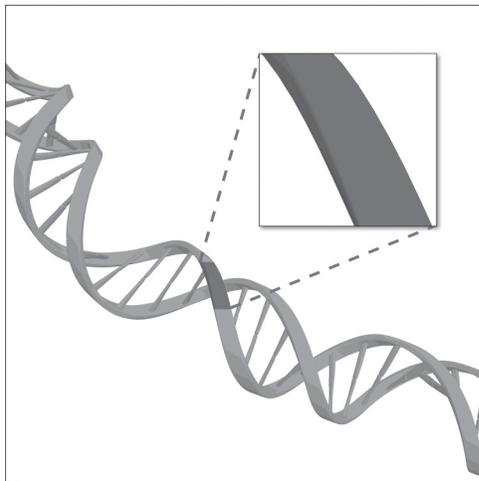
Activity 2: Connective Tissue Estimated time: 25 minutes	Page and Step
Ask, "What is connective tissue?" Explain that it's mostly made of proteins and forms tissues that help hold organs in place and that connect muscles to bones and bones to bones.	Page 82 Steps 1 and 2
Explain that students will use rubber bands to represent connective tissue and will compare the elasticity of two rubber bands.	Page 82 Step 3
Display Master 3.7 , read the instructions aloud, and make sure students understand how make the measurements.	Page 82 Step 4 
Arrange students in pairs. Give each pair <ul style="list-style-type: none"> • 1 meter stick • 1 rubber band from dish A (nonstretched) • 1 paper clip • 1 soda can containing about 2 ounces of water (or other 2–3-ounce weight) 	Page 82 Step 5
Instruct pairs to record in their notebooks <ul style="list-style-type: none"> • the question they are investigating and • how far down the meter stick the rubber band stretched. 	Page 82 Step 6
Collect the rubber bands. Give each pair a rubber band from dish B (previously stretched), and instruct pairs to make and record measurements as before.	Page 82 Step 7
Ask volunteers to report their conclusions. Did the two rubber bands perform differently and if so, how?	Page 83 Step 8
Explain that the rubber band from dish A (nonstretched) represents normal connective tissue. Ask, <ul style="list-style-type: none"> • "What do you think the rubber band from dish B represents?" • "How might looser connective tissue affect the body?" 	Page 83 Steps 9 and 10
Explain that now they will investigate whether Patrick has a rare disease affecting his connective tissue.	Page 83 Step 11

Activity 3: A Common Thread Estimated time: 50 minutes	Page and Step
Remind students that Patrick’s symptoms involve more than one body system and seem to have connective tissue in common. They will decide which, if any, rare disorder of connective tissue Patrick may have.	Page 83 Step 1
Arrange the class in pairs. Give each pair a copy of Master 3.8 and Master 3.9 . Instruct students to use information on Master 3.9 to complete Master 3.8.	Page 84 Steps 2-p and 3-p 
Ask volunteers to report their conclusions.	Page 84 Step 4
Agree that Marfan syndrome best explains for Patrick’s symptoms. Ask, <ul style="list-style-type: none"> • “What is the cause of Marfan syndrome?” • “What evidence is there to suggest that Patrick may have Marfan syndrome?” 	Page 85 Step 5
Explain that students will look on a handout for evidence of Marfan syndrome in Patrick’s family and record in their notebooks what they find. Give each student pair a copy of Master 3.10 .	Page 85 Step 6-p 
Remind students of the three major causes of disease. Ask, <ul style="list-style-type: none"> • “Did you find any evidence of Marfan syndrome in Patrick’s family?” • “Is there evidence to suggest that Patrick’s symptoms may have a different cause?” 	Page 86 Step 7
Explain that an early diagnosis of Marfan syndrome allows people to take steps to protect their health. Ask, “In what ways might having Marfan syndrome affect your life?”	Page 86 Step 8
Conclude by explaining that students will now consider how Marfan syndrome affects the lives of people who have it. Ask students to write in their notebooks <ul style="list-style-type: none"> • one question they would like to ask a doctor about Marfan syndrome and • one way they think having Marfan syndrome might affect their lives. 	Page 87 Step 9-p
Ask volunteers to report what they wrote.	Page 87 Step 10-p
Display Master 3.11 , and give students time to read it. Ask, <ul style="list-style-type: none"> • “Were the questions and comments from the young people on the master similar to yours?” • “How would you want to be treated by your classmates if you had Marfan syndrome?” 	Page 88 Steps 11-p and 12-p 

 = Involves making a transparency.  = Involves copying a master.

Lesson 4

The Importance of Medical Research



Elaborate

At a Glance

Overview

Lesson 4 introduces the idea that medical research is important for the treatment of a rare disease, childhood leukemia. In the first activity, students meet Jason and Kim, parents of a daughter named Hanna, who has been diagnosed with childhood leukemia. Students perform a simulated Web search to learn about the disease. They must sift through different Web hits to find relevant and accurate information about the disease. In considering a genetic cause of the disease, students perform a karyotype analysis on each family member. In the second activity, students are introduced to treatments for leukemia. They design a clinical trial to guide the treatment of the disease. Finally, students watch a brief video (or, for classes using the print version, act out an interview) of a leukemia survivor discussing what it's like to live with the disease.

Major Concepts

- Much medical information can be found on the Internet; however, this information must be examined carefully to assess its relevance and accuracy.
- Lack of appearance in a family history does not mean that a disease doesn't have a genetic cause.
- Leukemia is a cancer of the white blood cells.
- Clinical trials have greatly improved the survival rates of children with leukemia.

Objectives

After completing this lesson, students will

- have used a simulated Web search to learn about the cause, symptoms, and diagnosis of childhood leukemia;
- have performed a karyotype analysis to diagnose leukemia;
- have designed and tested a clinical trial for treating childhood leukemia; and
- have considered the challenges associated with living with leukemia.

Teacher Background

Consult the following sections in Information about Rare Diseases and Scientific Inquiry:

2.0 The Impact of Genomics on Rare Diseases (pages 24–27)

3.0 Rare Infectious Diseases (page 26)

4.0 Rare Diseases Caused by Environmental Toxins (pages 27–28)

5.3 Childhood Leukemia (pages 31–33)

In Advance

Web-Based Activities

Activity	Web Component?
1	Yes
2	Yes

Photocopies, Transparencies, Equipment, and Materials

Photocopies and Transparencies
Activity 1: An Unwelcome Diagnosis For Classes Using the Web-Based Activity: 1 transparency of Master 4.1 1 copy of Masters 4.2 and 4.5 for each student 1 transparency and 1 copy for each student of Master 4.3 1 copy of Master 4.4 for each pair of students For Classes Using the Print-Based Activity: 1 transparency of Master 4.1 1 copy of Masters 4.2, 4.5, 4.11, and 4.12 for each student 1 transparency and 1 copy for each student of Master 4.3 1 copy of Masters 4.4 and 4.10 for each pair of students

Continued

Photocopies and Transparencies

Activity 2: Clinical Trials

For Classes Using the Web-Based Activity

1 transparency of Master 4.6

1 copy of Masters 4.7, 4.8, and 4.9 **for each pair of students**

For Classes Using the Print-Based Activity:

1 transparency of Master 4.6

1 copy of Masters 4.7, 4.8, 4.9, 4.13, 4.14, 4.15, and 4.16 **for each pair of students**

2 copies of Master 4.17 **for the class**

Equipment and Materials

For Activities 1 and 2, Web-based versions, students will need computers with Internet access.

Preparation

Activities 1 and 2

For classes using the Web version, verify that the computer lab is reserved for your class or that classroom computers are set up for the activities.

Refer to Using the Web Site for details. Check that the Internet connection is working properly.

Log on to the Web Portion of Student Activities section at

<http://science.education.nih.gov/supplements/rarediseases/student>

Select “Lesson 4: The Importance of Medical Research.”

Procedure

Note: This is an Elaborate lesson. It gives students an opportunity to take what they have learned about rare diseases and scientific inquiry from the previous lessons and apply it in a new setting. In the first activity, students place themselves in the role of a parent whose child has just been diagnosed with childhood leukemia. They perform a simulated Web search to learn about the disease. This activity is designed to help students hone their skills in evaluating information for relevance and accuracy. The genetic link to the disease is made real to students by having them perform a simple karyotype analysis.

In the second activity, students exercise their understandings of scientific inquiry in the context of clinical trials. Designing a fair test is a common

inquiry skill. We selected childhood leukemia because it is a rare disease that has a genetic cause. It's a serious disease, but, at the same time, it represents a real success story in the application of medical research to treatment.

The activity includes a graph that shows how survival rates for children with leukemia have dramatically improved over the past few decades. The lesson concludes with a video (or a role-play) of a young woman who has come through treatment for the disease and is now pursuing a medical education. The inclusion of this story is designed to give students an opportunity to empathize with someone who has had leukemia and also to leave them with the vision of a positive outcome.

Activity 1: An Unwelcome Diagnosis

Estimated time: 100 minutes

- 1. Begin the lesson by explaining that students will investigate a case study involving a child with a rare disease.**

This case study introduces the use of clinical trials to obtain evidence about which treatment options are most effective. It's not important that students understand the clinical trials process. Instead, clinical trials provide a real-life example of how the practice of science (especially proper experimental design) can help improve people's health.

- 2. Display Master 4.1, *Doctor Visits*. Ask for volunteers to read aloud each section of text.**
- 3. Ask students how they would feel if they were Hanna's parent and received this disturbing news. Ask, "What would you do now that you have learned that your daughter has been diagnosed with leukemia?"**

Students' responses will vary. Some students may suggest getting a second opinion. Others may suggest researching cancer treatment centers. Accept all answers and guide the discussion to the need to obtain more information.

- 4. Explain that although the doctor described childhood leukemia and answered their questions during the office visit, Jason and Kim were so upset that they didn't take notes or remember much of what they were told. After returning home with Hanna, they performed an Internet search on leukemia.**



Content Standard C:

Disease is a breakdown in structures or functions of an organism. Some diseases are the result of intrinsic failures of the system. Others are the result of damage by infection by other organisms.

5. **Ask students,**
- “If you were Hanna’s parent, what information would you want to have about the disease?”
 - “Where could you find the information that you want?”

Make a list on the board of the types of information about leukemia the students request. Students may mention a variety of sources for this information, including their doctors, books, television programs, the Internet, and, possibly, friends and family who have had to cope with the disease.

6. **Give each student one copy each of Master 4.2, *Internet Search Results*, and Master 4.3, *Evaluating Internet Search Results*. Instruct students to view the list of hits on Master 4.2 and follow the instructions on Master 4.3 to rank the hits from most helpful to least helpful.**

This step is designed to challenge students to sort through information related to leukemia and decide

- which hits are most likely to contain the information they want and
- which hits are likely to contain information that is accurate and unbiased.

There is no single correct answer to ranking these eight hits. Rather, you should see whether students can sift through the lists to identify one or two of the best hits. Likewise, students should be able to identify another couple of hits as clearly not helpful to providing the information they want.

In this activity, students are ranking hits based on relevance and accuracy. There are, however, other criteria that students should use to assess the usefulness of Web sites. For example, the site should present information that is up to date, and the information should be as free of bias as possible, such as the bias associated with promoting a product or service.

Answer key for Web hits on Master 4.2, *Internet Search Results*

1. Federal Center for Cancer Research

Information about leukemia, its causes, symptoms, diagnosis, and treatment ...

Hit 1 is from a fictional U.S. government research organization, the Federal Center for Cancer Research. The Federal government, however, does support medical research, primarily through the

National Institutes of Health (NIH). For example, the Office of Rare Diseases Research (<http://rarediseases.info.nih.gov/>) and the National Cancer Institute (<http://www.cancer.gov/>) are parts of NIH and provide accurate medical information resources for the general public. Such government sites post information that has been reviewed by experts and is labeled “no commercial bias,” which means that the information presented hasn’t been selected to promote the use of any particular product or service. Such sites are a logical place to begin to learn about a rare disease.

2. My Leukemia Blog

Living with Cancer: Reflections and remembrances of a cancer survivor ...

Personal blogs can provide a window into the life of someone who has a rare disease. The person may or may not choose to include medical information as part of the blog. Furthermore, any medical information on the blog may reflect a possibly incomplete understanding by the author. Although such blogs can be helpful resources, they are not the best place to begin to learn about a rare disease.

3. The Cancer Research Center at Lincoln State University

Breast cancer, Prostate cancer, Leukemia, Lymphoma, ...

Research centers based at universities often provide medical information to the public. The information is reviewed by experts for accuracy. Often, the posted information is tied to the research interests of individual scientists and may be too specific to be a starting point for searching about a rare disease.

4. Information about Leukemia from the American Blood Cancer Society

Cells of the blood, Stem cells and leukemia, White blood cells and bacteria ...

Hit 4 is from a patient support group. Although the American Blood Cancer Foundation is fictional, a large number of patient-support organizations exist to promote medical research and support for people with rare diseases. In the case of leukemia, the Leukemia and Lymphoma Society (http://www.leukemia.org/hm_lls) is a very useful resource that provides reliable disease information as well as a variety of patient services. Such sites are a logical place to begin to learn about a rare disease.

5. **Leukemia—Medhealthopedia: The Do-It-Yourself Encyclopedia**

Leukemia is a form of cancer that is ...

Medhealthopedia is a fictional Web site that provides medical information to the public in a manner similar to Wikipedia. On such a site, the information posted is written collaboratively by users of the site. The information is often reliable, but there is no assurance that experts have reviewed it or that it is free of commercial bias.

6. **Cancer drugs for less! Leukemia**

Order drugs from overseas to treat leukemia and save!

Hit 6 is included as a reminder that some information about disease on the Internet is more concerned with making money for someone than with providing objective medical information.

7. **Fed approves new drug to treat leukemia**

Medical Business Weekly (Washington, DC)—The Food and Drug Administration today approved Hamilton Pharmaceutical's drug Arresta for the treatment of leukemia ...

Hit 7 is from a business publication. Although the information is likely to be accurate, it only describes one specific development in the field of leukemia research and is not a good place to begin to learn about the disease.

8. **Leukemia: Definition from Medical Jargon.com**

Leukemia—A form of cancer involving the white blood cells. White ...

Hit 8 comes from a medical dictionary and only provides a brief definition of the disease.

7. **Display Master 4.3. Ask for volunteers to report how they ranked the Web hits.**

Students' responses will vary. Allow several volunteers to report their rankings with explanations of their reasoning. Remember that the precise ranking of the Web sites is not important. Ideally, students will recognize that Hits 1 and 4 are the best places to begin to learn about leukemia. Hits 2, 3, and 5 can also be useful, but the information may not be as relevant or as accurate as that from Hits 1 and 4. Some students may reason that Hit 8, which provides a definition, is a good place to start. Hits 1 and 4, however, will also provide a definition along with a lot of other useful information. Hits 6 and 7 are clearly not very useful.



As students report how they ranked the hits from the simulated Web search, you have an opportunity to assess how well they use their critical-thinking skills to evaluate information for its relevance and accuracy.

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In classrooms using the Web version of the activity:



- 8-w. Arrange the students in pairs. Give each pair one copy of Master 4.4, *Summarizing Information about Leukemia*. Explain that student pairs will go to their computers and access information about leukemia from Hits 1 and 4 from the Internet search. Pairs should summarize on Master 4.4 the information from both Web hits.**

Computers should be at this URL:

<http://science.education.nih.gov/supplements/rarediseases/student>

This is a menu page that contains a link for this activity.

- 9-w. Direct the pairs to their computer stations and instruct them to click on “Lesson 4: The Importance of Medical Research,” then “Activity 1: An Unwelcome Diagnosis,” and then “Activity 1: Simulated Web Search.”**

“Activity 1: Simulated Web Search” contains information found on Hits 1 and 4, which were listed on Master 4.2. These are the hits judged to be the best places to begin a search for information about leukemia.

In classrooms using the print version of the activity:



- 8-p. Arrange the students into pairs. Give each pair one copy each of Master 4.4, *Summarizing Information about Leukemia*, and Master 4.10, *Information about Leukemia*.**

- 9-p. Explain that student pairs should look at the information on Master 4.10 and summarize it on Master 4.4.**

Master 4.10 contains information found on Hits 1 and 4, which were listed on Master 4.2. These are the hits judged to be the best places to begin a search for information about leukemia.

- 10. After students have completed the tasks, reconvene the class. Ask whether students have any questions about the information they found from the Internet search.**

Clarify any confusion and misunderstandings. If students ask about the case of leukemia, ask them to hold on because the class is about to consider that question.

11. Ask students to recall the three causes of disease.

If necessary, ask guiding questions to bring out the three causes: infectious agents, heredity (genetics), and exposure to environmental toxins.

12. Ask, “What types of information would you want to have to decide which of the three causes of disease applies to leukemia?”

Students may suggest information about a family history of leukemia and about exposure to toxic substances or pathogens.

13. Explain that the parents, Jason and Kim, have two children: Hanna, who was just diagnosed with leukemia, and her older brother, Rick, who is healthy. There is no history of leukemia in the family. Ask, “Does this rule out genetics as the cause of leukemia?”

Most students will conclude that it does. At this time, accept all answers.

14. Ask, “What about environmental exposure or infections?”

Some students may remark that Hanna shows signs of infection. Point out that the rest of the family is infection free. Also, if Hanna had been exposed to a dangerous substance in her environment, we might also expect that the rest of the family had also been exposed, but they remain healthy.

15. Acknowledge that so far, there isn’t good evidence to suggest a cause for Hanna’s leukemia. Return to the idea of genetics. Ask students to recall Information about Leukemia from the American Blood Cancer Society. Ask, “What happened to a stem cell that led to leukemia?”

Students should recall that a single stem cell acquired mutations and began to grow out of control, producing large numbers of unhealthy white blood cells.

Note: Since your students have a limited understanding of genetics, they may believe that mutations are something that only took place many years ago. You may need to stress the idea that mutations are happening now and can cause disease. Explain that cells have mechanisms that detect and correct mutations, but in rare cases, these mechanisms fail.

