BIOLOGICAL BODYGUARDS

a laboratory module investigating antibodies using the Enzyme Linked Immunosorbent Assay (ELISA)

Principal developer of Biological Bodyguards

Betty Brown, MS

Contributors to Biological Bodyguards

James "Maxx" Andersen, BFA
Lenis Chen, MEd
Cathy Fryar, MEd
Archana Gowda, BA
Dana Haine, MS
Jennifer Murphy, MA
Grant Parkins, MS
Lisa Pierce, MEd
Joy M. Salyers, MA
Amber Vogel, PhD
Jane Wright, MEd, Head of Revision Team
John Zhu, BA

Consultants during the development of Biological Bodyguards

Walter E. "Skip" Bollenbacher, PhD
Christine Muth, PhD
Brian Rybarczyk, PhD
Jory Weintraub, PhD

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Bio-Rad Explorer
ELISA Immuno Explorer Kit
Catalog #1662400EDU

bio-rad.com/ELISAkit
1-800-4BIORAD (1-800-424-6723)

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KEY TERMS

Acquired immunity — a specific response to specific foreign substances to which the body adapts with multiple exposures; also called adaptive immunity.

AIDS — acquired immunodeficiency syndrome, caused by the human immunodeficiency virus (HIV).

Anatomical barriers — natural barriers to infection such as skin, mucous membranes, ciliated epithelial cells, tears, and saliva.

Antibody — immunoglobulin protein formed in response to a challenge of the immune system by a foreign agent. Antibodies bind to specific antigens.

Antigen — any agent that provokes an immune response and is bound specifically by either antibodies or T cells. Also called immunogen.

Antiserum — blood serum containing antibodies defending against a specific antigen.

Assay — a test to detect the presence and/or concentration of a component, drug, or microorganism in the blood or other body fluids or tissues; see also ELISA.

Autoimmune disease — disease that results from the immune system making a mistake and mounting an immune response against one's own body; examples are systemic lupus erythematosus (lupus, SLE), rheumatoid arthritis, and multiple sclerosis (MS).

Bacteria — a diverse group of organisms whose members are unicellular and prokaryotic. Some members are deadly parasites.

Bacteriophage — a virus that infects bacteria, also called a phage; can be used to introduce foreign DNA into a bacterial genome.

B cells — one type of white blood cell (lymphocyte) which matures in the bone marrow; once activated, some B cells develop into plasma cells to make antibodies to the antigen and other B cells develop into memory B cells.

Cancer — a disease in which the body's own cells lose the ability to control growth.

Chromogenic — substrates that produce a colored product when acted upon by an enzyme.

Clone — a cell or group of cells that are all derived through cell division from the same parent cell and thus have identical genetic information.

Complement — one group of proteins that destroys bacterial cells.

Conjugate — a substance formed by the covalent bonding of two types of molecules such as HRP linked to an antibody.

Cytokine — any of a group of regulatory proteins secreted by cells of the immune system, including lymphokines (secreted by lymphocytes), monokines (secreted by macrophages), interferons (secreted by both) and interleukins (secreted by both). Cytokines bind to receptors on other cells to alter the behavior of cells.

ELISA — enzyme-linked immunosorbent assay, a tool which utilizes antibodies to detect a particular antigen.

Enzyme — a protein that acts as a biological catalyst. The molecule that an enzyme acts on is called its substrate; for example, the enzyme horseradish peroxidase oxidizes its substrate.

Epitope — a specific site on an antigen that is recognized and bound by an antibody.

Genetically modified organism (GMO) — an organism whose genetic material (DNA) has been altered in a way that does not occur naturally by mating or natural recombination.

HIV — human immunodeficiency virus, the virus that causes AIDS (acquired immunodeficiency syndrome).

Horseradish peroxidase (HRP) — an enzyme frequently used to label secondary antibodies.

Humoral response — also known as humoral immune response, occurs when B cells interact with the antigen, which eventually results in their transformation into antibody-producing plasma cells.

Hydrophobic — nonpolar compounds that are immiscible with water, literally "water fearing." The side chains of some amino acids are nonpolar, and hence protein sequences rich in these amino acids tend to locate to the interior of the protein in its native state, away from the presence of a solvent.

Immune cells — the cells of the immune system, including lymphocytes (B and T cells) and macrophages.

Immunocompetent — B cells and T cells that are fully developed and armed to fight infection. These will recirculate from blood to lymph to blood.

Immunodeficiency — weakening or defects of the immune response such that an individual is unable to mount an effective immune response; may have a genetic basis, result from a disease or other health factor, or be caused by immunosuppressive drugs.

Immunoglobulin (Ig) — general term for all types of antibodies; in the humoral response, B cells function to produce antibodies.

Immunology — the study of the immune system—the bodily system that protects the body from foreign substances, cells, and tissues by producing an immune response.

Interferon — one of the groups of proteins that alerts the body to the presence of an antigen; typically a virus or cancer. An adaptive or inflammatory response is then activated.

Interleukin — a type of protein released by T cells to activate immunocompetent B cells to make antibodies to respond to the antigen.

Innate immunity — the immunity with which a person is born. Nonspecific host defenses that exist prior to exposure to an antigen; includes cells such as circulating macrophages that respond to foreign invaders.

Lag time — the length of time (usually several days) from infection to antibody production.

Leukocyte — a white blood cell. The category includes lymphocytes, macrophages and other white blood cells.

Lymphocyte — type of white blood cell. Component of the immune system includes T cells (thymus - derived) and B cells (bone marrow-derived).

Lymphokine — proteins released by immunocompetent T cells into the blood stream that activate B cells to respond to the antigen. An example is interleukin.

Macrophage — a type of white blood cell that binds and engulfs foreign materials and antigens in a process called phagocytosis; two primary functions are 1) removing foreign cells and molecules from the blood, and 2) processing antigens and presenting them on their cell surfaces.

Memory B cells — as the activated B cell reproduces, it will also make memory B cells; these memory B cells have antigen-binding regions that are identical to those of the original parent B cell. The memory B cells persist in the body and the next time the antigen is encountered, it will be recognized more quickly and the response will be more vigorous.

Microplate — molded plastic plate consisting of multiple small wells. Usually in a 96-well format.

Multiple Sclerosis — an autoimmune disease that affects the central nervous system.

Opportunistic infections — infections that occur as a result of deficiencies in the immune system; for example, diseases like oral candidiasis and tuberculosis that occur in immunodeficient AIDS patients.

Passive immunity — the acquisition of antibodies from an external source; for example, antibodies passed from mother to infant or certain postexposure vaccines such as that for rabies. Passive immunity lasts only a few weeks and does not change with multiple exposures.

Pathogens — organisms that can cause disease. Pathogens include bacteria, viruses, fungi, infectious proteins called prions, and parasites.

Phage display — a method of producing novel antibodies to specific antigens using recombinant DNA technology.

Phagocytic barriers — white blood cells with the capacity to engulf and destroy microbes or antigens.

Phagocytosis — the ingestion and destruction of microorganisms, foreign matter, and debris from damaged cells by white blood cells (neutrophils and macrophages).

Physiological barriers — conditions within the body under which infectious agents cannot survive including body temperature and pH (as in the acid pH of the stomach).

Plasma cells — cells produced by activated B cells that release antibodies, which are proteins that bind to the antigen.

Primary antibody — the antibody in an immunoassay that binds a specific antigen, conferring specificity to the assay.

Rheumatoid arthritis — an autoimmune disease that causes joint pain.

Secondary antibody — in an immunoassay, the antibody that recognizes and binds the primary antibody, which is from a different species. Secondary antibodies are frequently labeled with an enzyme for easy detection.

Serum — the clear, sticky fluid obtained when the solid components (e.g., red and white blood cells) are removed from whole blood. The plural for serum from multiple patients or sources is sera.

Substrate — reactant produced by an enzyme-catalyzed reaction. The particular substrate frequently used in ELISA assays oxidizes to a blue color by the horseradish peroxidase enzyme.

T cells — one type of white blood cell (a lymphocyte) that starts in the bone marrow, enters the bloodstream, and matures in the thymus.

T helper cells — T_H cells (which are lymphocytes) must be activated by specific antigens before they become functional. These cells produce factors needed for the production of plasma cells and memory B cells.

Vaccination — the process of inducing acquired immunity by deliberately stimulating an immune response with a nonpathogenic form of a disease agent. Also called immunization. The first vaccination used cowpox to inoculate against smallpox.

Vectors — organisms that carry pathogens from one host to another. Vectors are frequently arthropods (e.g., ticks and mosquitoes).

Virus — ultramicroscopic infectious agent that replicates itself only within cells of living hosts; many are pathogenic.

Western blotting — a common technique for detecting proteins. The proteins are separated by electrophoresis based on size and/or charge.

White blood cell — another term for leukocytes.

SOURCES

BIO-RAD, ELISA Immuno Explorer™ Kit, Catalog #166-2400EDU

HBP310 Immunology. Retrieved August 25, 2006, from SUNY Stony Brook Web site: http://www.path.sunysb.edu/coursemat/hbp310immun.htm

The Key Components of the 5E Model

PHASE	WHAT THE TEACHER DOES THAT IS	
	Consistent with the 5E Model	Inconsistent with the 5E Model
ENGAGE 	• Creates interest • Generates curiosity • Raises questions • Elicits responses that uncover what students know or think about the concept/subject	• Explains concepts • Provides definitions and answers • States conclusions • Provides premature answers to students' questions • Lectures
EXPLORE 	• Encourages students to work together without direct instruction from teacher • Observes and listens to students as they interact • Asks probing questions to redirect students' investigations when necessary • Provides time for students to puzzle through problems • Acts as a consultant for students	• Provides answers • Tells or explains how to work through the problem • Tells students they are wrong • Gives information or facts that solve the problem • Leads students step-by-step to a solution
EXPLAIN 	• Encourages students to explain concepts and definitions in their own words • Asks for justification (evidence) and clarification from students • Formally provides definitions, explanations, and new labels • Uses students' previous experiences as the basis for explaining concepts	• Accepts explanations that have no justification • Neglects to solicit students' explanations • Introduces unrelated concepts or skills
ELABORATE 	• Expects students to use formal labels, definitions and explanations provided previously • Encourages students to apply or extend concepts and skills in new situations • Reminds students of alternative explanations • Refers students to existing data and evidence and asks "What do you already know?""Why do you think . . . ?"	• Provides definitive answers • Tells students they are wrong • Lectures • Leads students step-by-step to a solution • Explains how to work through the problem
EVALUATE 	• Observes students as they apply new concepts and skills • Assesses students' knowledge and/or skills • Looks for evidence that students have changed their thinking or behaviors • Allows students to assess their own learning and group process skills • Asks open-ended questions, such as "Why do you think . . . ?""What evidence do you have?""What do you know about x?""How would you explain x?"	• Tests vocabulary words, terms and isolated facts • Introduces new ideas or concepts • Creates ambiguity • Promotes open-ended discussion unrelated to concept or skill

(Trowbridge & Bybee, 1990), adapted by Biological Sciences Curriculum Study
Available online at http://science.education.nih.gov/supplements/nih1/diseases/guide/module3.htm

2005-06 North Carolina Standard Course of Study for Biology — Grades 9-12

*** Highlighted sections are objectives addressed in the Biological Bodyguards module

Strands: Nature of Science, Science as Inquiry, Science and Technology, Science in Personal and Social Perspectives. The strands provide the context for teaching of the content Goals and Objectives.

Competency Goal 1:
The learner will develop abilities necessary to do and understand scientific inquiry.

Objectives

1.01 Identify biological questions and problems that can be answered through scientific investigations.
1.02 Design and conduct scientific investigations to answer biological questions.
- Create testable hypotheses
- Identify variables
- Use a control or comparison group when appropriate
- Select and use appropriate measurement tools
- Collect and record data
- Organize data into charts and graphs
- Analyze and interpret data
- Communicate findings

1.03 Formulate and revise scientific explanations and models of biological phenomena using logic and evidence to:
- Explain observations
- Make inferences and predictions
- Explain the relationship between evidence and explanation

1.04 Apply safety procedures in the laboratory and in field studies:
- Recognize and avoid potential hazards
- Safely manipulate materials and equipment needed for scientific investigations

1.05 Analyze reports of scientific investigations from an informed, scientifically literate viewpoint including considerations of:
- Appropriate sample
- Adequacy of experimental controls
- Replication of findings
- Alternative interpretations of the data

Competency Goal 2:
The learner will develop an understanding of the physical, chemical and cellular basis of life.

Objectives

2.01 Compare and contrast the structure and functions of the following organic molecules:
- Carbohydrates
- Proteins
- Lipids
- Nucleic acids

2.02 Investigate and describe the structure and functions of cells including:
- Cell organelles
- Cell specialization
- Communication among cells within an organism.

2.03 Investigate and analyze the cell as a living system including:
- Maintenance of homeostasis
- Movement of materials into and out of cells
- Energy use and release in biochemical reactions

2.04 Investigate and describe the structure and function of enzymes and explain their importance in biological systems.

2.05 Investigate and analyze the bioenergetic reactions:
- Aerobic respiration
- Anaerobic respiration
- Photosynthesis

Competency Goal 3:
The learner will develop an understanding of the continuity of life and the changes of organisms over time.

Objectives

3.01 Analyze the molecular basis of heredity including:
- DNA replication
- Protein synthesis (transcription, translation)
- Gene regulation

3.02 Compare and contrast the characteristics of asexual and sexual reproduction.

3.03 Interpret and predict patterns of inheritance.
- Dominant, recessive and intermediate traits
- Multiple alleles
- Polygenic inheritance
- Sex-linked traits
- Independent assortment
- Test cross
- Pedigrees
- Punnett squares

3.04 Assess the impact of advances in genomics on individuals and society.
- Human genome project
- Applications of biotechnology

3.05 Examine the development of the theory of evolution by natural selection, including:
- Development of the theory
- The origin and history of life
- Fossil and biochemical evidence
- Mechanisms of evolution
- Applications (pesticide and antibiotic resistance)

Competency Goal 4:
The learner will develop an understanding of the unity and diversity of life.

Objectives

4.01 Analyze the classification of organisms according to their evolutionary relationships.
- The historical development and changing nature of classification systems
- Similarities and differences between eukaryotic and prokaryotic organisms
- Similarities and differences among the eukaryotic kingdoms: protists, fungi, plants, animals
- Classify organisms using keys

4.02 Analyze the processes by which organisms representative of the following groups accomplish essential life functions including:
- Unicellular protists, annelid worms, insects, amphibians, mammals, non vascular plants, gymnosperms and angiosperms
- Transport, excretion, respiration, regulation, nutrition, synthesis, reproduction, and growth and development

4.03 Assess, describe and explain adaptations affecting survival and reproductive success.
- Structural adaptations in plants and animals (form to function)
- Disease-causing viruses and microorganisms
- Co-evolution

4.04 Analyze and explain the interactive role of internal and external factors in health and disease:
- Genetics
- Immune response
- Nutrition
- Parasites
- Toxins

4.05 Analyze the broad patterns of animal behavior as adaptations to the environment.
- Innate behavior
- Learned behavior
- Social behavior

Competency Goal 5:
The learner will develop an understanding of the ecological relationships among organisms.

Objectives

5.01 Investigate and analyze the interrelationships among organisms, populations, communities, and ecosystems.
- Techniques of field ecology
- Abiotic and biotic factors
- Carrying capacity

5.02 Analyze the flow of energy and the cycling of matter in the ecosystem.
- Relationship of the carbon cycle to photosynthesis and respiration
- Trophic levels — direction and efficiency of energy transfer

5.03 Assess human population and its impact on local ecosystems and global environments.
- Historic and potential changes in population
- Factors associated with those changes
- Climate change
- Resource use
- Sustainable practices/stewardship

2005-06 North Carolina Standard Course of Study for Healthful Living — Grades 9-12

*** Highlighted sections are objectives addressed in the Biological Bodyguards module

Strands: Preparatory, Stress Management, Protecting Self/Others, Relationships, Nutrition/Weight Management, Substance Abuse, Personal Fitness, Healthful Lifestyles, Appreciation for Diversity, Social Wellness, Movement Forms, Fitness and Sport Literacy

Competency Goal 1:
The learner will direct personal health behaviors in accordance with own health status and susceptibility to major health risks.

Objectives

1.01 Assess own health status.

1.02 Accept responsibility for own health.

1.03 Determine individual control over health risks.

1.04 Compare relationship of health to quality of life.

1.05 Describe the procedures for organ donation, local and state resources, and benefits to society.

1.06 Identify the value for personal outcomes acquired from lifelong learning about health education.

Competency Goal 2:
The learner will apply skills of stress management to the prevention of serious health risks for self & others.

Objectives

2.01 Develop awareness of own control over stress.
2.02 Replace negative thoughts with positive.
2.03 Associate behaviors with personal, family, and cultural values.
2.04 Cope with losses appropriately.
2.05 Respond to others with empathy.
2.06 Identify symptoms of mental disorders and know where to seek professional assistance.

Competency Goal 3:
The learner will interpret health risks for self and others and corresponding protection measures.

Objectives

3.01 Interpret the importance of various health risks.
3.02 Explain activities taken for disaster preparedness.
3.03 Prioritize own health risks and construct a model health risk behavior self-management plan.
3.04 Identify risk behavior to manage.
3.05 Explain the importance of early detection, including medical examination and self-examination.
3.06 Assess behaviors and decisions as to their likelihood of resulting in infant morbidity and mortality.
3.07 Understand that a mutually faithful monogamous heterosexual relationship in the context of marriage is the best lifelong means of avoiding sexually transmitted diseases, including HIV/AIDS.
3.08 Refine skills and strategies for remaining or becoming abstinent from sexual intercourse, and avoiding sexually transmitted diseases, including HIV/AIDS.
3.09 Understand causes, consequences, and prevention of major health risk behaviors for own age group, including the transmission of HIV/AIDS.

Competency Goal 4:
The learner will apply relationship skills to the promotion of health and the prevention of risk.

Objectives

4.01 Analyze problems stemming from unhealthy relationships.
4.02 Implement skills which develop positive relationships.
4.03 Utilize anger management skills.
4.04 Identify resources for managing relationship problems.
4.05 Demonstrate conflict resolution skills.
4.06 Formulate principles for healthful dating relationships.

Competency Goal 5:
The learner will apply behavior management skills to nutrition-related health concerns.

Objectives

5.01 Provide detailed examples of how nutrition and physical activity can reduce the risk for chronic diseases.
5.02 Develop a personal healthful eating plan that incorporates food choices outside the home setting.
5.03 Develop specific eating plans to meet changing nutritional requirements, such as special dietary needs, athletic training, pregnancy, and food allergies.
5.04 Describe the pharmacological benefits of nutrients such as folic acid.
5.05 Evaluate specific diet plans found in popular magazines and books.
5.06 Design a plan for personal weight management based on a realistic and healthful body image.
5.07 Differentiate between healthful and harmful dietary habits.

Competency Goal 6:
The learner will choose not to participate in substance use.

Objectives

6.01 Recognize and seek help for depression.
6.02 Describe the potential effects on others of substance abuse by individuals.
6.03 Analyze motives for and consequences of steroid abuse.
6.04 Access services for dealing with substance abuse problems.
6.05 Explain behavior change strategies used in the treatment of substance abuse.
6.06 Delineate the risks involved in binge drinking.
6.07 Define "Fetal Alcohol Syndrome" and describe how it is prevented.

Competency Goal 7:
The learner will achieve and maintain an acceptable level of health-related fitness.

Objectives

7.01 Recognize and apply safety techniques, practices, and guidelines as related to fitness and nutrition.
7.02 Identify and analyze the principles of cardiovascular and strength development.
7.03 Complete a health related fitness test and assess personal level of physical fitness, including monitoring of the heart.
7.04 Interpret multiple sets of data in order to determine the best course of action for a healthy personal life-style.
7.05 Design and implement a personal activity program that demonstrates the relationship between physical activity, nutrition and weight management.
7.06 Recognize the implications of cardiovascular disease on healthy living.

Competency Goal 8:
The learner will exhibit regular physical activity.

Objectives

8.01 Identify resources in the community that can be accessed to maintain regular physical activity.
8.02 Evaluate the benefits of various physical activities.
8.03 Demonstrate and evaluate the importance of regular physical activity and proper diet.
8.04 Use goals and logical steps to develop an action plan to organize resources in order to be physically active.
8.05 Participate regularly in health-enhancing and personally rewarding physical activity outside the physical education class setting.
8.06 Appreciate and value the importance of regular physical activity.

Competency Goal 9:
The learner will demonstrate an understanding and respect for differences among people in physical activity settings.

Objectives

9.01 Execute respect for individual differences in physical activity settings.
9.02 Synthesize and evaluate knowledge about the role of physical activity in a diverse society.
9.03 Develop strategies for including persons of diverse backgrounds and abilities in physical activity settings.

Competency Goal 10:
The learner will demonstrate responsible personal and social behavior in physical activity settings.

Objectives

10.01 Work productively as a member of a team and contribute to the team's success through the assumption of a variety of noncompetitive duties.

10.02 Set personal goals for the development of skills, knowledge, and social responsibility, and work independently toward those goals.

10.03 Practice acceptable sportsmanship and fair play behaviors in physical activity settings.

10.04 Apply cooperative social skills to partner and group activities such as dance, outdoor activities, team building, problem solving, and cooperation games.

10.05 Demonstrate leadership in physical activities.

Competency Goal 11:
The learner will participate successfully in a variety of movement forms and gain competence towards lifetime physical activities.

Objectives

11.01 Participate at a competent level in small-sided games in at least one team sport.

11.02 Participate at a competent level in small-sided games in at least one individual or dual sport.

11.03 Participate at a competent level in at least one other movement form such as dance, gymnastics, aquatics, and outdoor pursuits.

11.04 Engage in various duties as they pertain to games and sport.

Competency Goal 12:
The learner will demonstrate a competent level of physical activity, sport, and fitness literacy.

Objectives

12.01 Exhibit knowledge of concepts in three different activities by officiating, judging, or refereeing.

12.02 Demonstrate competence in basic offensive and defensive strategies or tactics in team, individual, and dual activities.

12.03 Apply rules, biomechanical or movement principles, problem solving and fitness concepts to game and movement settings.

12.04 Know and apply safe practices in physical activity settings.

12.05 Apply statistical data about personal and group performance to the improvement of game play.

Biological Bodyguards
Correlation to the National Science Education Standards

The Teaching Standards	
Biological Bodyguards Correlation	
Each activity in the module provides short-term objectives for students. There is a conceptual flow of activities and help teachers plan a timeline for teaching the module. Use of this module helps teachers to update their curriculum in response to student interest in the topic. The module's focus is active, collaborative, and inquiry-based.	**Standard A: Teachers of science plan an inquiry-based science program for their students. In doing this, teachers** • develop a framework of yearlong and short-term goals for students. • select science content and adapt and design curriculum to meet the interest, knowledge, understanding, abilities, and experiences of students. • select teaching and assessment strategies that support the development of student understanding and nurture a community of science learners.
Student inquiry is encouraged by all activities in the module. The module promotes discourse among students, and challenges students to accept responsibility for their own learning by using hands-on, inquiry-based activities. The use of the 5E instructional model with collaborative learning is an effective way of responding to diversity in student backgrounds and learning styles.	**Standard B: Teachers of science guide and facilitate learning. In doing this, teachers** • focus and support inquiries while interacting with students. • orchestrate discourse among students about scientific ideas. • challenge students to accept and share responsibility for their own learning. • recognize and respond to student diversity and encourage all students to participate fully in science learning. • encourage and model the skills of scientific inquiry, as well as the curiosity, openness to new ideas and data, and skepticism that characterize science.
There are a variety of assessment components provided in the module, such as group discussion, data collection, and student writing activity. Answers are provided to help teachers analyze student feedback.	**Standard C: Teachers of science engage in ongoing assessment of their teaching and of student learning. In doing this, teachers** • use multiple methods and systematically gather data about student understanding and ability. • analyze assessment data to guide teaching.
The answers provided for teachers model respect for diverse ideas, skills, and experiences of all students. Students work collaboratively in teams to complete activities in the module. Discussion activities in this module model the rules of scientific discourse.	**Standard E: Teachers of science develop communities of science learners that reflect the intellectual rigor of scientific inquiry and the attitudes and social values conducive to science learning. In doing this, teachers** • display and demand respect for the diverse ideas, skills, and experiences of all students. • structure and facilitate ongoing formal and informal discussion based on a shared understanding of rules of scientific discourse. • model and emphasize the skills, attitudes, and values of scientific inquiry.

Biological Bodyguards
Correlation to the National Science Education Standards

The Content Standards	
Biological Bodyguards activity	
Pre-lab Activities **Wet Lab Activities** **Additional Activities:** Convince Your Peers Classroom guide to Arousing the Fury of the Immune System	**Standard A (Science as Inquiry) : As a result of activities in grades 9-12, all students should develop** **1. abilities necessary to do scientific inquiry.** • identify questions and concepts that guide scientific investigations • Use technology and mathematics to improve investigations and communications • Formulate and revise scientific explanations and models using logic and evidence • Recognize and analyze alternative explanations and models • Communicate and defend a scientific argument **2. understanding about scientific inquiry.**
Additional Activities Video: The Flu Immune System Animations	**Standard C (Life Science): As a result of their activities in grades 9-12, all students should develop understanding of** **1. the cell.** • Cells store and use information to guide their functions • Cells can differentiate, and complex multicellular organisms are formed as a highly organized arrangement of differentiated cells
Pre-lab Activities **Additional Activities** Super Bugs: An Evolving Concern	**2. molecular basis of heredity.** • In all organisms, DNA carries the instructions for specifying organism characteristics • Changes in DNA occur spontaneously at low rates
Additional Activities Superbugs Deadly Diseases Among Us	**3. biological evolution.** • Species evolve over time
Wet Lab Activities **Post-lab Activities** **Additional Activities**	**Standard E (Science and Technology): As a result of activities in grades 9-12, all students should develop understanding of** **1. abilities of technological design.** **2. science and technology.** • Scientists in different disciplines ask questions, use different methods of investigation, and accept different types of evidence to support these explanations • Science often advances with the introduction of new technologies • Creativity, imagination, and good knowledge base are all required in the work of science and engineering • Science and technology are pursued for different purposes
Additional Activities Protecting the Herd Prepare a pamphlet	**Standard F (Science in Personal and Social Perspectives): As a result of activities in grades 9-12, all students should develop understanding of** **1. personal and community health.** **5. human-induced hazards.** **6. science and technology in local, national and global challenges.**
Additional Activities Benefits of Biomedical Research	**Standard G (History and Nature of Science): As a result of activities in grades 9-12, all students should develop understanding of** **1. science as a human endeavor.** **2. nature of scientific knowledge.** **3. historical perspectives.**

INTRODUCTION

This module reviews various parts and functions of the immune system, in order to meet the following objectives:

1. To describe how the body defends itself against **pathogens** and antigens;
2. To identify the role of antibodies in the immune system;
3. To diagram the events of the humoral and cell-mediated immune responses of the immune system;
4. To describe the process of conducting an ELISA test, interpret the results, and recognize the real-life applications of such a test for the presence of **HIV**, pregnancy, and drug use;
5. To identify causes and preventative measures concerning the contraction of the HIV **virus** and to detail briefly the mechanisms of how the HIV virus works to infect a person.

BACKGROUND

The **immune system** of the body plays a crucial role in fighting illness and in preventing disease. Regardless of whether a person is attacked by something as common as an annoying cold virus or allergy, or as severe as **hepatitis** or **HIV**, it is the immune system that the body calls to action, in some cases more successfully than others. Although humans generally prove quite resilient against a host of bacterial and viral invasions, certain diseases can overwhelm the immune system. The progression of **AIDS** in an HIV-infected individual, for instance, cripples the immune system so that it can no longer sustain a person's health.

THE IMMUNE SYSTEM

Immunology is the study of the immune system, a system that protects the body from a host of foreign substances, toxins, and pathogens (agents that cause disease). A healthy immune system can tell the difference between so-called "self" and "non-self." Just as young children grow and learn to distinguish themselves from other people, so, too, does the immune system create a distinction between one's own body and outside substances. Typically, examples of "non-self" include foreign invaders such as **viruses** and **bacteria**. By fighting these "non-self" pathogens, the "self" ensures that it stays healthy.

A properly working immune system can also tell the difference between "self" and "altered-self." **Cancer**, or uncontrolled cell growth, is an example of "altered-self." Cancer cells change themselves to the point where they are destructive to the individual. The immune system works hard to get rid of these altered, cancerous cells. Other examples of "altered-self" include normal cells that become infected with a virus or bacteria. The infection alters the cells and makes them targets for the immune system.