16. Explain that although people sometimes inherit mutations from their parents, new mutations happen as well. Mutations in DNA can occur from exposure to sunlight or to substances in the environment, or sometimes they occur just because the cell makes a DNA-copying mistake during cell division that is



Content Standard C: Hereditary information is contained in genes, located in the chromosomes of each cell. Each gene carries a single unit of information. An inherited trait of an individual can be determined by one or by many genes, and a single gene can influence more than one trait. A human cell contains many thousands of different genes.

not corrected. If mutations occur in genes associated with cell growth, cancer can result.

This is an opportunity to have students think back to Lesson 3, which dealt with Marfan syndrome and a genetic mutation. Both diseases have a genetic association. If you think it would be helpful ask, “How are they similar? How are they different?”

17. **Explain that in some genetic disorders, the effects of mutations can be so large that they change the number and appearance of the chromosomes. Scientists call a photograph of chromosomes under a microscope a karyotype. Give each student one copy of Master 4.5, *Karyotype*.**

You may need to help students understand the idea of a chromosome. You can explain that the DNA in each cell is arranged in packages called chromosomes. Each different chromosome contains a single molecule of DNA.

18. **Explain that students first need to see what a normal karyotype looks like before they can understand what a karyotype with a large mutation looks like. Instruct students to read the information on Master 4.5 and answer the question at the bottom.**

While students are reading the handout, circulate and answer any questions they may have. For example, you may need to explain that the karyotype is made by squashing cells and taking a picture of the chromosomes through a microscope. Then, the photograph is cut up, and the chromosomes are rearranged in pairs to make it easier to see abnormal patterns.

Students may observe differences in the shapes of chromosome pairs in the karyotypes, but these shapes result from how the chromosomes were positioned when the cells were squashed and do not represent genetic mutations. A normal karyotype has 22 pairs of numbered chromosomes as well as a pair of sex chromosomes (X and Y). A male has one X chromosome and one Y chromosome. A female has two X chromosomes and no Y chromosome. The individual whose karyotype is depicted here is male because both an X and a Y chromosome are present.

19. **Explain that in the case of leukemia, the karyotype would be expected to show three, instead of the normal two, copies of one or more of the numbered (nonsex) chromosomes.**

Students should pay attention to the numbers of each chromosome. The presence of three copies of a chromosome is abnormal and helps diagnose leukemia.

(For print version, skip to Step 20-p on page 106.)



In classrooms using the Web version of the activity:

20-w. Direct student pairs back to their computers.

Explain that they will first observe karyotypes prepared from blood samples taken from each of Hanna’s family members. Instruct students to predict whether the karyotype for each family member will appear normal or abnormal.

Students should make predictions for Jason and Kim (Hanna’s parents), Hanna, and Rick (Hanna’s brother). They should recall that Hanna is the only family member with leukemia and, therefore, only her karyotype should appear abnormal.

Note: To reinforce the role of the sex chromosomes, you may want to ask students to identify the sex of each family member from the person’s karyotype.

21-w. Instruct student pairs to click on “Lesson 4: The Importance of Medical Research,” then “Activity 1: An Unwelcome Diagnosis,” and then “Activity 1: Karyotypes.” Students will see a karyotype from the parents, Jason and Kim, as well as from Hanna and her brother, Rick. Students should record in their notebooks whether each karyotype is normal or abnormal and whether the evidence supports their predictions.

22-w. Explain that the link labeled “View All of Hanna’s Karyotypes” will display three karyotypes from Hanna. The first karyotype was taken from her blood sample as before, the second was from her cheek cells, and the third, from her hair follicles. As before, instruct student to predict whether each karyotype will be normal or abnormal.

Students should predict that the karyotype from Hanna’s blood sample will appear abnormal, as it was earlier. Some students may not realize that the abnormal chromosomes are limited to the white blood cells. They will see, however, that the karyotypes from Hanna’s cheek cells and hair follicles are normal.

23-w. Ask, “How can you account for the appearance of the karyotypes taken from these three different tissues?”

Guide the discussion to bring out that the leukemia started with a single stem cell in the bone marrow that went on to produce a large population of unhealthy white blood cells, each with an abnormal karyotype. In contrast, the cheek cells and hair follicle cells are unaffected by leukemia and show normal karyotypes.

End of Web-based activity.



Evaluating karyotypes taken from different body tissues allows you to assess how well students understand the basic idea of cancer, namely, that the disease begins with mutations in a single cell in one part of the body.

In classrooms using the print version of the activity:



20-p. Explain that students will look at karyotypes prepared from blood samples taken from each of Hanna’s family members. Ask students to predict whether the karyotype for each family member will appear normal or abnormal and to record in their notebooks whether the evidence supports their predictions.

Students should make predictions for Jason and Kim (Hanna’s parents), Hanna, and Rick (Hanna’s brother). They should recall that Hanna is the only family member with leukemia and, therefore, only her karyotype should appear abnormal.

Note: To reinforce the role of the sex chromosomes, you may want to ask students to identify the sex of each family from the person’s karyotype.

21-p. Give each student pair one copy of Master 4.11, *Family Karyotypes*. Instruct students to examine the karyotypes and note whether their predictions were confirmed.

If any pairs struggle with this task, remind them that each numbered chromosome should exist as a pair. If a third copy of any chromosome is present, it represents a mutation and helps diagnose leukemia.

22a-p. Explain that students will now look at three different karyotypes, all from Hanna. One karyotype is taken from her blood as before, one is from her cheek cells, and another, from her hair follicles. As before, instruct students to predict whether each karyotype will be normal or abnormal and to record their predictions in their notebooks.

Students should predict that the karyotype from Hanna’s blood sample will appear abnormal, as it was earlier. They likely will predict that the karyotypes from her cheek cells and hair follicles will also be abnormal.

22b-p. Give each student pair one copy of Master 4.12, *Hanna’s Karyotypes*. Instruct students to examine the karyotypes and note whether their predictions were confirmed.

Some students may not realize that the abnormal chromosomes are limited to the white blood cells.

23-p. Ask, “How can you account for the appearance of the karyotypes taken from these three different tissues?”

Guide the discussion to bring out that the leukemia started with a single stem cell in the bone marrow that went on to produce a large population of unhealthy white blood cells, each with an abnormal karyotype. In contrast, the cheek cells and hair follicle cells are unaffected by leukemia and show normal karyotypes.



Evaluating karyotypes taken from different body tissues allows you to assess how well students understand the basic idea of cancer, namely, that the disease begins with mutations in a single cell in one part of the body.

Activity 2: Clinical Trials

Estimated time: 50 minutes

1. **Display Master 4.6, *Another Doctor Visit*. Ask for volunteers to read aloud each section of text.**

Ethical concerns cause the design of clinical trials to sometimes differ from that of animal studies. If a treatment for a disease is known to have some benefit, then it is unethical to replace that treatment with another one whose value is unknown.

2. **Explain that doctors often compare the effectiveness of cancer treatments by looking at the percentage of patients who are still alive five years after treatment. This helps explain why a series of clinical trials takes so long to improve survival rates.**
3. **Explain that students will now go back in time to the year 1970 and play the roles of doctors trying to improve the survival rates of children with leukemia. Still working in their pairs, students will have the opportunity to design, carry out, and assess the effectiveness of a clinical trial.**

Over the past 50 years, steady progress has been made in improving the survival rates for children with leukemia. We chose the period around 1970 for this activity because one specific treatment (of the central nervous system, or CNS) led to a very significant gain in survival rate. Students will see the value of clinical trials when they examine survival rates over time on Master 4.9, *Survival Rates for Children with Leukemia*.

4. **Give each student pair one copy of Master 4.7, *Treating Leukemia*. This handout describes the treatment options students can include in the clinical trial:**
 - **Three different drugs (A, B, and C) are available. Each drug has been shown to improve the survival rates of patients taking its standard dose. Research also indicates that the best results are achieved when the three drugs are used in combination.**
 - **For each drug, three different doses are available:**
 - standard dose
 - increased dose
 - decreased dose

- **The CNS treatment follows the drug treatment described above. It involves irradiating the patient’s head with X-rays while drug C (methotrexate) is injected into the spinal fluid. This approach is intended to kill cancer cells that may have escaped the effects of the earlier drug treatment and are lurking in the CNS.**

(For print version, skip to Step 5-p on page 110.)



In classrooms using the Web version of the activity:

- 5-w. Explain that student pairs will use the computer to design and carry out a clinical trial. Before moving to the computers, make the students aware of the following:**
- **The standard therapy (control) for treating leukemia is a combination therapy using the standard doses of drugs A, B, and C.**
 - **Pairs select the characteristics (drug doses and use or nonuse of the CNS treatment) of the therapy they want to compare with the standard treatment.**
 - **After students select the treatment, they submit it, and the trial design is analyzed by the computer software. If the trial design is appropriate, then the trial is approved, and the pair can run the trial and learn the results. If a flaw is found in the trial design, then students have an opportunity to correct it and go on to run the trial.**

In designing the clinical trial, students may be tempted to use more of everything. Remind students that each treatment is associated with side effects that are sometimes very harmful.

Although proper trial design involves a number of aspects, we are focusing on just one—control of variables. Students should understand that a proper design involves changing just one variable while keeping other variables constant relative to the comparison (control) group of patients. Students must remember that their proposed treatment will be compared with the standard treatment (using drugs A, B, and C at their standard doses *without* the CNS treatment).

- Pairs that decide to use the CNS treatment must keep drugs A, B, and C at the standard doses.
- Pairs that decide not to use the CNS treatment can change the dose of *one* of the three drugs while keeping the other two drugs at the standard doses.

Note: After students submit a design that is approved, run the trial, and get the results, they can try other designs by simply changing their selections and resubmitting a new design.



Content Standard A: Students should develop general abilities, such as systematic observation, making accurate measurements, and identifying and controlling variables.

6-w. Give one copy of Master 4.8, *Designing a Clinical Trial*, to each student pair. Instruct students to use this handout to record the treatment options they select as well as the trial results (survival rate data) and conclusions they draw from the data.

7-w. Explain that in a clinical trial such as this, the experimental treatment is compared with the standard treatment. Ask, “Should the clinical trial also include a group that receives no treatment?”

Students’ responses may vary. Students who think just in terms of good experimental design may respond that including a no-treatment group would better indicate how well the experimental treatment performs. Others may point out that it would not be fair to withhold treatment from a group of patients. In fact, the latter view prevails. For ethical reasons, a no-treatment group would not be included in the design of such a clinical trial.

8-w. Direct the students back to their computers and instruct them to click on “Lesson 4: The Importance of Medical Research,” then “Activity 2: Clinical Trials.”

- **Students will see the treatment options and boxes where they can make their selections.**
- **After selecting the treatment options, students click the “Submit” button to have the trial design analyzed.**

If the design is judged to be appropriate, then a letter will appear that instructs the students to proceed with the clinical trial. A “Run treatment” button appears. When it is clicked, the trial results are shown on a graph of survival over time.

If the design is judged to not be appropriate, then a letter will appear that reminds the students to change just one variable at a time. A “Try again” button appears. When it is clicked, the treatment options reappear, and the pair has an opportunity to redesign the trial.

When doctors carry out clinical trials, they first submit the study design to a committee called an institutional review board (IRB). The IRB members discuss the proposed study and decide whether it is designed correctly and meets the ethical standards for experimenting with humans.

9-w. Give pairs about 15 minutes to run the clinical trial, record the results, and draw a conclusion.

The results of each clinical trial are presented as a graph with the percentage of surviving patients on the y-axis and time



As students design and test the clinical trials, you have an opportunity to assess how well they understand the concept of controlling variables.

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(in years) on the x -axis. One line on the graph corresponds to the standard treatment (control), and a second line corresponds to the experimental treatment group. On the basis of these data, students should recommend either the standard treatment or the experimental treatment. Students should provide evidence that supports their recommendation.

Continue with Step 10 on page 112.

In classrooms using the print version of the activity:



5-p. Explain that pairs will design and carry out a clinical trial. Make the students aware of the following:

- **The standard therapy (control) for treating leukemia is a combination therapy using the standard doses of drugs A, B, and C.**
- **Student pairs select the characteristics (drug doses and use or nonuse of the CNS treatment) of the therapy they want to compare with the standard treatment.**
- **After students select the treatment, they submit it to you for analysis. If the trial design is appropriate, then approve the trial and give the pair the results. If you find a flaw in the trial design, then give students an opportunity to correct it before proceeding.**

In designing the clinical trial, students may be tempted to use more of everything. Remind them that each treatment is associated with side effects that are sometimes very harmful.

Although proper trial design involves a number of aspects, we are focusing on just one—control of variables. Students should understand that a proper design involves changing just one variable while keeping other variables constant relative to the comparison (control) group of patients. Students must remember that their proposed treatment will be compared with the standard treatment (using drugs A, B, and C at their standard doses *without* the CNS treatment).

- Student pairs that decide to use the CNS treatment must keep drugs A, B, and C at the standard doses.
- Pairs that decide not to use the CNS treatment can change the dose of *one* of the three drugs while keeping the other two drugs at the standard doses.

6-p. Explain that in a clinical trial such as this, the experimental treatment is compared with the standard treatment. Ask, “Should the clinical trial also include a group that receives no treatment?”



Content Standard A:

Students should develop general abilities, such as systematic observation, making accurate measurements, and identifying and controlling variables.

Students' responses may vary. Students who think just in terms of good experimental design may respond that including a no-treatment group would better indicate how well the experimental treatment performs. Others may point out that it would not be fair to withhold treatment from a group of patients. In fact, the latter view prevails. For ethical reasons, a no-treatment group would not be included in the design of such a clinical trial.

- 7a-p. Give each student pair one copy of Master 4.8, *Designing a Clinical Trial*. Instruct students to**
- use Master 4.8 to record the treatment options they select and
 - submit their design to you for evaluation.

Students will need only about five minutes to discuss the trial design and make their selections.

- 7b-p. Explain that a clinical trial must be approved by an institutional review board (IRB) before it is carried out. The IRB determines whether the trial is both ethical and properly designed. As each pair submits a clinical trial design, check that only one variable is being tested.**

A correct design will vary the dose of a single drug or will keep all three drugs at the standard doses and test the effect of the CNS treatment.

- 8-p. After each pair has submitted a properly designed clinical trial, explain that the trial was performed, and you have the results. Give each student pair the appropriate handout:**
- Pairs that chose to test the dose of drug A receive Master 4.13, *Changing the Dose of Drug A*.
 - Pairs that chose to test the dose of drug B receive Master 4.14, *Changing the Dose of Drug B*.
 - Pairs that chose to test the dose of drug C receive Master 4.15, *Changing the Dose of Drug C*.
 - Pairs that chose to test the effect of the CNS treatment receive Master 4.16, *Central Nervous System Treatment*.

The results of each clinical trial are presented as a graph with the percentage of surviving patients on the y-axis and time (in years) on the x-axis. One line on the graph corresponds to the standard treatment (control), and a second line corresponds to the experimental treatment group.

- 9-p. Instruct student pairs to summarize the data on Master 4.8 in the box labeled “Clinical Trial Results.” On the basis of the results, students should recommend treating Hanna with the standard treatment or the experimental treatment. They should**



As students design and test their clinical trials, you have an opportunity to assess how well they understand the concept of controlling variables.

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state their recommendation and explain their reasoning in the box labeled “Conclusion from the Clinical Trial.”

If pairs chose to vary the dose of one of the three drugs, the results will show little difference between the standard treatment (control) and the experimental treatment (altered dose). Students should look at the graph on the handout and estimate the five-year survival rates for the control and experimental groups of patients.

If pairs chose to test the effect of the CNS treatment, they will see a significant difference between the control and experimental groups.

- 10. Reconvene the class and ask for volunteers to report which treatment they compared with the standard treatment and to indicate whether their treatment was better or worse than the standard treatment.**

Keep track of and display results as they are reported. Changing the dose of one of the three drugs used to treat leukemia produces only modest differences when compared with the standard treatment. In contrast, the CNS treatment produces much greater gains in the survival rate.

- 11. Give each student one copy of Master 4.9, *Survival Rates for Children with Leukemia*. Explain that the doctor showed this graph to Jason and Kim to help them understand how effective clinical trials have been in improving the survival rates of children with leukemia.**

Master 4.9 is a graph depicting how survival rates of children with leukemia have improved over the past 50 years. Ask questions to gauge students' understanding of the graph. The main point of the graph is that studies carried out in the past showed five-year survival rates that were lower than studies conducted more recently. This means that the results of earlier clinical trials have been successfully used to improve the survival rates of patients.

- 12. Ask students to think back to the Web search they performed during the first part of the lesson. Remind them that they evaluated the results to find the hits most likely to give them relevant and accurate information about childhood leukemia. Ask, “What other results from the Web search could give us a different type of perspective about childhood leukemia?”**

Some students will likely suggest that the leukemia blog would provide a patient's perspective on the disease.

(For print version, skip to Step 13-p on page 114.)



In classrooms using the Web version of the activity:

13-w. Acknowledge that blogs and videos created by cancer survivors can offer an important perspective on what it's like to live and cope with leukemia. Conclude the lesson by explaining that students will watch a brief video called "Hailey's Story." It was made by a young woman who was diagnosed with childhood leukemia when she was in middle school. Before directing the pairs to their computers, instruct students to write in their notebooks some questions that they would like to ask Hailey about her experiences.

14-w. Direct the students to their computers and instruct them to click on "Lesson 4: The Importance of Medical Research," and then "Activity 2: Hailey's Story."

The video is brief, five minutes long. If you have the ability to project the computer image, it may be simpler to watch the video as a group.

15-w. After student pairs have watched the video, reconvene the class. Ask for volunteers to describe their reactions to the video and how it addressed (or did not address) the questions they wrote in their notebooks.

During the video, Hailey mentions that the Leukemia and Lymphoma Society presented her with the Spirit of Tom Landry Award. Tom Landry was the coach of the Dallas Cowboys football team. He died from leukemia in 2000.

Hailey mentions that she wants to fight cancer by becoming a pediatric oncologist. You may need to explain to the class that a pediatric oncologist is a doctor who treats cancer in children.

The video will not answer all of the students' questions. Suggest that they perform a Web search to access information from foundations and patient support groups that can answer their questions.

Note: In the video, Hailey mentions that more than 12,000 children and teenagers will be diagnosed with cancer this year and that about 1 in 3 will die from it. Students may find this confusing since the graph on Master 4.9 shows a current survival rate of about 90 percent. Explain that the lower survival rate Hailey mentioned comes from combining the survival rates from all forms of cancer and not just leukemia, which responds better to treatment.

End of Web-based activity.

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In classrooms using the print version of the activity:



13-p. Acknowledge that blogs and videos created by cancer survivors can offer an important perspective on what it's like to live and cope with the illness. Conclude the lesson by explaining that the class will conduct a brief interview with a high school senior who was diagnosed with leukemia when she was in eighth grade.

Note: During the interview, Hailey mentions missing a year of school. As she explains in her video, she missed school while undergoing chemotherapy and kept up with her studies with the help of a tutor.

14-p. Explain that the interview is based on the words of an actual cancer survivor named Hailey. Ask for one volunteer to ask the questions and another to play Hailey and read her responses.

Students may become interested in Hailey's story and want to see her video. If so, give them the link to the Web site.

15-p. Give the student interviewer and the student playing Hailey each a copy of Master 4.17, *Interview with Hailey*. Instruct the two student actors to come to the front of the room and conduct the interview.

During the interview, Hailey mentions that the Leukemia and Lymphoma Society presented her with the Spirit of Tom Landry Award. Tom Landry was the coach of the Dallas Cowboys football team. He died from leukemia in 2000.

Hailey mentions that she wants to fight cancer by becoming a pediatric oncologist. You may need to explain to the class that a pediatric oncologist is a doctor who treats cancer in children.

16-p. After the student actors return to their seats, ask for volunteers to describe their reactions to the interview.

Students may still have questions about leukemia. Suggest that they perform a Web search to access information from foundations and patient support groups that can answer their questions.

Lesson 4 Organizer: Web Version



Activity 1: An Unwelcome Diagnosis Estimated time: 100 minutes	Page and Step
Explain that students will explore a case study of a child who has a rare disease. <ul style="list-style-type: none"> • Display Master 4.1. • Ask volunteers to read paragraphs aloud to the class. 	Page 98 Steps 1 and 2 
Ask, "What would you do now that you have learned that your daughter has been diagnosed with leukemia?"	Page 98 Step 3
Explain that after the upsetting visit to the doctor, Jason and Kim performed an Internet search on leukemia.	Page 98 Step 4
Ask students: <ul style="list-style-type: none"> • "If you were Hanna's parent, what information would you want to have about the disease?" • "Where could you find that information?" 	Page 99 Step 5
Give each student a copy of Masters 4.2 and 4.3 . Instruct students to rank on Master 4.3 the usefulness of the hits listed on Master 4.2.	Page 99 Step 6 
Display Master 4.3 . Ask volunteers to report how they ranked the Web hits.	Page 101 Step 7 
Arrange the class in pairs. Give each pair a copy of Master 4.4 . Explain that students will now access information about leukemia from Hits 1 and 4 from the Internet search and summarize on Master 4.4 what they learn.	Page 102 Step 8-w 
Instruct students to click on "Activity 1: An Unwelcome Diagnosis" and then on "Activity 1: Simulated Web Search."	Page 102 Step 9-w 
Reconvene the class and ask whether students have questions about the information from the Web hits.	Page 102 Step 10
Remind students about the three general causes of disease. Ask, "What types of information would you want to have in order to decide which of the three causes of disease applies to leukemia?"	Page 103 Steps 11 and 12



<p>Explain that Jason and Kim have two children: Hanna, who has leukemia, and Rick, her healthy older brother. Also, say that there's no history of leukemia in the family. Ask,</p> <ul style="list-style-type: none"> • "Does this rule out genetics as the cause of leukemia?" • "What about environmental exposure or infections?" 	<p>Page 103 Steps 13 and 14</p>
<p>Acknowledge that so far, there isn't good evidence to suggest a cause for Hanna's leukemia. Remind students about the Animation about Leukemia. Ask, "What happened to a stem cell that led to leukemia?"</p>	<p>Page 103 Step 15</p>
<p>Explain that new mutations happen from exposure to sunlight and substances in the environment or from an uncorrected DNA-copying mistake. Mutations in genes associated with cell growth can lead to cancer.</p>	<p>Page 103 Step 16</p>
<p>Explain that mutations can affect the number and appearance of chromosomes and that a photograph of chromosomes under a microscope is a karyotype. Give each student a copy of Master 4.5.</p>	<p>Page 104 Step 17</p> 
<p>Instruct students to read Master 4.5 and answer the question at the bottom. Explain that in leukemia, we expect a karyotype to show three, not two, copies of one or more of the numbered (nonsex) chromosomes.</p>	<p>Page 104 Steps 18 and 19</p>
<p>Direct student pairs back to the computers. Explain that they will view karyotypes from Hanna and her immediate family. Instruct students to predict whether each karyotype will appear normal or abnormal.</p>	<p>Page 105 Step 20-w</p> 
<p>Instruct students to click on "Activity 1: An Unwelcome Diagnosis" and then on "Activity 1: Karyotypes."</p>	<p>Page 105 Step 21-w</p> 
<p>Explain that the link labeled "View All of Hanna's Karyotypes" displays karyotypes from three cell types: blood, cheek, and hair follicles. Ask pairs to predict how each karyotype will appear and to record their predictions in their notebooks.</p>	<p>Page 105 Step 22-w</p>
<p>Ask, "How can you account for the appearance of the karyotypes taken from these three different tissues?"</p>	<p>Page 105 Step 23-w</p>

Activity 2: Clinical Trials Estimated time: 50 minutes	Page and Step
Display Master 4.6 . Ask volunteers to read it aloud.	Page 107 Step 1 
Explain that doctors compare the effectiveness of cancer treatments by looking at the percentages of patients still alive after five years.	Page 107 Step 2
Explain that students will go back to the year 1970 and assume the roles of doctors trying to improve the survival rates of children with leukemia by conducting a clinical trial.	Page 107 Step 3
Give each student pair a copy of Master 4.7 . Explain that it describes the treatment options they can include in their clinical trial.	Page 107 Step 4 
Explain that student pairs will use computers to design and carry out their clinical trial. Explain that <ul style="list-style-type: none"> • The standard therapy is a combination of the standard doses of drugs A, B, and C. • Pairs will select drug doses and the use or nonuse of the central nervous system treatment. • They will submit the design for approval. Once approved, the trial will be carried out and students will learn the results. 	Page 108 Step 5-w
Give each pair a copy of Master 4.8 . Instruct students to record their treatment options, trial results, and conclusions on it.	Page 109 Step 6-w 
Explain that in a clinical trial such as this, the experimental treatment is compared with the standard treatment. Ask, "Should the clinical trial also include a group that receives no treatment?"	Page 109 Step 7-w
Direct students to their computers and instruct them to click on "Activity 2: Clinical Trials." Student pairs should select the treatments and then click "Submit." <ul style="list-style-type: none"> • If approved, students can click "Run treatment" and learn the results. • If rejected, students can redesign the trial. • After recording the trial results, students should make and record their conclusions. 	Page 109 Steps 8-w and 9-w 
Reconvene the class. Ask volunteers to report the designs and results of the trials and how their treatment compared with the standard treatment.	Page 112 Step 10

Give each student a copy of Master 4.9 and explain that this is what the doctor showed Hanna’s parents to help them see how effective clinical trials have been in improving survival rates of children with leukemia.	Page 112 Step 11	
Remind students of the Web search they performed about leukemia. Ask, “What other results from the Web search could provide us with a different perspective about childhood leukemia?”	Page 112 Step 12	
Conclude the lesson by explaining that students will watch a brief video created by a young woman who is a leukemia survivor. Ask students to write in their notebooks some questions they would like to ask the young woman about her experiences.	Page 113 Step 13-w	
Instruct students to click on “Activity 2: Hailey’s Story” and watch the video.	Page 113 Step 14-w	
Reconvene the class and ask volunteers to describe their reactions to the video and to explain how it addressed (or did not address) the questions they wrote in their notebooks.	Page 113 Step 15-w	



= Involves making a transparency.



= Involves copying a master.



= Involves using the Internet.

Lesson 4 Organizer: Print Version



Activity 1: An Unwelcome Diagnosis Estimated time: 100 minutes	Page and Step
Explain that students will explore a case study of a child who has a rare disease. <ul style="list-style-type: none"> • Display Master 4.1. • Ask volunteers to read paragraphs aloud to the class. 	Page 98 Steps 1 and 2 
Ask, "What would you do now that you have learned that your daughter has been diagnosed with leukemia?"	Page 98 Step 3
Explain that after the upsetting visit to the doctor, Jason and Kim performed an Internet search on leukemia.	Page 98 Step 4
Ask students: <ul style="list-style-type: none"> • "If you were Hanna's parent, what information would you want to have about the disease?" • "Where could you find that information?" 	Page 99 Step 5
Give each student one copy of Masters 4.2 and 4.3 . Instruct students to rank on Master 4.3 the usefulness of the hits listed on Master 4.2.	Page 99 Step 6 
Display Master 4.3 . Ask volunteers to report how they ranked the Web hits.	Page 101 Step 7 
Arrange the class in pairs. Give each pair a copy of Masters 4.4 and 4.10 . Ask students to read Master 4.10 and summarize the information on Master 4.4.	Page 102 Steps 8-p and 9-p 
Reconvene the class and ask whether students have questions about the information from the Web hits.	Page 102 Step 10
Remind students about the three general causes of disease. Ask, "What types of information would you want to have in order to decide which of the three causes of disease applies to leukemia?"	Page 103 Steps 11 and 12
Explain that Jason and Kim have two children: Hanna, who has leukemia, and Rick, her healthy older brother. Also, say that there's no history of leukemia in the family. Ask, <ul style="list-style-type: none"> • "Does this rule out genetics as the cause of leukemia?" • "What about environmental exposure or infections?" 	Page 103 Steps 13 and 14
Acknowledge that so far, there isn't good evidence to suggest a cause for Hanna's leukemia. Remind students about the Animation about Leukemia. Ask, "What happened to a stem cell that led to leukemia?"	Page 103 Step 15

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Explain that new mutations happen from exposure to sunlight and substances in the environment or from an uncorrected DNA-copying mistake. Mutations in genes associated with cell growth can lead to cancer.	Page 103 Step 16
Explain that mutations can affect the number and appearance of chromosomes and that a photograph of chromosomes under a microscope is a karyotype. Give each student a copy of Master 4.5 .	Page 104 Step 17 
Instruct students to read Master 4.5 and answer the question at the bottom. Explain that in leukemia, we expect a karyotype to show three, not two, copies of at least one of the numbered (nonsex) chromosomes.	Page 104 Steps 18 and 19
Explain that students will now view karyotypes from Hanna and her immediate family. Ask students to predict whether each karyotype will appear normal or abnormal and to record in their notebooks whether the evidence supports the predictions.	Page 106 Step 20-p
Give each student pair a copy of Master 4.11 . Ask them to note whether their predictions were confirmed.	Page 106 Step 21-p 
Explain that students will now look at three different karyotypes from Hanna: from her blood, cheek, and hair follicles. Ask pairs to predict how each karyotype will appear and to record their predictions.	Page 106 Step 22a-p
Give each student pair a copy of Master 4.12 . Ask students to note whether their predictions were confirmed.	Page 106 Step 22b-p 
Ask, "How can you account for the appearance of the karyotypes taken from these three different tissues?"	Page 106 Step 23-p

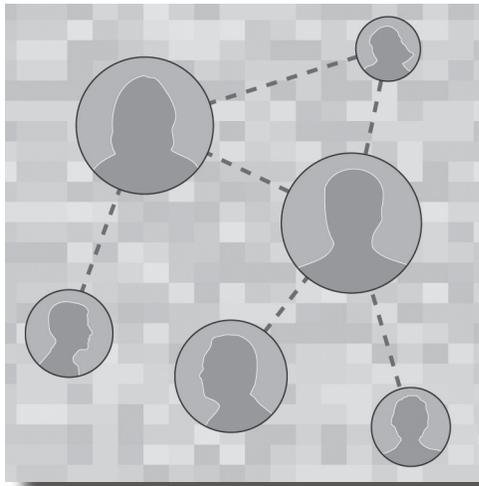
Activity 2: Clinical Trials Estimated time: 50 minutes	Page and Step
Display Master 4.6 . Ask volunteers to read it aloud.	Page 107 Step 1 
Explain that doctors compare the effectiveness of cancer treatments by looking at the percentages of patients still alive after five years.	Page 107 Step 2
Explain that students will go back to the year 1970 and assume the roles of doctors trying to improve the survival rates of children with leukemia by conducting a clinical trial.	Page 107 Step 3
Give each student pair a copy of Master 4.7 . Explain that it describes the treatment options they can include in their trial.	Page 107 Step 4 
Tell students that they will work in their pairs to design and carry out a clinical trial. Explain that <ul style="list-style-type: none"> • the standard therapy is a combination of the standard doses of drugs A, B, and C, • pairs will select drug doses and the use or nonuse of the central nervous system treatment, and • they will submit the design to you for analysis. 	Page 110 Step 5-p
Explain that in clinical trials, an experimental treatment is compared with the standard treatment. Ask, “Should the clinical trial also include a group that receives no treatment?”	Page 110 Step 6-p
Give each pair a copy of Master 4.8 . Instruct students to record on it the treatment options they select, and then to submit it to you. Explain what an Institutional Review Board is, and check that student designs test only one variable.	Page 111 Steps 7a-p and 7b-p 
Once you’ve approved all the clinical trial designs, give each student pair the appropriate handout (Master 4.13, 4.14, 4.15, or 4.16)	Page 111 Step 8-p 
Ask student pairs to summarize the data and their conclusions and reasoning on Master 4.8 .	Page 111 Step 9-p
Reconvene the class and ask volunteers to report which treatment they used and whether it was better than the standard one.	Page 112 Step 10
Give each student a copy of Master 4.9 and explain that this is what the doctor showed Hanna’s parents to help them see how effective clinical trials have been in improving survival rates of children with leukemia.	Page 112 Step 11 
Remind students of the Web search they performed about leukemia. Ask, “What other results from the Web search could give us a different perspective about childhood leukemia?”	Page 112 Step 12

<p>Acknowledge that blogs and videos by cancer survivors can offer important perspectives on what it's like to live with that illness. Conclude by explaining that the class will conduct a brief interview with a high school senior who was diagnosed with leukemia in eighth grade.</p>	<p>Page 114 Step 13-p</p>
<p>Ask for one volunteer to play Hailey and one to play the interviewer, give each of them a copy of Master 4.17, and have them conduct the interview in front of the class.</p>	<p>Page 114 Steps 14-p and 15-p</p> 
<p>Ask volunteers to describe their reactions to the interview.</p>	<p>Page 114 Step 16-p</p>

 = Involves making a transparency.  = Involves copying a master.

Lesson 5

Communicating about Rare Diseases



Evaluate

At a Glance

Overview

Lesson 5 gives students the opportunity to reflect on what they have learned about rare diseases and scientific inquiry during this supplement. Students role-play staff members of a patient-support organization and are tasked with creating informational posters for the public about Marfan syndrome and childhood leukemia. After students create the posters, they evaluate another poster for a different disease. Finally, students return to the reality TV show scenario that began the supplement. They revisit their initial ideas about rare disease and their attitudes toward people affected by them. They reexamine their answers to the questions about rare diseases posed in Lesson 1 and discuss how their thinking has changed.

Major Concepts

- Diseases have three main causes:
 - genetics
 - environmental exposure
 - infectious agents
- Rare diseases may become common, and common diseases may become rare.
- Some rare diseases can be cured, while many others can be managed through treatment.
- People with rare diseases must sometimes cope with the stigma associated with their condition.

Objectives

After completing this lesson, students will have

- revisited their preconceptions about the nature of disease in light of scientific conceptions,
- summarized information about childhood leukemia and Marfan syndrome, and
- considered their feelings about people affected by rare diseases.

Teacher Background

Consult the following sections in Information about Rare Diseases and Scientific Inquiry:

2.0 The Impact of Genomics on Rare Diseases (pages 24–26)

3.0 Rare Infectious Diseases (page 26)

4.0 Rare Diseases Caused by Environmental Toxins (pages 27–28)

5.1 Necrotizing Fasciitis (pages 28–29)

5.2 Marfan Syndrome (pages 29–31)

5.3 Childhood Leukemia (pages 31–33)

In Advance

Web-Based Activities

Activity	Web Component?
1	No
2	Yes

Photocopies, Transparencies, Equipment, and Materials

Photocopies and Transparencies
Activity 1: Creating an Informational Poster 1 transparency and 1 copy of Master 5.1 for each student pair 1 copy of Master 5.2 for each student pair addressing Marfan syndrome 1 copy of Master 5.3 for each student pair addressing childhood leukemia 1 transparency and 1 copy for each student pair of Master 5.4 1 copy of Master 5.5 for each student pair
Activity 2: Reflecting on Rare Diseases For Classes Using the Web-Based Version 1 copy of Master 5.6 for each student

Continued

Photocopies and Transparencies

Activity 2: Reflecting on Rare Diseases

For Classes Using the Print-Based Version

1 copy of Master 5.6 **for each student**

1 transparency of Master 5.7

Equipment and Materials

For Activity 1, students will need chart paper and colored marking pens.

For Activity 2, Web-based version, students will need computers with Internet access.

Preparation

Activity 1

Gather chart paper and colored marking pens for each student pair. Make photocopies and transparencies.

Activity 2

For classrooms using the Web version, verify that the computer lab is reserved for your class or that classroom computers are set up for the activities. Refer to Using the Web Site for details about the site. Check that the Internet connection is working properly.



Log on to the Web Portion of Student Activities section of the site at

<http://science.education.nih.gov/supplements/rarediseases/student>

Select “Lesson 5: Communicating about Rare Diseases” so students can begin the activity right away.

Procedure

Activity 1: Creating an Informational Poster

Estimated time: 50 minutes

Note: This is an Evaluate lesson. It’s not designed to teach new content but rather to give you a chance to assess how well students have learned the major concepts about rare diseases and scientific inquiry.

1. **Begin by explaining that in this final lesson of the supplement, students will play the roles of staff members working for an**

**Content Standard C:**

Disease is a breakdown in structures of functions of an organism. Some diseases are the result of intrinsic failures of the system. Others are the result of damage by infection by other organisms.