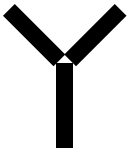
Unfortunately, cases exist in which one's own body will turn against itself. **Autoimmune diseases** occur when the body no longer recognizes the "self"; in these cases, the body will attack itself. Like a dog chasing its tail because it cannot recognize the tail as its own, the body cannot recognize its own cells and systems. Examples of autoimmune diseases include common but serious conditions such as **multiple sclerosis** and **rheumatoid arthritis**.

KEY PLAYERS

An **antigen** is any substance that triggers an immune response. When an antigen such as a bacteria or virus attacks the body, the body makes proteins called **antibodies** that bind tightly to, neutralize, and help destroy specific antigens. Also known as **immunoglobulins**, antibodies have Y-shaped structures. As shown in Figure 1, they have four polypeptide chains – two so-called "heavy" chains and two "light" chains.

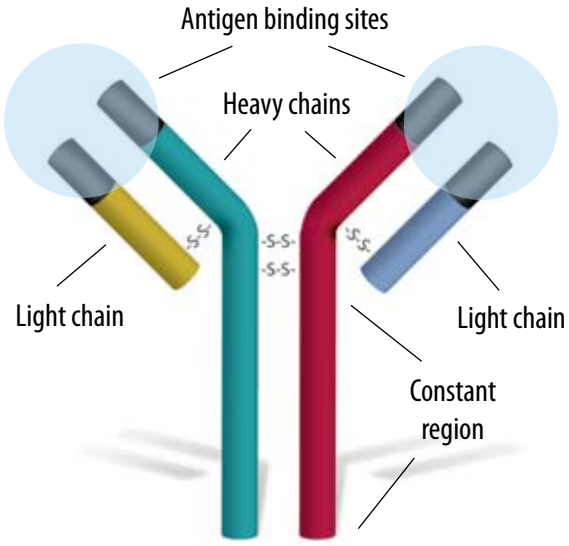
The antigen-binding portion of the antibody contains portions of both the heavy and light chains. Often called the "hypervariable" region, it allows for specificity of binding between antibody and antigen. This variable region of the antigen binding site can differ greatly from one antibody to another.

WHAT'S YOUR SIGN?

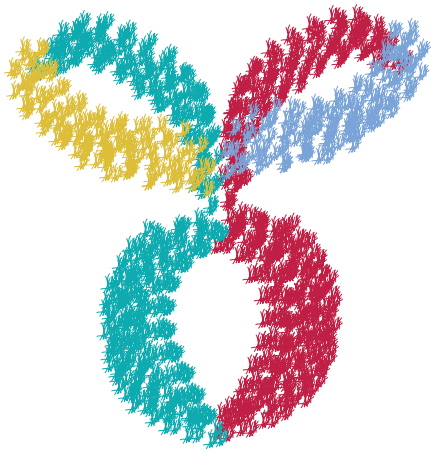


Antibodies are usually represented by a Y-shaped symbol.

FIGURE 1: ANATOMY OF AN ANTIBODY



An antibody's protein structure



Computer model of an antibody molecule

WEIGHTY ISSUES

An antibody's "heavy" and "light" chains are so called because of the length of each chain. The heavy chain has 440 amino acids, while the light chain has 220.

White blood cells (also known as **leukocytes**) play a key role in the body's immune system. The body responds to foreign invaders by calling white blood cells into action. White blood cell (WBC) counts often become elevated during infection. In cases of **immunodeficiency**, however, WBC counts tend to fall as a result of the body's inability to adequately fight infection. People infected with HIV, for instance, typically have low WBC counts.

One white blood cell that plays a key role in the immune response is the **lymphocyte**. Humans have approximately twenty trillion (20,000,000,000,000 or 2 x10^{13}) lymphocytes. These cells exist mostly in blood and the **lymphatic system**, a part of the circulatory system that supplies fluids to maintain balance in the body. The lymphatic system assists with the body's immune response.

Yet another important white blood cell of the immune system is the **macrophage**. Macrophages scout the body for foreign invaders and devour them. A macrophage is an example of a **phagocyte** (or "eating cell"), which is a cell that engulfs and takes in foreign material.

IMMUNITY

Immunity is the body's ability to respond to antigens. Many different types of immunity exist and they represent the variety of ways in which our bodies arm themselves to ward off infection. The body responds to antigens in the following ways:

1) INNATE IMMUNITY

The innate immune system serves as a first line of defense against antigens (infectious agents). It has four parts:

- **Anatomical barriers** are parts of the body, such as intact skin and mucous membrane, that act as barriers to infectious agents.

- **Physiological barriers** include body conditions, such as temperature and pH, that do not allow invaders to survive. For example, our body temperature of 98°F is a harsh temperature that kills many invaders. A fever kills many of the invaders that can survive under our normal body temperature. The acid in our stomach also kills organisms that enter. The set of physiological barriers also contains two important kinds of protein, **interferon** and **complement**.

Interferon alerts the body to the presence of an antigen (typically a virus or cancer); it then activates an adaptive and/or inflammatory response. Complement destroys bacterial infections.

• **Phagocytic barriers** are created when the white blood cells seek and destroy infected cells through a process known as **phagocytosis**.

• **Inflammatory response** is the release of interferon that triggers chemical signals to fight infection. Some common physical responses include fever, pain, redness, and swelling. All these responses increase blood flow to damaged body areas in order to repair and eliminate infectious agents.

2) ADAPTIVE IMMUNITY

If antigens sneak through the first lines of defense, the body responds by eliminating the antigen and remembering it, so it does not cause disease again. Two types of adaptive responses exist. The **humoral response** makes antibodies. The **cell-mediated response** makes specialized cells that kill infected cells or recruit other cells to kill.

WHAT'S IN A NAME?

The B and T cells are named after the first letters of the body parts where they mature. The B cell matures in the bone marrow. The T cell starts to develop in the bone marrow, but it travels through the bloodstream and matures in the thymus.

There are two types of lymphocytes involved in adaptive immunity. **B cells** produce antibodies in the humoral response. **T cells**, of which there are two types, produce the cell-mediated response:

• **Helper T cells** (T_H Cells) secrete proteins that activate B and T cells in response to an antigen.

• **Cytotoxic T** cells seek out and kill infected cells.

THE IMMUNE SEQUENCE

First, an antigen triggers the development of B and T cells, both of which come from a precursor cell made in the bone marrow. When B and T cells are fully developed and armed to fight against infection, they are **immunocompetent**. They re-circulate from blood to lymph to blood.

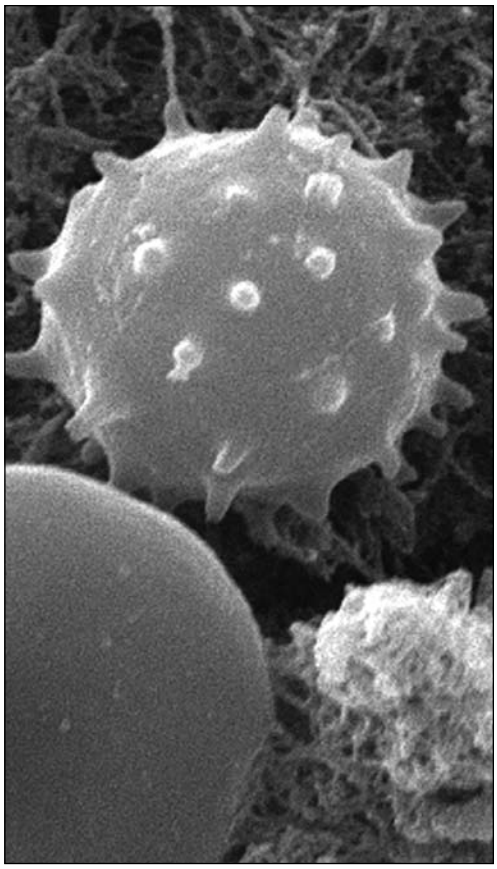


Photo by Janice Carr | Centers For Disease Control and Prevention

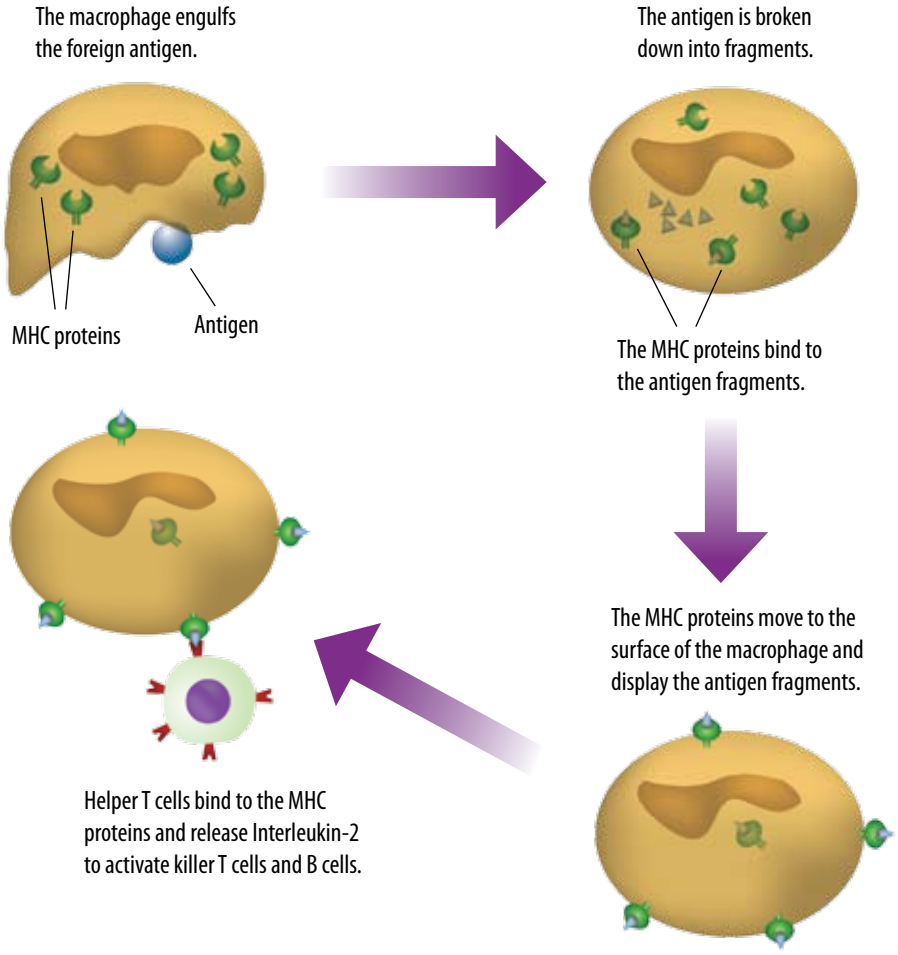
A scanning electron micrograph (SEM) of a white blood cell, magnified 7,766 times.

When a foreign invader such as a virus enters the body, a macrophage engulfs it. Once inside the macrophage, the virus is broken into many pieces. These viral pieces attach to a protein inside the macrophage called **major histocompatibility complex I (MHC)** (Figure 2). Once the MHC protein binds to the viral pieces, it moves to the plasma membrane of the macrophage and presents the viral proteins—the "antigens"—on the outside surface of the macrophage cell.

Now that the viral proteins are on the outside of the macrophage, an immunocompetent T cell circulating in the blood stream can respond. Acting as a sort of "intelligence-gathering" cell, the T cell senses a virus present in the body and triggers the adaptive immune Response. The T cell then releases proteins called **lymphokines**, an example of which is **interleukin**. The lymphokine moves through the blood stream and activates immunocompetent B cells. The B cells multiply and dif-

FIGURE 2: MAJOR HISTOCOMPATIBILITY COMPLEX (MHC)

A major histocompability complex protein binds to a foreign antigen after it has been engulfed by a macrophage and displays it on the surface of the cell to alert Helper T cells.



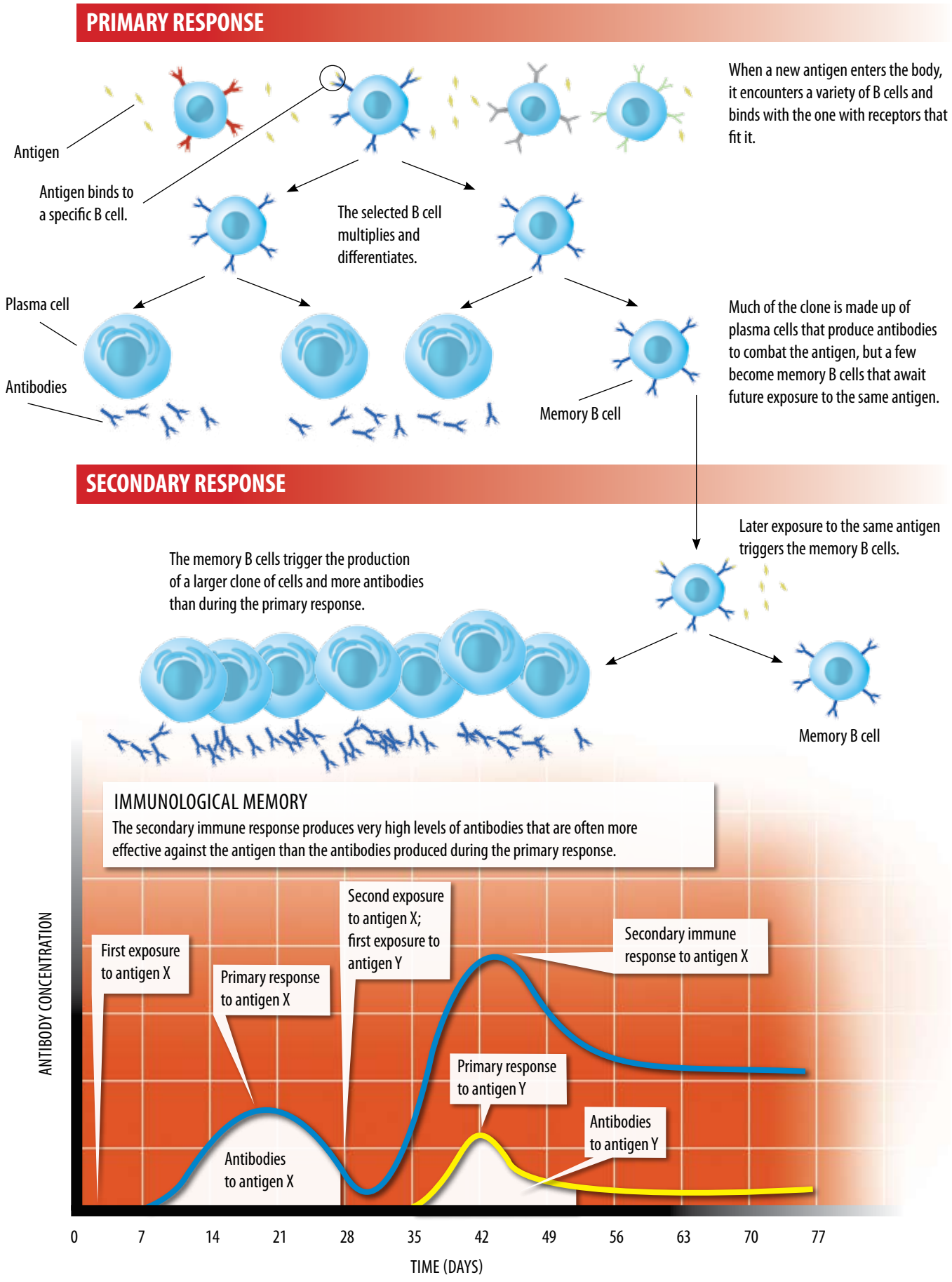
ferentiate into two types of cells — **plasma cells** and memory B cells. Plasma cells act as the "weapons experts" to produce the antibodies that are specific to the antigen.

This elaborate sequence of events, from infection to antibody production, typically takes several days, a delay referred to as **lag time**. The secondary response occurs much faster because of the formation of **memory B cells** that act as "historians" to remember the antigens. During a second infection of the same antigen, **memory B cells** work quickly to rid the body of the remembered invader (Figure 3).

Vaccinations are examples of passive immune transfer. Vaccinations take advantage of this rapid secondary response by intentionally exposing an organism to a harmless or less harmful form of a pathogen in order to stimulate the specific antibody response. If the organism encounters another exposure to the same pathogen, the quicker secondary response is launched by the memory B cells.

The term **passive immunity** is used whenever preformed antibodies are transferred from an immune organism to one that is not immune. For instance, passive immunity occurs when a mother transfers her antibodies to the fetus. Passive immunity is widely used in the treatment of immunodeficiency diseases.

FIGURE 3: PRIMARY AND SECONDARY RESPONSES



PRE-LAB

The pre-lab of this module introduces students to a range of different diseases and how they can be transmitted. Additionally, by assuming the characters of various cells and foreign substances, students engage in a kinesthetic role play to understand how the different parts of the immune system work together in the body's defense. Through this activity, students recognize that the different cells and parts of the immune system all have unique parts to play in fighting disease. The role play illustrates a sequence of events that rids the body of unwanted material, and strengthens it through the use of "memory" cells that can operate in future "attacks."

Students learn the importance of specificity within the immune system: antibodies will bind to an antigen with a particular shape or specific sequence (**epitope**). In this case, the way in which the antibody's shape in the role play will bind only to the specific antigen that "fits" mimics the way that true antibodies and antigens fit together biochemically.

WET LAB

In order to show how quietly, rapidly, and widely a virus such as HIV can be transmitted from person to person, the wet lab begins with an activity in which students "exchange fluids" with classmates. A pH indicator called phenolphthalein is used at the end of the exercise as a "test" to see who in the class has contracted the virus.

In addition to illustrating how quietly a virus like HIV can spread, this activity also provides a good review of acids and bases, since the "virus" is actually NaOH, or sodium hydroxide, which is a base.

In order to further promote awareness of HIV, and to provide students with first-hand scientific knowledge of how HIV testing is performed in real life, students perform an **ELISA (enzyme-linked immunosorbent assay)**. In addition to testing for antibodies to HIV, the ELISA also forms the basis for pregnancy and drug tests.

HIV: HOW IT FUNCTIONS

HIV, or human immunodeficiency virus, is known as a **retrovirus**. Instead of DNA, the HIV virus contains RNA. Using an enzyme known as **reverse transcriptase** (recall that the process of **transcription** normally produces one strand of mRNA from DNA), the virus makes DNA from RNA, which is a process that is essentially the reverse of that in regular transcription. The virus then incorporates its newly formed DNA into the DNA of the host cell. Once integrated into the host genome, the virus's genetic information replicates thousands of times to produce new viruses, which can then infect other cells.

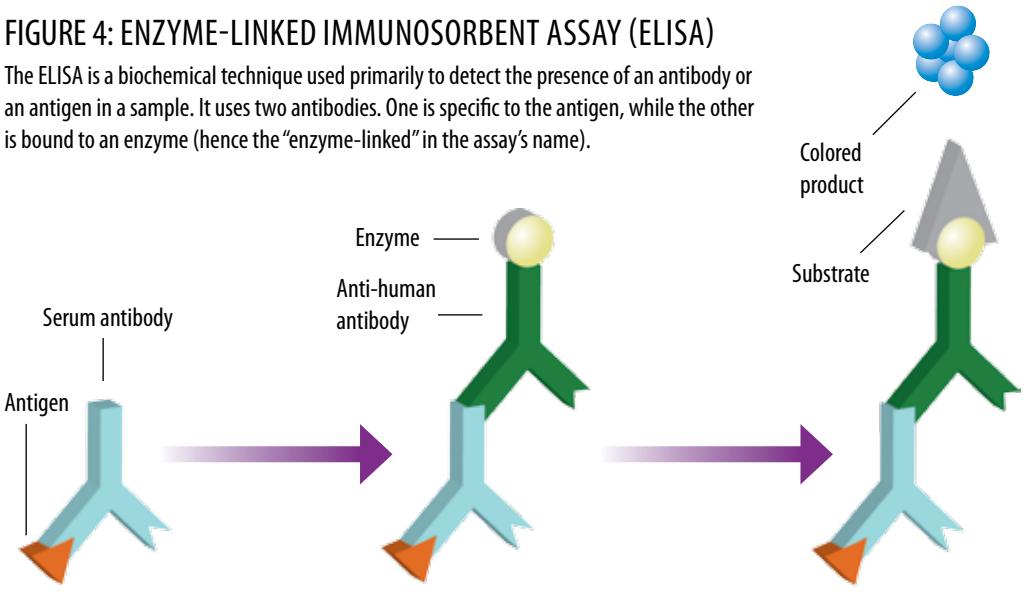
The presence of the HIV virus affects the level of **CD4** cells, or helper T cells, in the body. The number of CD4 cells in the body directly relates to the **viral load**, which reflects blood levels of HIV. The higher the amount of HIV in the blood, the higher the viral load and the lower the CD4 count. Research has shown that low CD4 counts, particularly those below 200 cells/µl, indicate a much higher susceptibility to opportunistic infection. Because a person with AIDS has a weakened immune system, the system proves less able to fight infections. Typically, people do not die because of the HIV virus itself; rather, they die because their weakened immune systems cannot fight the host of opportunistic infections that take advantage of this weakness. Criteria for a diagnosis of AIDS (as opposed to HIV) include a CD4 count below 200, as well as certain clinical criteria that relate to opportunistic infections.

THE ELISA

The enzyme-linked immunoabsorbent assay (ELISA) offers a quick and accurate test that can detect diseases in people, animals, and plants, determine indoor air quality, and establish if foods are labeled accurately. Diseases spread by exchange of bodily fluids such as HIV and SARS, diseases spread by food-borne agents like E.coli 0157:H7, and also diseases caused by **vector** transfers (e.g., a tick transmitting Lyme disease) can be detected using ELISA. The many varieties of dipstick tests, including home pregnancy

FIGURE 4: ENZYME-LINKED IMMUNOSORBENT ASSAY (ELISA)

The ELISA is a biochemical technique used primarily to detect the presence of an antibody or an antigen in a sample. It uses two antibodies. One is specific to the antigen, while the other is bound to an enzyme (hence the "enzyme-linked" in the assay's name).



A patient's serum is exposed to the antigen. If the corresponding antibody exists, it will bind to the antigen.

An anti-human antibody (secondary antibody) is added and binds to the constant region of the serum antibody. An enzyme is bound to this secondary antibody.

A substrate is added to the enzyme, resulting in a colored product. The colored product indicates the presence of the antigen and the antibody specific to that antigen.

tests and tests for illegal drug use, can show results in a matter of minutes. Dipstick tests use immunochromatography, which relies on many different antibodies to yield positive or negative results.

A person exposed to a particular antigen produces very specific antibodies in response. These specific antibodies, contained in the **antiserum**, can be detected by an ELISA test. ELISA is a lab tool that takes advantage of this specificity of antibodies.

To determine if these antibodies are present in a patient's **serum**, the serum is exposed to the corresponding antigen bound to the plastic surface of a plate. The antigen, which is a protein, attaches to the plastic as a result of interactions between the **hydrophobic** areas of the protein and the nonpolar surface of the plastic. If an antibody to the antigen is present in the serum, it will bind with the antigen when added to the plate, as in Figure 4.

Even though the antibody and antigen bind to each other, the reaction cannot be observed without some kind of indicator. The next step is to create an anti-human antibody that will bind to the constant region of the patient's serum antibody.

This anti-human antibody is commonly made by injecting a goat or rabbit with the constant region of human antibodies. The animal's immune system responds by making anti-human antibodies. A **conjugate** is formed when these anti-human antibodies are covalently bonded. Next, these anti-human antibodies are covalently bonded to **chromogenic enzymes** that produce a color with addition of a **substrate** (Figure 4). Commonly used enzymes include **horseradish peroxidase**, alkaline phosphatase, and ß-galactosidase.

TREATMENTS FOR COMMON ILLNESSES

So what happens when you feel sick and go to the doctor? Often, the doctor will prescribe **antibiotics** if you are not feeling well, in response to a **bacterial** infection. An example of a bacterium that causes disease is streptococcus, which causes strep throat.

Antibiotics, commonly prescribed for bacterial infections, kill both good and bad bacteria.

At other times, your doctor may tell you only to rest and drink plenty of fluids. In this case, you likely have a viral infection. Examples of **viral** infections include chicken pox and the flu. Such infections cannot be treated with antibiotics, which may destroy components of the bacterial cell wall or affect a bacteria's metabolism.

Fortunately, some viruses such as these, as well as some bacteria, can be prevented with the help of a **vaccine**. A vaccine carries a weakened or dead form of a bacteria, virus, or part of the virus. It provides material against which your body can make antibodies as part of an immune response; however, the material is not strong enough to make you sick. The next time your body gets the real bacteria or virus, it remembers that you have already been infected with the weaker version, and it can quickly respond.

In some cases, physicians do prescribe antibiotics to people with viral infections, particularly when their immune systems are weak and susceptible to opportunistic bacterial infections. It is important for patients to take the full round of antibiotics prescribed, even if they are feeling better after just the first or second dose. The antibiotics are designed to eliminate bacteria from the body; but if only the first few doses are taken, then some residual bacteria hang around and can multiply. Because antibiotics kill both good and bad bacteria, sometimes doctors recommend eating foods like yogurt in addition to taking antibiotics. Yogurt contains bacterial cultures that help to re-supply the body with good bacteria.

Recently, there has been growing concern about the overuse of antibiotics, because these could lead to antibiotic resistance. The idea is that, due to the process of natural selection, bacteria with favorable characteristics will survive the antibiotics. After these bacteria survive and multiply, they will pass along genes that are resistant to particular antibiotics. In this way, greater numbers of bacteria are likely to be created that hold a genetic resistance to antibiotics. This is another reason to take all antibiotics prescribed and to use antibiotics only when needed.

INTERDISCIPLINARY BRIDGES

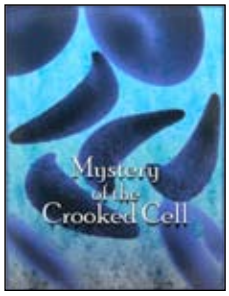
ELISA forms the basis for a wide array of tests, including drug tests. Many high schools across the country, including some in North Carolina, have now adopted randomized drug testing for students participating in extracurricular activities. A 2002 Supreme Court ruling stated that this randomized testing is constitutional, as long as the school restricts the testing to those involved in extracurricular activities. One of the interdisciplinary bridges asks students to discuss personal feelings about this testing and conduct a debate about the potential benefits and harms of such tests. Finally, they will place the issue within the context of the Bill of Rights and individual privacy.

CONNECTION TO OTHER MODULES

The module Biological Bodyguards examines the vital role of the body's immune system in fighting illness and preventing disease. Using an enzyme-linked immunosorbent assay (ELISA), students screen hypothetical patients for the presence of human immunodeficiency virus (HIV). The modules with accompanying wet-lab activities presented here are all health science-related. They also provide students the first-hand experience they need to understand common practices used by biotechnologists in their labs daily.

MYSTERY OF THE CROOKED CELL

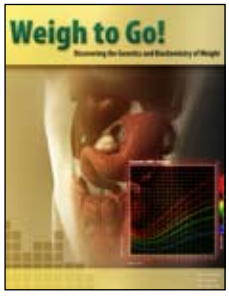
In this module developed by Boston University School of Medicine's CityLab, students



learn about the genetic basis for sickle cell anemia. Students observe functional differences in normal hemoglobin and sickle cell hemoglobin, which result from a point mutation. Electrophoresis is used as a tool to diagnose hypothetical patients for sickle cell disease. Both Mystery of the Crooked Cell and Biological Bodyguards introduce students to important diagnostic techniques used in molecular biology labs.

WEIGH TO GO!

This module invites to students to explore connections between obesity, diabetes, high



blood pressure, and high cholesterol. Using hydrophobic interactive chromatography, a key process in biotechnology research, students purify a genetically engineered designer protein (simulated leptin) from transformed bacteria cells. Biological Bodyguards and Weigh to Go! examine the body's immune system and the genetics and biochemistry of specific diseases.

BIOBUSINESS

In BioBusiness, students discover how businesses use recombinant DNA technology to tailor products to meet customers' needs. Students perform a procedure known as genetic transformation, which occurs when a cell takes up and expresses a new piece of genetic material — DNA. The resulting organism is known as a **genetically modified organism** or GMO. In medicine, diseases caused by defective genes are being treated by gene therapy, which is genetically transforming a sick person's cells with healthy copies of the gene involved in their disease. Like Biological Bodyguards, BioBusiness is health related and introduces students to concepts relating to the genetics and biochemistry of specific diseases.

SEQUENCE OF MODULES

A sequence relating the four modules is summarized below:

1. **MYSTERY OF THE CROOKED CELL**
   Students learn the genetic basis of sickle cell anemia and diagnose patients for the disease using gel electrophoresis.

2. **WEIGH TO GO!**
   Students learn about the genetics and biochemistry of weight. They examine obesity as a disease that has reached epidemic proportions.

3. **BIOLOGICAL BODYGUARDS**
   Students examine the vital role of the body's immune system in fighting illness and preventing disease.

4. **BIOBUSINESS**
   Students perform a procedure known as genetic transformation, which occurs when a cell takes up and expresses a new piece of genetic material.

HIV FACT SHEET

WHAT IS HIV?

HIV (human immunodeficiency virus) is the virus that causes **AIDS**. This virus may be passed from one person to another when infected blood, semen, or vaginal secretions come in contact with an uninfected person's broken skin or mucous membranes. In addition, infected pregnant women can pass HIV to their babies during pregnancy or delivery, as well as through breast-feeding. People with HIV have what is called HIV infection. Some of these people will develop AIDS as a result of their HIV infection.

WHAT IS AIDS?

- AIDS – stands for acquired immunodeficiency syndrome.
- Acquired – means that the disease is not hereditary but develops after birth from contact with a disease causing agent (in this case, HIV).
- Immunodeficiency – means that the disease is characterized by a weakening of the immune system.
- Syndrome – refers to a group of symptoms that collectively indicate or characterize a disease. In the case of AIDS this can include the development of certain infections and/or cancers, as well as a decrease in the number of certain cells in a person's immune system.

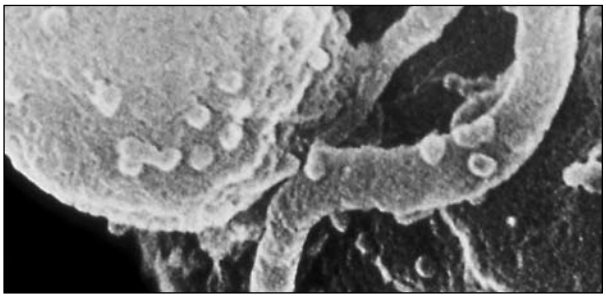
A diagnosis of AIDS is made by a physician using specific clinical or laboratory standards.

HOW DOES HIV CAUSE AIDS?

HIV destroys a certain kind of blood cell (CD4+ T cells) that is crucial to the normal function of the human immune system. In fact, loss of these cells in people with HIV is an extremely powerful predictor of the development of AIDS. Studies of thousands of people have revealed that most people infected with HIV carry the virus for years before enough damage is done to the immune system for AIDS to develop. However, sensitive tests have shown a strong connection between the amount of HIV in the blood and the decline in CD4+ T cells and the development of AIDS. Reducing the amount of virus in the body with anti-retroviral therapies can dramatically slow the destruction of a person's immune system.

HOW IS HIV PASSED FROM ONE PERSON TO ANOTHER?

HIV transmission can occur when blood, semen (cum), pre-seminal fluid (pre-cum), vaginal fluid, or breast milk from an infected person enters the body of an uninfected person.



A scanning electron micrograph of HIV viruses (the small round bumps) budding from a lymphocyte.

HIV can enter the body through a vein (e.g., injection, drug use), the lining of the anus or rectum, the lining of the vagina and/or cervix, the opening to the penis, the mouth, other mucous membranes (e.g., eyes or inside of the nose), or cuts and sores. Intact, healthy skin is an excellent barrier against HIV and other viruses and bacteria.

These are the most common ways that HIV is transmitted from one person to another:

- by having sex (anal, vaginal, or oral) with an HIV-infected person;
- by sharing needles or injection equipment with an injection drug user who is infected with HIV; or
- from HIV-infected women to their babies before or during birth, or through breast-feeding after birth.

HIV also can be transmitted through receipt of infected blood or blood-clotting factors. However, since 1985, all donated blood in the United States has been tested for HIV. Therefore, the risk of infection through transfusion of blood or blood products is extremely low. The U.S. blood supply is considered to be among the safest in the world.

Some health-care workers have become infected after being stuck with needles containing HIV-infected blood or, less frequently, when infected blood comes in contact with a worker's open cut or is splashed into a worker's eyes or nose. There has been only one documented instance of a health-care worker infecting patients—an HIV-infected dentist in Florida who apparently infected some patients while performing dental work.

WHAT ARE THE DIFFERENT HIV SCREENING TESTS AVAILABLE IN THE U.S.?

In most cases the EIA (enzyme immunoassay), performed on blood drawn from a vein, is the standard screening test used to detect the presence of antibodies to HIV. A reactive EIA must be used with a follow-up confirmatory test such as the **Western blot** to make a positive diagnosis.

BIOLOGICAL BODYGUARDS IMPLEMENTATION PLAN — PRE-LAB			
Activity	Estimated Time	Materials/Equipment	Purpose/Objectives/ Essential Question
Engagement	10 minutes	Bag containing 6 stuffed microbes responsible for the following diseases: HIV, kissing disease (mono), Ebola, syphilis, tuberculosis, and influenza (or 6 index cards, each listing one of the diseases) Engagement Activity: Disease List With Symptoms sheet Glogerm powder	**Purpose:** • To identify the anatomical and physiological barriers related to the immune system • To explain the process involved in the immune system's operation • To understand the concept of clonal selection **Objectives:** • To develop and articulate ideas about the body's defense against pathogens • To identify the role of antibodies in the immune system • To sequence the events of the humoral response of the immune system **Essential Questions:** • How does the body defend itself against pathogens? • What are the steps that make up the humoral response?
Exploration	25 minutes	Overhead transparency of humoral response One copy of the descriptions and diagrams of the components of the humoral response for each group Props for role play exercise: instructions, labels for participants, water bottle, models of antibodies and antigens, (optional) Christy Lane's Sports & Novelty Themes music	
Explanation	15 minutes	Television Show, "Dial in for a Dialogue with a Doc" Basic features of the immune system; 3rd line of defense: special features (specificity, diversity, self/nonself, recognition, memory)	
Elaboration	30 minutes	Television Show, "Dial in for a Dialogue with a Doc" Types of immunity; passive, active Dual defense: humoral and cell-mediated responses B and T cells What happens when immune response goes awry; autoimmune diseases	
Evaluation	10 minutes	Paper, pencil, worksheet to create concept map of the humoral response	

Alignment with NC Competency Goals	
Biology	Healthful Living
Goal 1 Objectives 1.01,1.02,1.03, 1.04, 1.05 Goal 2 Objectives 2.01, 2.02, 2.03, 2.04 Goal 3 3.01,3.04 Goal 4 Objectives 4.01, 4.03,4.04	Goal 1 Objectives 1.02, 1.06 Goal 3 Objectives 3.01, 3.04, 3.07, 3.08, 3.09

BIOLOGICAL BODYGUARDS PRE-LAB ACTIVITIES: UTILIZING THE 5E INSTRUCTIONAL MODEL

ENGAGEMENT

The teacher greets each student with a handshake as they enter the room, and secretly transfers Glogerm powder from his or her hand to the students' hands. Students then join one of six groups in the classroom.

As the bag of stuffed disease microbes is passed among the six groups of students, one student from each of the six groups selects a stuffed disease microbe from the bag or selects an index card with the name of the disease written on it from six index cards. The teacher then uses a black light to detect the Glogerm on the students' hands and explains that this Glogerm indicates the students have come into contact with a disease-causing organism. The teacher circulates throughout the six groups identifying symptoms of each group's particular disease. Finally, the teacher asks students to reflect on how their bodies respond to the invasion of these organisms.

EXPLORATION

Students are asked to describe in their own words the steps in the overhead transparency of the immune system process known as the humoral response. After the

students share their descriptions with the class, they take on the roles of the "major players" in the immune response and engage in a role play exercise. This role play activity allows the class to visualize the antigen invasion and the immune response when students take on the "roles" of the immune system's key players; antigen, macrophage, B cell (Plasma cell), Helper T cell and Memory B cell.

EXPLANATION/ELABORATION

A television show called "Dial in for a Dialogue with a Doc" provides a format for a more complete investiga-

tion of the immune system. One group of students call in with their questions and are provided answers by a group of students playing a panel of doctors.

During this elaboration phase, students have an opportunity to correctly use technical vocabulary and apply scientific reasoning. The instructor acts as a mediator and facilitates the discussion between the two groups. Some of the concepts covered during this "television show" are as follows:

- Causes of disease, including a review of Koch's Postulates
- Nonspecific immunity versus specific immune responses
- Lymphatic system involvement in the immune response
- The body's lines of defense in the fight against infection
- Two categories of the immune system response: cell-mediated response and the humoral response
- Autoimmune diseases
- Immunodeficiency diseases: SCID, HIV, and those induced by immunosuppressive drugs

EVALUATION

The evaluation activity serves to assess whether students have grasped the answer to the essential question:

how does your body defends itself against foreign invaders? Students are asked to complete a concept map to assess their understanding of the body's humoral response, including the major components and the order in which they appear.

BIOLOGICAL BODYGUARDS PRE-LAB ACTIVITIES

PURPOSES

- To identify the anatomical and physiological barriers related to the immune system
- To explain the process involved in the immune system's operation
- To understand the concept of clonal selection

OBJECTIVES

- To develop and articulate ideas about the body's defense against pathogens
- To identify the role of antibodies in the immune system
- To sequence the events of the humoral response of the immune system

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ENGAGEMENT ACTIVITY

MATERIALS NEEDED

- Glogerm powder
- Bag of 6 stuffed microbes (one per group) or 6 index cards, with one of these diseases written on each card: HIV, mononucleosis ("kissing disease"), Ebola, syphilis, tuberculosis (TB), and influenza.
- Engagement Activity: Disease List With Symptoms sheet.

INSTRUCTIONS FOR TEACHERS

- Secretly put Glogerm powder on your hands before class and shake hands with each student, or as many students as possible, as they enter the classroom.

- Arrange the students into six groups. Have one student from each of the six groups choose one stuffed disease microbe from the microbe bag (or one of the index cards) and encourage them to pass it around to members of their group.

- Start to cough, then explain that some of the students have been exposed to organisms that may cause a cold or influenza when they shook your hand as they entered the room.

- Use a black light to detect Glogerm powder on students' hands, indicating that students have come in contact with a disease-causing organism.

- Ask the students, "How do you feel?" Explain that they do not look very good. Then move around the room identifying symptoms expressed by each group based upon which stuffed microbe or index card they selected. (Symptoms for each disease can be found on the following page entitled Disease List With Symptoms.)

- Explain that the students' bodies have been invaded by these villains and ask the students, "How does your body respond to infection/infections?" Allow five minutes for students to reflect before asking them to share

Stuffed microbes, each representing a disease.

DISEASE LIST WITH SYMPTOMS

Sources: adapted from information available at www.webmd.com and www.disability.vic.gov.au

Ebola Hemorrhagic Fever (HF)

The signs and symptoms of Ebola HF are not the same for all patients. The table below outlines symptoms of the disease, according to the frequency with which they have been reported in known cases.

Time frame	Symptoms that occur in most Ebola patients	Symptoms that occur in some Ebola patients
Within a few days of becoming infected with the virus	High fever, headache, muscle aches, stomach pain, fatigue, diarrhea	Sore throat, hiccups, rash, red and itchy eyes, vomiting blood, bloody diarrhea
Within one week of becoming infected with the virus	Chest pain, shock, and death	Blindness, bleeding

Researchers do not understand why some people are able to recover from Ebola HF and others are not. However, it is known that patients who die usually have not developed a significant immune response to the virus at the time of death.

Human Immunodeficiency Virus (HIV) Infection

HIV infection progresses in stages. These stages are based on an individual's symptoms and the amount of the virus in the blood.

Initial stage: Flu-like symptoms often appear within 3 to 6 weeks of initial exposure to the virus, although symptoms can develop within just a few days. This first stage is called acute retroviral syndrome. Symptoms of acute retroviral syndrome are often mistaken for symptoms of another viral infection, such as influenza or mononucleosis, and may include:

- Abdominal cramps, nausea, or vomiting
- Diarrhea
- Enlarged lymph nodes in the neck, armpits, and groin
- Fever
- Headache
- Muscle aches and joint pain
- Skin rash
- Sore throat
- Weight loss.

Influenza

The symptoms of influenza (flu) appear suddenly and often include:

- Fever of 100°F (37.8°C) to 104°F (40°C), which can reach 106°F (41.1°C) when symptoms first develop. Fever is usually continuous, but it may come and go. And it may be lower in older adults than in children and younger adults.
- Shaking chills.
- Body aches and muscle pain (often severe), commonly in the back, arms, or legs
- Headache
- Pain when moving the eyes.
- Fatigue, a general feeling of sickness (malaise), and loss of appetite
- A dry cough, runny nose, and a dry or sore throat. The infected individual may not notice these during the first few days of the illness, when other symptoms are more severe. As the fever goes away, these symptoms may become more evident.

Mononucleosis

The early symptoms of mononucleosis, which resemble those of the flu, include:

- Deep fatigue
- Sore throat
- Headache
- Chills, followed by a fever
- Muscle aches.

After a day or two, the following additional symptoms may occur:

- Swollen lymph nodes
- Jaundice (a yellow tinge to the skin and eyes).
- A measles-like skin rash anywhere on the face or body. (Sometimes the rash develops suddenly after the infected individual takes amoxicillin for a severe sore throat.)
- Tiny red spots or bruise-like areas inside the mouth, especially on the roof of the mouth (palate)
- Soreness in the upper-left abdomen (from an enlarged spleen).

Tuberculosis (TB)

Individuals who have *latent* TB do not have symptoms and cannot spread the disease to others. Individuals who have *active* TB do have symptoms and can spread the disease to others. The specific symptoms depend on whether the infection is in the lungs (the most common site) or in another part of the body (extrapulmonary TB).

Symptoms of active TB in the lungs: Symptoms of active TB begin gradually and develop over a period of weeks or months. Someone infected with TB may have one or two mild symptoms and not even be aware of having the disease. Common symptoms may include:

- Coughing up thick, cloudy, and sometimes bloody mucus (sputum) from the lungs for more than two weeks
- A rapid heartbeat
- Swelling in the neck (because lymph nodes in the neck become infected).

Syphilis

Syphilitic infection unfolds in 3 distinct stages.

First Stage (4 to 6 weeks): At this stage, syphilis can be recognized by one or more sores on the penis, vulva (lip of the vagina), anus, or mouth. These sores, which are usually painless, may also be hidden from view in the rectum or on the cervix. This symptom usually appears 3-4 weeks after infection, but can occur between 10 and 90 days after infection. The sores usually heal completely in 4-6 weeks.

Second Stage (0-12 months): This stage of syphilis is characterized by a highly contagious rash on the soles of the feet or palms of the hands. This flat, red rash may also cover the entire body. Other symptoms include enlarged lymph nodes, hair loss, lumps on the genitals, and general tiredness. Individuals who do not receive treatment can remain infectious for up to two years.

Third Stage (may occur years later): If left untreated, the syphilitic infection may progress to this stage, which is characterized by severe problems with the heart, brain, and nerves. Results can include blindness, dementia, impotency, and even death.

EXPLORATION ACTIVITY, PART 1

MATERIALS NEEDED

• Copies of the sheets listing the steps of the humoral response
• Transparency of the humoral response

INSTRUCTIONS FOR TEACHERS

Using the same small student groups, give each group a sheet listing the main components of the humoral response and place the overhead transparency of humoral response (Figure 5) for the class to see. Ask students to list and describe the steps in the humoral response in their own words.

NAME _____

EXPLORATION ACTIVITY: PART 1

In your own words, describe the steps in the diagram of the immune system process (humoral response).

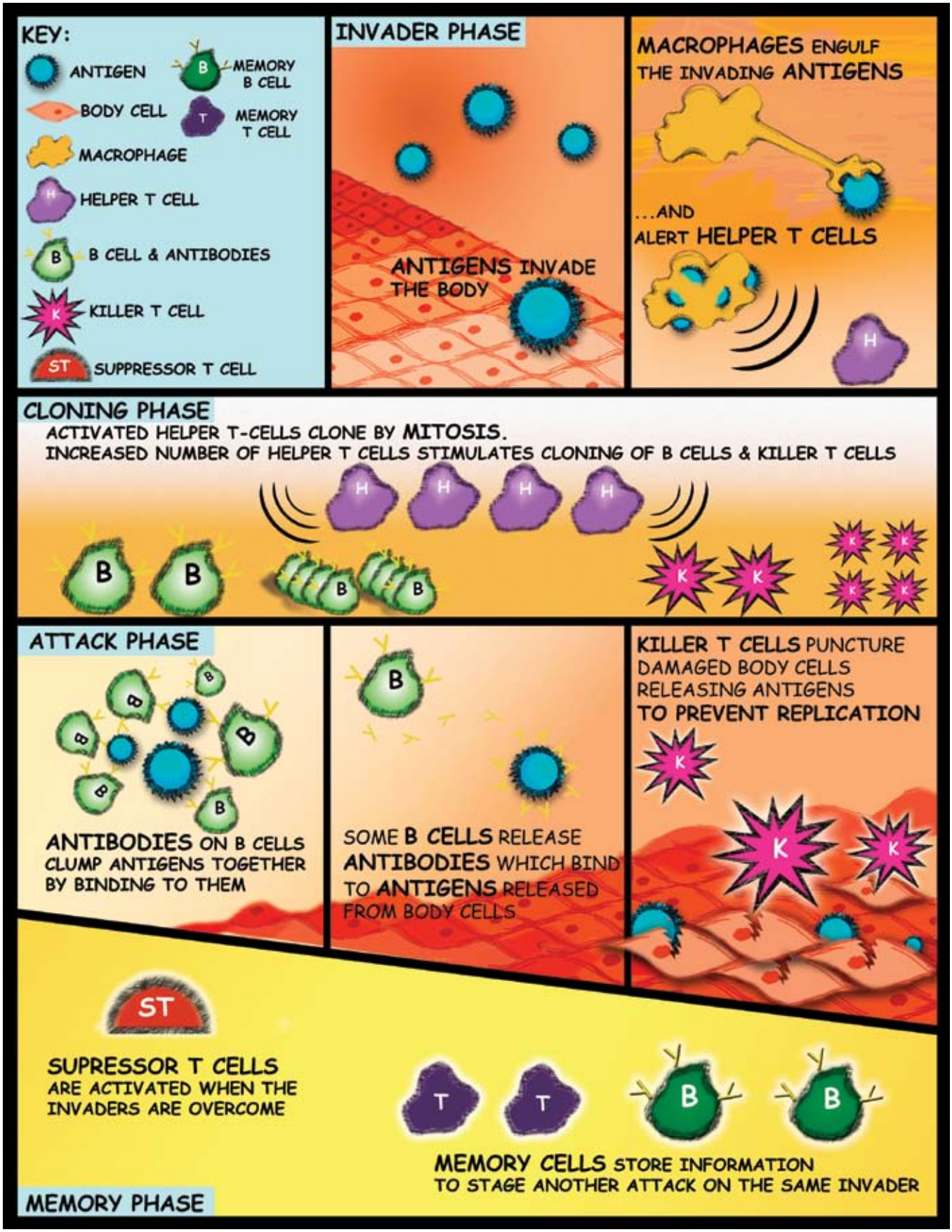
Invader identification phase

Cloning phase

Attack phase

Slowdown/memory cell phase

FIGURE 5: HUMORAL RESPONSE



EXPLORATION ACTIVITY, PART 2

Students will act out the invasion of the body by an antigen. Using the analogy of the armed forces, students take on the defensive roles of the humoral response.

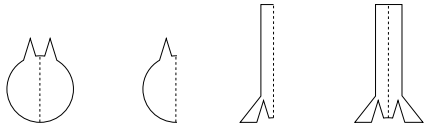
MATERIALS NEEDED

- (optional) Christy Lane's Sports & Novelty Themes music CD (available at www.christylane.com)
- CD player
- Water bottle for the Helper T cell to spray or activate the B cell to make antibodies
- Role-play cards with instructions
- Labels for participants
- Shapes of antibodies and antigens (print color copies on color card stock and cut out ahead of time)
    - 2 copies of shape A (fold one of the shapes along the center line to form shape B)
    - 10-15 copies of shape D (fold 2 copies along the center line to form shape C)

INSTRUCTIONS FOR TEACHERS

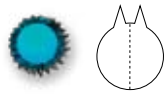
- Select several participants to be the actors in this role-play exercise.
- Give all participants time to read their role play cards and then allow them to act out the scene of an antigen invasion.
- Provide the shapes of the antigens and antibodies to the participants as follows.

Shapes:



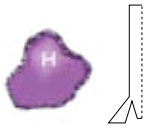
Roles for the participants:

- Antigen (The Body's Alien Invader) — Enter when you hear track #34, Jaws. Acting as an antigen, you will carry shape A with you. This shape is detected by the macrophage as a "wrong uniform" and stimulates macrophages into action.

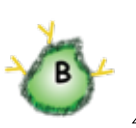


- Macrophage (The Inspector General) — Enter when you hear track #43, Pink Panther Theme. Acting as the "Inspector General" in the body, you are on the lookout for any foreign invaders. You can identify these foreign invaders by the "uniform" or shape they carry. Once you ID a foreign invader (antigen), carry shape B to activate Helper T cells.

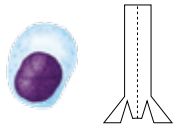
- Helper T cell (Central Intelligence Agency, or CIA, of the body) — Enter when you hear track #10, Mission Impossible. You can discern what is needed to battle the antigen. Once a macrophage, the "Inspector General," shows you shape B, you spring into action. To accomplish your job, you must pass shape C onto the B cells as you squirt the B cell with water (**cytokine**) to activate them into action.



- B Cell (The Arms Expert) — Enter when you hear track #25, Stars & Stripes Forever. You can launch a precise campaign by producing the precise ammunition to attack the antigens. Once the Helper T cell presents shape C to you and has activated you by squirting you with water (cytokine), you will mature into plasma cells to produce the "exact fit" antibodies to destroy the antigen.

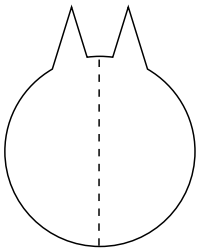
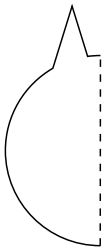


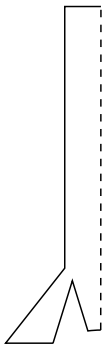
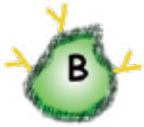
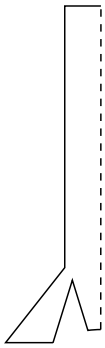
- Plasma Cell — As a plasma cell, take shape C and unfold it to form the "exact fit" (shape D) to latch onto the antigen. Throw these "exact fit" antibodies out among the antigen. These weapons (antibodies) will destroy only the antigens with shapes complementary to them.

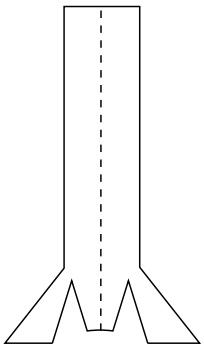
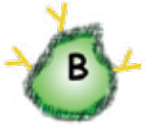


- Memory B Cell (The Chronicler/Archivist) — Enter when you hear track #7, Na Na Hey Hey. As you chronicle the events that occur when the immune system launches this specific response, you must record the wrong "uniform" of marker molecules (shape A) worn by this particular antigen and also the antibody shape used to stop the attack (shape D). The next time the enemy invades, you are authorized to immediately direct B Cell to start production of those particular weapons (antibodies).

EXPLORATION ACTIVITY, PART 2 ROLE PLAY CARDS

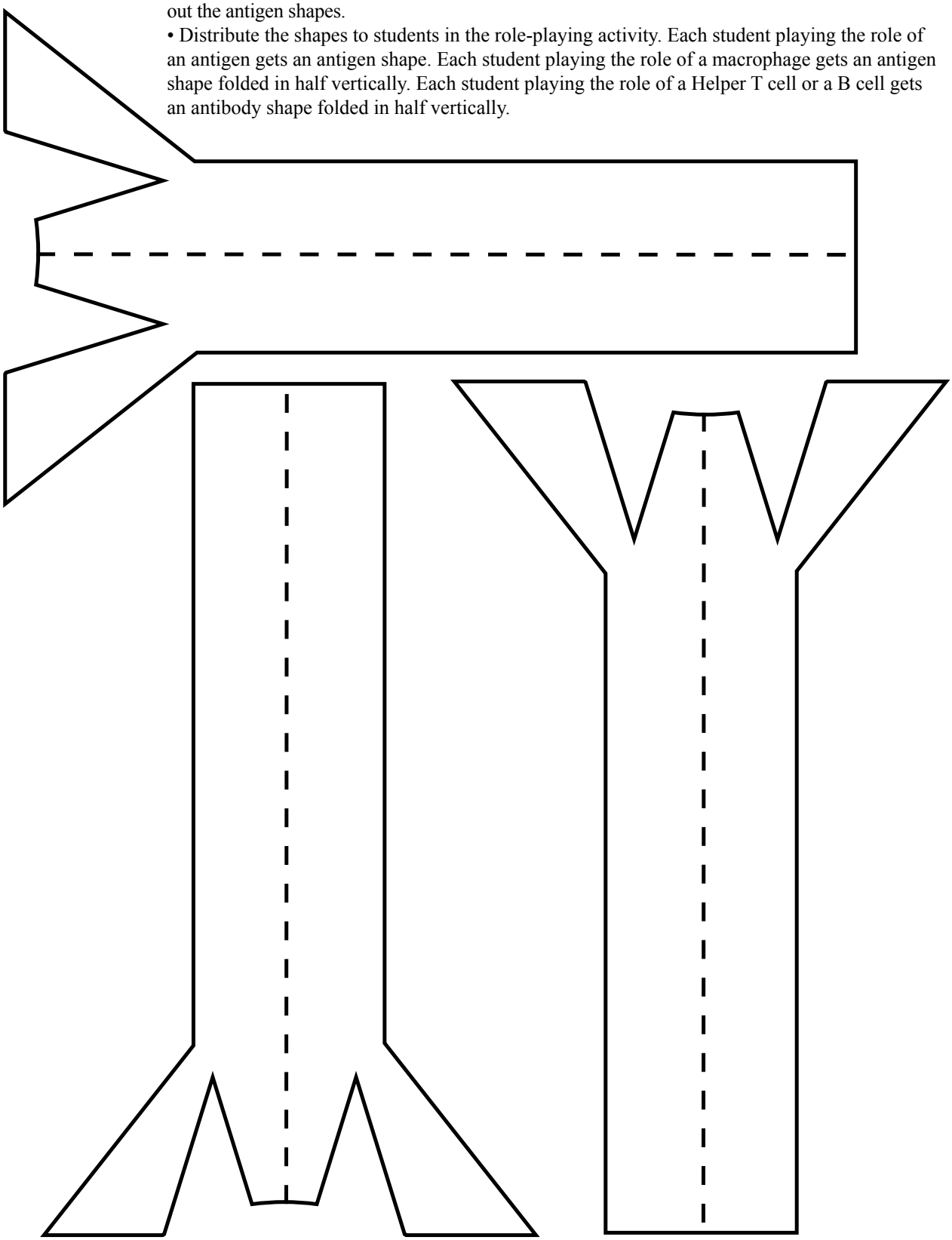
Role	Shape	Instructions
ANTIGEN (THE BODY'S ALIEN INVADER) 	 A	Enter when you hear track #34, "Jaws." Acting as an antigen, you will carry shape A with you. This shape is detected by the macrophage as a "wrong uniform," identifying you as an invader and stimulating macrophages into action.
MACROPHAGE (THE INSPECTOR GENERAL) 	 B	Enter when you hear track #43, "Pink Panther Theme." Acting as the "Inspector General" in the body, you are on the lookout for any foreign invaders. You can identify these foreign invaders by the uniform or shape they carry. Once you ID a foreign invader (antigen), carry shape B to activate Helper T cells.