**Content Standard A:**

Students should base their explanations on what they observed, and as they develop cognitive skills, they should be able to differentiate explanation from description—proving causes for effects and establishing relationships based on evidence and logical argument.

organization that informs and support patients with rare diseases and their families. Explain the following:

- Many rare diseases have support groups that raise awareness and money to support research about the disease.
- The task is for pairs to prepare informational posters that explain important aspects of a rare disease to patients, family members, and other interested people.

Students may feel unqualified to prepare informational posters about rare diseases. You can explain that the posters will deal with the rare diseases they have been studying. Furthermore, the goal of the poster is to communicate information to the public, so the posters should use language that everyone can understand.

2. **Arrange students into pairs again. Explain that each pair will create a poster about childhood leukemia or Marfan syndrome. Assign half of the pairs to childhood leukemia and the other half to Marfan syndrome. Explain that after each pair creates a poster, they will evaluate a poster about the other rare disease.**

You may allow student pairs to select the disease they prefer. If selections heavily favor one disease over the other, you may need to instruct some pairs to switch diseases to maintain a balance between the two.



Tip from the field test: If your classroom has the technical capacity, consider allowing students to create a PowerPoint presentation instead of a poster.

3. **Display Master 5.1, *Guidelines for the Poster*, and give each pair a copy to use as a reference. Explain that the handout lists the types of information that should be in the poster. Briefly go over the items on the handout and answer any questions students have.**

Make sure that students have access to the notebooks that contain their work from previous lessons. This work will help students complete the first part of the poster.

Note: The purpose of this activity is to assess students' learning from the previous lessons. Therefore, do not allow students to conduct a research project using the Internet or other outside resources.

4. **Explain that the second part of the poster will contain a brief summary of a recent clinical trial or research study about the disease. Give each student pair one copy of Master 5.2, *Research Study on Marfan Syndrome*, or Master 5.3, *Clinical Trial on Childhood Leukemia*, depending on student preference.**

These handouts contain the information needed to complete the second part of the poster.

Marfan study

Students should conclude that the drug losartan helped keep the aortas of mice with the Marfan mutation at a healthy size. This suggests that the drug also may be able to help humans with Marfan syndrome.

Leukemia clinical trial

Students should conclude that the survival rate of patients who received drug combination therapy with brain irradiation was essentially the same as that of patients who received combination drug therapy alone. This means that patients can be spared the brain irradiation and the risk of its harmful side effects.

5. **Display Master 5.4, Evaluation Rubric. Explain that student pairs will use it to evaluate the poster created by another pair. Briefly go over the criteria on the handout.**

It's important to provide the pairs with evaluation criteria before they create the posters. Otherwise, they may feel that it is unfair to be given this information after it's too late to revise the posters.

6. **Make available to pairs chart paper and colored marking pens. Explain that pairs will first make an outline of the information they plan to include on the poster. When they are satisfied with it, they should transfer it to a piece of chart paper.**
7. **As the student pairs work, circulate around the room and assign a code number to each poster.**

Allow students at least 15 minutes to complete this task. The code number allows you to know which students worked on which poster and prevents the students from knowing who created the poster they will evaluate.

8. **After student pairs have completed the posters and each has been assigned a code number, collect all posters.**

Place the posters about childhood leukemia in one pile and those about Marfan syndrome in another pile.

9. **Give each pair a poster to evaluate. Make sure that each pair evaluates a poster about the rare disease they did not create a poster for.**

If multiple classes will be making posters, consider having one class serve as peer reviewers for another class.

10. Give each student pair one copy each of Master 5.4 and Master 5.5, *Poster Score Sheet*.

Give students about 20 minutes to complete the evaluation, and then collect the score sheets. Of course, the students' explanations for their scores are more revealing than the numbers themselves.

Activity 2: Reflecting on Rare Diseases

Estimated time: 50 minutes

1. Remind the class about the producer of the reality TV show who wanted to film a student with a rare disease joining the class. Instruct students to look in their notebooks where, in Lesson 1, they wrote down questions they would ask the student with the rare disease.

(For print version, skip to Step 2-p on page 130.)



In classrooms using the Web-based activity:

- 2-w. Explain that student pairs will go to their computers and watch a video made by a young man with Marfan syndrome. Instruct students to keep in mind the questions they posed and the feelings they expressed about rare diseases and the people affected by them.

Computers should be at the URL:

<http://science.education.nih.gov/supplements/rarediseases/student>

This is a menu page that contains a link for this activity.

- 3-w. Direct students to their computer stations and instruct them to click on “Lesson 5: Communicating about Rare Diseases.”

The video is about 12 minutes long and illustrates the story of Kevin, a young man who has Marfan syndrome.

- 4-w. After they have watched the video, allow students to express their feelings about it.

If students focus on feelings of sorrow or pity, call attention to comments made by Kevin's mother about how important he is to their family and to those around him. Marfan syndrome certainly has affected him, but not only in negative ways. It has helped Kevin direct his life.

- 5-w. Ask for volunteers to read from their notebooks**
- a question they wanted to ask the student with the rare disease or
 - a feeling they expressed about having the student join the class.

If their thinking has changed since the beginning of the supplement, ask them to explain how and why.

The point of this step is to revisit questions, concerns, and fears about people with rare diseases that students expressed at the start of the supplement. We hope that after learning about rare diseases and hearing from people who live with them, students become more empathetic and sensitive to those who cope with rare diseases.

- 6-w. Explain that you want to conclude the supplement by revisiting the students' initial ideas about disease. Give each student one copy of Master 5.6, *What Do You Think Now?* Instruct students to answer each question on the handout.**

Give students 5–10 minutes to answer the questions. Students may recognize that they answered these questions during the Lesson 1. Answering the same questions gives them the opportunity to reflect on how their thinking has changed as a consequence of participating in the supplement.

- 7-w. Have students retrieve the copy of Master 1.2, *Thinking about Disease*, that they filled out in Lesson 1. Instruct students to compare the answers they just wrote with those on Master 1.2.**

- 8-w. After students have had a chance to compare both sets of answers, ask the following:**
- “Have any of your answers changed since Lesson 1?”
 - “If so, what caused your thinking to change?”

Allow different students to respond. Some of the students' answers to the questions will probably have changed. Even if some students' attitudes are essentially the same, the knowledge gained during the supplement may influence their opinions later, after they have had more experiences.

End of Web-based activity.

In classroom using the print version of the activity:



- 2-p. Display Master 5.7, *Another Letter from the Producer*. Ask for a volunteer to read it aloud to the class.**
- 3-p. Remind students that during Lesson 1, they wrote in their notebooks some questions they would ask a student with a rare disease who was about to join the class. Instruct students to look back at the questions they posed and the feelings they expressed about sharing their classroom with this student.**
- 4-p. Explain that you wonder whether participating in the lessons in this supplement has caused anyone to change their attitude about people with rare disease. Ask for volunteers to read from their notebooks**
- a question they wanted to ask the student with a rare disease *or*
 - a feeling they expressed about having the student join the class.

If their thinking has changed since the beginning of the supplement, ask them to explain how and why.

The point of this step is to revisit questions, concerns, and fears about people with rare diseases that students expressed at the start of the supplement. We hope that after learning about rare diseases and hearing from people who live with them, students become more empathetic and sensitive to those who cope with rare diseases.

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- 6-p. Have students retrieve the copy of Master 1.2, *Thinking about Disease*, they filled out in Lesson 1. Instruct them to compare the answers on Master 5.6 with those on Master 1.2.**

7-p. After students have had a chance to compare both sets of answers, ask the following:

- **“Have any of your answers changed since Lesson 1?”**
- **“If so, what caused your thinking to change?”**

Allow different students to respond. Some of the students' answers to the questions will probably have changed. Even if some students' attitudes are essentially the same, the knowledge gained during the supplement may influence their opinions later, after they have had more experiences.

Lesson 5 Organizer: Web Version



Activity 1: Creating an Informational Poster Estimated time: 50 minutes	Page and Step	
Explain that students will play the roles of staff members working for a patient support group. Student pairs will prepare informational posters for the public.	Page 125 Step 1	
Arrange the class in pairs again. Explain that each pair will make a poster about a rare disease (half will address Marfan syndrome and half will address childhood leukemia) and then evaluate another pair's poster.	Page 126 Step 2	
Display Master 5.1 and give each pair a copy. Go over the master and answer students' questions.	Page 126 Step 3	 
Explain that the second part of the poster will contain a summary of a clinical trial or research study. Give each pair a copy of either Master 5.2 or Master 5.3 , depending on student preference.	Page 126 Step 4	
Display Master 5.4 , and explain that students will use it to evaluate another pair's poster.	Page 127 Step 5	
Give pairs chart paper and marking pens. <ul style="list-style-type: none"> • Instruct students to first make an outline of the poster, then transfer it to the chart paper. • Circulate around the room and assign a code number to each poster. • When students have finished, collect the posters. 	Page 127 Steps 6–8	
Give each pair a poster of the disease they did not work on.	Page 127 Step 9	
Give each pair a copy of Masters 5.4 and 5.5 . After students have completed the work, collect the score sheets.	Page 128 Step 10	

Activity 2: Reflecting on Rare Diseases Estimated time: 50 minutes	Page and Step
Remind the class about the reality TV scenario from Lesson 1. Instruct students to retrieve the questions and feelings about the scenario they recorded in their notebooks.	Page 128 Step 1
Tell students to watch a video on their computers made by a young man who has Marfan syndrome (at “Lesson 5: Communicating about Rare Diseases”). Afterwards, allow students to express their feelings about the video.	Pages 128 Steps 2w–4w 
Ask volunteers to read from their notebooks <ul style="list-style-type: none"> • a question they wanted to ask the student with the rare disease <i>or</i> • a feeling they expressed about having the student join their class. If their thinking has changed since the beginning of the supplement, ask them to explain how and why.	Page 129 Step 5-w
Revisit students’ initial ideas about disease. Give every student a copy of Master 5.6 , and instruct them to answer the questions on it.	Page 129 Step 6-w 
Have students retrieve their copies of Master 1.2 and compare these answers with those on Master 5.6 .	Page 129 Step 7-w
Conclude by asking, <ul style="list-style-type: none"> • “Have any of your answers changed since Lesson 1?” • “If so, what caused your thinking to change?” 	Page 129 Step 8-w

 = Involves making a transparency.

 = Involves copying a master.

 = Involves using the Internet.

Lesson 5 Organizer: Print Version



Activity 1: Creating an Informational Poster Estimated time: 50 minutes	Page and Step
Explain that students will play the roles of staff members working for a patient support group. Student pairs will prepare informational posters for the public.	Page 125 Step 1
Arrange the class in pairs again. Explain that each pair will make a poster about a rare disease (half will address Marfan syndrome and half will address childhood leukemia) and then evaluate another pair's poster.	Page 126 Step 2
Display Master 5.1 and give each pair a copy. Go over the master and answer students' questions.	Page 126 Step 3  
Explain that the second part of the poster will contain a summary of a clinical trial or research study. Give each pair a copy of either Master 5.2 or Master 5.3 , depending on student preference.	Page 126 Step 4 
Display Master 5.4 , and explain that students will use it to evaluate another pair's poster.	Page 127 Step 5 
Give pairs chart paper and marking pens. <ul style="list-style-type: none"> • Instruct students to first make an outline of the poster, then transfer it to the chart paper. • Circulate around the room and assign a code number to each poster. • When students have finished, collect the posters. 	Page 127 Steps 6–8
Give each pair a poster of the disease they did not work on.	Page 127 Step 9
Give each pair a copy of Masters 5.4 and 5.5 . After students have completed the work, collect the score sheets.	Page 128 Step 10 

Activity 2: Reflecting on Rare Diseases Estimated time: 50 minutes	Page and Step
Remind the class about the reality TV scenario from Lesson 1. Instruct students to retrieve the questions and feelings about the scenario they recorded in their notebooks.	Page 128 Step 1
Display Master 5.7 , and ask a volunteer to read it aloud. Ask students to reflect on the questions and feelings they wrote about in their notebooks during Lesson 1.	Page 130 Steps 2-p and 3-p 
Ask volunteers to read from their notebooks <ul style="list-style-type: none"> • a question they wanted to ask the student with the rare disease <i>or</i> • a feeling they expressed about having the student join their class. If their thinking has changed since the beginning of the supplement, ask them to explain how and why.	Page 130 Step 4-p
Revisit students' initial ideas about disease. Give every student a copy of Master 5.6 , and instruct them to answer the questions on it.	Page 130 Step 5-p 
Have students retrieve their copies of Master 1.2 and compare those answers with the ones on Master 5.6 .	Page 130 Step 6-p
Conclude by asking, <ul style="list-style-type: none"> • "Have any of your answers changed since Lesson 1?" • "If so, what caused your thinking to change?" 	Page 131 Step 7-p

 = Involves making a transparency.
  = Involves copying a master.

Masters

Lesson 1—What Is a Rare Disease?

Activity 1: What Is a Rare Disease?

- Master 1.1, *Letter from a Producer* transparency
Master 1.2, *Thinking about Disease*..... student copies

Lesson 2—What Causes Rare Diseases?

Activity 1: Causes of Disease

- Master 2.1, *Medical Officer Report Form*..... transparency and student copies
for each pair
Master 2.2, *Visits to the Infirmary, Week 1** student copies for each pair
Master 2.3, *Test Results, Week 1** student copies for each pair

Activity 2: Is a Rare Disease Present?

- Master 2.4, *Follow-up on Week 1 Infirmary Visits** student copies for each pair
Master 2.5, *Visits to the Infirmary, Week 2** student copies for each pair
Master 2.6, *Medical Reference Manual: Necrotizing Fasciitis** student copies for each pair
Master 2.7, *Questions about a Rare Disease* student copies for each pair

Lesson 3—The Difficulty of Diagnosis

Activity 1: A Parent’s Dilemma

- Master 3.1, *To Play or Not to Play?*..... transparency
Master 3.2, *Medical Specialty Report Form* student copies
Master 3.3, *Heart and Circulatory System** student copies for each group of 4
Master 3.4, *Vision System** student copies for each group of 4
Master 3.5, *Respiratory System** student copies for each group of 4
Master 3.6, *Skeletal System** student copies for each group of 4

Activity 2: Connective Tissue

- Master 3.7, *Measuring Elasticity* transparency

Activity 3: A Common Thread

- Master 3.8, *Diagnosing a Connective Tissue Disorder*. student copies for each pair
Master 3.9, *Medical Reference Manual: Disorders
of the Connective Tissue** student copies for each pair
Master 3.10, *Patrick’s Family** student copies for each pair
Master 3.11, *Living with Marfan Syndrome** transparency

Lesson 4—The Importance of Medical Research

Activity 1: An Unwelcome Diagnosis

- Master 4.1, *Doctor Visits 1 and 2* transparency
Master 4.2, *Internet Search Results*..... student copies

*Print version only

Master 4.3, <i>Evaluating Internet Search Results</i>	transparency and student copies
Master 4.4, <i>Summarizing Information about Leukemia</i>	student copies for each pair
Master 4.5, <i>Karyotype</i>	student copies

Activity 2: Clinical Trials

Master 4.6, <i>Another Doctor Visit</i>	transparency
Master 4.7, <i>Treating Leukemia</i>	student copies for each pair
Master 4.8, <i>Designing a Clinical Trial</i>	student copies for each pair
Master 4.9, <i>Survival Rates for Children with Leukemia</i>	student copies for each pair
Master 4.10, <i>Information about Leukemia*</i>	student copies for each pair
Master 4.11, <i>Family Karyotypes*</i>	student copies
Master 4.12, <i>Hanna’s Karyotypes*</i>	student copies
Master 4.13, <i>Changing the Dose of Drug A*</i>	student copies for each pair
Master 4.14, <i>Changing the Dose of Drug B*</i>	student copies for each pair
Master 4.15, <i>Changing the Dose of Drug C*</i>	student copies for each pair
Master 4.16, <i>Central Nervous System Treatment*</i>	student copies for each pair
Master 4.17, <i>Interview with Hailey*</i>	2 copies for the class

Lesson 5—Communicating about Rare Diseases

Activity 1: Creating an Informational Poster

Master 5.1, <i>Guidelines for the Poster</i>	transparency and student copies for each pair
Master 5.2, <i>Research Study on Marfan Syndrome</i>	student copies for each pair
Master 5.3, <i>Clinical Trial on Childhood Leukemia</i>	student copies for each pair
Master 5.4, <i>Evaluation Rubric for Poster</i>	transparency and student copies for each pair
Master 5.5, <i>Poster Score Sheet</i>	student copies for each pair

Activity 2: Reflecting on Rare Diseases

Master 5.6, <i>What Do You Think Now?</i>	student copies
Master 5.7, <i>Another Letter from the Producer*</i>	transparency

*Print version only

Letter from a Producer



Dear Principal:

I am a producer for People Reality Productions, a company that develops reality television shows for broadcast over several cable TV channels. We are thinking about creating a series that follows the life of a student who has a rare disease.

We are still working out the details of the series. At this point, we haven't identified the student who will participate or even which rare disease will be featured in the series. As a first step, we are interested in learning what concerns and questions your teachers and students have about a student with a rare disease joining their class.

Please share this letter with your teachers. After they have had a chance to discuss it with their students, I will call you to learn about their thoughts and concerns.

Thank you for your help with this project.

Sincerely,

Vincent Shifflett
Senior Producer
People Reality Productions

Thinking about Disease

Name: _____

Questions

1. What is a disease?
2. How do doctors tell if someone has a disease?
3. What do you think causes disease?
4. Make a list of list 10 different diseases.

Table 1. List of Diseases

5. What does it mean to call a disease “rare”?
6. In simple terms, curing a disease means that the patient has been restored to good health and there is little chance of the disease coming back.

It is not possible to cure all diseases. Controlling a disease means that the disease symptoms are lessened and the quality of the life for the patient is improved, but the disease has not been cured.

Which of the diseases you listed in Step 4 do you think are curable, controllable, or incurable?