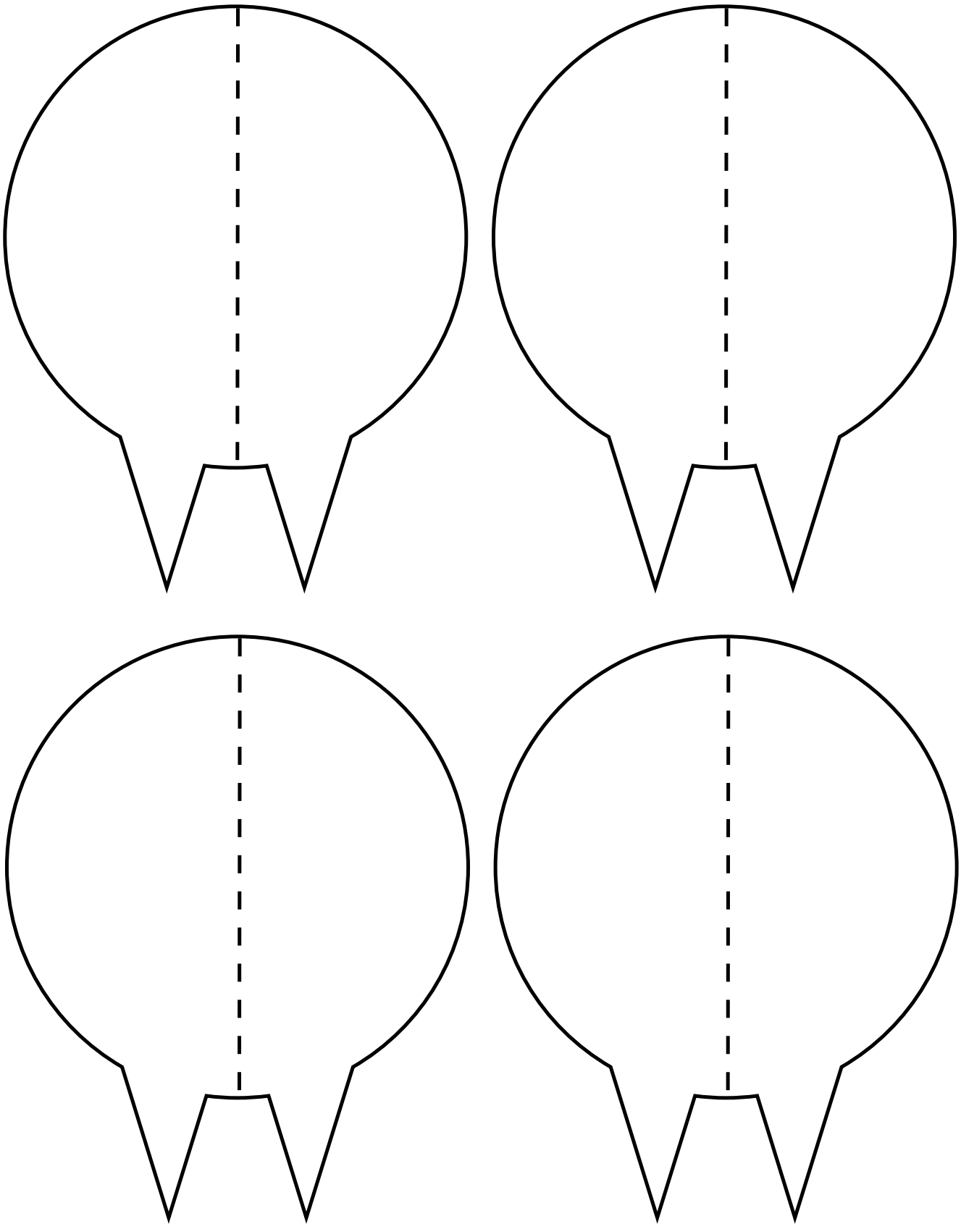
Role	Shape	Instructions
HELPER T CELL (CENTRAL INTELLIGENCE AGENCY, OR CIA, OF THE BODY) 	 C	Enter when you hear track # 10, "Mission Impossible." You can discern what is needed to battle the antigen. Once a macrophage, the "Inspector General," shows you shape B, you spring into action. To accomplish your job, you must pass shape C onto the B cells as you squirt the B cell with water (cytokine) to activate them into action.
B CELL (THE ARMS EXPERT) 	 C	Enter when you hear track # 25, "Stars & Stripes Forever." You can launch an exact campaign by producing the precise ammunition to attack the antigens. Once the Helper T cell presents shape C to you and has activated you by squirting you with water (cytokine), you will mature into plasma cells to produce the "exact fit" antibodies to destroy the antigen.

Role	Shape	Instructions
PLASMA CELL 	 D	As a plasma cell, take shape C and unfold it to form the "exact fit" (shape D) to latch onto the antigen. Throw these "exact fit" antibodies out among the antigen. These weapons (antibodies) will destroy only the antigens with shapes complementary to them.
MEMORY B CELL (THE CHRONICLER/ ARCHIVIST) 		Enter when you hear track #7, "Na Na Hey Hey." When you chronicle the events that occur as the immune system launches this specific response, you must record the wrong "uniform" of marker molecules (shape A) worn by this particular antigen and also the antibody shape used to stop the attack (shape D). The next time the enemy invades, you are authorized to immediately direct B Cell to start production of those particular weapons (antibodies).

INSTRUCTIONS FOR TEACHERS

• Make copies of this page on color card-stock paper and cut out the antibody shapes.
• Make copies of the next page (antigen shapes) on card-stock paper of a different color and cut out the antigen shapes.
• Distribute the shapes to students in the role-playing activity. Each student playing the role of an antigen gets an antigen shape. Each student playing the role of a macrophage gets an antigen shape folded in half vertically. Each student playing the role of a Helper T cell or a B cell gets an antibody shape folded in half vertically.





EXPLANATION/ELABORATION BACKGROUND INFORMATION

The following topics are addressed in the "Dial in for a Dialogue with a Doc" activity that follows.

THE CAUSES OF DISEASES

Antigens are not whole pathogens. They are molecules that may be chemical components of a pathogen's surface. Pathogens are types of antigens that cause disease and include viruses, bacteria, fungi, protozoan, and prions.

Koch's Postulates (Figure 8) established the germ theory of disease in 1876.

THE BODY'S DEFENSE SYSTEM

Lymphatic system (thymus and lymph nodes; Figure 9)

Types of immunity

- Innate
- Acquired or adaptive vs. passive (transferring antibodies)
- Supplemental body defenses
  - Vaccines
  - Antibiotics

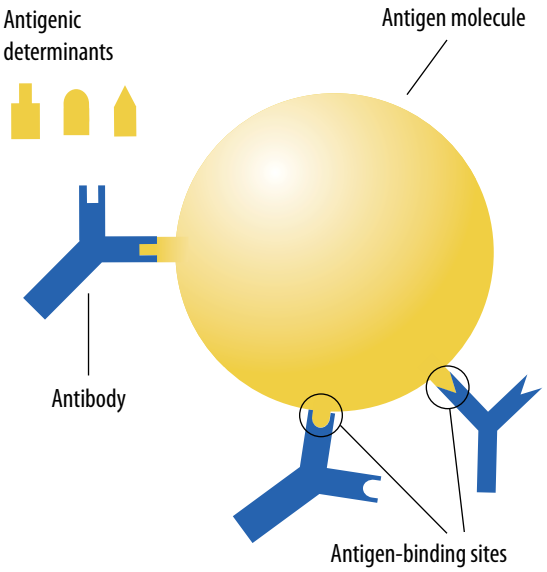
Nonspecific immunity (Figure 10A)

1. First line of defense
   - Skin and mucous membranes
   - Cilia, sweat, and tears (many body secretions contain lysosomes)
   - Acid secretions of the stomach
   - Fever
   - Symbiotic bacteria

2. Second line of defense: nonspecific mechanisms
   - Interferon (IFNs) — secreted by cells invaded by viruses that stimulate neighboring cells to produce proteins that help them defend against viruses.
     - Genetic engineering and mass production of interferons began in the early 1980s.
     - Interferons show promise against many viral diseases and some cancers.
   - Natural killer (NK) cells, phagocytic cells (neutrophils and monocytes)
   - Complement system — a group of about 20 proteins that "complement" defense reactions. They help attract phagocytes to foreign cells and destroy foreign cells by promoting cell lysis.
   - Inflammatory response — mast cells — initiate the immune response
     - Mast cells produce histamines, which increases blood flow to the surrounding tissues.
     - Antihistamines

FIGURE 6: ANTIGENIC DETERMINANTS

Antibodies bind to specific regions on the antigen molecule called antigenic determinants. Antibodies' antigen-binding sites and the antigenic determinants they bind to have complementary shapes. An antigen molecule usually has several different determinants, so different antibodies can bind to the same antigen.



3. Third line of defense (Figure 10B): immune response (targeted at specific antigens)
   - Specificity: self /nonself recognition, MHC (tissue rejections)
     - MHC (major histocompatibility complex) or HLA (human leukocyte antigens)
     - Antigen antibody specificity
       Five classes of antibodies, each associated with a particular activity: IgG; IgA; IgM; IgD; IgE
     - Antibody Structure/epitopes (antigenic determinants, Figure 6)
       Diversity — explanation of how the immune system produces millions of different antibodies
   - Lymphocytes: formation of T cells and B cells
     - Types of T Cells — pass through the thymus (Helper T CD4+, CD8+ Killer or cytotoxic, Memory T)
     - B Cells originate and mature in bone marrow, become plasma cells, memory B cells
     - Immunocompetence
   - Immunological memory (Memory B & T cells)
     - Primary and secondary immune response

The responses of the immune system are categorized into two kinds of reactions:

1. Cell-mediated (mostly uses T cells and responds to any nonself cell, including cells invaded by pathogens)
2. Humoral response (or antibody-mediated response)

What happens when the immune system goes awry?

- Hypersensitivity (Figure 11) — occurs when the immune system overreacts to an antigen. Examples include: allergy, anaphylactic reactions, and contact sensitivity (such as to poison ivy).
- Immunodeficiency — occurs when individuals cannot mount an effective immune response (SCID or "bubble boy" disease, HIV, or immunosuppressive drugs).
- Autoimmune diseases result from the immune system inappropriately mounting an immune response against itself.
  - Examples include: lupus (systemic lupus erythematosus, SLE), rheumatoid arthritis, scleroderma, and Sjogren's syndrome, which affect a wide range of tissues; diabetes (insulin dependent), which affects the pancreas; Crohn's disease, which affects the bowel; Graves disease, which affects the thyroid; chronic fatigue syndrome.

Clonal selection occurs when an antigen introduced into the body activates only a tiny number of lymphocytes. These "selected" cells then proliferate, forming a **clone** of cells (a population of genetically identical B cells or T cells).

Monoclonal antibodies (Figure 7) occur when all cells producing the antibodies are descendants of a single cell. Monoclonal antibodies are harvested from cell cultures rather than from animals. They show great promise in treating diseases such as cancer.

FIGURE 7: MONOCLONAL ANTIBODIES

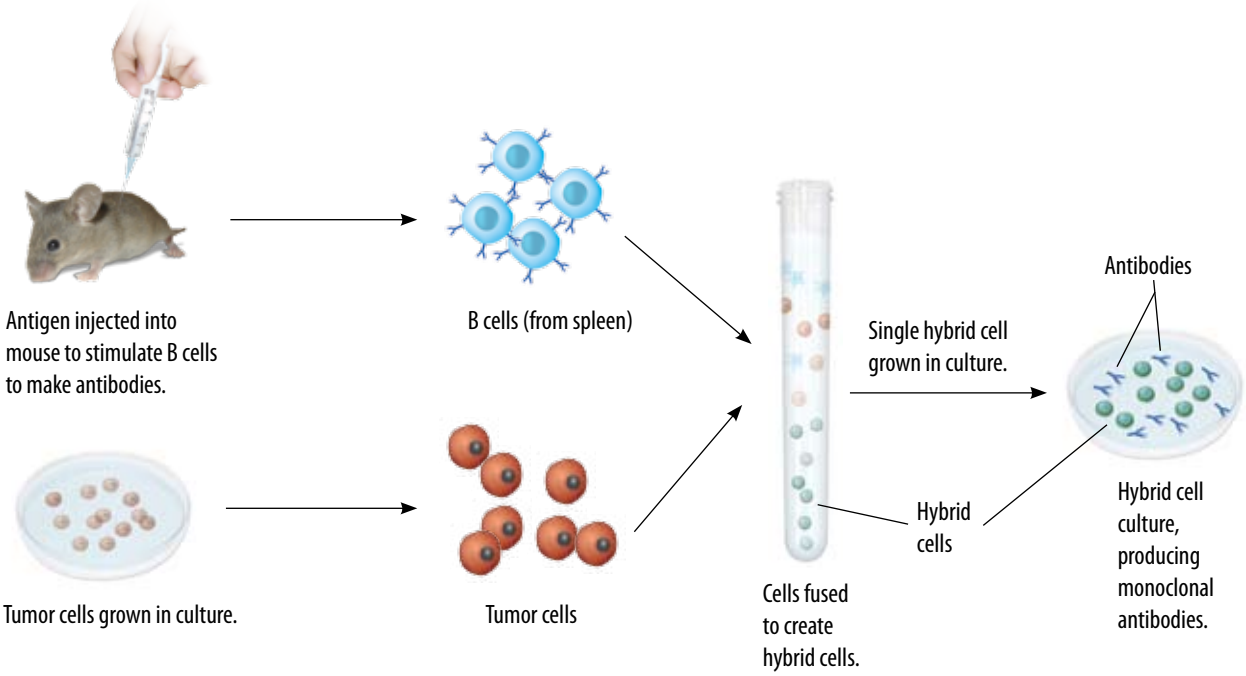


FIGURE 8: KOCH'S POSTULATES

FINDING THE CAUSE

Robert Koch, a German physician who discovered rod-shaped bacteria in the blood of cattle suffering from anthrax, used these four diagnostic criteria for identifying disease-causing bacteria:

1. The same, specific pathogen must be identified in each animal (host) that has the disease.
2. The pathogen must be isolated from a host and grown in a pure culture, one in which no other kinds of cells are present.
3. The original disease must be produced in experimental hosts that are inoculated with the pathogen from the pure culture.
4. The same pathogen must be isolated from the experimental hosts after the disease develops in them.

USUAL PROCEDURE FOR DEMONSTRATING KOCH'S POSTULATES

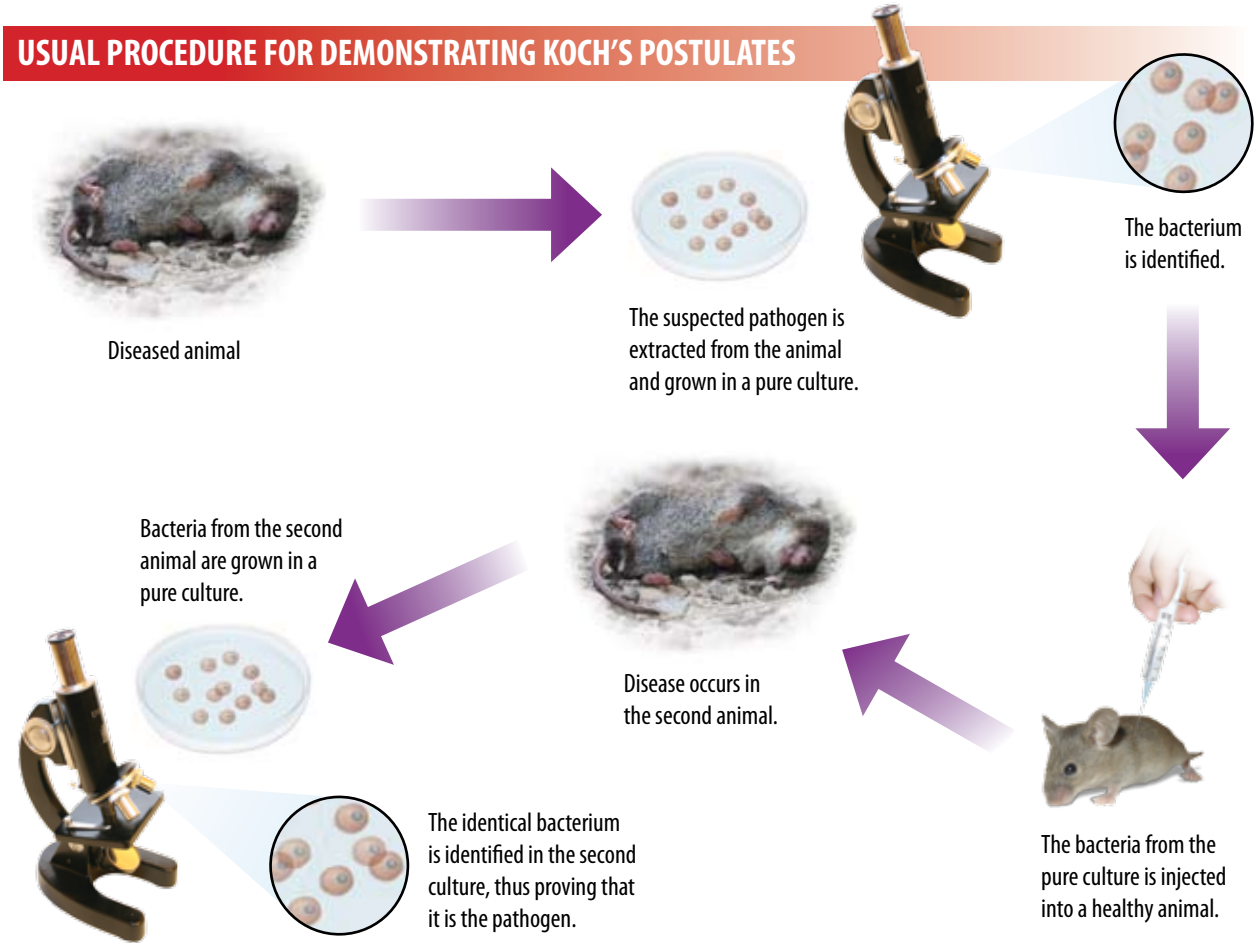
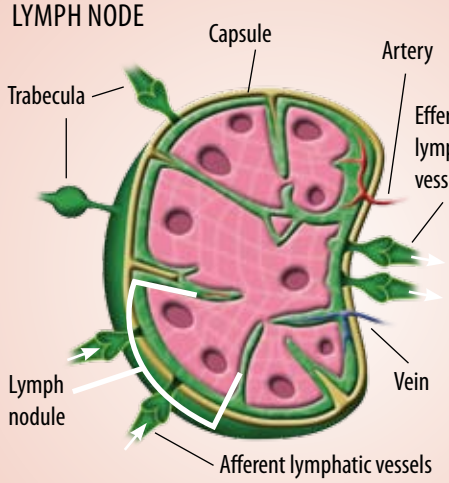


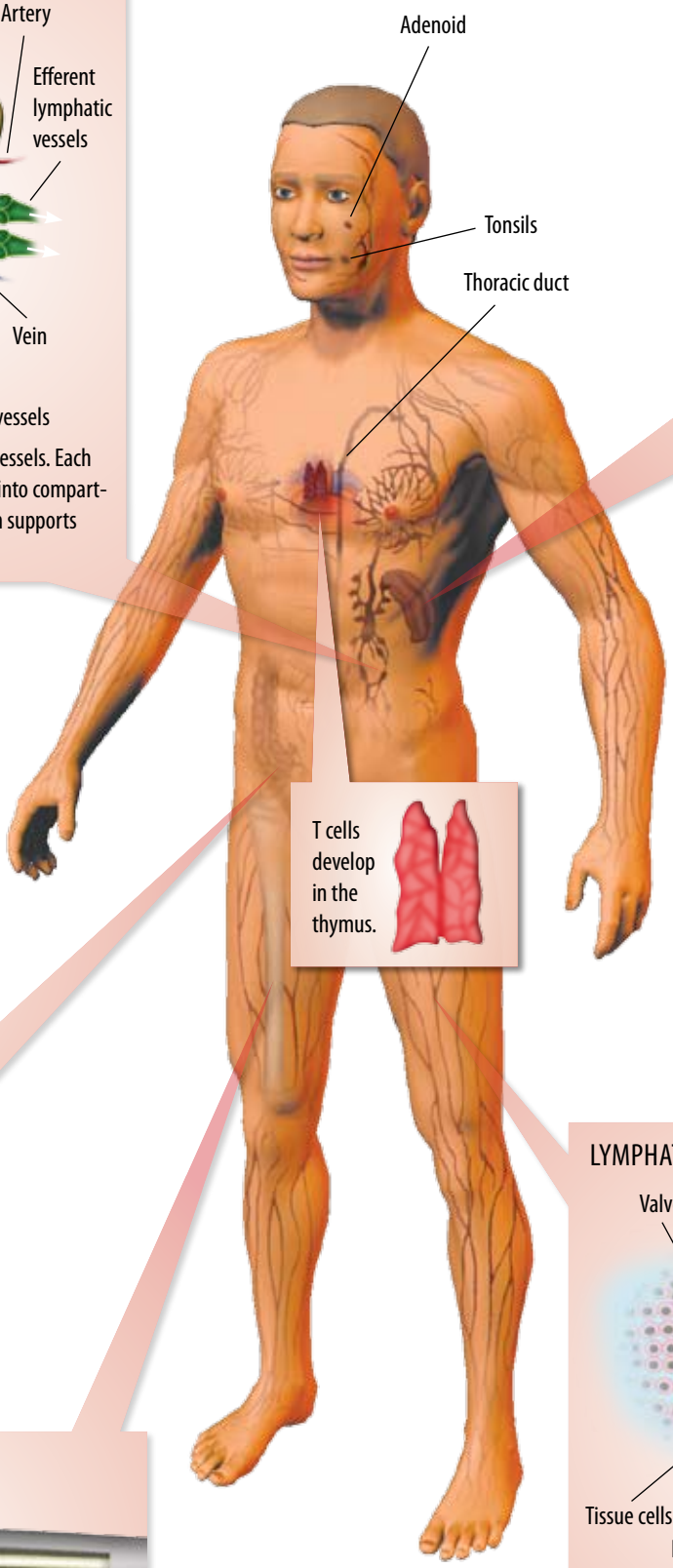
FIGURE 9: THE LYMPHATIC SYSTEM

The lymphatic system is a network of vessels, tissues, and organs that helps the body regulate fluid balance and fight infection.

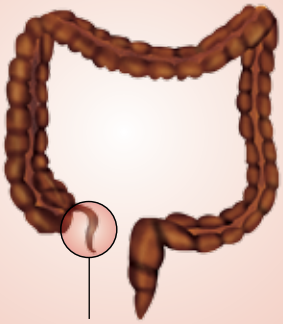
LYMPH NODE



Lymph nodes are clustered along lympathic vessels. Each node is surrounded by a capsule and divided into compartments that contain a network of fibers, which supports lymphocytes and macrophages.

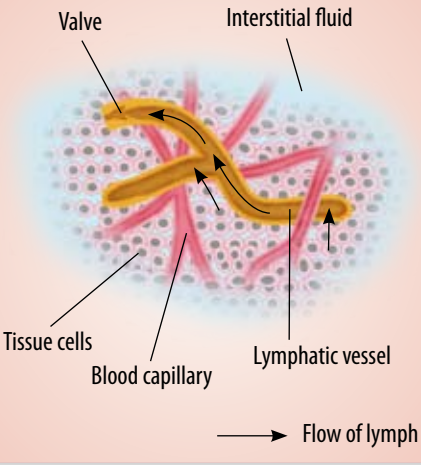


The spleen is the largest lymphoid organ and acts as a blood reservoir where worn-out red blood cells are removed from the blood.



T cells develop in the thymus.

LYMPHATIC VESSELS



B cells develop in the bone marrow.

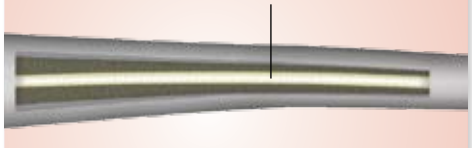
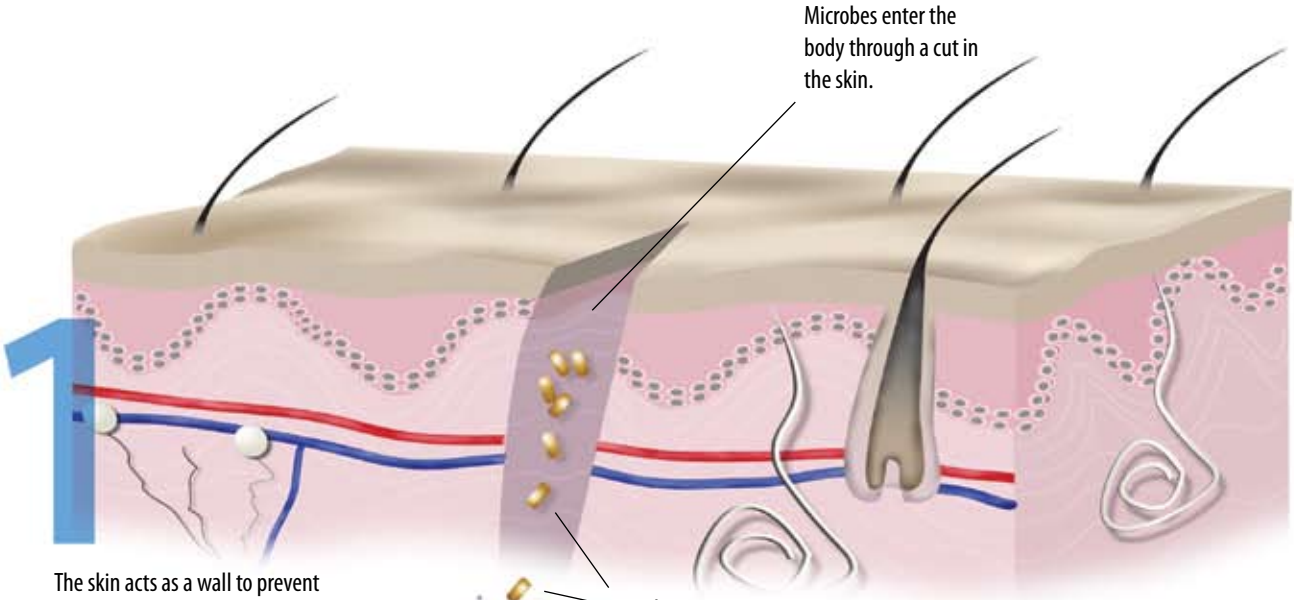
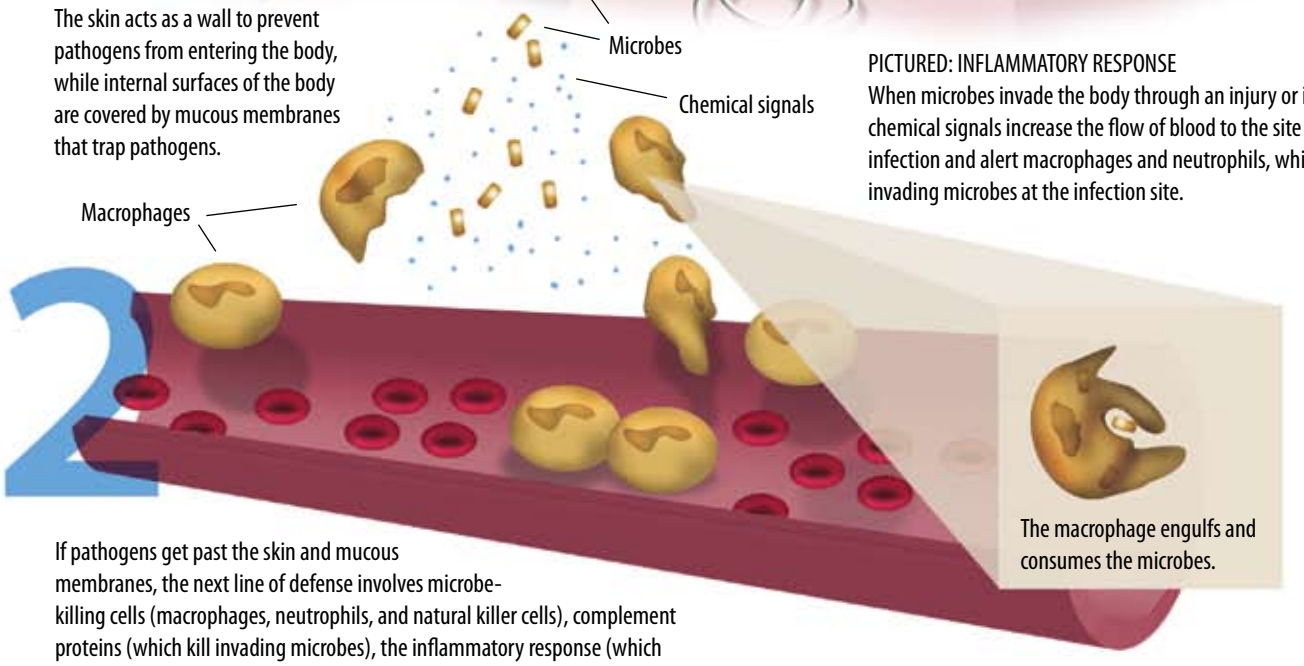


FIGURE 10A: THE THREE LINES OF DEFENSE

The human body has three layers of defense mechanisms against infection.

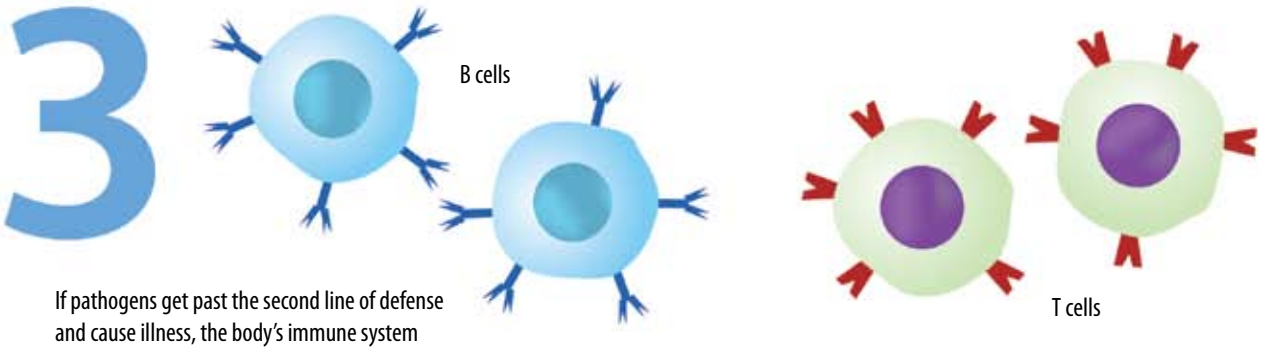


The skin acts as a wall to prevent pathogens from entering the body, while internal surfaces of the body are covered by mucous membranes that trap pathogens.