Medical Officer Report Form

Name(s): _____

Questions

1. Summarize the reasons that soldiers came to the infirmary during Week 1.

2. Fill out the form for ordering lab tests.

Test Order Form

Soldier	Test ordered	Why was the test ordered?
1		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
16		
17		
18		
19		
20		
21		

Visits to the Infirmary, Week 1

Soldier	Barracks	What's wrong?	Test ordered	Test results	Diagnosis	Treatment
1	A	Sore, red, itchy eyes				
2	D	Sore toe				
3	A	Sore, red, itchy eyes				
4	A	Sore, red, itchy eyes				
5	G	Sore throat				
6	A	Sore, red, itchy eyes				
7	E	Skin rash				
8	A	Sore, red, itchy eyes				
9	F	Cut on left leg				
10	G	Sore throat				
11	I	Shortness of breath				
12	A	Sore, red, itchy eyes				
13	H	Sore toe				
14	G	Sore throat				
15	E	Skin rash				
16	G	Sore throat				
17	G	Sore throat				
18	B	Ankle pain				
19	G	Sore throat				
20	D	Sore toe				
21	C	Sore toe				

Test Results, Week 1

Soldier	Barracks	What's wrong?	Test ordered	Test results	Diagnosis	Treatment
1	A	Sore, red, itchy eyes	Test 1	+ for bacteria C	Pinkeye	Antibiotic eyedrops
2	D	Sore toe	Test 1	+ for bacteria A	Blister from boots	Dressing
3	A	Sore, red, itchy eyes	Test 1	+ for bacteria C	Pinkeye	Antibiotic eyedrops
4	A	Sore, red, itchy eyes	Test 1	+ for bacteria C	Pinkeye	Antibiotic eyedrops
5	G	Sore throat	Test 1	+ for bacteria A	Strep throat	Antibiotic
6	A	Sore, red, itchy eyes	Test 1	+ for bacteria C	Pinkeye	Antibiotic eyedrops
7	E	Skin rash	Test 2	+ for poison ivy	Poison ivy	Steroid skin cream
8	A	Sore, red, itchy eyes	Test 1	+ for bacteria C	Pinkeye	Antibiotic eyedrops
9	F	Cut on left leg	No test			Stitches
10	G	Sore throat	Test 1	+ for bacteria A	Strep throat	Antibiotic
11	I	Shortness of breath	No test		Asthma	Inhaler
12	A	Sore, red, itchy eyes	Test 1	+ for bacteria C	Pinkeye	Antibiotic eyedrops
13	H	Sore toe	Test 1	+ for bacteria A	Blister from boots	Dressing
14	G	Sore throat	Test 1	+ for bacteria A	Strep throat	Antibiotic
15	E	Skin rash	Test 2	+ for poison ivy	Poison ivy	Steroid skin cream
16	G	Sore throat	Test 1	+ for bacteria A	Strep throat	Antibiotic
17	G	Sore throat	Test 1	+ for bacteria A	Strep throat	Antibiotic
18	B	Ankle pain	No test	X-ray	No break	Bandage
19	G	Sore throat	Test 1	+ for bacteria A	Strep throat	Antibiotic
20	D	Sore toe	Test 1	– for all bacteria	Blister from boots	Dressing
21	C	Sore toe	Test 1	+ for bacteria A	Blister from boots	Dressing

Follow-up on Week 1 Infirmary Visits

Summary of Patients' Responses to Treatment from Week 1

- Six soldiers from Barracks A with pinkeye tested positive for infection by bacterial species C. They were treated with eyedrops containing antibiotics. In all cases, the infection has cleared up.
- Six soldiers from Barracks G with sore throats tested positive for infection by bacterial species A. They were treated with antibiotics. Although two soldiers returned to the infirmary, all are responding to the antibiotics and the infections have largely disappeared.
- Four soldiers developed blisters from wearing new boots. Three of the four tested positive for infection by bacterial species A, and the fourth soldier tested negative for species A, B, and C. One soldier received a cut on the left leg, which was closed with stitches. He has no evidence of infection.
- One soldier twisted his ankle. X-rays showed no broken bones. The ankle was bandaged, and the soldier has been assigned to light duty.
- Two soldiers from Barracks E tested positive for exposure to poison ivy. They were treated with steroid cream, and the skin rashes are disappearing.
- One soldier, who was short of breath, was diagnosed as having asthma and was given an inhaler, which eased her symptoms.

Visits to the Infirmary, Week 2

Return Visits to the Infirmary from Week 1 Soldier Visits

Soldier	Barracks	What's wrong?	Tests ordered	Test results	Diagnosis	Treatment
2	D	Swollen, blistered lower leg				
16	G	Sore throat				
19	G	Sore throat				

New Visits to the Infirmary, Week 2

Soldier	Barracks	What's wrong?	Tests ordered	Test results	Diagnosis	Treatment
22	G	Sore throat				
23	A	Sore throat				
24	E	Cut on head				
25	G	Sore throat				
26	G	Sore throat				
27	B	Skin rash				
28	G	Sore throat				
29	D	Ankle pain				
30	A	Sore throat				
31	B	Sore toe				
32	F	Skin rash				

Medical Reference Manual: Necrotizing Fasciitis (Flesh-Eating Bacteria)

What is it?

Flesh-eating disease is a bacterial infection that destroys skin and fat tissue. The disease is very rare. The odds of getting it are about 1 in 100,000. However, it is very serious. About 2 out of 10 people who get this infection die from it.

What causes it?

The disease can be caused by different species of bacteria, including the one that causes strep throat. The bacteria enter the body through open wounds, where they interact with the immune system to produce the disease. Flesh-eating disease is rare because the immune system of most people will stop the infection before it becomes serious.

What are the symptoms?

The skin reddens, becomes swollen, and is painful to the touch. Other symptoms include nausea, vomiting, and diarrhea. The symptoms start suddenly, may get better for a day or two, then quickly worsen. If not treated, the disease may result in organ failure and death.

Figure 1. Early infection. (Donald E. Low, University Health Network/Mount Sinai Hospital)



Figure 2. Late infection. (Donald E. Low, University Health Network/Mount Sinai Hospital)



How is it treated?

Patients with flesh-eating disease need immediate hospital care. Treatment involves antibiotics and surgery to remove diseased tissue and stop the spread of the disease.

Questions about a Rare Disease

Name(s): _____

1. What evidence suggests that bacterial species A causes both sore throat and foot infection?
2. What evidence suggests that the soldier with the foot infection has flesh-eating disease?
3. Why are there many cases of sore throat but only one case of flesh-eating disease?
4. What evidence is there that flesh-eating disease is a rare disease?
5. What should be the next step in treating the soldier with the foot infection? Explain your reasoning.

To Play or Not to Play?

Patrick is a 13-year-old middle school student who loves to play basketball. He came home excited from school and explained to his parents that the school basketball team will be holding tryouts next month and he wants to participate.

Patrick's parents are both happy and concerned for him. They are happy because they know Patrick loves sports, and they feel that the exercise will be good for him. They also know that Patrick has been occasionally teased because he is tall and thin. Maybe by joining the basketball team he will make new friends and feel more accepted by his classmates.

Patrick's parents are concerned because he has some health problems. When Patrick was a toddler, the family doctor diagnosed him with a heart murmur. The doctor explained that a heart murmur refers to a sound that the blood makes as it flows through the heart. She further explained that heart murmurs are usually harmless and that Patrick could lead a normal life.

When he was nine, Patrick developed a problem with his eyesight, and it was discovered that one of his eye lenses was detached and had to be repaired. When Patrick was 10, he was diagnosed with asthma. The doctor explained that asthma causes the tubes carrying air in and out of the lungs to become sore and swollen. This can cause coughing and wheezing and make it difficult to breathe. The doctor created a treatment plan for Patrick that helped him recognize his symptoms and use an inhaler to make breathing easier. She also explained that, with proper management of his asthma, Patrick could play sports and that the exercise might even improve his condition.

Finally, just last year, Patrick was diagnosed with scoliosis, or curvature of the spine. The doctor explained that Patrick's scoliosis was moderate and, as with most children, the cause was unknown. He further explained that in 90 percent of cases, no future treatment is needed.

Medical Specialty Report Form

Name(s): _____

Patient's name _____

Medical specialty _____

Patient's medical history

Results from physical exam

Possible causes

Heart and Circulatory System

Cardiologist Report

Medical history

Patient was previously diagnosed with a heart murmur. An echocardiogram reveals mitral valve prolapse and an enlarged aorta.

Physical exam

The presence of a heart murmur was confirmed. An echocardiogram revealed the presence of mitral valve prolapse.

Medical Reference Manual: *Heart and Circulatory System*

Heart murmur

When doctors use a stethoscope to listen to the heartbeat, they hear a lub-DUB sound made by heart valves opening and closing as blood flows through the heart. The term “heart murmur” refers to an unusual whooshing sound doctors hear when listening to the heartbeat.

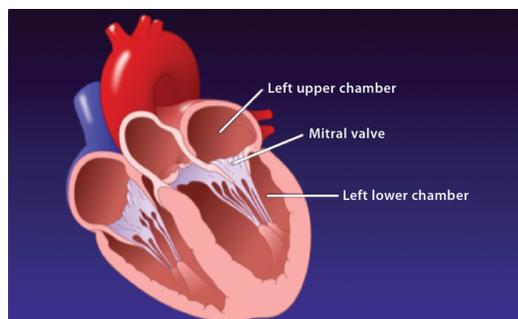
Doctors diagnosis heart murmurs in many children at some point in their lives. Most heart murmurs are harmless and need no treatment. Other heart murmurs are called abnormal and may be associated with defects in the heart that were present at birth.

Mitral valve prolapse

In the condition called mitral valve prolapse, one of the heart’s valves doesn’t work properly. The valve flaps are “floppy” and don’t close properly. This sometimes causes blood to flow backward from its normal direction. This backflow of blood may be associated with shortness of breath or chest pain.

The cause of mitral valve prolapse is not known. Most people with the condition are born with it. It tends to run in families and is associated with connective tissue disorders such as Marfan syndrome.

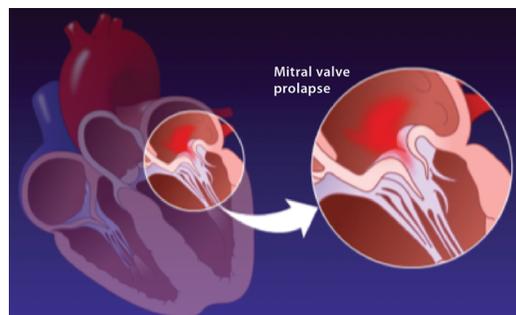
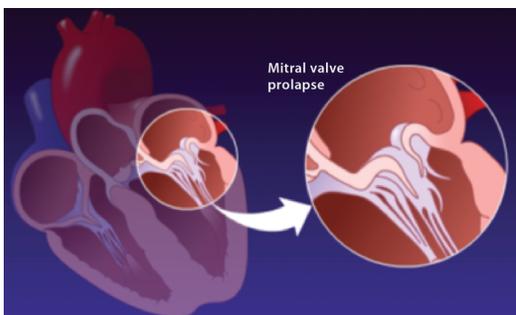
Figure 1. *Mitral valve prolapse.*



The mitral valve is a valve that lies between the left upper and lower chambers of the heart.

In mitral valve prolapse, the valve flaps are too large and don’t form a tight seal when they close.

This lack of a tight seal can cause a small amount of blood to flow backward, resulting in a heart murmur.



Vision System

Ophthalmologist Report

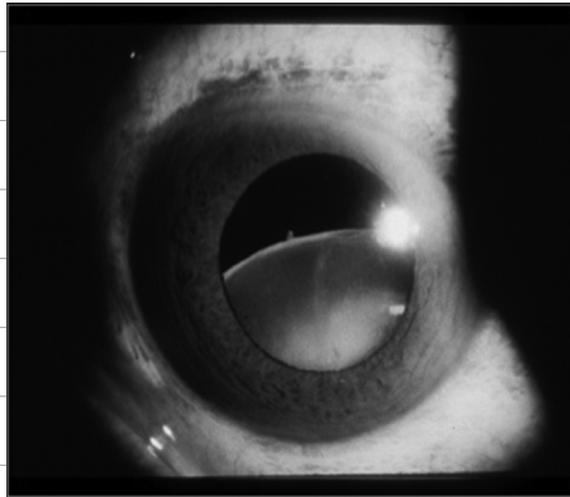
Medical history

The patient is myopic (nearsighted). When he was nine years old, he was being fitted for eyeglasses when an exam revealed that his left lens was dislocated.

Physical exam

An eye exam confirmed myopia and a repaired detached left lens.

Figure 1. Slit lamp exam: Photo from a slit lamp exam of a patient's eye showing a detached left lens. (Kevin J. Blinder, MD, The Retina Institute, Washington University School of Medicine)



Medical Reference Manual: *Vision System*

Myopia (nearsightedness)

Nearsightedness is caused by a change in the shape of the eyeball so that it is egg shaped instead of round. This egg-shaped eyeball focuses light a little in front of the retina instead of directly on it, resulting in blurry vision. Myopia is a common condition affecting 30 to 40 percent of the American population.

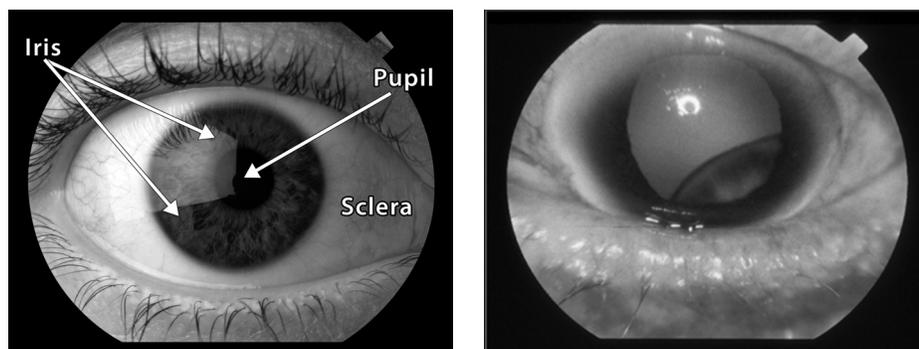
Detached lens

A detached, or dislocated, lens means that the lens has shifted from its normal position (centered behind the pupil). If the dislocation is moderate, the problem may be corrected with glasses. A severe lens dislocation may require surgery to correct.

Detached lenses are rare in the general population. They are often caused by a blow to the eye. The condition is much more common among people with certain diseases involving connective tissue such as Ehlers-Danlos syndrome and Marfan syndrome.

Figure 2. Photos from slit lamp exams: Left, a normal lens; right, a detached lens.

((left) Corbis, (right) Kevin J. Blinder, MD, The Retina Institute, Washington University School of Medicine)



Respiratory System

Pulmonologist Report

Medical history

Patient has been diagnosed with asthma. When seven years old, he experienced a collapsed lung.

Physical exam

Exam confirmed the diagnosis of asthma. Lung volume was normal. Chest X-ray was normal.

Figure 1. Patient photo: Patrick at age 10.



Medical Reference Manual: *Respiratory System*

Table 1. Information about Asthma

What are the symptoms of asthma?	<ul style="list-style-type: none">• Coughing• Wheezing• Difficulty breathing
What causes asthma attacks?	<p>Asthma attacks are a response to environmental triggers that leads to</p> <ul style="list-style-type: none">• Inflammation of the airways. This swelling and irritation inside the airways leads to difficulty breathing.• Bronchospasms. The muscles surrounding the airways go into spasm, leading to their narrowing. <p>In rare cases, asthma is associated with disorders of the connective tissue.</p>
What are the triggers for asthma attacks?	<ul style="list-style-type: none">• Dust• Mold• Pollen• Pets• Cigarette smoke• Pollution• Illness (infection by bacteria and viruses)
How is asthma treated?	<p>Inhaled drugs, such as albuterol, help widen the airways during asthma attacks and make it easier to breathe.</p> <p>For long-term management of asthma, inhaled steroids are safe and can be used every day.</p>

Skeletal System

Orthopedist Report

Medical history

Patient was previously diagnosed with mild scoliosis (curvature of the spine).

Physical exam

A physical exam and X-rays confirmed the presence of mild scoliosis. The curvature was measured to 15 degrees. It was noted that the patient has unusually long, slender arms, fingers, and feet.

Figure 1. Patient X-ray: X-ray taken when patient was five years old.

(© Ldambies | Dreamstime.com)



Medical Reference Manual: *Skeletal System*

Scoliosis (curvature of the spine)

Scoliosis refers to an abnormal curvature of the spine. About 10 percent of adolescents show some degree of scoliosis, but less than 1 percent need treatment for the condition. The severity of scoliosis is described by the extent of the curvature.

Table 1. Severity of Scoliosis

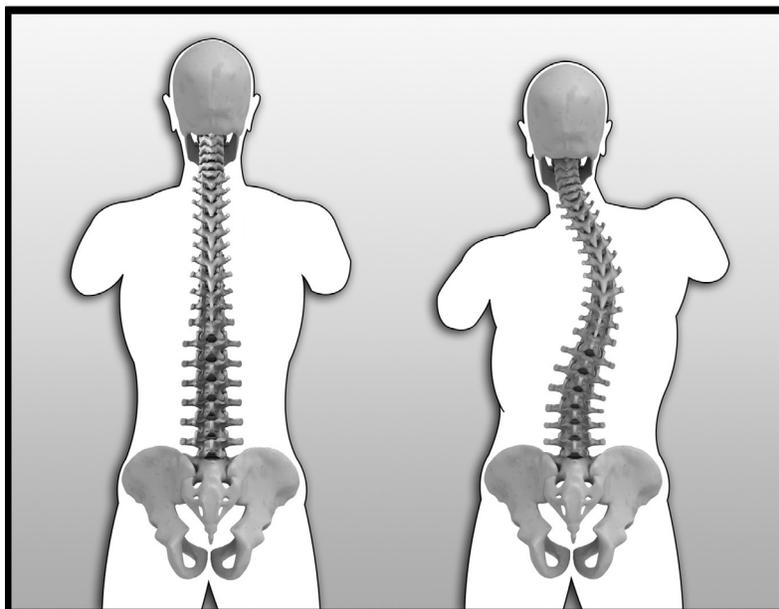
Amount of Curvature	Severity
Curvature less than 20 degrees	Mild
Curvature between 20 and 70 degrees	Moderate
Curvature greater than 70 degrees	Severe

Patients with mild scoliosis usually don't require treatment beyond examination to see whether the condition worsens. Patients with moderate and severe scoliosis are treated with back braces or surgery.