PICTURED: INFLAMMATORY RESPONSE
When microbes invade the body through an injury or infection, chemical signals increase the flow of blood to the site of the infection and alert macrophages and neutrophils, which attack invading microbes at the infection site.

If pathogens get past the skin and mucous membranes, the next line of defense involves microbe-killing cells (macrophages, neutrophils, and natural killer cells), complement proteins (which kill invading microbes), the inflammatory response (which suppresses infection and speeds healing after an injury or local infection), and the temperature response (macrophages send signals to cause a fever, which raises the body's temperature to suppress bacteria growth).



If pathogens get past the second line of defense and cause illness, the body's immune system responds (see Figure 10B for details).

FIGURE 10B: THE THIRD LINE OF DEFENSE — THE IMMUNE SYSTEM

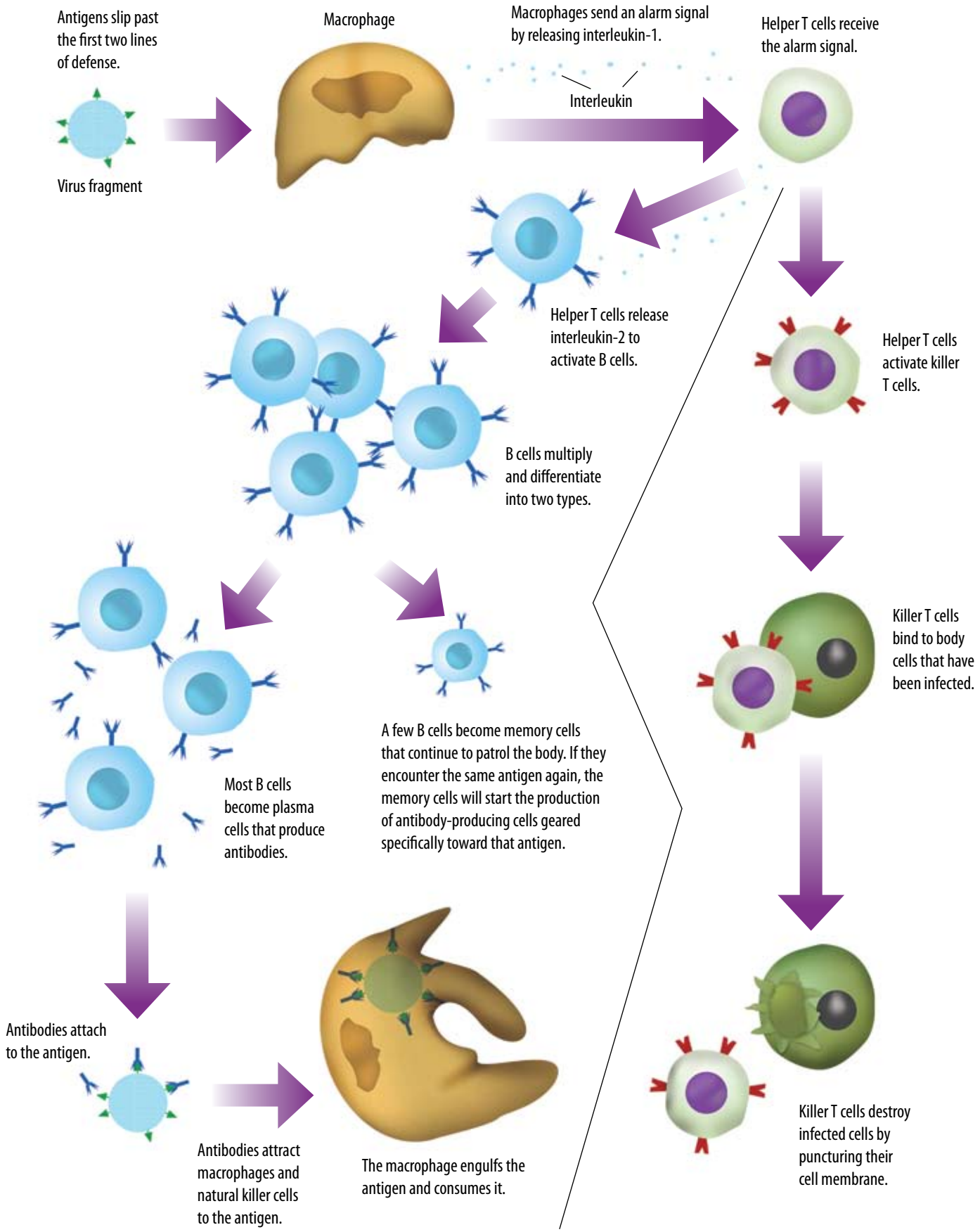
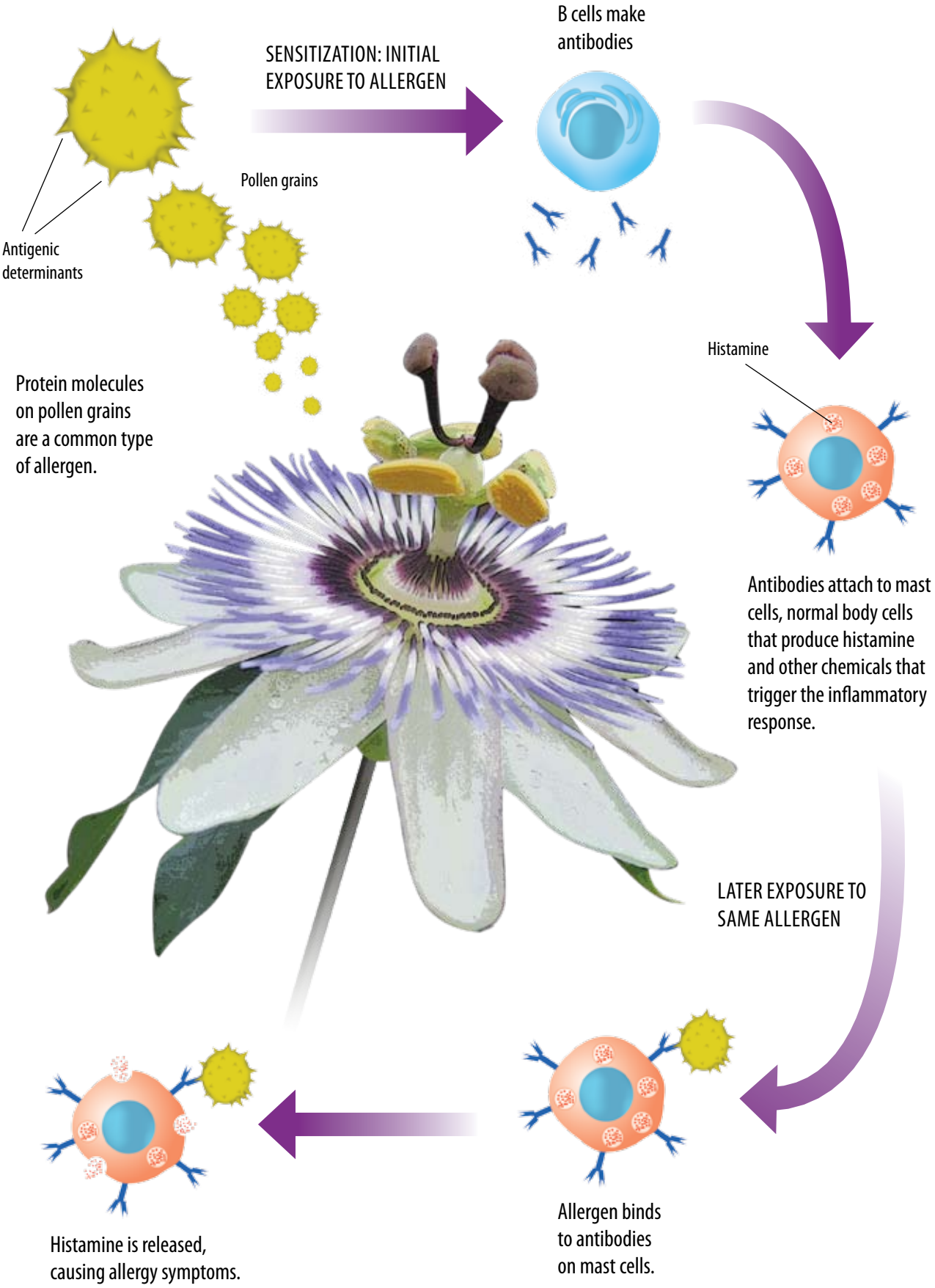


FIGURE 11: STAGES OF AN ALLERGIC REACTION



EXPLANATION/ELABORATION ACTIVITY: TV SHOW, DIAL IN FOR A DIALOGUE WITH A DOC

INSTRUCTIONS FOR TEACHERS

Make a copy of the questions and questions with answers. Cut the strips apart and distribute the questions to one group of students and the questions with answers to the other group of students.

EXTENSION

Have students come up with some questions of their own. They can research the answers and report back to the group.

QUESTIONS

1. I don't feel well. What could make me so sick?

2. How does the body defend itself against disease? What are the body's first line of defense, second line of defense and third line of defense? Why are burn patients more likely to have infection?

3. How is a vaccination like an artificial infection? Is the protection resulting from a vaccination considered active or passive immunity?

4. What are interferons and what do they interfere with? What is our complement system and what does it complement?

5. I got a splinter in my finger and the doctor said my inflammatory response would protect me. What is the inflammatory response?

6. How does an antibody differ from an antibiotic?

7. What would happen if a person was born without a thymus? What is the function of the lymph system? Why do lymph nodes swell when you have an infection?

8. How are MHC surface markers analogous to your fingerprints? What is the significance of the MHC in the immune response?

9. I have heard that the B and T cells are soldiers of the immune response. How and where are T cells and B cells formed? What is meant by the term immunocompetence?

10. How is my body capable of making so many different types of antibodies? How does the structure of an antibody promote its function?

11. Why do we refer to certain diseases, such as mumps, as "childhood diseases"? What is the difference between the primary and secondary immune responses?

12. I have heard that the immune response does not always involve the production of antibodies. Is this true?

13. I have allergies and I am especially sensitive to poison ivy. What causes this?

14. My aunt is to receive a liver transplant. What can be done to increase the chances that it will be successful?

15. My friend's mother has cancer and she is being treated with monoclonal antibodies. What are monoclonal antibodies?

16. Why is it so difficult to develop an effective vaccine against AIDS?

17. Why are you more likely to get sick during final exams than during summer vacation?

EXPLANATION/ELABORATION ACTIVITY: DIAL IN FOR A DIALOGUE WITH A DOC

KEY

1. I don't feel well. What could make me so sick?

Antigens. They are not whole pathogens; they are molecules that may be chemical components of a pathogen's surface. Pathogens are types of antigens that cause disease, including viruses, bacteria, fungi, protozoan, and prions.

Koch's Postulates — presently known as the germ theory of infectious disease. German bacteriologist Robert Koch came up with these rules for proving that a specific type of organism causes a specific type of disease:

i. The microorganism should always be found in the body of the host organism and not in a healthy organism.
ii. The microorganism must be isolated and grown in a pure culture away from the host.
iii. When the microorganisms grown in pure culture are injected into a new host organism, they produce disease.
iv. The same microorganisms should be reisolated from the second host and grown in pure culture, after which the microorganisms should still be the same as the original microorganisms.

Koch's Postulates still guide microbiology and epidemiology, but there are many exceptions. Many pathogens (including the ones that cause AIDS and syphilis) cannot be grown in culture, making the second statement, postulate ii, impossible to achieve.

2. How does the body defend itself against disease? What are the body's first line of defense, second line of defense and third line of defense? Why are burn patients more likely to have infection?

First line of defense

- Skin and mucous membranes
- Cilia, sweat and tears (many body secretions contain lysosomes)
- Acid secretions of the stomach
- Fever
- Symbiotic bacteria

Second line of defense: nonspecific mechanisms

- Interferon (IFNs) — Secreted by cells invaded by viruses that stimulate neighboring cells to produce proteins that help them defend against viruses.
  - 1980 genetically engineered and mass produced; shows promise against many viral diseases and some cancers
- Natural killer (NK) cells, phagocytic cells (neutrophils and monocytes).
- Complement system — a group of about 20 proteins that "complements" defense reactions. They help attract phagocytes to foreign cells and destroy foreign cells by promoting cell lysis.
- Inflammatory response – mast cells – initiate the immune response
  - Mast cells produce histamines (increase blood flow to the surrounding tissues)
  - Antihistamines

Third line of defense: immune response (targeted at specific antigens)

Burn victims are more likely to have an infection because their skin, the first line of defense, is damaged.

3. How is a vaccination like an artificial infection? Is the protection resulting from a vaccination considered active or passive immunity?

A vaccination contains dead or attenuated pathogens. Vaccinations cause the body to make its own antibodies so it is considered to be acquired or adaptive and active immunity.

4. What are interferons and what do they interfere with? What is our complement system and what does it complement?

   Inteferons are substances secreted by cells invaded by viruses that stimulate neighboring cells to produce proteins that help them defend against the virus.

   Complement is a group of about 20 proteins that "complement" defense reactions. These proteins help attract phagocytes to foreign cells and help destroy foreign cells by promoting cell lysis.

5. I got a splinter in my finger and the doctor said my inflammatory response would protect me. What is the inflammatory response?

   The inflammatory response consists of a series of nonspecific events that occur in response to pathogens. Histamines are produced by mast cells, causing dilation of the blood vessels. Chemical gradients of complements attract phagocytes to the injury, where they engulf pathogens and damaged cells.

6. How does an antibody differ from an antibiotic?

   Antibiotics are produced by living organisms and combat disease by weakening certain microorganisms, such as bacteria and fungi. Antibodies are produced by B cells and combat specific antigens.

7. What would happen if a person was born without a thymus? What is the function of the lymph system? Why do lymph nodes swell when you have an infection?

   Your T cells would not be immunocompetent. T cells must pass through the thymus to become immunocompetent. The lymph system consists of the thymus and bone marrow and is the site where white blood cells develop. It also consists of the lymph nodes which filter bacteria. (These swell when you are fighting infection, as a result of the multiplication of defensive lymphocytes.)

8. How are MHC surface markers analogous to your fingerprints? What is the significance of the MHC in the immune response?

   MHC markers are unique to each individual. The MHC (major histocompatability complex), also known as the HLA (human leukocyte antigens), consists of about 20 different proteins located on the surfaces of body cells that identify "self" to the immune system. Identical twins would have identical MHC proteins.

9. I have heard that the B and T cells are soldiers of the immune response. How and where are T cells and B cells formed? What is meant by the term immunocompetence?

   B cells are lymphocytes that originate and mature in the bone marrow (B for bone). B cells respond to antigens. The plasma membrane surface of B cells has specialized antigen receptors called antibodies, which serve as biological ammunition.

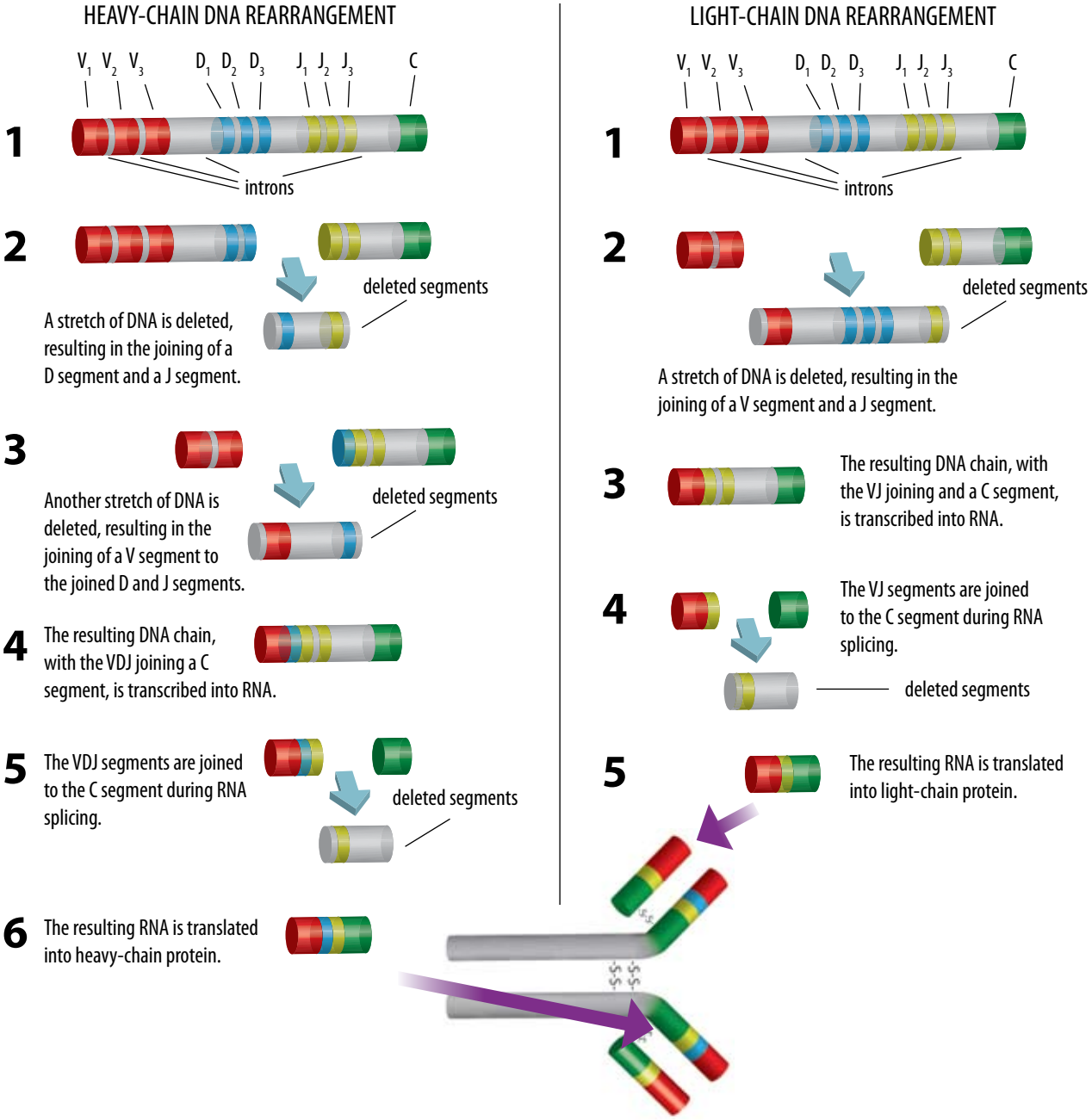
   T cells are lymphocytes that originate in the bone marrow, but mature in the thymus gland (T for thymus). The plasma membranes of T cells have antigen receptors that are recognition sites for molecules displayed by nonself cells. When T cells encounter nonself cells, they divide and produce cytotoxic T cells (or killer T cells) and helper T cells, which stimulate the proliferation of B cells and cytotoxic T cells.

10. How is my body capable of making so many different types of antibodies? How does the structure of an antibody promote its function?

Because of the randomness of possible combinations of specific parts of antibody genes that are cut, reshuffled, and assembled, billions of different combinations of antibodies are possible. Only cells producing antibodies to invading antigens are selected to multiply.

Genes are expressed in two stages. First, the V, D, and J gene segments move closer together when enzymes remove the introns (segments that separate the coding regions). Second, the resulting DNA chain is transcribed into RNA, along with RNA representing the C portion of the gene. This RNA is translated into an antibody protein (Figure 12).

FIGURE 12: ANTIBODY DIVERSITY



11. Why do we refer to certain diseases, such as mumps, as "childhood diseases"? What is the difference between the primary and secondary immune responses?

    Because once you have the disease, which usually occurs during childhood, you are generally protected for the rest of your life. The primary response refers to the initial phase of your body's response when you first come into contact with the pathogen. It occurs more slowly than the secondary response, which results from a second exposure to the same antigen.

12. I have heard that the immune response does not always involve the production of antibodies. Is this true?

    Yes. The responses of the immune system are categorized into two kinds of reactions:
    - Cell-mediated (mostly uses T cells and responds to any nonself cell, including cells invaded by pathogens)
    - Humoral response (or antibody-mediated response)

13. I have allergies and I am especially sensitive to poison ivy. What causes this?

    Hypersensitivity occurs when the immune system overreacts to an antigen (allergy, anaphylactic reactions, and contact sensitivity to substances such as poison ivy).

14. My aunt is to receive a liver transplant. What can be done to increase the chances that it will be successful?

    Using immunosuppressive drugs to suppress the immune response.

15. My friend's mother has cancer and she is being treated with monoclonal antibodies. What are monoclonal antibodies?

    Monoclonal antibodies are harvested from cell cultures rather than from animals. All cells producing the antibodies are descendents of a single cell. Monoclonal antibodies, which recognize one specific region on one protein or immunogen, show great promise in treating diseases such as cancer.

16. Why is it so difficult to develop an effective vaccine against AIDS?

    The HIV virus evolves so rapidly that it is difficult to develop an effective vaccine. New therapies such as drug combinations called the drug cocktails (composed of protease and RT inhibitors) have provided hope and at least temporary relief from disease progression.

17. Why are you more likely to get sick during final exams than during summer vacation?

    Stress suppresses the immune response.

EVALUATION ACTIVITY: THE HUMORAL RESPONSE CONCEPT MAP

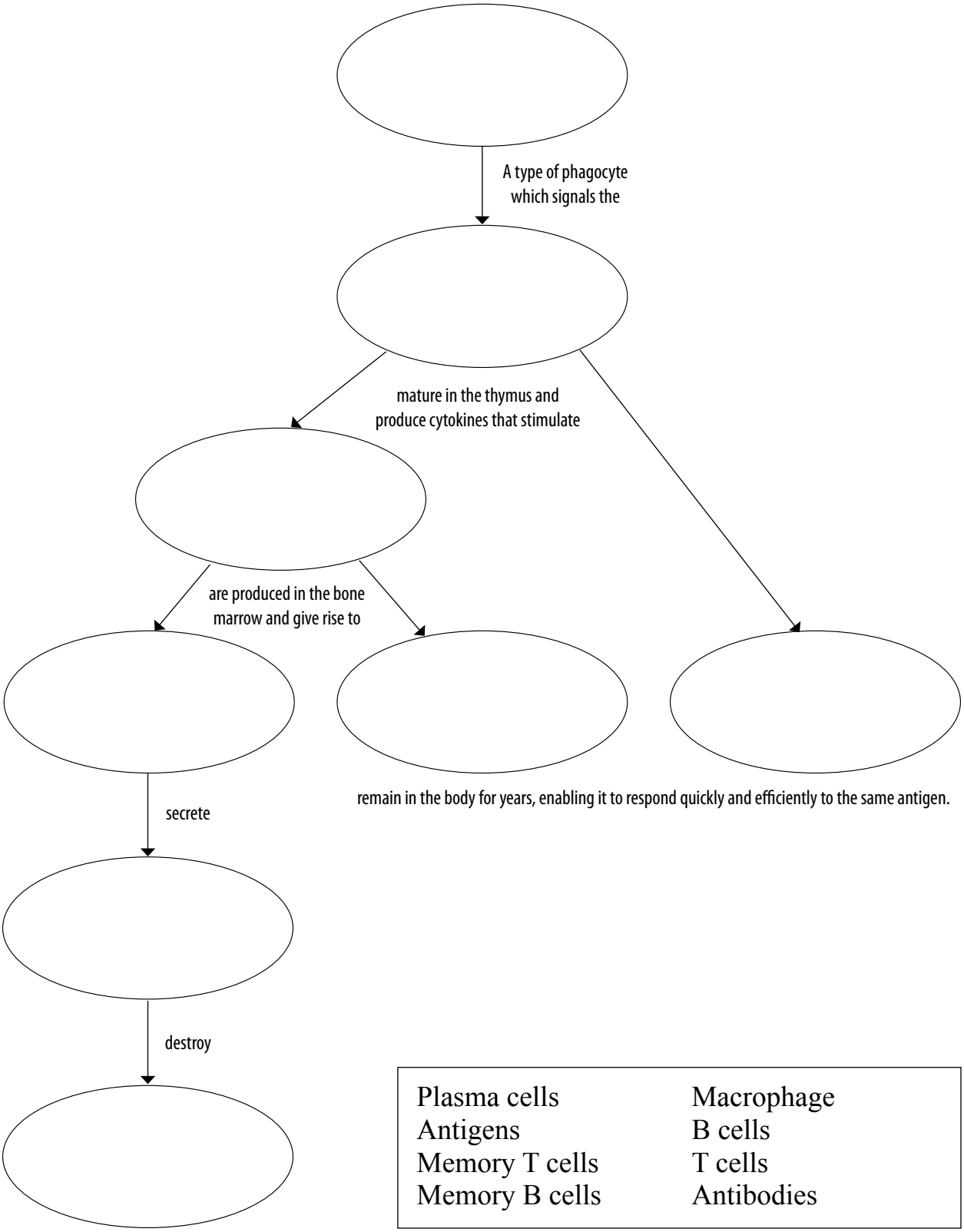
INSTRUCTIONS FOR TEACHERS

Make copies of the blank concept map. Have students complete the concept map to check their understanding of the humoral response.

Each student should create a concept map of the humoral response. Depending on the familiarity of the students with concept maps, you may choose to give the students the list of terms and have them create their own concept maps and explain the connections for each term to the class.

EVALUATION ACTIVITY: THE HUMORAL RESPONSE CONCEPT MAP

Fill in each oval using the appropriate vocabulary from the box below.

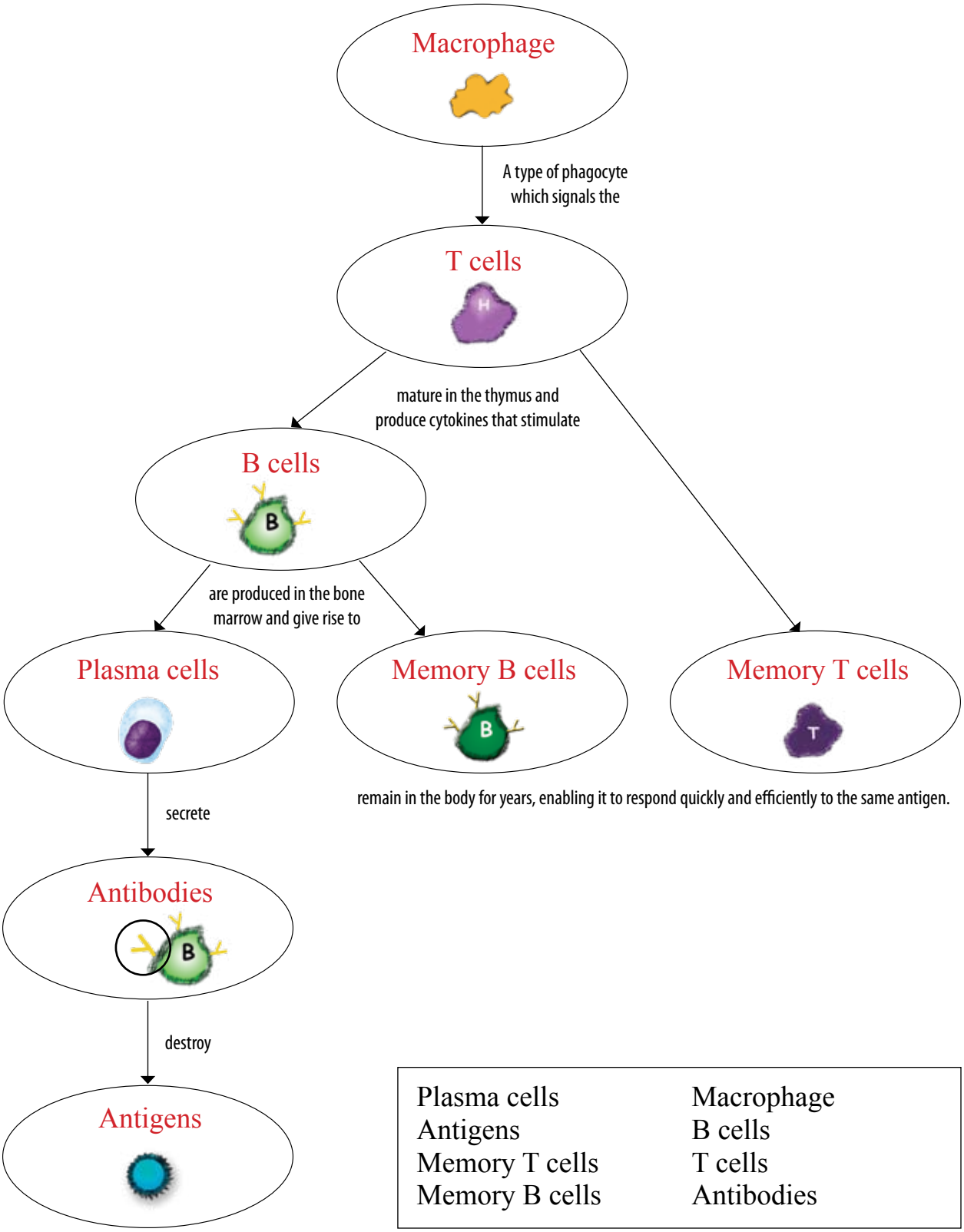


Plasma cells	Macrophage
Antigens	B cells
Memory T cells	T cells
Memory B cells	Antibodies

EVALUATION ACTIVITY: THE HUMORAL RESPONSE CONCEPT MAP

KEY

Fill in each oval using the appropriate vocabulary from the box below.



Plasma cells	Macrophage
Antigens	B cells
Memory T cells	T cells
Memory B cells	Antibodies

BIOLOGICAL BODYGUARDS IMPLEMENTATION PLAN — WET LAB			
Activity	Estimated Time	Materials/Equipment	Purpose/Objectives/ Essential Question
Engagement: HIV simulation activity Note: This activity may be done one day prior to the ELISA test or in place of the ELISA test.	20 minutes	Centrifuge tubes labeled with numbers (one for each student) 30 mL of 0.1% NaOH (sodium hydroxide) for one student's centrifuge tube 30 mL of water in each of the other tubes (one for each student) Label each tube with a number Phenolphthalein to use as an indicator One plastic pipette for each student Index cards Optional: Party hats, music	**Purpose:** To apply the specificity of antibodies to a diagnostic test using the ELISA technique. **Objectives:** • To define a method of testing for HIV, when given models of antibodies and antigens • To perform an ELISA test to diagnose fictional patients for possible exposure to HIV • To analyze the results of the ELISA **Essential Question:** Which of our patients' sera has antibodies that may be specific to HIV?
Explanation of the ELISA test	5 minutes	Transparencies	
ELISA test	60 minutes	Materials described in ELISA prep section of this notebook or Bio-Rad's ELISA ImmunoExplorer™ Kit Student data observation sheets Focus question sheets	
Closure: Analyze the results to see which patient has HIV	5 minutes	Student data observation sheets Focus question sheets	

Alignment with NC Competency Goals	
Biology	Healthful Living
Goal 1 Objectives 1.01, 1.02, 1.03, 1.04, 1.05 Goal 2 Objectives 2.01, 2.02, 2.03, 2.04 Goal 3 Objectives 3.01, 3.04 Goal 4 Objectives 4.01, 4.03, 4.04	Goal 1 Objectives 1.02, 1.06 Goal 3 Objectives 3.01, 3.04, 3.07, 3.08, 3.09

REAL-WORLD APPLICATIONS OF ELISA: ENZYME-LINKED IMMUNOSORBENT ASSAY

Adapted from Bio-Rad's ELISA Immuno Explorer Kit™ Instruction Manual

BACKGROUND

Over 100 years ago biologists discovered that the immune system of animals responds to the invasion of foreign substances or antigens. A quick and inexpensive test known as ELISA (Enzyme-Linked ImmunoSorbent Assay) is a sensitive immunoassay that uses an enzyme linked to an antibody or antigen as a marker for the detection of a specific protein, especially an antigen or antibody. ELISA can determine exposure to a particular infectious agent, such as the human immunodeficiency virus (HIV), the causative agent of AIDS (acquired immunodeficiency disease) by identifying antibodies present in the blood sample.

ELISA is widely used for tracking disease outbreaks and detecting antigens and antibodies. Variations of ELISA have been developed to allow for qualitative detection or quantitative measurement of either the antigen or the antibody. Qualitative responses result in a Yes/No answer, can be obtained using ELISA, and are definite and rapid. Quantitative results can be measured because as the concentration of the antibody or antigen increases, so does the intensity of the blue color in the wells. The blue color absorbs light at a specific wavelength and this absorbance can be measured with a **microplate** reader.

ELISA is a powerful diagnostic tool in human medicine. As you examine the table below, you will see that the technique is used in a variety of other fields.

Human & veterinary medicine	• Diagnose a variety of diseases, such as West Nile virus (in people and animals), HIV, SARS, Lyme disease, trichinosis, tuberculosis, and many more by detecting serum antibodies
Veterinary	• Detect viruses such as feline leukemia virus (FLV) and feline immunodeficiency virus (FIV) in cats • Detect parasites, such as heartworms, in dogs • Diagnose thyroid problems in dogs and cats by measuring serum thyroxine (T4) concentrations • Diagnose equine encephalitis in horses by detecting arboviruses
Agriculture: crops	• Detect viruses, such as potato roll leaf virus and cucumber mosaic virus, in food crops • Detect mycotoxins in crops, such as aflatoxin in cereal grains and corn • Detect viruses in decorative plants, such as bean yellow mosaic virus in gladiolus • Track adulteration of non-genetically modified (non-GMO) crops with GMO products (e.g., detecting Roundup Ready and Bt content)
Environmental	• Test indoor air quality, such as detecting mold toxins in buildings
Food safety and quality	• Prevent transmission of bovine spongiform encephalitis (mad cow disease, BSE) by screening for central nervous system tissues in raw meat, in processed and cooked meats, and on surfaces • Determine if food labeling is correct (e.g., by checking for cow milk proteins in goat milk products or for non-durum wheat in durum wheat products) • Prevent allergic reactions by detecting ingredients that aren't listed on food content labels (e.g., detecting peanuts in products in which peanuts are not listed as an ingredient)
Other	• Detect restricted or illegal drug use (e.g., performance-enhancing drugs, marijuana, methamphetamine, cocaine, etc.) • Confirm pregnancy by detecting human chorionic gonadotropin (hCG) in urine

WET LAB ENGAGEMENT ACTIVITY: HIV SIMULATION: TRACKING A DISEASE OUTBREAK

Note: This activity may be done one day prior to the ELISA test or in place of the ELISA test.

MATERIALS

- Transparency of the data on shared partners for the overhead
- 50 mL centrifuge tubes with caps (one for each student)
- Tap water
- 0.1% NaOH (sodium hydroxide, 30 mL)
- 3" x 5" cards (one for each student)
- Plastic pipettes (one for each student)
- Centrifuge tube with phenolphthalein

PRE-LAB PREP

1. Make up 30 mL of 0.1% NaOH for one centrifuge tube. Place one or two NaOH pellets in the tube.

2. Place 30 mL H_2O in each of the other tubes (for the remainder of the students).

3. Label all tubes with a number. **NOTE: Remember which tube contains the NaOH solution.** Place all tubes in a styrofoam holder.

INSTRUCTIONS FOR TEACHERS

1. Each student should receive a 3 x 5 index card, a plastic pipette, and a numbered centrifuge tube.

2. Instruct the students to "exchange" fluid with three other people, using the plastic pipettes to obtain fluid from each other's tubes. Students should note on the 3 x 5 card the number of each tube with which they exchange fluid and the order in which these fluid exchanges occur.

Remind students that it is important for them to exchange fluid and to turn the tube upside down to mix the solutions (with the cap on, of course). The point is to mix thoroughly between each exchange.

3. When three exchanges have been made, you can test the tubes for "HIV" by adding phenolphthalein to the solutions. If the solutions turn pink, the tube has tested positive for "HIV." If the solution remains clear, the tube has tested negative for "HIV." An alternative to phenolphthalein is phenol red. You will get either a pale pink color indicating "normal" (no infection) or a bright violet color indicating a positive HIV test. An analysis can then be made to find out who had the original vial of "HIV." Students can start by working backward to find out who had the contaminated tube.

Students will be amazed by how many people get "HIV" from only three contacts.

This activity can be embellished by pretending that the students are going to a party and that they become exposed to the fluids of other people at the party. To set the mood, party music and hats should be available for use.

Note: Be sure to rinse tubes with vinegar before they are used for another class.

HIV SIMULATION: TRACKING A DISEASE OUTBREAK

INSTRUCTIONS FOR STUDENTS

1. Each person should receive a 3 x 5 index card, a plastic pipette, and a numbered centrifuge tube.

2. Using your plastic pipette, "exchange" fluid from the tubes of three other people. Note on the 3 x 5 card the number of each tube with which you exchange fluid and the order in which these fluid exchanges occur. It is important to exchange fluid and to turn the tube upside down to mix the solutions (with the cap on, of course). The point is to mix thoroughly between each exchange.

3. After the three exchanges have been made, the instructor can test the tubes for "HIV." If the solutions turn pink, the tube has tested positive for "HIV." If the solution remains clear, the tube has tested negative for "HIV." An analysis can then be made to find out who had the original vial of "HIV." You can start by working backward to find out who had the contaminated tube.

4. If your numbered tube tested positive, record a "+" in the number column for your tube.
   OR
   If your numbered tube tested negative, record a "–" in the number column for your tube.

HIV SIMULATION: TRACKING A DISEASE OUTBREAK CLASS RESULTS

Make an overhead transparency of this page to use with the data of shared partners.

Student #	Sharing Partners (+ or -)																								
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
1																									
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BIOLOGICAL BODYGUARDS WET LAB

PURPOSE

• To apply the specificity of antibodies to a diagnostic test using the ELISA technique.

OBJECTIVES

• To define a method to test for HIV, when given models of antibodies and antigens.
• To perform an ELISA test to diagnose fictional patients for exposure to the HIV virus.
• To analyze the results of the ELISA.

EXPLANATION OF ELISA TEST

Introduce the investigation by telling students they will be given serum from two patients who are theoretically being tested for HIV. They will test the patients for the presence of HIV antibodies. Before entering the lab, safety procedures should be reviewed.

ELISA TEST

Each student will determine whether the patients test positive or negative for HIV. The results may be analyzed at this time based on a qualitative analysis of color.

EVALUATION

Ask each group what their diagnosis is for each patient. Encourage discussion by asking other groups whether they agree or disagree. Ask students to explain their diagnoses.

FOCUS QUESTIONS: ELISA

1. How does the immune system protect us from disease?

2. How do doctors use the immune response to protect you from disease?

3. How are antibodies made in your body?

4. What do the terms below mean?

   a. AIDS

   b. HIV

   c. ELISA

   d. Opportunistic infection

5. What are the characteristic ways that a person can get HIV?

ANSWERS TO FOCUS QUESTIONS: ELISA

KEY

1. How does the immune system protect us from disease?

   The innate immune system includes physical barriers (e.g., the skin and mucous membranes that prevent pathogens from entering the body) and cellular responses (e.g., circulating macrophages that respond to foreign invaders). Our acquired immune system mounts a specific antibody response upon exposure to a foreign invader, and our immune cells attack the foreign invader.

2. How do doctors use the immune response to protect you from disease?

   Doctors use the immune response when we are vaccinated against disease. Our immune system remembers diseases we were exposed to and the next time we are exposed to the disease our immune system attacks the disease more quickly and efficiently. Doctors take advantage of this priming effect by exposing us to inactivated diseases (either killed or weakened organisms that cannot make us sick) so that if we are later exposed to the disease our body will mount a strong and immediate antibody response, reducing or eliminating the chance that the disease will make us sick.

3. How are antibodies made in your body?

   Antibodies are produced in response to specific antigens. B cells produce antibodies.

4. What do the terms below mean?

   a. AIDS

      Acquired Immunodeficiency Syndrome — the stage of the disease when the characteristic symptoms appear, and CD4+ T cell count drops.

   b. HIV

      Human immunodeficiency virus — the virus that causes AIDS

   c. ELISA

      Enzyme-linked immunosorbent assay — the first test that doctors use to detect HIV

   d. Opportunistic infection

      An infection by an organism to which a healthy body would normally be resistant

5. What are the characteristic ways that a person can get HIV?

   Sexual contact, transfer of infected body fluids to a non-infected person

EXPLANATION OF ELISA TEST

Introduce the wet lab by telling students they will be given serum from two patients who are theoretically being tested for HIV. Choose from any of the two patients listed below. The students will test the patients for the presence of HIV antibodies. Before entering the lab, safety procedures should be reviewed.

BIOGRAPHICAL SKETCHES

SAMPLE A

Bill C. Age 40 Sex M
Occupation: Transient, lives on the streets
Time after possible exposure: unknown
Reason to suspect HIV infection: Appears to be a habitual drug user. Has "needle tracks" on both arms. He denies using intravenous drugs. Is attempting to donate blood to a blood bank in the inner city.

SAMPLE B

Amy B. Age 26 Sex F
Occupation: Elementary school teacher
Time after possible exposure: 6 months
Reason to suspect HIV infection: Assisted a student who fell off playground equipment and cut his head. Amy was not wearing protective gloves and noticed the scratches on her hand she had received from weeding her garden.

SAMPLE C

Roger T. Age 15 Sex M
Occupation: High school student
Time after possible exposure: 3 years to present
Reason to suspect HIV infection: He has just learned that his older brother has AIDS. Fears that he may have been infected due to frequent contact from sharing same bedroom, bathroom, and eating utensils. Insists on being tested for HIV.

SAMPLE D

John K. Age 17 Sex M
Occupation: High school student
Time after possible exposure: 0 months
Reason to suspect HIV infection: Has recently begun dating a fellow student seriously. He and his new partner have agreed to be tested before becoming sexually active.

SAMPLE E

Norma T. Age 36 Sex F
Occupation: Policewoman
Time after possible exposure: 4 months
Reason to suspect HIV infection: While making an arrest, she was scratched, bitten, and spat upon by a person claiming to be HIV positive.

SAMPLE F

Susan J. Age 25 Sex F
Occupation: Nurse
Time after possible exposure: 3 months
Reason to suspect HIV infection: While she was working with an AIDS patient, a hypodermic needle punctured her latex glove.

SAMPLE G

Lucy L. Age 33 Sex F
Occupation: Homemaker
Time after possible exposure: 7 years to present
Reason to suspect HIV infection: Her husband was formerly heavily involved in a promiscuous lifestyle. He tested positive for HIV before their marriage, and they have taken all recommended precautions to protect her from contracting the disease. However, she has recently heard of a Center for Disease Control report stating that the virus can be transmitted by kissing, if the person with HIV has bleeding gums. Her husband has the early stages of gum disease.

SAMPLE H

Tom M. Age 25 Sex M
Occupation: Computer Programmer
Time after possible exposure: 10 years
Reason to suspect HIV infection: Has had persistent infections and has been in generally poor health over the last few months. Has had a few homosexual relationships in the past and is currently in a monogamous homosexual relationship.

WET LAB PROTOCOL: ELISA ANTIBODY TEST

From Bio-Rad's ELISA Immuno Explorer Kit Instruction Manual

1. Label the yellow tubes (if necessary) to identify the samples being tested.

2. Label your 12-well strip. On each strip label the first three wells with a "+" for the positive controls and the next three wells with a "-" for the negative controls. Label the remaining wells to identify the samples being tested (three wells each).

3. Use a fresh pipet tip to transfer 50 µl of purified antigen (AG) into all 12 wells of the microplate strip.

4. Wait 5 minutes for the antigen to bind to the plastic wells.

5. WASH:
   a. Tip the microplate strip upside down onto the paper towels, and gently tap the strip a few times upside down.
   b. Discard the top paper towel.
   c. Use a transfer pipet to fill each well with wash buffer.
   d. Tip the microplate strip upside down onto the paper towels and tap.
   e. Discard the top 2-3 paper towels.

6. Use a fresh pipet tip to transfer 50 µl of the positive control (+) into the three "+" wells.

7. Use a fresh pipet tip to transfer 50 µl of the negative control (-) into the three "-" wells.

8. Transfer 50 µl of each of your team's serum samples into the appropriately initialed three wells, using a fresh pipet tip for each serum sample.

9. Wait 5 minutes for the antibodies to bind to their targets.

10. Wash the unbound **primary antibody** out of the wells by repeating all of wash step 5.

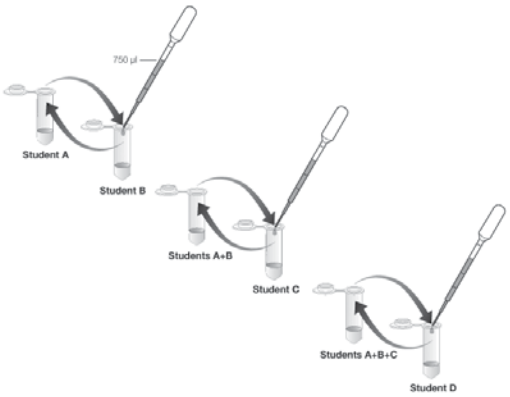
11. Use a fresh pipet tip to transfer 50 µl of **secondary antibody** (SA) into all 12 wells of the microplate strip.

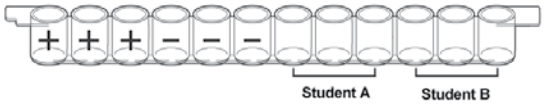
12. Wait 5 minutes for the antibodies to bind to their targets.

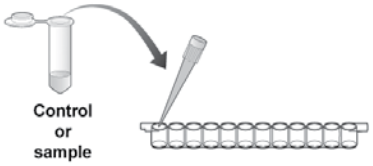
13. Wash the unbound secondary antibody out of the wells by repeating wash step 5 two times.

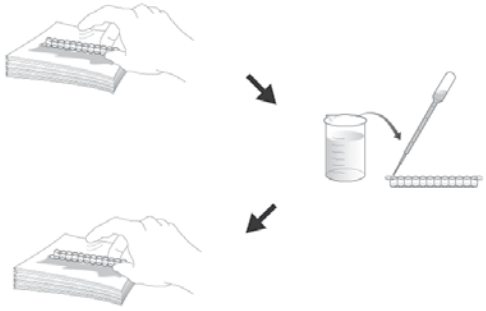
14. Use a fresh pipet tip to transfer 50 µl of enzyme substrate (SUB) into all 12 wells of the microplate strip.

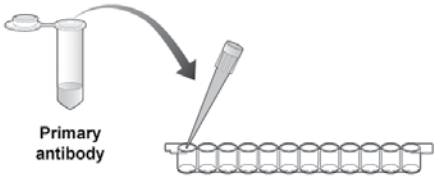
15. Wait five minutes. Observe and record the results.

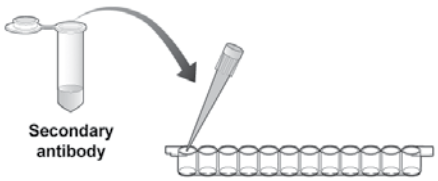


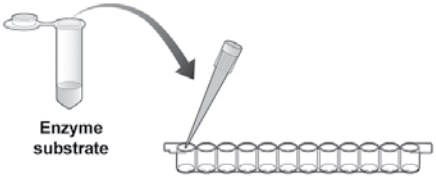










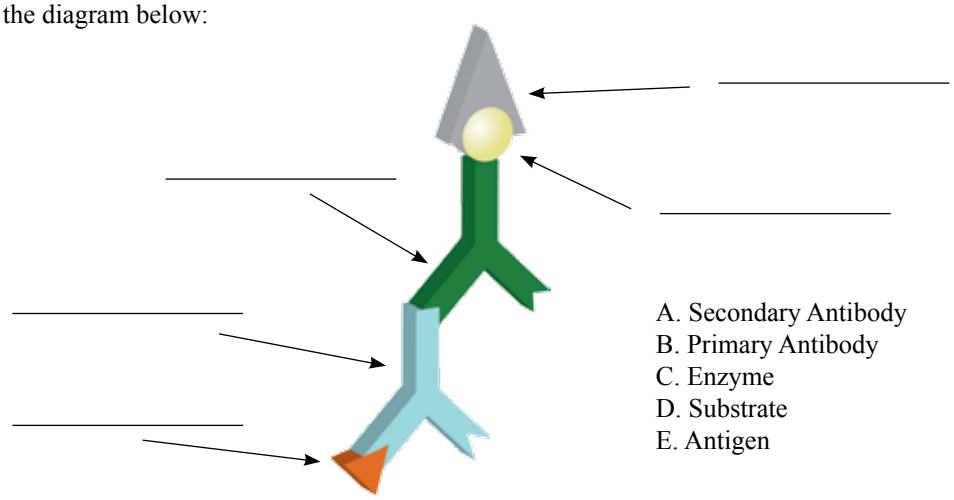


NAME _____

DATA/OBSERVATION SHEET

1. During this lab, you are testing for the presence of _____ in a patient's serum.

2. A positive ELISA test would occur assuming each of the molecules below interacted accordingly. Label each molecule in the diagram below:



A. Secondary Antibody
B. Primary Antibody
C. Enzyme
D. Substrate
E. Antigen

3. What is the function of the secondary antibody?

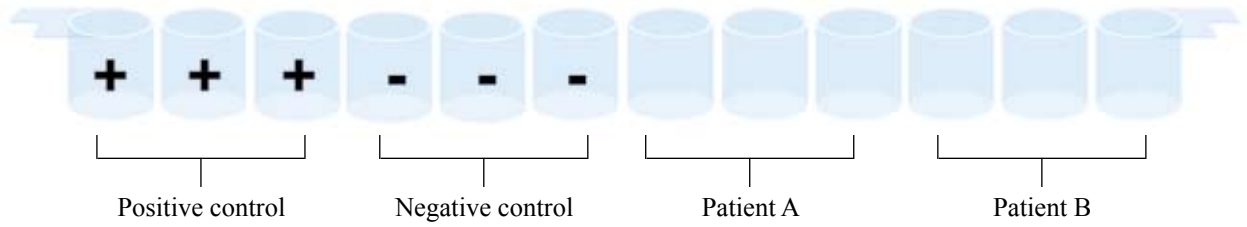
4. What is the function of the viral extract in this assay?

5. In a patient who is HIV negative, which molecule would be missing from the ELISA test?

6. Why did you assay your samples in triplicate (three times)?

RESULTS

Indicate which wells below exhibited a blue color by shading the appropriate well(s).



7. Which patient tested positive for HIV?

Note: A positive result using ELISA would need to be confirmed with a Western blot prior to diagnosing a patient with HIV.

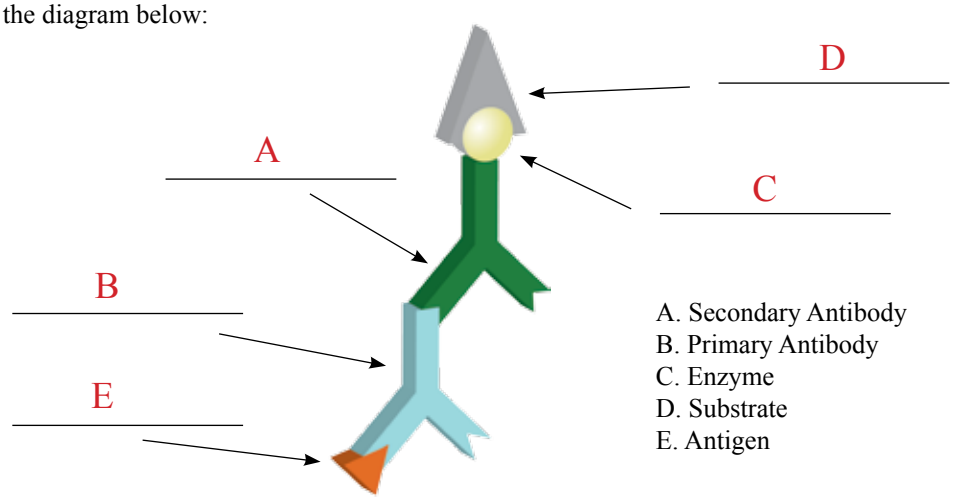
8. Does a positive HIV test mean that this patient has AIDS? Explain your answer.

KEY

DATA/OBSERVATION SHEET

1. During this lab, you are testing for the presence of antibodies to HIV in a patient's serum.

2. A positive ELISA test would occur assuming each of the molecules below interacted accordingly. Label each molecule in the diagram below:



A. Secondary Antibody
B. Primary Antibody
C. Enzyme
D. Substrate
E. Antigen

3. What is the function of the secondary antibody?
   To recognize and bind to the primary antibody. In this case, the primary antibody is specific for HIV.

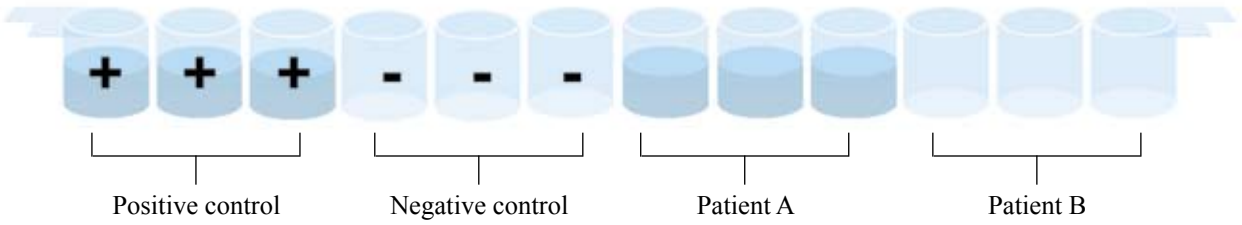
4. What is the function of the viral extract in this assay?
   To provide the antigen to which the primary antibody can bind. A simulated HIV viral extract is used in this assay.

5. In a patient that is HIV negative, which molecule would be missing from the ELISA test?
   The primary antibody would be absent from a patient who is HIV negative.

6. Why did you assay your samples in triplicate (three times)?
   This represents another experimental control, since the results for all three wells for a particular patient should be the same. If the same result is not achieved for all three wells, this indicates an experimental error.

RESULTS

Indicate which wells below exhibited a blue color by shading the appropriate well(s).



7. Which patient tested positive for HIV?
   Patient A is HIV positive.

8. Does a positive HIV test mean that this patient has AIDS? Explain your answer.
   A positive HIV test does NOT mean that an individual has AIDS. An HIV positive patient is clinically diagnosed with AIDS if two criteria are met: 1) the presence of one or more AIDS indicator illnesses (opportunistic infections) and 2) a T_H cell count below 200 cells/µl.