In most cases, the cause of scoliosis is not known; however, it does seem to run in families. In some cases, the condition is caused by an injury. In other cases, the condition is a result of a muscle, nerve, or connective tissue disease.

Figure 2. *The spine and scoliosis: Left, normal spine; right, spine showing scoliosis.*

(© Sebastian Kaulitzki | Dreamstime.com)

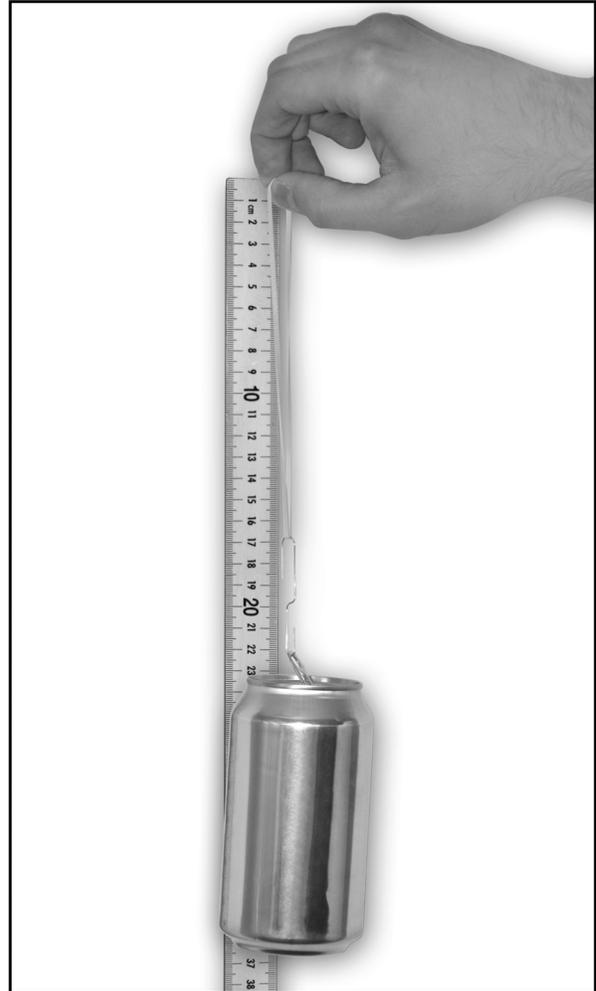


Measuring Elasticity

Steps for measuring the elasticity of rubber bands

1. Unfold the paper clip into an S shape.
2. Slip one end of the paper clip through the pulled tab on top of the soda can.
3. Place the other end of the paper clip through the rubber band.
4. Hold a meter stick upright on a hard surface so that the end reading “100 centimeters” is resting on the surface and the end reading “0 centimeters” is up in the air.
5. Hold the top of rubber band (the end away from the paper clip) up to the end of the meter stick that reads “0.”
6. Observe and record in your notebook how far down the meter stick the rubber band has stretched.
7. Repeat Steps 2 through 6 for the second rubber band.

Figure 1. Measuring elasticity.



Diagnosing a Connective Tissue Disorder

Name(s): _____

1. You will try to match Patrick's medical symptoms to four different disorders of connective tissue.
2. For each of Patrick's symptoms listed in the table under "medical history," decide whether that symptom is consistent with each of the four connective tissue disorders written across the top row. Use the information supplied in the Medical Reference Manual.
3. Place a check mark in the appropriate box when the symptom is consistent with the connective tissue disorder.

Table 1. Checklist of Patrick's Symptoms

Patrick's medical history	Ehlers-Danlos syndrome	Marfan syndrome	Osteogenesis imperfecta	Scleroderma
Myopia				
Detached eye lens				
Asthma				
Collapsed lung				
Heart murmur				
Leaky heart valve				
Long arms and legs				
Curvature of spine				

Medical Reference Manual: Disorders of the Connective Tissue

Connective tissues are made of proteins and fats. They support your body's organs and give your tissues their shape. Cartilage is an important connective tissue. It is stiff but more flexible than bone. Cartilage helps your bones move and glide over each other. It also gives shape to body parts such as your nose and ears.

Connective tissue may be damaged by injury or through an infection. It can also be damaged by a large number of genetic disorders that occur rarely in the population. A few of them are described below.

Ehlers-Danlos syndrome

Ehlers-Danlos syndrome refers to a collection of related disorders that weaken connective tissues. Symptoms can be mild to life threatening. They include the following:

- heart valves that leak
- weakened blood vessels
- loose joints
- abnormal wound healing
- soft, stretchy skin that bruises easily
- muscle weakness
- joint dislocations

Ehlers-Danlos syndrome is an inherited disorder. Treatment involves managing symptoms and learning how to protect the joints and prevent injuries.

Scleroderma

Scleroderma is a group of related disorders involving abnormal growth of connective tissue. One type of scleroderma affects only the skin. Another type can also affect other body systems. The cause of scleroderma is not known. It is more common in females than males. Other symptoms may include the following:

- calcium deposits in connective tissues
- narrowing of blood vessels in the hands and feet
- swelling of the esophagus (tube between the throat and stomach)
- thick, tight skin on fingers
- red spots on hands and face

Treatment involves managing the symptoms.

Marfan syndrome

Marfan syndrome is a disorder of connective tissue that is due to mutations in a gene that codes for a connective tissue protein called fibrillin. Symptoms can be mild to severe. Often, people with Marfan syndrome are tall and thin and have loose joints. Their fingers and feet may be unusually long. Other symptoms may include the following:

- heart valves that leak
- heart murmur
- weakened blood vessels
- curvature of the spine
- flat feet
- sudden lung collapse, sometimes asthma
- nearsightedness and problems with the eye lens
- stretch marks on the skin
- teeth that are crowded together

Marfan syndrome is an inherited disorder. Treatment involves managing symptoms and adopting physical activity guidelines that are specific to each person.

Osteogenesis imperfecta

Osteogenesis imperfecta is an inherited disorder that causes bone weakness. The disorder is caused by mutations to a gene involved with making the protein collagen. Sometimes, bones break for no apparent reason. Symptoms can be mild to severe. Other symptoms may include the following:

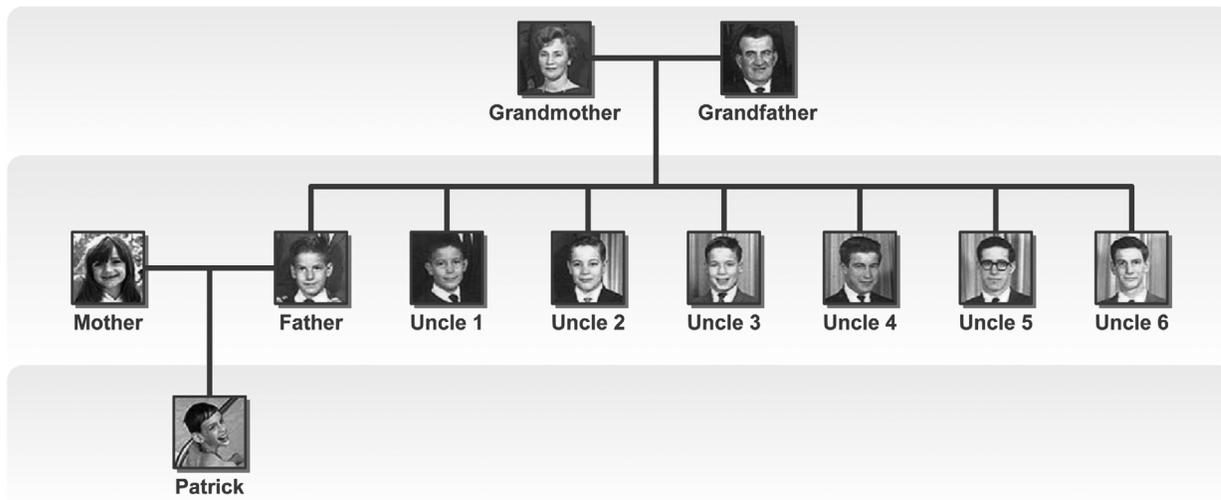
- muscle weakness
- curvature of the spine
- loose joints
- hearing loss
- skin that bruises easily
- brittle teeth

Treatment involves exercise, physical therapy, braces, and surgery.

Patrick's Family

Figure 1. Patrick's family on his father's side.

Patrick's Family Tree



Grandmother: In good health

Grandfather: Died after several heart operations

Mother: In good health

Father: Has had two heart operations and has mild scoliosis

Uncle 1: Died from brain cancer

Uncle 2: In good health

Uncle 3: In good health

Uncle 4: Has had a heart operation and a collapsed lung

Uncle 5: Died after several heart operations and had a detached eye lens

Uncle 6: Has type 2 diabetes

Living with Marfan Syndrome

Questions to a doctor from young people who have Marfan syndrome

1. “Is there any possible way for the Marfan gene to be detected before a child is born and maybe find a way to prevent it from mutating itself?”
2. “When they measured my heart with the echocardiogram, they told my mom they don’t think I should do marching band. I was wondering, if I don’t exert myself too much, if I take it at my own pace, do you think I could do it?”

Comments from those young people about the most frustrating part of having Marfan syndrome

1. “The most frustrating thing for me is ... I can’t drive. I tried to get my permit, and I couldn’t pass the vision test because I did have my retina detached.”
2. “The thing that frustrates me the most is all the aches and pains in my joints and sternum.”
3. “When it comes to how you’re socially accepted, high school is really lame. In a couple of years, it’s not going to matter what sport you played or anything. It is going to matter what you know and what you do with the knowledge that you know.”

Doctor Visits 1 and 2

Background

Jason and Kim are the parents of a five-year old girl, Hanna. They are concerned because she has had flu-like symptoms for three weeks and has not responded to treatment. The family doctor was concerned that something more serious than flu might be responsible for Hanna's symptoms. He referred Hanna to another doctor for further examination.

First visit

The doctor examined the child and immediately noticed that she had signs of an infection. She felt the child's abdomen and observed that the liver appeared to be swollen. The doctor asked the parents about their daughter's health and the health of the rest of the family. Finally, she ordered some blood tests.

Second visit

During the follow-up visit, the doctor explained that the results of the blood tests showed there was a problem. The doctor explained that Hanna had developed a cancer of the blood called leukemia. Jason and Kim were understandably upset to hear this news. The doctor further explained the nature of the disease and how it would be treated. She told them that childhood leukemia such as Hanna's is treatable. About 80 percent of children with leukemia are cured after treatment.

Internet Search Results

1. **Federal Center for Cancer Research**
Information about [leukemia](#), its causes, symptoms, diagnosis, and treatment ...
2. **My [Leukemia](#) Blog**
Living with Cancer: Reflections and remembrances of a cancer survivor ...
3. **The Cancer Research Center at Lincoln State University**
Breast cancer, Prostate cancer, [Leukemia](#), Lymphoma, ...
4. **Information about [Leukemia](#) from the American Blood Cancer Society**
Cells of the blood, Stem cells and [leukemia](#), White blood cells, bacteria ...
5. **[Leukemia](#)—Medhealthopedia: The Do-It-Yourself Encyclopedia**
Leukemia is a form of cancer that is ...
6. **Cancer drugs for less! [Leukemia](#)**
Order drugs from overseas to treat [leukemia](#) and save!
7. **Fed approves new drug to treat [leukemia](#)**
Medical Business Weekly (Washington, DC)—The Food and Drug Administration today approved Hamilton Pharmaceutical's drug Arresta for the treatment of [leukemia](#) ...
8. **[Leukemia](#): Definition from medicaljargon.com**
[Leukemia](#)—A cancer of the white blood cells. White blood cells ...

Evaluating Internet Search Results

Name(s): _____

Questions

1. Hanna's parents searched the Internet because they wanted to find information about childhood leukemia. They wanted to answer such questions as
 - What causes leukemia?
 - What are its symptoms?
 - How is it diagnosed?
 - How is it treated?
 - How likely is it that the treatment will help?
2. When thinking about the results of an Internet search, for each hit, ask yourself:
 - Is this site likely to contain the information that I want?
 - Is this site likely to contain information that is accurate?
3. The Internet search returned the eight hits on your handout. Rank each hit in the table below by placing its number in one of the boxes. The most helpful hit is on the left side, and the least helpful hit is on the right side.

Table 1. Ranking the Hits

Most helpful				Least helpful			

Summarizing Information about Leukemia

Name(s): _____

Federal Center for Cancer Research

Disease definition

Disease symptoms

Disease diagnosis

American Blood Cancer Society

- List types and functions of blood cells.
- Where are blood cells made?
- What is a stem cell?
- What is the relationship between stem cells and leukemia?
- Why are people with leukemia more likely to get bacterial infections?

Karyotype

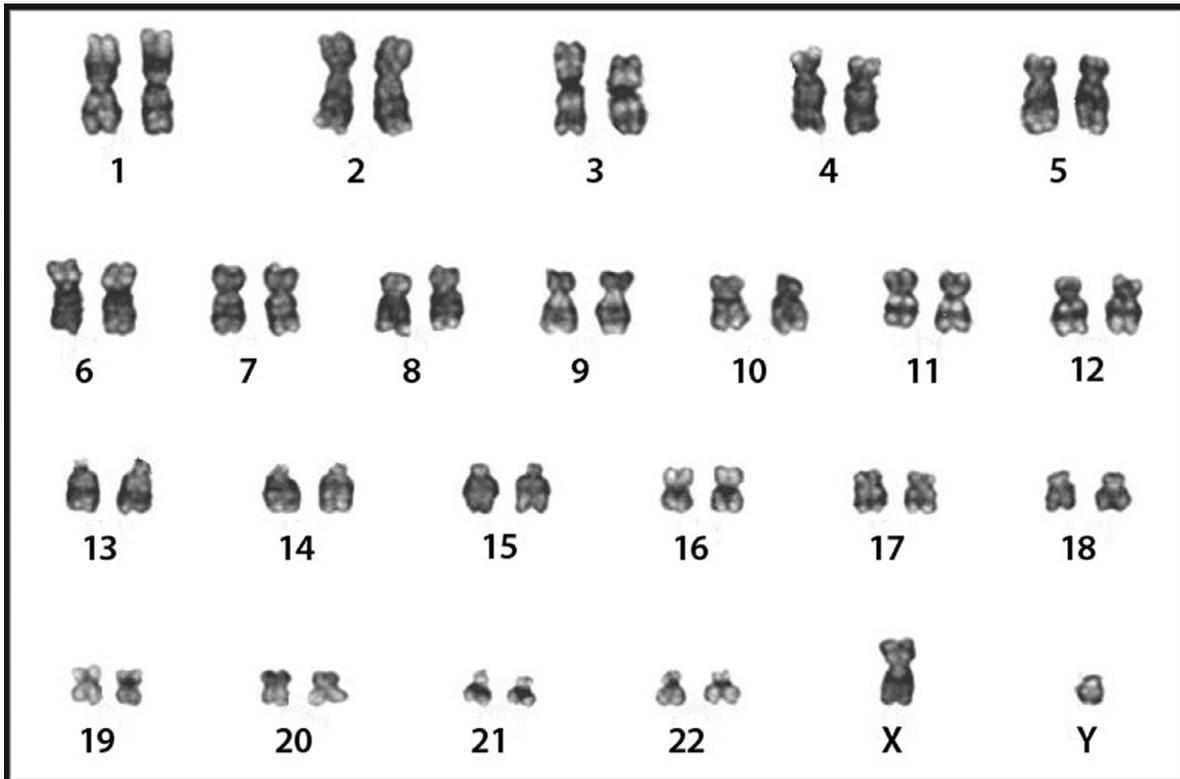
A karyotype is a photograph of a person's complete set of chromosomes.

A healthy human karyotype shows 22 pairs of numbered chromosomes (arranged by size), where one member of each pair comes from the mother and the other comes from the father.

There is an additional pair called the sex chromosomes. An individual with one X chromosome and one Y chromosome is male. Someone with two X chromosomes and no Y chromosome is female.

What is the sex of the person whose karyotype is above?

Figure 1. Sample karyotype. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine.)



Another Doctor Visit

Jason and Kim returned to the doctor's office with Hanna to discuss her treatment. The doctor suggested having Hanna participate in something called a clinical trial. She explained that a clinical trial is a process in which groups of patients receive treatments that differ in one feature of their treatment.

Jason and Kim were alarmed at this suggestion. They asked,

- “Does this mean that you don't know what to do for her?”
- “Do you mean that Hanna may receive a sugar pill instead of a real drug?”

The doctor replied that for decades, most children with leukemia have participated in clinical trials. The results from these clinical trials have helped greatly improve survival rates. The doctor further explained that, during a clinical trial, patients are never given a sugar pill because effective treatment options are available. Instead, a control group of patients receives the standard therapy while another group of patients receives some experimental treatment.

Treating Leukemia

Treatments for childhood leukemia in 1970

Standard treatment: Chemotherapy

The standard treatment for childhood leukemia uses three drugs taken together. This combination of drugs and their doses have been guided by the results of many clinical trials:

- **Drug A is prednisone.** Cells have the ability to kill themselves if they become damaged. This helps keep the body free of unhealthy cells. Prednisone works by helping the body kill damaged white blood cells.

Side effects: Increased appetite, indigestion, and nervousness

- **Drug B is vincristine.** When cells divide, each new cell must receive an identical set of chromosomes. Vincristine interferes with this process and stops white blood cells from dividing.

Side effects: Hair loss, constipation, and nerve damage

- **Drug C is methotrexate.** When cells divide, they need to make more DNA, RNA, and protein molecules. Cancer cells are dividing rapidly compared with normal cells. Methotrexate interferes with the ability of all cells to make DNA, RNA, and proteins.

Side effects: Stomach pain, shortness of breath, and blood in urine

Central nervous system treatment

Doctors observed that often after chemotherapy treatment was stopped, leukemia reappeared in the central nervous system (brain and spinal cord). To kill cancer cells “hiding” in this part of the body, the patient’s head is exposed to X-rays and the drug methotrexate is injected directly into the spinal fluid.