DESTINY - UNC-CHAPEL HILL - CB# 7448, Morehead Planetarium and Science Center Annex - Chapel Hill, NC 27599-7448 - (919) 843-9036 - www.destiny.unc.edu

Equipment Needed for Biological Bodyguards Wet Lab						
Vendor	**Catalog Number**	**Item**	**Unit**	**Price**	**Minimum Needed**	**TOTAL**
REQUIRED EQUIPMENT						
Bio-Rad	166-0507EDU	20-200 digital micropipet	1	$159.00	8	$1272.00
					EQUIPMENT TOTAL	**$1272.00**
REQUIRED CONSUMABLES						
Bio-Rad	166-2400EDU	ELISA Immuno Explorer Kit	1 kit	$99.99	½ kit	$49.50
Bio-Rad	223-9347EDU	Racked pipet tips TBR-35 tips	1 box of 1,000	$35.20	64 tips	$2.26
					CONSUMABLES TOTAL	**$134.20**
					Approximate price per class of 24 students/8 student groups	**$51.76**
OPTIONAL EQUIPMENT						
Bio-Rad	166-0501EDU	Mini incubation oven	1	$295.00		
Bio-Rad	166-0504EDU	Water bath	1	$505.00		
Carolina Biological	21-5570	Micro-test tube rack, polypropylene	1	$4.00		
Bio-Rad	166-0709EDU	Rocking platform	1	$575.00		
		Microwave oven				

BIOLOGICAL BODYGUARDS IMPLEMENTATION PLAN — POST-LAB			
Activity	Estimated Time	Materials/Equipment	Purpose/Objectives/ Essential Question
Biological Bodyguards Quiz Game	20 minutes	Questions and answers provided in notebook or on CD	**Purpose:** To analyze the results of the ELISA test to see which patient/patients may have HIV **Objectives:** • To analyze the results visible on the test plate • To successfully explain the diagnosis of each patient tested **Essential Question:** Which of our patients' sera has antibodies that may be specific to the HIV virus?
Post-lab focus questions	15 minutes	Copies of post-lab focus questions	
Homework assignment: Investigate one of the proposed theories concerning the body's immune system	30 minutes	Copies provided in notebook and on CD	
Video: An Inside Look: The Flu (Discovery Channel School)	27 minutes	Video (www.discovery.com, Item# 745042)	

Alignment with NC Competency Goals	
Biology	Healthful Living
Goal 1 Objectives 1.01, 1.02, 1.03,1.04 1.05 Goal 2 Objectives 2.01, 2.02, 2.03, 2.04 Goal 3 Objectives 3.01, 3.04 Goal 4 Objectives 4.01, 4.03, 4.04	Goal 1 Objectives 1.02, 1.06 Goal 3 Objectives 3.01, 3.04, 3.07, 3.08, 3.09

BIOLOGICAL BODYGUARDS QUIZ GAME QUESTIONS

	Fact or Fiction	Immune System Players	Biological Body-guards	ELISA	Diseases	Hodge Podge
200	Fact or Fiction: The only way to fight disease is by using medication.	Which molecule acts as the foreign invader, stimulating your body's immune response?	The ELISA in the wet lab tested for possible exposure to what antigen?	When performing the ELISA during the wet lab, why did you test three replicates of each sample?	True or False: All bacteria cause diseases in humans and should therefore be eliminated.	What is the shape of an antibody?
400	Fact or Fiction: The only way your body develops acquired immunity for a disease is by contracting that disease.	Which cells act as scouts, engulfing antigens and presenting them to specific white blood cells for identification?	What was the function of the viral extract in the wet lab?	If you test positive for an antibody using ELISA, does that mean that you definitely have been exposed to the antigen?	What does AIDS stand for?	What does HIV stand for?
600	Fact or Fiction: Your body has a "memory" for antigens, allowing for a quicker immune response.	What is the name of the white blood cells that act as the intelligence agent, signaling other cells to attack the foreign invaders?	What do we call an infection by an organism to which a healthy body normally would be resistant?	Other than testing for exposure to HIV, what other ways is ELISA used?	What is the difference between HIV and AIDS?	Name two body parts that act as physical barriers to prevent pathogens from entering the body.
800	Fact or Fiction: T cells are produced in the thymus.	What is the term for white blood cells that give rise to plasma cells, which create the antibodies necessary to destroy invaders (antigens)?	Based on the wet lab, did either of the patients possibly have the antibodies for HIV? Explain.	What does ELISA stand for?	Aside from your immune response, list 3 ways your body resists acquiring diseases.	During the wet lab, why did you make positive and negative control wells?
1000	Fact or Fiction: In order for an immune system to completely prevent a disease, the body must have been previously exposed to the antigen that causes that disease.	What cells record the characteristics of the antigen so that the B cell will immediately be activated the next time that antigen invades?	Assume you are a doctor and you performed an ELISA test on a patient to test for HIV. The test returned a positive result. What do you tell your patient?	Explain the steps of an HIV ELISA test (such as that used in the wet lab) and describe the results you would expect to find when testing a patient who is positive for the antibody.	What are vectors? Define and give examples.	What are three common ways that HIV is transmitted?

BIOLOGICAL BODYGUARDS QUIZ GAME ANSWERS

KEY

	Fact or Fiction	Immune System Players	Biological Bodyguards	ELISA	Diseases	Hodge Podge
200	Fiction. Your body's immune system is able to fight off disease without medication.	Antigens. Examples of antigens include viruses, bacteria, and pollen.	HIV virus.	By triplicating the test, you will be better able to know if the results are accurate.	False. A relative few bacteria actually cause disease; many others are actually very useful.	Antibodies are Y-shaped.
400	Fiction. Vaccines stimulate an acquired immunity without actually giving you the disease.	Macrophages.	It contained the antigen to which the primary antibody, if present, could bind.	Not necessarily. Further tests should be given (i.e., Western blot, immunoblot).	Acquired ImmunoDeficiency Syndrome.	Human Immunodeficiency Virus.
600	Fact. Memory B cells recall familiar antigens.	T cells.	Opportunistic infection.	Test for pregnancy, drug use (marijuana, cocaine).	HIV is the virus that causes AIDS. AIDS is only diagnosed if two criteria are present: 1) one or more AIDS indicator illnesses (opportunistic infections) and 2) a Helper T cell count below 200 cells/microliter. It can take 10+ years for HIV to develop into AIDS. During this time, an infected person can still transmit HIV to others.	Skin and mucous membranes.
800	Fiction. T cells are produced in the bone marrow, and mature in the thymus.	B cells. The B cells act as the weapons expert.	Yes, patient A. That assay turned out blue like the positive control.	Enzyme Linked ImmunoSorbent Assay.	Skin, mucous membranes, and internal body temperature act as barriers to infection.	Controls are used to make sure the test works properly.
1000	Fiction. You are born with what is called innate immunity. The four components of this are anatomical barriers (skin, etc.), physiological barriers (body temp too high for some bacteria to live), phagocytic barriers, and inflammatory response which destroy new infectious cells.	Memory B cells. Because our bodies have these cells, our immune system quickly responds to familiar antigens.	The test came back positive, meaning that the patient may have the virus. A further test, the Western blot, must be run to determine if HIV is definitely present and to eliminate the possibility of a false positive. In case it is HIV, the patient should take steps to prevent the spread of HIV to others until the final results are in.	1. Place antigen (such as HIV) into 3 wells; the antigen will attach to the wells. 2. Place patient's serum into wells; in a positive patient, a primary antibody will bind to the antigen. 3. Place secondary antibodies into wells; in a positive patient, these will bind to primary antibodies. 4. Place enzyme substrate into wells; in a positive patient, this will bind to secondary antibodies, creating a blue color. If negative, no binding or color change will occur.	Organisms that carry pathogens from one host to another (bacteria, viruses, ticks, mosquitoes).	HIV is transmitted in numerous ways, such as sexual activity, sharing hypodermic needles with an infected person, and from mother to baby during birth and breastfeeding.

POST-LAB FOCUS QUESTIONS

From Bio-Rad's ELISA Immuno Explorer™ Kit Instruction Manual

1. Did your serum have antibodies to the disease?

2. If you tested positive for antibodies, does this mean that you have been exposed to the disease?

3. What reasons could there be for a positive test when you actually do not have the disease?

4. Why did your assay include three replications of each sample?

5. When you added serum samples to the wells, what happened to the serum antibodies if the serum sample was positive? What if it was negative?

6. Why did you need to wash the wells after every step?

7. When you added secondary antibody, what happened if your serum sample was positive? What if the serum sample was negative?

8. What ELISA-type tests can you buy at your local pharmacy?

POST-LAB FOCUS QUESTIONS

From Bio-Rad's ELISA Immuno Explorer™ Kit Instruction Manual

KEY

1. Did your serum have antibodies to the disease?

Students explain using data from their results.

2. If you tested positive for antibodies, does this mean that you have been exposed to the disease?

A positive result does not necessarily mean that you have been exposed to the disease.

3. What reasons could there be for a positive test when you actually do not have the disease?

It could be a false positive. Not all assays are specific for a single disease agent. For example, the ELISA for exposure to Lyme disease, which tests for IgG and IgM against the bacteria that cause the disease, has only 72% specificity, and a positive ELISA must be confirmed by a more specific test such as a Western blot or an immunoblot.

Another cause of false positives is past exposure to a disease. For example, most adults have been exposed to Epstein-Barr virus (EBV; the cause of many, but not all, cases of mononucleosis), and some people maintain levels of antibodies to EBV for years after clearing the disease. If they present to their physician with a fever and sore throat, they may test positive for EBV, but EBV may not be the cause of their symptoms.

A third cause of false positives is experimental error, such as putting a positive control into a well where you thought you were putting an experimental sample.

4. Why did your assay include three replications of each sample?

Assaying the samples in triplicate is another control. If you do not get the same result in all triplicate wells, you have a problem with your experimental technique or you have made a pipetting error. In a clinical laboratory, the experiment would have to be repeated.

5. When you added serum samples to the wells, what happened to the serum antibodies if the serum sample was positive? What if it was negative?

If the sample was positive, serum antibodies that recognized the purified antigen in the wells bound to the antigen. If the sample was negative, no antibodies bound.

6. Why did you need to wash the wells after every step?

Washing removes any proteins that have not bound to the plastic wells and any antibodies that have not bound to their targets, thus preventing unbound proteins (either antigen or antibodies) from giving false positive results.

7. When you added secondary antibody, what happened if your serum sample was positive? What if the serum sample was negative?

If the sample was positive, the secondary antibody bound to the serum antibodies that were bound to the purified antigen adsorbed to the wells. If the sample was negative, there were no serum antibodies bound in the wells and therefore the secondary antibody had nothing to bind to and was washed away.

8. What ELISA-type tests can you buy at your local pharmacy?

Test kits that are based on the same principles as the ELISA include home pregnancy and ovulation tests, and tests for the presence of illegal drugs such as marijuana and cocaine.

VIDEO COMPREHENSION QUESTIONS: AN INSIDE LOOK: THE FLU

From DiscoverySchool.com

1. What happens immediately after viruses and bacteria enter the body?

2. How does a virus take advantage of the way human cells work?

3. Why does the entire body rather than just the throat experience flu symptoms?

4. How does a T cell become activated, and what happens immediately after it's been called into duty?

5. What are antibodies, and what is their role in fighting the flu?

6. What causes immunity to the flu?

ANSWERS TO VIDEO COMPREHENSION QUESTIONS: AN INSIDE LOOK: THE FLU

KEY

From DiscoverySchool.com

1. What happens immediately after viruses and bacteria enter the body?

When viruses and bacteria first enter the body through the nose, they encounter the hairs lining the nostrils. These hairs trap nearly every particle that's inhaled, and they contain mucus that dissolves bacteria. A virus may survive, however, if it becomes detached from a nose hair and is sucked deeper into the nose. From the back of the nose, the virus can either go to the stomach, where it will be destroyed, or make its way to the throat, beginning the process of giving the person the flu.

2. How does a virus take advantage of the way human cells work?

It impersonates one of the proteins that cells use to communicate with each other. A cell can therefore be fooled into thinking the virus is a harmless protein and will permit the virus to enter it. Once inside the cell, the virus begins to use the cell's structure to manufacture components for new viruses.

3. Why does the entire body rather than just the throat experience flu symptoms?

As the flu viruses multiply, macrophages in the throat release interleukins, which are chemicals that go through the bloodstream to summon reinforcements to the throat. The interleukins cause nerves to be hypersensitive, making even slight touches uncomfortable. They also raise the body's temperature to make it a less hospitable environment for the virus. This temperature increase tricks the body into feeling cold. Blood vessels around the brain swell, causing a headache. All of these symptoms help remind the flu victim to slow down so that energy can be channeled into defeating the virus.

4. How does a T cell become activated, and what happens immediately after it's been called into duty?

Dendritic cells gather fragments of the flu virus and then search the body's lymph glands for an appropriate T cell. Once this T cell has been located, it begins to divide. The new T cells then move to the throat through the bloodstream and selectively destroy the infected throat cells.

5. What are antibodies, and what is their role in fighting the flu?

Antibodies are tiny proteins manufactured by B cells. They lock onto the spikes of newly produced viruses, paralyzing the viruses and preventing them from infecting new cells.

6. What causes immunity to the flu?

Some T cells remain as memory cells, patrolling the body for the rest of the person's life. If the virus tries to enter the body again, these memory cells will instantly wipe it out, unless it has mutated.

HOMEWORK ASSIGNMENT

STUDENT OBJECTIVES

- Determine the basis for scientific theories
- Address this question: do scientific theories change over time?

Listed below are several theories that have been proposed concerning the body's immune system:

- 1st century belief that the cause of disease was magical or divine in source
- Cause of disease tinged with Old Testament morality and belief
- 1700s — Edward Jenner's smallpox vaccination
- Louis Pasteur's germ theory of disease
- Eating your way to immunity
- Smoking and depression of the immune system
- Immunity associated with vaccinations
- Exercising your way to immunity
- Robert Koch and Koch's Postulates
- Viral mutation/evolution
- Resistant strains of bacteria

Using the media center and/or the Internet, research one of these theories to discover:

- the evidence or beliefs on which the theory was founded.
- if your chosen theory would be considered valid based on scientific evidence today.
- if there is a need for further research to verify or validate your theory.

Report back to the class on your findings.

BIOLOGICAL BODYGUARDS IMPLEMENTATION PLAN — ADDITIONAL ACTIVITIES & RESOURCES

Activity	Estimated Time	Materials/Equipment	Subjects Covered	Suggestions
Deadly Disease among Us: Pamphlet on a Disease Scoring Rubric Students select and research a disease, design an instructional pamphlet, and present it to the class.	90 minutes	Access to the Internet or media center; computer access for pamphlet production	English, AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	Located in notebook
Lab: The Sensitivity Range of a Home Pregnancy ELISA Test for Human Chorionic Gonadotropin	60 minutes	Human chorionic gonadotropin (HCG) CBS #BA85-4240 Home pregnancy tests (Ask pharmacist for outdated kits or available at The Dollar Store)	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	Arousing the Fury located in notebook
AIDS: The Effect on the Immune Response Graphing activity comparing the normal immune response to an AIDS-infected immune response	90 minutes	Copies of 2-page worksheet for each student 2 sheets graph paper per student Optional: Excel	Mathematics	Located in notebook
ELISA Antibody TEST, Flash Animation	5 minutes	Access to the Internet www.tracy.k12.ca.us/thsadvbio/biorad/ELISAwonderflash.swf	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	
Your World: Biotechnology and You — AIDS issue	30-60 minutes	Many activities in teacher's guide Magazine and activities for class	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	AIDS issue provided in workshop. Your World is also available to download for free at www.biotechinstitute.org/resources/your_world_magazine.html
Immune System Animations. These include T cell, B cell, and machrophage animations.	20 minutes	Access to the Internet http://highered.mcgraw-hill.com/sites/0072919183/student_view0/chapter39/elearning.html	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	
Protecting the Herd NIH Curriculum Supplement Series	90 minutes	Make copies for students or transparencies of materials	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	Available for free at science.education.nih.gov/customers.nsf/HSDiseases?OpenForm
Superbugs: An Evolving Concern NIH Curriculum Supplement Series	90 minutes	Copies of Bacterial Growth Experiment	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	Available for free at science.education.nih.gov/customers.nsf/HSDiseases?OpenForm
Deadly Diseases Among Us NIH Curriculum Supplement Series	30 minutes	Causes of death quiz (transparency) Set of disease cards for each group of 5 students	AP Biology, Allied Health I and II, Health Occupations, Medical Sciences I & II, Anatomy and Physiology	Available for free at science.education.nih.gov/customers.nsf/HSDiseases?OpenForm

Additional Resources:
cellsalive.com
www.biointeractive.org
www.accessexcellence.org
www.hhmi.org/news/schatz.html
www.cancer.gov/cancertopics/understandingcancer/immunesystem

DEADLY DISEASE AMONG US: PAMPHLET ON A DISEASE

Assignment: Select and research one disease from the list below or one of your own and prepare an instructional pamphlet to present to the class.

SCORING RUBRIC

1 - Criterion: Quality of Research				
1	2	3	4	5
1 source		3 sources		5 sources
2 - Criterion: Question and Answer				
1	2	3	4	5
Many factual errors		Some factual errors		No factual errors
3 - Criterion: Graphics				
1	2	3	4	5
No Graphics		Graphics that describe the disease		Graphics that instruct as well as dazzle!
4 - Criterion: Organization				
1	2	3	4	5
Little evidence of design and planning		Some evidence of design and planning		Strong evidence of design and planning
5 - Criterion: Oral Presentation				
1	2	3	4	5
Did little to describe disease, symptoms, cause, and cure		Explained disease, symptoms, cause, and cure adequately		Grabbed everyone's attention

Examples of types of diseases to select from are: AIDS, cholera, Creutzfeldt-Jakob Disease (CJD), Ebola, Guinea worm disease, influenza, Legionnaire's disease, Lyme disease, malaria, strep throat, plague, pneumonia, polio, schistosomiasis, tuberculosis, anthrax, smallpox.

ELISA ADDITIONAL LAB ACTIVITY

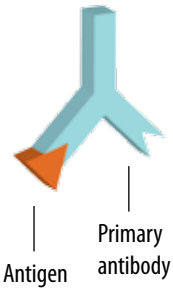
THE SENSITIVITY RANGE OF A HOME PREGNANCY ELISA TEST FOR HUMAN CHORIONIC GONADOTROPIN (HCG)

OBJECTIVES

Students will gain knowledge of the process for screening human urine to detect the presence of human chorionic gonadotrophin, commonly known as HCG, using the ELISA technique of immunological assay.

BACKGROUND INFORMATION

ELISA is a very common immunological assay used in labs, as well as the privacy of homes, across the country today. This process can even detect horse meat in hamburger and antibiotics in milk. However, probably the most important application of this technique is in the clinical setting. ELISA is an important tool in the screening for HIV exposure, as the basis for pregnancy tests, and in ovulation predictor testing, which are all based on the binding ability of antibodies.



Rather than testing for the presence of a condition or antigen itself, ELISA tests for the presence of antibodies specific to the condition or antigen of interest. This relies on antibodies' property of binding to specific antigens and/or to other antibodies. Knowing which antibody binds to which antigen (see diagram) allows a search for an antigen by searching for the antibody that responds to it.

Therefore, when an individual is tested for HIV, the lab technician does not screen the blood for HIV, but for the antibodies to HIV. If HIV antibodies are detected in the blood, one can conclude that exposure to HIV has occurred.

Another familiar use of this ELISA technique is in home pregnancy-testing kits. The antigen known as human chorionic gonadotrophin (HCG), is detected in these kits. HCG is a hormone that is secreted in bodily fluids of a female during pregnancy. The responsibility of this hormone is to prevent the destruction of the corpus luteum at the end of the menstrual cycle. With the presence of HCG, the corpus luteum also begins to secrete massive amounts of estrogen and progesterone hormones. These hormones are responsible for stimulating the endometrial lining of the female uterus to grow and store adequate amounts of the nutrients needed for fetal development. HCG can then be detected in the urine of the mother soon after the fertilized embryo implants itself into the endometrial lining of the uterus. ELISA can detect the anti-HCG antibody that will bind to the HCG in the urine. This complete HCG concept is the basis for home pregnancy tests. Most home pregnancy tests will detect the HCG concentration levels in the very early weeks of pregnancy due to the rapid increase of this hormone (see data table below).

Week of Pregnancy	Amount of HCG in Urine (mIU/mL)
3	5 – 50
4	3 - 426
5	19 – 7,340
6	1,080 – 56,500
7-8	7,650 – 229,000
9-12	25,700 – 288,000
13-16	13,300 – 254,000
17-24	4,060 – 165,400
25-40	3,640 – 117,000

ESSENTIAL QUESTION

What is the sensitivity range of a home pregnancy ELISA test for human chorionic gonadotropin?

MATERIALS NEEDED

- Vial of 10,000 international units (IU) of dried HCG (available through Carolina Biological Supply Company)
- 200 mL tap water
- Yellow food coloring
- 4 "stock bottles" – or comparable containers
- Home pregnancy test kit (available at pharmacy stores, as well as the Dollar Store)
- Small bottle large enough for 5 mL (one bottle for each group of students)

PRE-LAB TEACHER PREPARATIONS

1. Reconstitute the entire vial of dried HCG by adding 200 mL tap water. Mix completely dissolving the HCG. The stock concentration of HCG is now 50 IU per mL.

2. Add enough yellow food coloring so the mixture resembles dark urine.

3. Using tap water, prepare dilutions of the stock solution using the formula $C_1V_1 = C_2V_2$.

C_1 = stock concentration of 50 IU/mL
C_2 = diluted concentration
V_1 = 200 mL of stock concentration
V_2 = 2 mL (approximate – check the directions on the pregnancy test kit to determine the volume of "urine" needed for the test)

4. Dilute a set of samples within the range of detectable levels of HCG in the third week of pregnancy as shown in the previous chart.

5. Provide each lab team with 2 mL of a different dilution representing the "urine" to be tested.

INSTRUCTIONS FOR STUDENTS

Each lab team will be testing a different concentration of "urine."

1. Follow the directions in the test kit to test your "urine" sample for the presence of HCG. The sample has been prepared in advance by your teacher.

2. Record your lab group's results in the provided space:

_____

3. Report your results to the teacher. All groups will enter their data into the Class Data Chart below by lab group number.

4. After reviewing the class results, answer the following questions for this activity.

a. How reliable is this test?

b. Is it more likely to give positive or false negative results? Why?

c. What factors might contribute to incorrect (false positive or false negative) results?

5. As a lab team, draw an illustration of how ELISA might work in these kits. For example, what might be the components of each of the reagents provided in the test kit?

GOING FURTHER

Have students investigate the accuracy of outdated home pregnancy kits in comparison to kits that are current.

Have students compare different test kits with the same concentration levels.

CLASS DATA CHART BY LAB GROUP

#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15

NAME _____ DATE _____ CLASS _____

AIDS: THE EFFECT ON THE IMMUNE RESPONSE

BACKGROUND

Acquired Immunodeficiency Syndrome (AIDS) is a disease caused by the human immunodeficiency virus (HIV) and results from the destruction of an individual's immune system. HIV is passed from one person to another when infected blood, semen, or vaginal secretions come in contact with an uninfected person's broken skin or mucous membranes. Infected pregnant women can pass HIV to their babies during pregnancy or delivery, as well as through breast-feeding. People with HIV have what is called an HIV infection. Some of these people will develop AIDS as a result of their HIV infection.

HOW DOES HIV DESTROY THE IMMUNE SYSTEM?

The body's immune response involves white blood cells called lymphocytes. The two main kinds of lymphocytes involved in the immune response are T cells and B cells. Certain types of T cells destroy antigens directly. B cells produce antibodies with the help of other kinds of T cells known as T_H cells (for helper). When HIV enters the body, the virus destroys the T_H cells that facilitate the production of antibodies. Therefore, the immune system's ability to fight disease causing pathogens is impaired. The criteria for AIDS diagnosis is a T_H cell count below 200 cells/µl. The person usually dies from accumulation of secondary infections called opportunistic infections. Some examples include tuberculosis, P. carinii, and Karposi sarcoma.

STUDENT OBJECTIVES

- Plot data in graph form to demonstrate a healthy body's normal immune response.
- Plot data in graph form to demonstrate an HIV-infected body's immune response.
- Compare and interpret these two different immune responses.

MATERIALS

- colored pencils (red, blue, green, and yellow)
- graph paper (1 sheet)

PROCEDURE: PART A. THE NORMAL IMMUNE RESPONSE

Tables 1 and 2 refer to hypothetical numbers of microbes and immune response (units). Immune response (units) summarizes all the activities of the immune system, including antibody production and direct attack on invaders.

1. Examine Table 1, Normal Immune Response.

TABLE 1: NORMAL IMMUNE RESPONSE

Months	Number of Microbes	Immune Response (units)
0	1	0
3	1,000	0
6	10,000	1
36	1,000	100
48	10	1,000
60	1	1,000
72	0	1,000
84	0	100
96	0	10
108	0	1
120	0	1

2. Follow these steps to construct a graph of the data in Table 1 located above:

- Label the vertical axis (Y-axis) "Number of Microbes." Using an appropriate scale, number the Y-axis from 1 to 100,000.
- Label the horizontal axis (X-axis) "Number of Months." Using an appropriate scale, number the X-axis from 0 to 120.
- Use a red pencil to plot the number of microbes against the number of months.
- Use a blue pencil to plot the immune response (units) against the number of days.
- Be sure to give your graph a title and provide a key indicating the color code.

TABLE 2: IMMUNE RESPONSE IN PERSON WITH HIV

Months	Number of Microbes	Immune Response (units)
0	1	1
3	1,000	50
6	100,000	1,000
36	10	10,000
48	1	10,000
60	1	1,000
72	1	500
84	10	100
96	100	1
108	1,000	0
120	100,000	0

4. On the same sheet of graph paper, include the data from Table 2 located above:

- Use a green pencil to plot the number of microbes against the number of months.
- Use a yellow pencil to plot the immune response (units) against the number of months.

STUDENT ANALYSIS

Use your graph of the Normal Immune Response to answer the following questions.

1. What happens to the number of microbes:

during the first 3 months? _____

during months 6 through 60? _____

2. What happens to the immune response:

during the first 3 months? _____

during months 6 through 60? _____

3. Summarize in 2-3 sentences what happens during a normal immune response.

_____

_____

_____

Use your graph of the Immune Response of a Person with HIV to answer the questions below.

4. What happens to the number of HIV:

during the first 3 months? _____

during months 6 through 60? _____

during months 72 through 120? _____

5. What happens to the immune response in a person with HIV:

during the first 48 months? _____

during months 60 through 120? _____

6. Summarize in 2-3 sentences what happens during the immune response in a person with HIV.

_____

_____

_____

Compare and Contrast:

7. How do the time periods in the two graphs differ? _____

8. How is the HIV graph similar to that of the normal immune response? _____

_____

_____

9. How is the HIV graph different from that of the normal immune response? _____

_____

_____

10. How do you explain the increase in the number of HIV viruses during months 84 through 120? _____

_____

_____

Further Research: Find out some of the other diseases that affect the immune system.

BIOLOGICAL BODYGUARDS IMPLEMENTATION PLAN — INTERDISCIPLINARY BRIDGES							
Activity	Arts	English	Health	Math	Science	Social Studies	Provided materials
Using Drugs? You're in Trouble		X	X		X	X	Activity sheet
"Global State of Emergency: Government's Role in Curbing the AIDS Crisis"						X	One copy of handout per student, or access to internet. www.state.gov/s/gac/rl/or/c11652.htm
Battling Bioterrorism: Understanding the Science and Politics	X	X				X	Copies from notebook or CD. Internet access for research of diseases. PowerPoint access, if available, for student presentations
A Discovery-Based Approach to Understanding Clinical Trials		X	X		X	X	3 Handouts (attached): Engagement Activity, FAQ and Glossary (Understanding Clinical Trials), Exploration Activity (choose either "Strategies for Delivering Anti-HIV Therapy in South Africa" or "Safety of and Immune Response to a Bird Flu Virus Vaccine in Healthy Adults") Optional website: ClinicalTrials.gov.
Germs In the Arts & Humanities	X	X				X	List of related music and literature

NAME _____ DATE _____ CLASS _____

USING DRUGS? YOU'RE IN TROUBLE

Many high schools across the country, including some in North Carolina, have now adopted randomized drug testing for students participating in extracurricular activities. A 2002 Supreme Court ruling states that this randomized testing is constitutional, as long as the school restricts the testing to those involved in extracurricular activities.

1. Think. Pair. Share.

Ask each student to jot down a few answers to the following questions. After 5-10 minutes, place the students in small groups to discuss their answers. Each group will then share their thoughts with the class.

- Do you assume that someone who refuses a drug test has something to hide? What other reasons would a person have for refusing a test?

- Do you think that randomized testing will prevent students from taking drugs?

2. Debate.

Randomly assign half the class to the "pro" side of drug testing, and the other half to the "con" side. Give each side about 15 minutes to prepare an answer to their assigned question.

- Pro question: What are the benefits of randomized drug testing?

- Con question: What negative impact could testing have?

Allow each group 5-10 minutes to present their case, without interruption. After each team presents, the opposing side will ask questions. Allow each team 10-15 minutes to respond to the questions.

3. Final Question.

Why was the issue of randomized student drug testing brought before the Supreme Court? Allow students to discuss for a few minutes. If no one brings up the Bill of Rights, present the students with the text of the Fourth Amendment. Students may discuss or write an essay that addresses whether a school system has "probable cause" to subject students to drug testing.

The Fourth Amendment to the Constitution
The right of the people to be secure in their persons, houses, papers, and effects, against unreasonable searches and seizures, shall not be violated, and no Warrants shall issue, but upon probable cause, supported by Oath or affirmation, and particularly describing the place to be searched, and the persons or things to be seized.

4. Homework.

Students research the various methods used to conduct drug testing. They may also research the effectiveness of randomized testing as a deterrent to drug use.

ANSWERS FOR USING DRUGS? YOU'RE IN TROUBLE

KEY

Many high schools across the country, including some in North Carolina, have now adopted randomized drug testing for students participating in extracurricular activities. A 2002 Supreme Court ruling states that this randomized testing is constitutional, as long as the school restricts the testing to those involved in extracurricular activities.

1. Think. Pair. Share.

Ask each student to jot down a few answers to the following questions. After 5-10 minutes, place the students in small groups to discuss their answers. Each group will then share their thoughts with the class.

- Do you assume that someone who refuses a drug test has something to hide? What other reasons would a person have for refusing a test?
  - o Refusals are often based on the claim that it invades a student's privacy.
  - o Students who have never done anything illegal may feel they are being treated unfairly, when they are targeted for testing.

- Do you think that randomized testing will prevent students from taking drugs?
  - o Many argue that randomly testing those participating in extracurricular activities targets the very people who are the least likely to take drugs.
  - o Two recent studies conducted by the University of Michigan have shown that random drug testing does not reduce student drug use.

2. Debate.

Randomly assign half the class to the "pro" side of drug testing, and the other half to the "con" side. Give each side about 15 minutes to prepare an answer to their assigned question.