Side effects: Learning problems and increased risk for heart disease

Designing a Clinical Trial

Name(s): _____

Clinical trial design

Drug A

- Decrease
- Standard dose
- Increase

Drug B

- Decrease
- Standard dose
- Increase

Drug C

- Decrease
- Standard dose
- Increase

Central nervous system treatment

- Yes
- No

Clinical trial results

Conclusion from the clinical trial

Survival Rates for Children with Leukemia

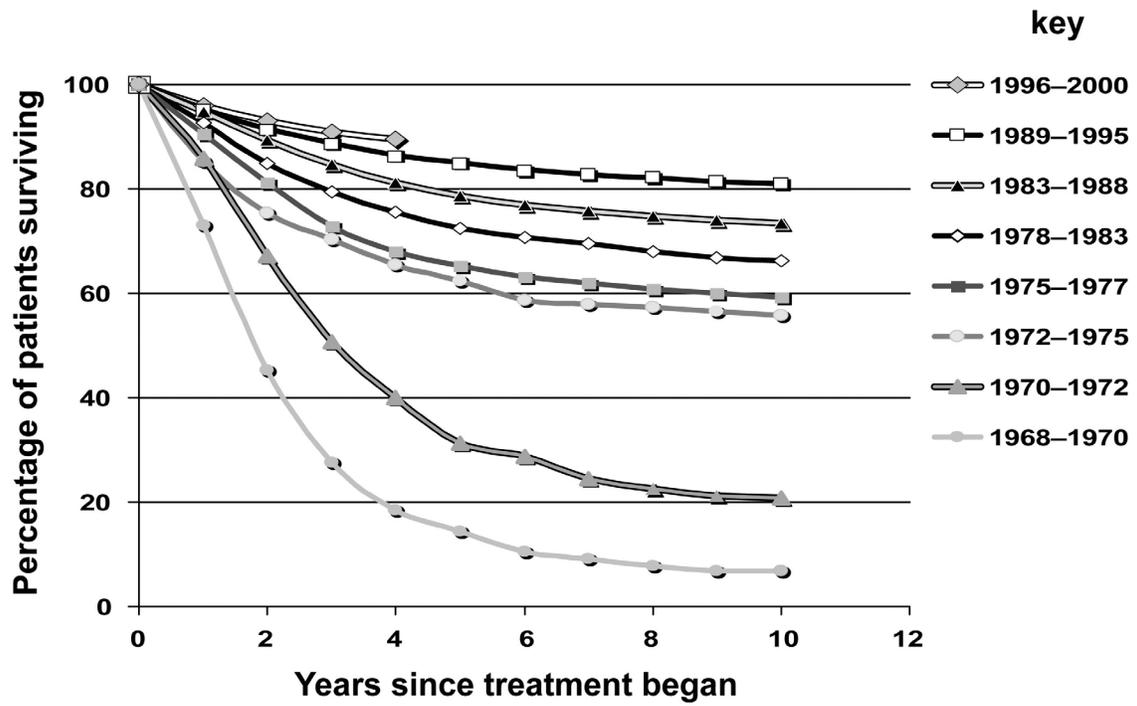


Image courtesy of Dr. Timothy Garrington

Information about Leukemia

Federal Center for Cancer Research

Leukemia: A cancer of the white blood cells. White blood cells associated with leukemia are abnormal, and they are produced in very high numbers. Although it is a rare disease, leukemia can affect both children and adults. One type of the disease can appear in a short period of time (days to weeks), while another type of the disease develops more slowly.

Disease symptoms catalog Leukemia

- Too few red blood cells and platelets
- Repeated infections by viruses and bacteria
- Pain in the joints
- Pain in the abdomen
- Wheezing and coughing

Diagnosing leukemia

Diagnosis of leukemia begins with a physical examination of the patient.

The doctor will

- look for signs of infection, such as runny nose, fever, and cough;
- feel the abdomen to see if the liver or spleen is enlarged;
- take a medical history that involves questions about
 - patient symptoms,
 - family health, and
 - medications and allergies; and
- order blood tests to measure the numbers of white blood cells, red blood cells, and platelets.

If the physical exam and blood test results suggest the possibility of leukemia, then the doctor may order the following tests:

- Bone marrow biopsy: A piece of bone marrow is taken from the back of the hip and checked for the presence of abnormal cells.
- Lymph node biopsy: As with the bone marrow biopsy, a sample is examined for the presence of abnormal white cells. (Lymph nodes are found throughout the body and help trap and destroy viruses and bacteria.)
- Lumbar puncture (spinal tap): A sample of spinal fluid is removed and checked for the presence of abnormal cells. The presence of abnormal cells can indicate that leukemia has spread to the central nervous system.

American Blood Cancer Society

As an adult, your body will contain about 10 pints of blood. This precious fluid flows through thousands of miles of veins, arteries, and capillaries. Let's take a look at the three most-common types of cells found in the blood. First are the **red blood cells**. They transport oxygen and nutrients to the body's cells. Second are the **platelets**. They help stop bleeding and repair wounds. Last, the **white blood cells** help protect against infection by viruses and bacteria.

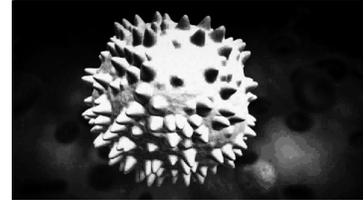
Figure 1. Red blood cell.



Figure 2. Platelet.

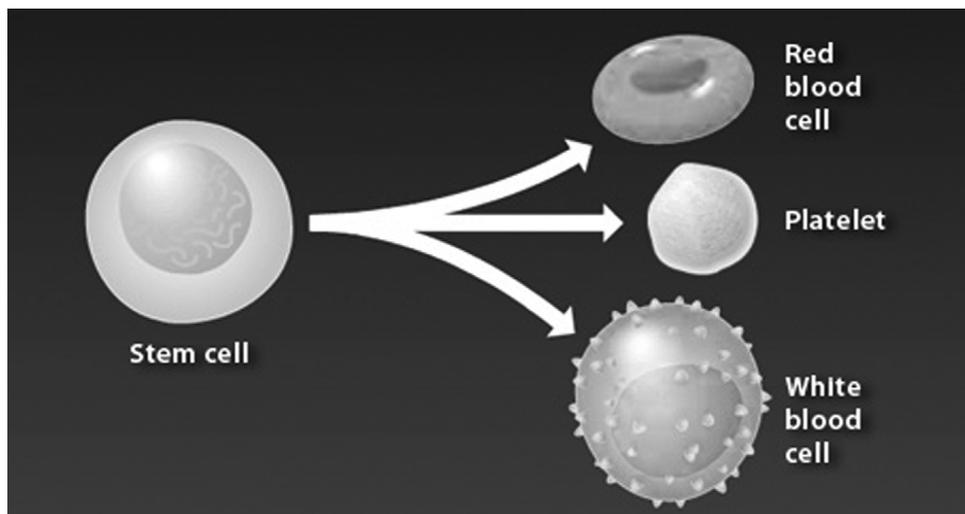


Figure 3. White blood cell.



Red blood cells, platelets, and white blood cells are not made in the blood itself. Instead, they are made in a spongy tissue called **bone marrow** found in the hollow portions of bones. The bone marrow produces cells called **stem cells**. The stem cells can divide to form red blood cells, platelets, and white blood cells, which enter the bloodstream, where they do their work.

Figure 4. A stem cell in the bone marrow can produce a red blood cell, a platelet, or a white blood cell.



American Blood Cancer Society (continued)

Leukemia and stem cells

In leukemia, a stem cell becomes mutated and begins to produce unhealthy white blood cells in large numbers. Leukemia is a cancer of the stem cells that are responsible for making white blood cells. As a result, unhealthy white blood cells are produced in great numbers and crowd out the healthy white blood cells. This also causes fewer red blood cells and platelets to be made. When healthy white blood cells encounter bacteria in the blood, they engulf and destroy them. But unhealthy white blood cells produced due to leukemia are not able to attack and destroy invading bacteria.

Figure 1. A mutated stem cell produces another mutated stem cell as well many unhealthy white blood cells.

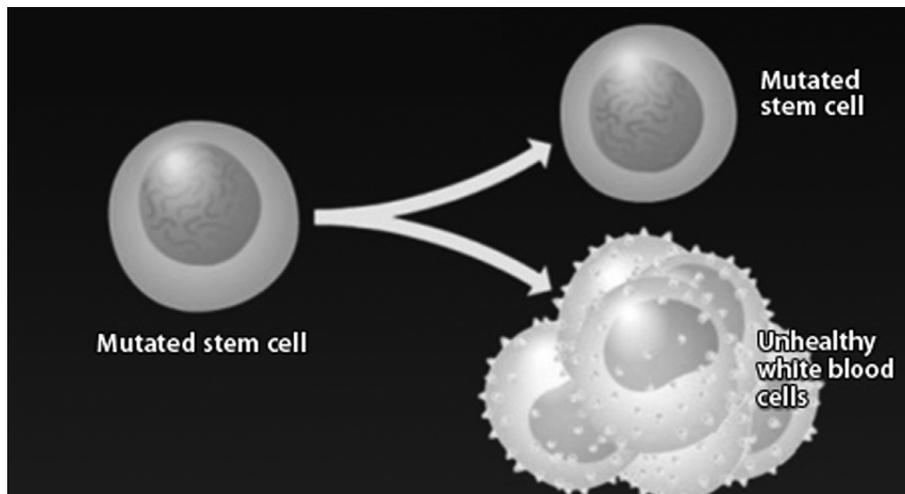


Figure 2. Healthy white blood cells engulf and destroy bacteria.

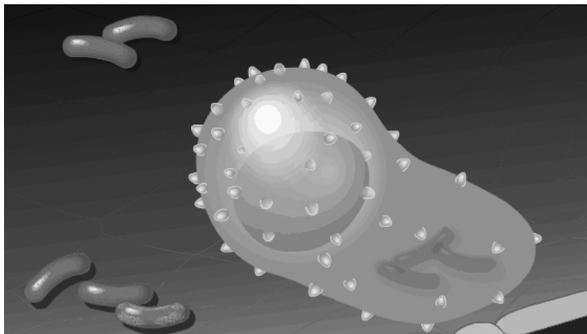


Figure 3. Unhealthy white blood cells do not engulf bacteria.



Family Karyotypes

Figure 1. Hanna. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)

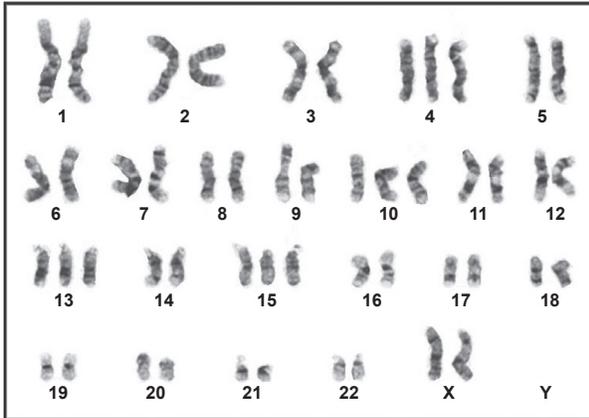


Figure 2. Kim. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)

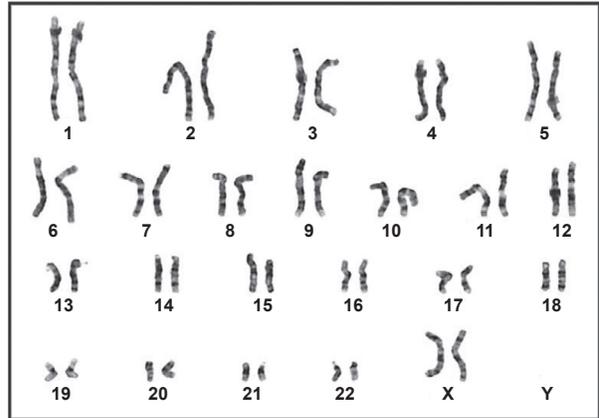


Figure 3. Rick. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)

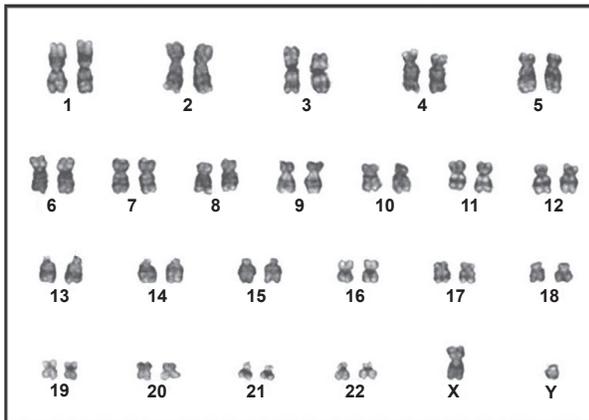
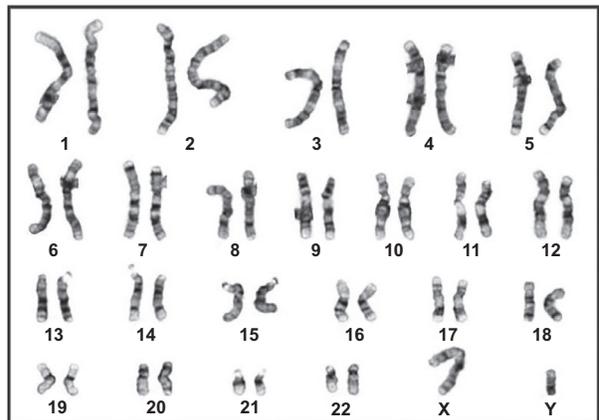


Figure 4. Jason. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)



Hanna's Karyotypes

Figure 1. Hanna's blood cells. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)

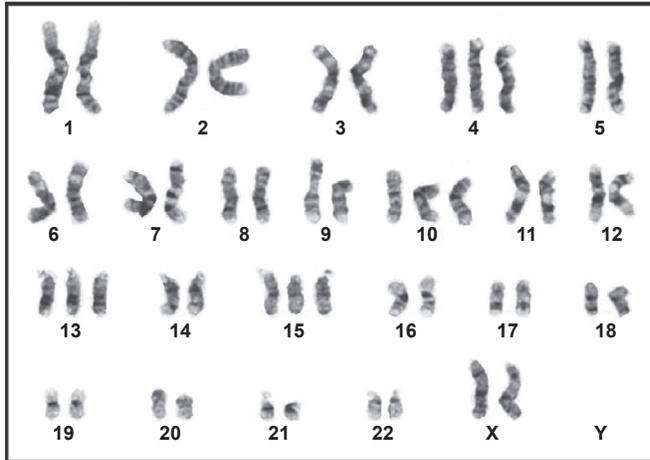


Figure 2. Hanna's hair follicle cells. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)

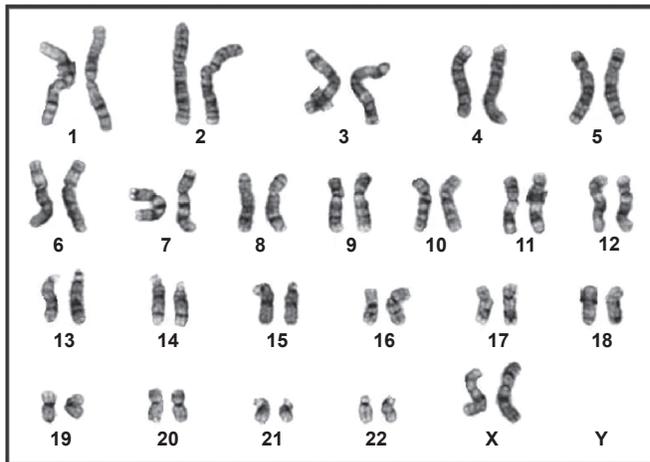
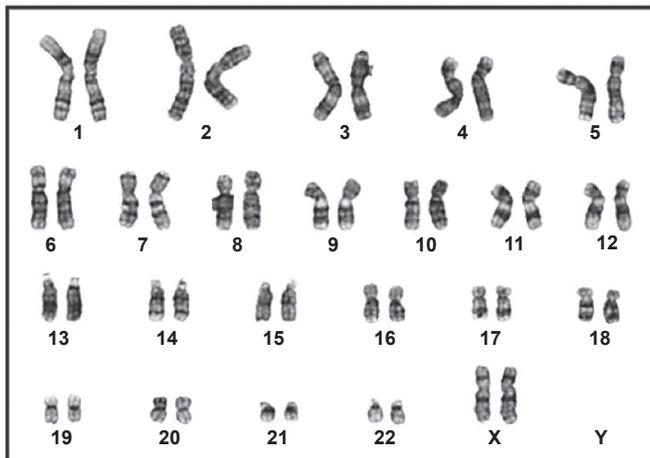


Figure 3. Hanna's cheek cells. (Genetics Department, Affiliated Laboratories, Inc., Bangor, Maine)



Changing the Dose of Drug A

Figure 1. Drug A, increased dose.

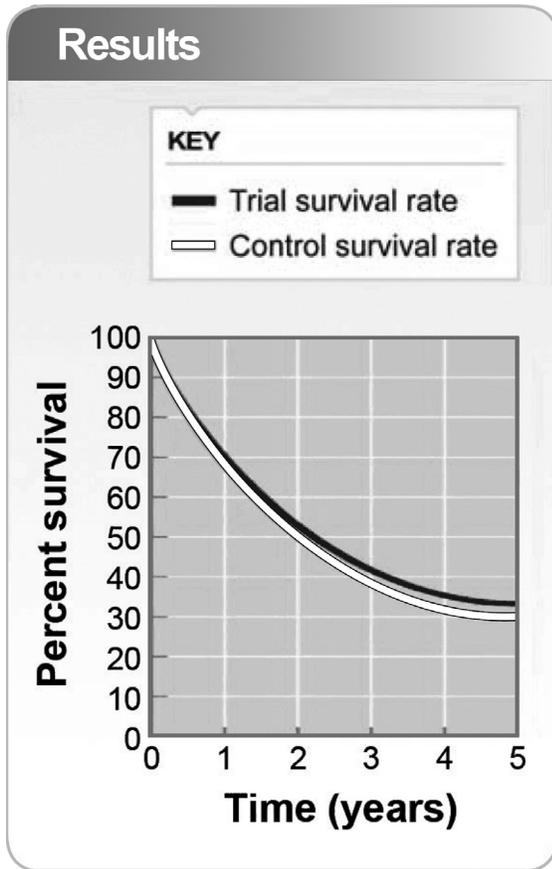
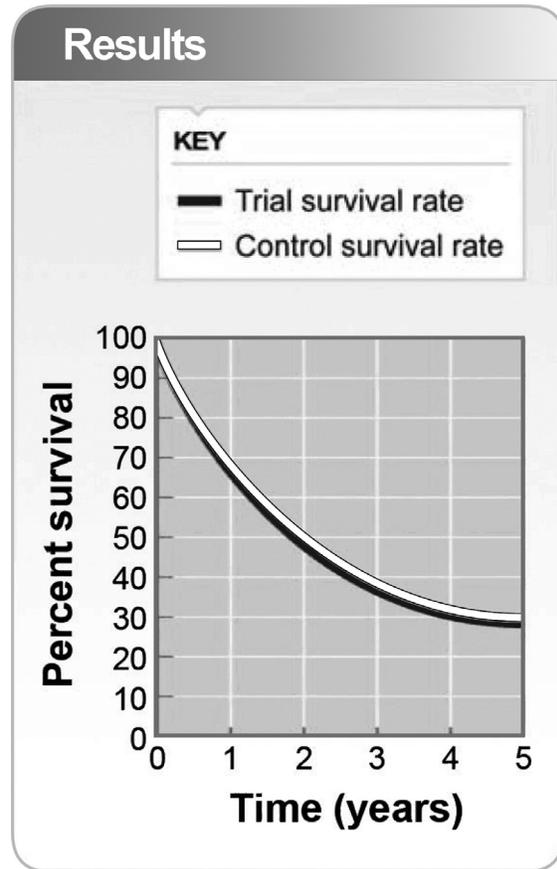


Figure 2. Drug A, decreased dose.



Changing the Dose of Drug B

Figure 1. Drug B, increased dose.

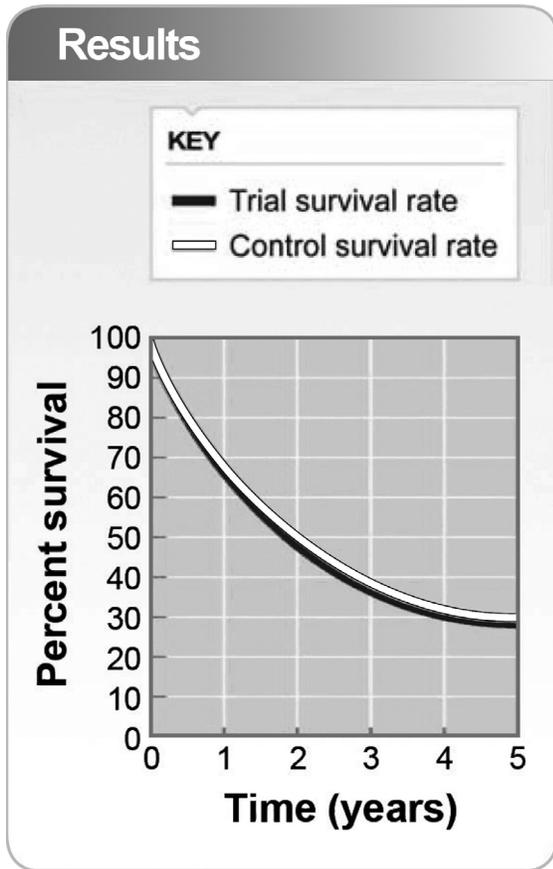
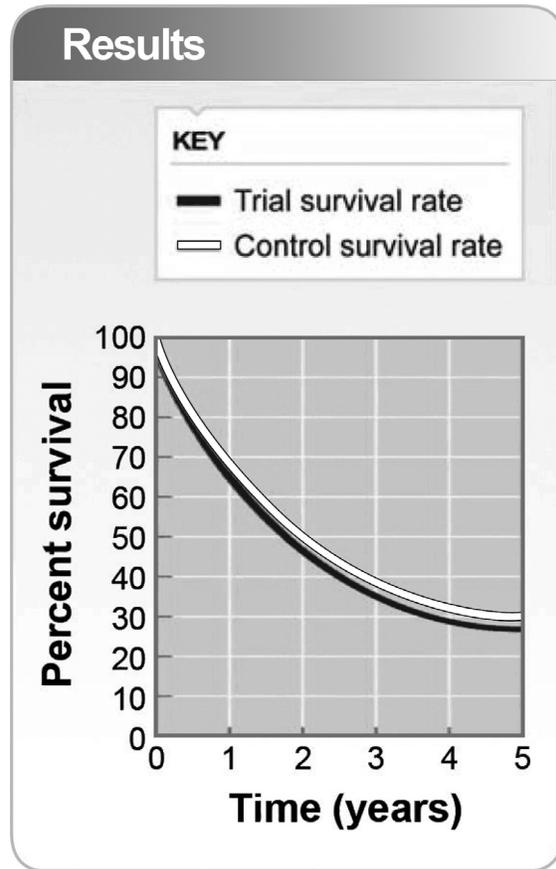


Figure 2. Drug B, decreased dose.



Changing the Dose of Drug C

Figure 1. Drug C, increased dose.

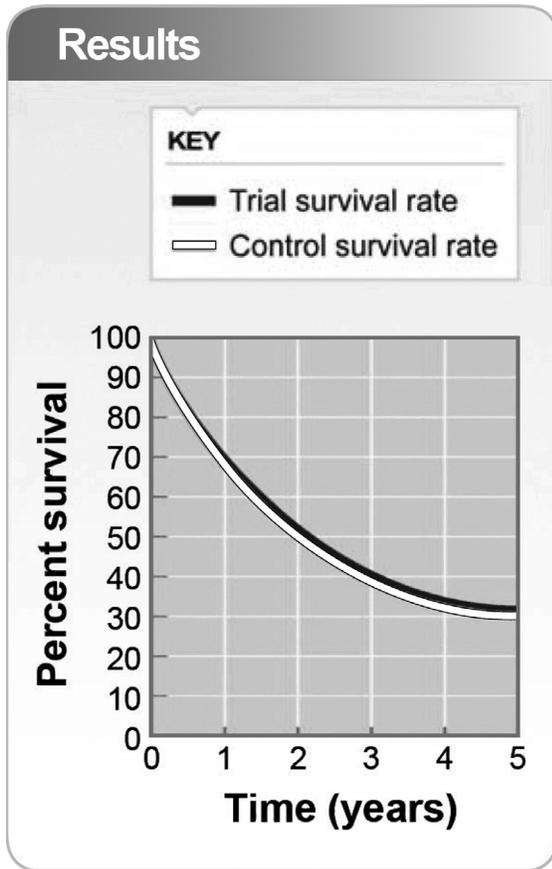
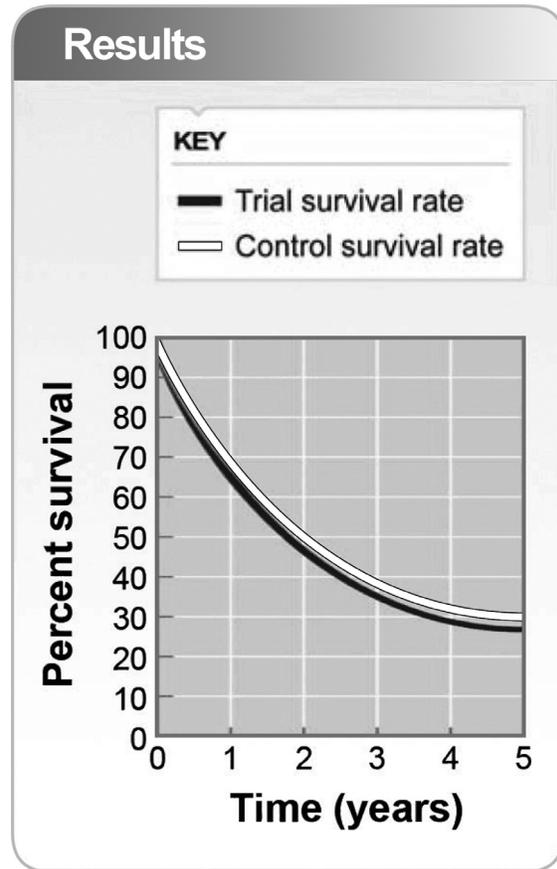
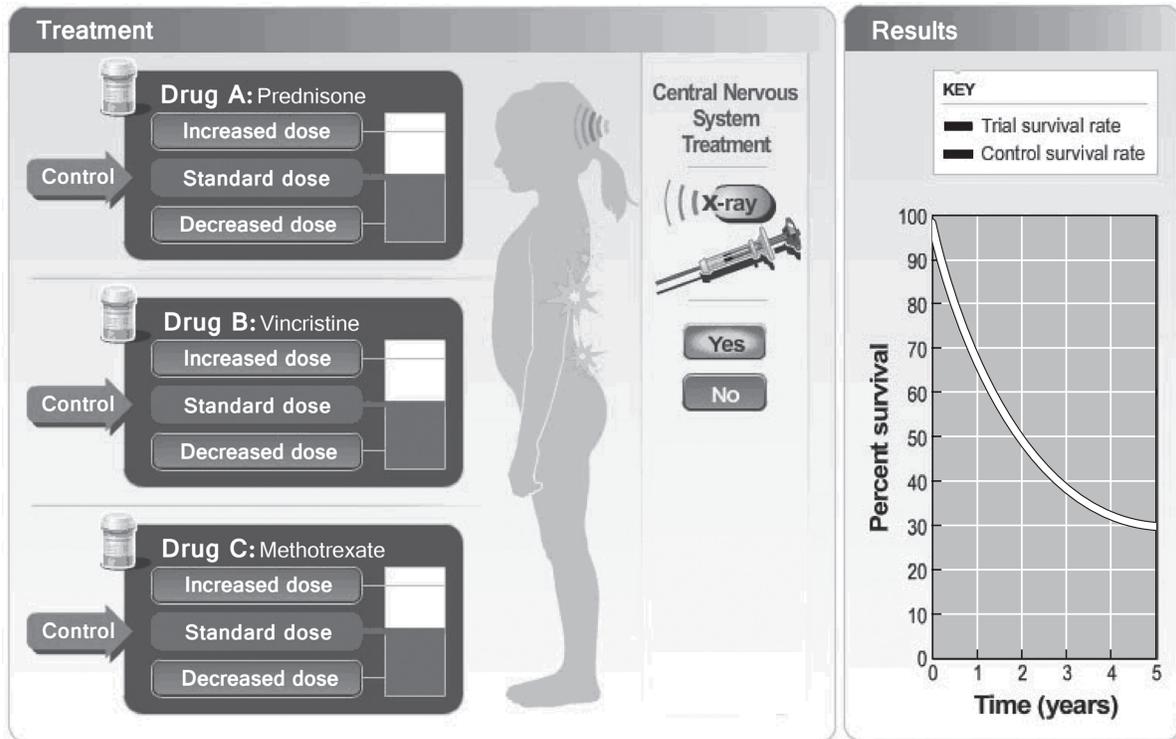


Figure 2. Drug C, decreased dose.



Central Nervous System Treatment

Figure 1. Designing a clinical trial. Left: Design of an experiment using standard doses of drugs A, B, and C with and without the central nervous system treatment. Right: Results of the experiment, where Trial is with the CNS treatment and Control is without it.



Interview with Hailey

INTERVIEWER: What was it like to go to a new high school after undergoing treatment for leukemia?

HAILEY: Being a freshman is hard already, but for me, it was even harder. After a year away, I didn't really fit in. I wasn't the same as the other kids. They were thinking about cars, cell phones, and dating. Some days, all I could think about was dragging myself to the next class without throwing up. It was strange; here I was, surrounded by 2,000 other people, and I felt more alone than I'd ever been in my entire life.

INTERVIEWER: So what happened?

HAILEY: Slowly, things started to change. I met new friends who made me laugh, and I reconnected with old friends I'd known since elementary school. My teachers helped me, too. Mr. Brinthom got me involved in theater, which made every day a new adventure. Dr. Bradley and my other teachers helped me discover a love of learning, especially science.

INTERVIEWER: Now that you're through with your treatment, what has cancer taught you?

HAILEY: Having cancer changed me. I had a new purpose. I wanted to help other teens who were going through the same thing.

INTERVIEWER: How did you go about helping teens with cancer?

HAILEY: I started delivering gift bags to a local hospital. Some people noticed and started sending me money to keep going—and I got noticed by the Leukemia and Lymphoma Society. I was even awarded the Spirit of Tom Landry Award last year by Mrs. Landry herself.

INTERVIEWER: What are your plans for the future?

HAILEY: I want to devote my life to fighting cancer as a pediatric oncologist. In the meantime, I'm helping out at events like a fashion show just for cancer patients.

INTERVIEWER: What can the rest of us do?

HAILEY: You don't have to find the cure for cancer to help someone in your own community. Sometimes, you just have to be there. Just get involved and do something—big or small.

Guidelines for the Poster

The information on your poster should be written in clear sentences in paragraph form.

Part 1: Information about the Disease

- What is the name of the disease?
- Is it a common or a rare disease?
- What are the disease symptoms?
- Who gets the disease?
- What causes the disease (and how do we know)?
- How is the disease treated?
- How might having the disease affect a person's
 - ability to participate in normal activities?
 - relationships with family, friends, classmates, and strangers?

Part 2: Summary of a Clinical Trial or Research Study

- What is the purpose of the clinical trial or research study?
- Describe how the clinical trial or research study was carried out.
- What were the results of the clinical trial or research study?
- What can you conclude from the evidence presented?

Research Study on Marfan Syndrome

Figure 1. Mice with the Marfan mutation. (© Brandon Laufenberg | iStockphoto.com)



1. Background

A drug called losartan is used to treat people with high blood pressure.

Many problems caused by Marfan syndrome, such as an enlarged aorta (blood vessel), are due to a substance that works as a signal between cells. If too many signals are sent, the aorta grows too big. When it becomes too big, it is weaker and tears more easily. Researchers wonder if a drug called losartan can block this substance and keep the aorta at the normal size. They are testing this drug first in mice with Marfan syndrome and then, they hope, in humans.

2. Study design

The study used three groups of mice:

Group 1: Healthy mice (without Marfan syndrome). They received no treatment.

Group 2: Mice with Marfan syndrome. They received no treatment.

Group 3: Mice with Marfan syndrome. They received the drug losartan.

After receiving the drug (or not) for six months, the amount of growth in the heart's aorta was measured.

Table 1. Marfan Study Results

Treatment group	Average amount of growth in aorta
Healthy mice (no drug)	0.20 millimeters
Marfan mice (no drug)	0.66 millimeters
Marfan mice (treated with drug)	0.18 millimeters

Clinical Trial on Childhood Leukemia

Figure 1. Combination drug therapy. (EyeWire)



Figure 2. Brain irradiation. (© Colleen Butler | iStockphoto.com)



1. Background

Since the 1960s, children with leukemia have had their heads X-rayed to prevent brain cancer. This treatment has worked well. Survival rates of children with leukemia have improved. Unfortunately, this treatment can also harm the ability of the brain to carry out its job.

Using more than one drug at the same time also has helped improve survival rates of children with leukemia. Researchers wondered whether the careful use of multiple drugs could keep survival rates high without using X-rays.

2. Study design

Children were assigned to one of two groups:

Group 1: Received combination drug therapy alone.

Group 2: Received combination drug therapy along with brain irradiation.

Table 1. Childhood Leukemia Study Results

Treatment group	5-year survival rate
Drug combination therapy without brain irradiation	94 percent
Drug combination therapy with brain irradiation	93 percent

Evaluation Rubric for Poster

Category	Excellent (5 points)	Good, but could be better (3 points)	Needs a lot of improvement (1 point)
Information about the disease is complete.	Each item on Part 1 of Master 5.1 is addressed.	Some items on Part 1 of Master 5.1 are not addressed.	Most items on Part 1 of Master 5.1 are not addressed.
Information about the clinical trial or research study is complete.	Each item on Part 2 of Master 5.1 is addressed.	Some items on Part 2 of Master 5.1 are not addressed.	Most items on Part 2 of Master 5.1 are not addressed.
Information on the poster is accurate.	Statements about the disease are supported by all relevant facts. Facts are accurate. Unrelated facts are not included.	Some supporting facts are missing or some supporting facts are not accurate. Some supporting facts are not relevant.	Most supporting facts are missing or they are inaccurate.
Information on the poster is clear and well written.	There are no errors in spelling or grammar.	There are a few errors in spelling or grammar.	There are many errors in spelling and grammar.
Poster design is creative and well executed.	Poster design is especially attractive, and the information is clearly presented.	Poster design is reasonably attractive, and most of the information is clearly presented.	Poster looks like it was made without much thought to an attractive and clear presentation.

Poster Score Sheet

Name: _____

Use the evaluation rubric to score the poster. Enter your score for each category on this score sheet. Include a specific reason (or reasons) for each score given.

Code number for the poster being evaluated _____

Category	Score	Reason for score (For example, if you find an inaccurate statement on the poster, list it here and include a correction.)
Information about the disease is complete.		
Information about the clinical trial or research study is complete.		
Information on the poster is accurate.		
Information on the poster is clear and well written.		
Poster design is creative and well executed.		
Total score		

What Do You Think Now?

Name: _____

1. What is a disease?
2. How do doctors tell if someone has a disease?
3. What do you think causes disease?
4. What does it mean to call a disease “rare”?

Another Letter from the Producer



Dear Principal:

I am pleased to learn that you are still interested in helping us develop our reality television show. We have been busy interviewing young people who have a rare disease, and we have selected a boy named Kevin to be the focus of the show.

Kevin has been diagnosed with a rare disease called Marfan syndrome. He is outgoing and loves sports, though recently he has had to give up playing because of his Marfan syndrome. Kevin has developed an interest in videography and has a real talent for it. He is eager to join the class and even wants to film parts of the show himself!

I will be bringing Kevin to the school sometime next month to meet you, your staff, and, most importantly, the students who will become his classmates. Of course, if you have any questions, please contact me.

Once again, thank you for your help with this project.

Sincerely,

Vincent Shifflett
Senior Producer
People Reality Productions