- Pro question: What are the benefits of randomized drug testing?
  - o Deterrent to drug use
  - o Early detection of student drug use allows for more effective intervention

- Con question: What negative impact could testing have?
  - o Fewer students involved in extracurricular activities
  - o Students become more sneaky about drug use
  - o Refusal to test, while the right of the student, may lead to false assumptions about the student
  - o Feeling that the student is "guilty" just because he or she was chosen for a test

Allow each group 5-10 minutes to present their case, without interruption. After each team presents, the opposing side will ask questions. Allow each team 10-15 minutes to respond to the questions.

3. Final Question.

Why was the issue of randomized student drug testing brought before the Supreme Court? Allow students to discuss for a few minutes. If no one brings up the Bill of Rights, present the students with the text of the Fourth Amendment. Students may discuss or write an essay that addresses whether a school system has "probable cause" to subject students to drug testing.

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4. Homework.

Students research the various methods used to conduct drug testing. They may also research the effectiveness of randomized testing as a deterrent to drug use.

Global State of Emergency: Government's Role in Curbing the AIDS Crisis

Subjects: World History, Civics and Economics, U.S. History, American Government

Overview of Lesson Plan: In this lesson, students will explore the role of the United States in controlling the AIDS pandemic. Specifically, students will analyze The President's Emergency Plan for AIDS Relief (PEPFAR) and discuss future measures that the U.S. might take in the global fight against AIDS.

Resources: Handout (attached); copies of The President's Emergency Plan for AIDS Relief (found at www.state.gov/s/gac/rl/or/c11652.htm)

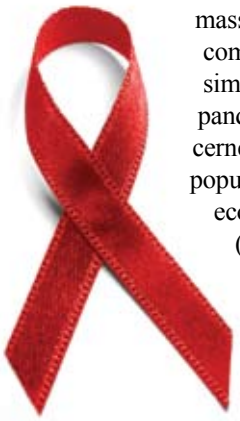
ACTIVITIES/PROCEDURES

1. (15 minutes) Give each student a hand-out (attached) with the following quote from Donna Shalala. Allow students 10-15 minutes to write down their thoughts on the listed questions.

In 2000, the Clinton Administration designated HIV/AIDS as a threat to national security. This was the first time that a disease has been added to the list of things that threaten U.S. security. Clinton's U.S. Secretary of Health, Donna Shalala, said,

> We know that infectious diseases know no borders, they can affect this country, and in this case it is both in our economic interest and in our national security interest to work on these infectious diseases abroad. The high rates of AIDS in Africa are putting security and stability at risk by disabling national armies, disrupting economies and killing off people who might become the next generation of leaders. Basically AIDS is uncoupling the economic gains in Africa as African countries are forced to shift more resources to their health care systems from their economic investments . . . . Eastern Europe has an AIDS problem, Russia has it, India has it, every country in the world that we do business with, but more importantly our need to be politically stable, is suffering from this huge onslaught of AIDS. And that makes the relationship economically and from the security point of view relevant to America's national security.

Do you think AIDS is a threat to America's national security? This statement was made prior to 9/11. Since then, bioterrorism has become a very real threat. How are the effects of bioterrorism (e.g., mass numbers of our population coming down with smallpox) similar to the effects of an AIDS pandemic? Why would we be concerned about mass numbers of the population dying? Is it a threat to our economy? The global economy? (Loss of workforce, goods, cost of health care.) Are there other reasons that the U.S. should get involved in the fight against AIDS? (Humanitarian mission.) List other instances of U.S. humanitarian assistance in U.S. History. Should the fight be restricted to the U.S. or should we try to help other countries as well? (Tie in with global economy and humanitarianism.)



2. (20 minutes) As a class, read pp. 15-16 of PEPFAR, "1. The Global HIV/AIDS Emergency: A Severe and Urgent Crisis."

a. Define "pandemic":
   i. Epidemic over a wide geographic area and affecting a large proportion of the population
   ii. An epidemic is an outbreak of a contagious disease that spreads rapidly and widely.

b. Discuss the "significant challenges that face all nations, donors, institutions, and individuals." Have students offer suggestions for meeting each of the challenges, including what groups should be involved.
   i. Treatment — antiretroviral drugs (A substance that stops or suppresses the activity of a retrovirus such as HIV. AZT, ddC, ddI and d4T are examples of antiretroviral drugs.) Problems include cost and monitoring
   ii. Lack of basic care and support services
   iii. Limited infrastructure and human resource capacity

iv. Growing orphan population straining community support
v. Inadequate leadership
vi. Stigma of HIV
vii. Inefficient use of funds, due to poor planning and lack of evaluation for the programs in place

c. Discuss why there is no longer a debate over "prevention" versus "treatment."
i. In the beginning of the AIDS outbreak, there was no known treatment. Some argued that money was better spent on preventing new people from getting the disease while others said that treating those who had it could stop its spread. Both prevention and treatment are necessary to address all the challenges.

3. (40 minutes)
a. Divide students into four groups and give each group the relevant section of PEPFAR — leadership (pp. 19-21), prevention (pp. 23-32), treatment (pp. 33-41) and care (43-51).

b. Ask each group to read over their section and come up with a brief summary and critique of that portion of PEPFAR to share with the class.

4. (15 minutes)
a. Wrap-up: Discuss the pandemic as it affects the entire planet. Why is the President's plan called an "emergency plan"? Could it be posited that the U.S. is currently treating the pandemic by focusing on the 15 countries that are the most affected? What is being done to prevent spread throughout the world? Specifically, China, India and Russia are on the brink of a massive AIDS outbreak. What should they do to prevent this? How are these countries different socially and economically from the ones that the U.S. is helping through PEPFAR? Should the U.S. handle these countries differently?

b. Homework: Ask students (individually or as a group project) to research AIDS in China, Russia or India and come up with a proposal to give to the leaders of the U.S. and of their chosen country, to address this impending crisis. A good introductory article on this subject is "The Future of AIDS" by Nicholas Eberstadt, found at www.foreignaffairs.org/20021101faessay9990/nicholas-eberstadt/the-future-of-aids.html

HANDOUT: GOVERNMENT'S ROLE IN CURBING THE AIDS CRISIS

In 2000, the Clinton Administration designated HIV/AIDS as a threat to national security. This was the first time that a disease has been added to the list of things that threaten U.S. security. Clinton's U.S. Secretary of Health, Donna Shalala, said,

> We know that infectious diseases know no borders, that they can affect this country, and in this case it is both in our economic interest and in our national security interest to work on these infectious diseases abroad. The high rates of AIDS in Africa are putting security and stability at risk by disabling national armies, disrupting economies and killing off people who might become the next generation of leaders. Basically AIDS is uncoupling the economic gains in Africa as African countries are forced to shift more resources to their health care systems from their economic investments . . . . Eastern Europe has an AIDS problem, Russia has it, India has it, every country in the world that we do business with, but more importantly our need to be politically stable, is suffering from this huge onslaught of AIDS. And that makes the relationship economically and from the security point of view relevant to America's national security.

Do you think AIDS is a threat to America's national security?

Is it a threat to our economy? The global economy?

Are there other reasons that the U.S. should get involved in the fight against AIDS?

Should the fight be restricted to the U.S. or should we try to help other countries as well?

Battling Bioterrorism: Understanding the Science and Politics

Developed by Susan Hirsch, East Wake High School, and Brian Wood, Enloe High School

OVERVIEW

The fear of an attack of bioterrorism has increased tremendously since September 11, 2001, and the U.S. government has budgeted an unprecedented amount of money to be used for research on this topic. In the following activities, students assume the role of research scientists from different government agencies who do research and other studies in order to prepare and prevent an attack where chemical or biological agents are used.

Learning about bioterrorism brings the study of science into your classroom while following the Social Studies standard course of study. It allows the students to research a very timely topic and discover how many agencies are involved in the defense of our country against a bioterrorist attack. The four activities described below can be used with a unit on the Legislative Branch and Congress or while teaching economics and the government's budgets.

OBJECTIVES

- Explore an aspect of the United States' anti-terrorism preparations
- Learn about the role of scientific research in governmental activities
- Discuss the roles of the U.S. Legislative Branch and Congress
- Learn about the national budget
- Develop public speaking skill

I. CONGRESSIONAL COMMITTEE HEARING SIMULATION ON BIOTERRORISM

Students work in pairs or alone to research a government agency that has been assigned by the U.S. government to research, prepare, and prevent a biological or chemical attack. Let each student/group draw numbers and whoever draws #1 gets to pick which agency they want. Continue this practice until all students have chosen. Before the students choose their agency, briefly explain what each agency is doing.

Government Agencies

- Centers for Disease Control and Prevention (CDC)
  www.cdc.gov
- Food and Drug Administration (FDA)
  www.fda.gov
- Health and Human Services (HHS)
  www.hhs.gov
- Homeland Security
  www.dhs.gov
- Center for Civilian Biodefense Strategies
  Johns Hopkins — www.hopkins-biodefense.org
- USDA
  www.usda.gov
- Environmental Protection Agency (EPA)
  www.epa.gov
- Federal Trade Commission (FTC)
  www.ftc.gov
- Department of Justice
  www.usdoj.gov
- Department of Labor (OSHA)
  www.osha.gov
- U.S. Army Medical Research
  www.usamriid.army.mil/education
- FBI
  www.fbi.gov
- CIA
  www.cia.gov
- National Institute of Allergy and Infections (NIAID)
  www.niaid.nih.gov
- Project Bio Shield
  www.whitehouse.gov/bioshield

After students have completed their research, each student or group of students will prepare a 2- to 4-minute oral presentation, including some type of visual — it may be poster/s, a PowerPoint, or individual sheets for each of the other students. Students make their presentations before a congressional committee (class and teacher). The job of each agency (student or group of students) is to convince the congressional committee

that their agency deserves be the lead in all research on bioterrorism. The committee will decide which agency will take the lead and receive funding for bioterrorism research.

Each presentation should address the following questions:

• What is the main emphasis of the current research being conducted? (diseases, data reporting, storage, biodefense, vaccines, preparation, prevention)
• What are the plans for future research?
• How much money has been budgeted for your agency to spend?

II. BIOTERRORISM "HYPE OR THREAT" ACTIVITY

Each of the following possible biological warfare agents should be placed on a sign. Make a masking tape line on the floor. One end of the line represents a low threat and the other end a high threat based on a scale from 1 to 10. Threat will be defined as likelihood that the agent would make a practical biological terrorist agent. The signs should be distributed to students, and the students will rank each agent in terms of the perceived list. Make a digital camera picture of the rankings.

Possible Biological Warfare Agents

Anthrax
Plague
Tularemia
Brucellosis
Q fever
Smallpox
Equine encephalitis viruses
Foot and Mouth Disease
Ebola virus
Hemorrhagic fevers (other than Ebola)
Influenza virus
Staph enterotoxin B
Ricin
Botulism toxins
Trichothecene mycotoxins

Students work in pairs or alone to research specific diseases or biological agents and develop a five- to ten-minute poster or PowerPoint presentation on their assigned biological warfare agent. Let each student/group draw numbers and whoever draws # 1 gets to pick which disease or agent they want to research. Continue this practice until all students have chosen.

The presentations should include the following information:

• History of the bacteria, virus, or toxin
• Any use as a biological weapon in the past
• Structure (what does it look like)
• Changes such as mutations to make it a more efficient biological weapon
• Mode of transmission including host species
• Symptoms and diagnosis
• Treatment
• Containment options if an outbreak should occur
• Social implications including the economic and political impact of an outbreak

A good starting point for research is the Center for Disease Control website: www.cdc.gov. Emphasize that students should cite their sources.

During the presentation the teacher should give students participation forms with a section for notes on each disease. Students take notes during the presentations and turn them in for evaluation.

After all of the presentations, the students will repeat the first exercise to see if their perceptions of the risk of each agent have changed and determine if their previous concerns were based on science or media hype.

III. SUPPLEMENTARY BIOTERRORISM LESSON PLANS

• Write a handbook on how to clean up a community after a biological or chemical attack.

• Discuss the Hippocratic Oath and the responsibility of the physician to the infected if there was a biological attack. If you were in the medical profession, would you knowingly treat someone who had been infected with a contagious disease?

• Write a grant application to a Biotech company where you are a researcher wanting to sequence a recently discovered virus. Give past, present and future uses of this process and convince your supporter that this research is important. (Persuasive letter)

• Discuss the economic importance of a biological attack on the U. S. economy. What about on the world economy?

- Create a mock drill on how a region would react to a smallpox outbreak.
- Write a report on how the government should prioritize those who should get vaccinated if there is an outbreak of a contagious disease.
- Keep a two-week journal as if you were being quarantined because of an outbreak of a contagious disease.
- Research the history of a disease such as smallpox and present to the class.
- Go to the Center for Disease Control (CDC) website and create 10-15 thought-provoking questions about bioterrorism and/or plagues that could be used as a lesson for the rest of the class.
- Research different companies and corporations as to how they handle their mail since the anthrax and ricin-laced letters were mailed in 2001 and 2004 respectively.
- Imagine that you work for the post office. Write a list of procedures that should be in place to safely handle mail.

IV. PAIDEIA SEMINARS: "EFFECTS OF BIOTERRORISM" AND *THE SPECKLED MONSTER*

Paideia comes from "pediatrician" and "encyclopedia", an ancient Greek belief of education that all children should have a general knowledge base. *Paideia* is the general learning that should be the possession al all children.

The Paideia seminar is a formal discussion based on text, in which the leader of the discussion asks open-ended questions designed to precipitate spirited and thoughtful dialogue. As a result, the participants are asked to articulate, justify, and clarify their own ideas as well as their responses to the ideas of others. The ultimate goal of a seminar is that all participants develop a more sophisticated understanding of the text through thoughtful interaction with the ideas of others. Neither consensus nor closure should signal the end of a seminar; rather continued inquiry and reflection should flow directly out of the experience.

There are four components of a successful seminar activity:

- Pre-seminar activity — Once the text is given to the participants, questions or an assignment that focused on content should be assigned so that before the seminar, the participants will have read and understood the text.
- Coaching activity — In this component, students develop in-depth understanding of the topic by problem solving and application.
- Seminar — The teacher becomes the facilitator and leads the students in a discussion of the assigned texts. The participation of the students consists of thinking, listening, speaking, referring to the text, and respecting all participants.
- Post-seminar activity — An assignment such as a writing assignment is made to assess and apply both content and process.

SEMINAR ON "EFFECTS OF BIOTERRORISM"

This seminar activity consists of three readings and can be used in its entirety or in small parts as class discussions, outside or in-class readings, cooperative learning activities or as seminars. The readings are "Prologue" from The Anthrax Letters by Leonard Cole and "The Horror of Halabja" and "What Leaders and Citizens Can Do," from Avoiding Armageddon, with quotes from former President Mikhail Gorbachev of the Soviet Union and former President Jimmy Carter of the U. S.

Pre-Seminar Activity: After reading the three selections, complete all activities on this page on your own paper in ink and answer any questions in complete sentences.

The Anthrax Letters

1. Write five questions as if you were an investigator that you would ask people who lived on and around Nassau Street in Princeton, New Jersey.
2. Describe how anthrax was used in the Bible according to the author.
3. Why is anthrax the preferred instrument of terror?
4. List the steps that anthrax spores go through once it get in the body.
5. Describe how you would react if you had been Pat Hallengren on August 10, 2002.

"Horror of Halabja"

Write a one-day journal entry as if you were the Iraqi Air Force pilot who flew over Halabja on March 16, 1988.

"What Leaders Can Do"

Summarize what both Gorbachev and Carter said was right and wrong with the world. Next, explain who you agree with the most and why.

Coaching Activity: Divide the class into cooperative learning groups with four students per group and give each student a copy of the readings "Definition of Bioterrorism" and "History of Biowarfare and Bioterrorism" (www.hs.state.az.us/phs/edc/edrp/es/bioterror.htm) and a large piece of poster board or construction paper. Divide the reading into four parts and assign each student in the group one section to read. Then have them divide their poster board in four by drawing a line down and across. Let them use colored pencils or magic markers and illustrate what they had read on the poster. Once everyone is finished, have each group present it to the class.

Opening seminar question: What scares you the most about bioterrorism?

Core seminar questions:

1. Pat Hallengren's first thought was of her mailman, Mario. What would be your first reaction if you had been in her situation?
2. You are the postal inspector in 2001. What are some rules you would make to keep the mail safe?
3. The person who sent anthrax has not been found as of yet. If you were an investigator and in the process of trying to solve the crime, what are some questions that you would ask the public to try to arrive at the truth?
4. What punishment would you recommend for the person who committed this crime, if they are found?
5. The secret code for the dropping of nerve gas in Halabja was "Rain, Rain, Rain." Think of another secret code that you may have used.
6. Describe how you would react if you were told to drop a chemical gas and kill innocent people or die.
7. Explain what punishment you would inflict on the pilot if you were an American soldier and you arrested him.
8. Analyze one way that what Gorbachev said is different from what Carter said.

Closing Question: The President of the United States is in the room. What is one thing you would say to him about bioterrorism?

Post-Seminar Activity: Write entries in a journal for 14 days as if you had been exposed to a biological or chemical agent but had no symptoms. Each entry must be dated and be at least one half of a page. Create a cover for this journal.

Seminar on *The Speckled Monster: A Historical Tale of Battling Smallpox*

This book by Jennifer Lee Carrell tells the dramatic story–both historical and timely–of two parents who dared to fight back against smallpox. This unit concentrates on the introduction (www.speckledmonster.com/intro.html) to the book, and the chapter "Rosebuds in Lily Skin" (www.speckledmonster.com/partone.html), which tells how Lady Mary Wortley Montagu saved her daughter and helped save the city of London from the deadliest disease mankind had known. We suggest reading the introduction of the book to the students so that they have a frame of reference as what and how this chapter fits into the entire story.

Pre-seminar Activity: Answer all questions in ink on your own paper and in complete sentences.

1. How did Lady Mary react to John Dryden's quote: Blisters with pride swelled, which through's flesh did sprout / Like rosebuds stuck i' th' lily skin about."
2. What do you think about the above quote?
3. Explain the line "the smallpox had been slashing its way through her friends and family."
4. Why did Lady Mary not take Princess Anne's death personally?
5. How did Lady Mary protect her daughter, Mary?
6. How did King George I react when his son, Prince of Wales, challenged his power in Parliament?
7. What brought the father and son back together?
8. How did the people of London react to the outbreak of smallpox?
9. What could have prevented the nurse from contacting smallpox?
10. What was Lady Mary's request of Mr. Maitland?
11. What were Mr. Maitland's demands and why did they change?
12. What preparations did Lady Mary want to avoid?
13. How did little Mary react to the doctor's procedure?
14. Who is the hero in this story and why?

Coaching Activity: Divide the class into cooperative learning groups with four students per group and give each student a copy of the reading the "Definition of Bioterrorism" and the "History of Biowarfare and Bioterrorism" (www.hs.state.az.us/phs/edc/edrp/es/bioterror.htm) and a large piece of poster board or construction paper. Divide the reading into four parts and assign each student in the group one section to read. Then have them divide their poster board in four by drawing a line down and across. Let them use colored pencils or magic markers and illustrate what they had read on the poster. Once everyone is finished, have each group present it to the class.

Opening Seminar Question: All vaccinations risk killing or harming some percentage of otherwise healthy people, in order to protect the majority. What criteria should be used to decide when to begin vaccinating the majority of the population? Also, who should decide and who, if anyone is to blame, when things go wrong?

Core Seminar Questions:

1. Explain what made Lady Mary and others like her willing to risk inoculation in 1721 for themselves and their family members? Consider the following arguments:
   - Emotional and personal
   - Scientific
   - Religious
   - Political
   - Economic
2. How do the above issues relate to modern concerns about vaccination?
3. Compare the fears in London of the spread of smallpox to our fear of a bioterrorist attack today. How are they alike and how are they different?
4. In 1721 the British government tested smallpox inoculation on prisoners under sentence of death; it did so with the prisoners' consent, and in exchange for pardons. In researching cures and vaccines for various diseases, the U. S. government has in the past run tests on human subjects both with and without their informed consent. What would have to happen to make you volunteer to be a part of medical testing for a cure for a deadly disease?
5. If no one consents to be tested, how should scientists test the safety of new vaccines and medicines?
6. If you were Lady Mary, how would you have reacted if your child or you may be exposed to a deadly disease?
7. If you were Princess Caroline, what would you have done in her situation—pick your spouse or your children?

Closing Seminar Question: Who was the medical hero in our story?

Post-Seminar Activity: Write a one- to two-page report to be presented to the Department of Homeland Security on how the government should prioritize those who should get vaccinated if there is an outbreak of a contagious disease. Include a list of people who should be charged, if you feel there should be any. Think about citizens and non-citizens, young and old, healthy and sick, rich and poor, etc.

Online Resources

- www.globallink.org.uk/Esc2Saf/Rebwar.htm — Story and artwork by survivor of chemical attack on the Kurdish in Halabja, Iraq
- www.pbs.org/wgbh/nova/bioterror/linksandbooks.html — NOVA online information on bioterrorism
- www.pbs.org/newshour/health/bioterrorism/threat_m.html — Online "News Hour with Jim Lehrer" about bioterrorism
- www.pbs.org/newshour/extra/features/july-dec02/bio.html — Jim Lehrer's Web page for students concerning bioterrorism
- academic.udayton.edu/health/syllabi/Bioterrorism/00intro02.htm — On the early biological war on Native Americans

A Discovery-Based Approach to Understanding Clinical Trials

Subjects: English, Health, Science, Social Studies

Overview: In modern society, the drugs we take and the medical procedures we undergo are the result of extensive research. Most people have seen the ads for clinical trials recruiting people with heart disease, high blood pressure, or some other possible ailment. Yet, many do not fully understand the procedures involved in clinical research. According to the U.S. National Institute of Health website, ClinicalTrials.gov, clinical research is the "fastest and safest way to find treatments that work in people and ways to improve health."

This lesson plan, designed to be covered in one 90-minute class (or at the end and beginning of two successive classes), will help students learn about the make-up of clinical research and the provisions in place to ensure the safety of the human participants.

These activities will also be useful in teaching critical reading and informational writing skills. Social Studies teachers may wish to expand on the content provided here by focusing on the history, ethics, and regulations of clinical trials. General information may be found at "The history of clinical testing and its regulation" (http://www.roche.com/pages/facets/18/histclinte.htm).

Objectives: Students think critically about the ways in which scientific researchers approach health problems, while also learning to analyze texts and write informational, science-based compositions.

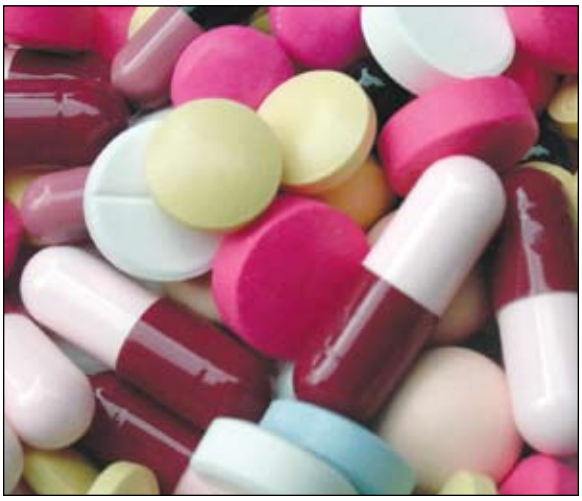
RESOURCES

• 3 Handouts (attached): Engagement Activity, FAQ and Glossary (Understanding Clinical Trials), Exploration Activity (choose either "Strategies for Delivering Anti-HIV Therapy in South Africa" or "Safety of and Immune Response to a Bird Flu Virus Vaccine in Healthy Adults")
• Students and teachers may also wish to consult the website ClinicalTrials.gov.

ACTIVITIES/PROCEDURES

I. Engagement Activity (15 minutes)

a. At the beginning of class, provide each student with a copy of the attached "Engagement Activity" handout, which lists four different clinical trials. (Alternatively, place the handout on an overhead projector.)



b. Ask the students to look over the handout and jot down answers to the following questions:
   i. What is the purpose of each of these trials?
   ii. Would you consider participating in one of these trials, if you met the requirements? Why?
   iii. Would you do it if you got paid?
   iv. What questions would you want to ask the researchers before you agreed to participate?
   v. Would you be interested in the results of any of these trials? Why?

II. Explore (this activity may also be assigned as individual or group homework) (45 minutes)

a. Divide students into small groups and provide each group with copies of the attached "Exploration Activity" handout — "Strategies for Delivering Anti-HIV Therapy in South Africa" or "Safety of and Immune Response to a Bird Flu Virus Vaccine in Healthy Adults" and the attached "FAQ and Glossary" handout — "Understanding Clinical Trials" (or direct them to the ClinicalTrials.gov website).
b. Ask students to complete the "Student Activities" section of the "Exploration Activity" handout.

III. Explain (15 minutes)

a. Students share the answers to the "Student Activities" section of the "Exploration Activity" handout with the entire class.

IV. Elaborate (homework) – choose a or b
   a. Students may locate 2 additional clinical trial descriptions from either the unchealthcare.org website (clinical trials are listed under "Health & Patient Care") or the ClinicalTrials.gov website, and use the descriptions to answer questions 2, 3, and 4 from the "Student Activities" section of the "Exploration Activity" handout.
   b. Using the "Strategies for Delivering Anti-HIV Therapy in South Africa" or "Safety of and Immune Response to a Bird Flu Virus Vaccine in Healthy Adults" as a model, students devise their own proposed clinical trial. They, of course, will not conduct this trial but will outline the protocol, exclusion/inclusion criteria, time-line and include a description of the proposed trial. Suggestions for possible trials:
      i. The effect of video games on violence in teenagers
      ii. The effect of fast food advertising on teenage food purchases
      iii. The correlations between wearing sandals and blistered and calloused feet
V. Evaluate
   a. Teachers may choose to evaluate students based on class participation and completion of the homework assignment(s)

ENGAGEMENT ACTIVITY

Think You Might Have Gum Disease?

RESEARCH PATIENTS NEEDED

UNC Center for Inflammatory Disorders
-and-
UNC Center for Oral and Systemic Diseases

Male and female subjects with periodontal (gum) disease are needed for a clinical research study. This study will assess the effect of gum treatments on general health. Eligible subjects will receive certain treatments at reduced fees or no charge.

For information please call or e-mail the
UNC School of Dentistry GO Health Center.

Lung Study

Do you currently smoke cigarettes?

Have you quit smoking, but smoked for at least 10 years?

The Center of Environmental Medicine at UNC is looking for individuals for a research study. This study involves 1 visit and a total of 1½ hours of your time.

You will be reimbursed for completion of the study. If you participate, you will have a breathing test and learn more about your lungs. Participants that are interested in quitting smoking will be given information and guidance to help them quit.

Genetic Study of Anorexia Nervosa in Families

We are seeking families with at least two members who have or had anorexia nervosa, and who would be willing to participate. Experts from around the world are working to help identify the genes that might predispose individuals to develop anorexia nervosa.

UNC Eating Disorders Program

African American Couples Needed for a Research Study

If you have been living with your partner for at least 9 months, are not taking anti-hypertensive or anti-depressant medications, are between the ages of 18 and 50, and are willing to have blood samples and blood pressure taken, then you may qualify for a study about the benefits of partner relationships.

Receive up to $200 per couple for completion of 2 lab visits.

If interested, please call the UNC
Stress and Health Research Program.

All advertisements on this page were retrieved on April 27, 2005, from unchealthcare.org

UNDERSTANDING CLINICAL TRIALS

FREQUENTLY ASKED QUESTIONS

What is a clinical trial? (*from* University of Maryland's brochure "Thinking about Enrolling in a Clinical Trial")

A clinical trial is an experimental research study that evaluates the effect of a new drug or medical device on human beings. Clinical research is a process of discovery that is intended to improve medical care. Researchers attempt to answer questions such as "Which medication works better?" or "What is the best way to treat a medical problem?"

Who can participate in a clinical trial? (*from* University of Maryland's brochure "Thinking about Enrolling in a Clinical Trial")

All participants in a clinical trial are volunteers who have agreed to participate in a particular study. Some volunteers seek out clinical trials, and some are referred to clinical trial opportunities by their physicians. There are research opportunities in clinical trials for persons with specific diseases and conditions and for persons in generally good health. Volunteers participating in a study are referred to as "subjects" or "participants." Volunteers can leave a study at any time for any reason.

What are the benefits and risks of participating in a clinical trial? (*from* ClinicalTrials.gov)

Benefits
• Play an active role in personal health care.
• Gain access to new research treatments before they are widely available.
• Obtain expert medical care at leading health care facilities during the trial.
• Help others by contributing to medical research.

Risks
• There may be unpleasant, serious or even life-threatening side effects to experimental treatment.
• The experimental treatment may not work for the participant.
• The trial may require more time and attention than standard treatment, including trips to the study site, more treatments, hospital stays or complex requirements.
• The participant may be placed in the "placebo" group

How is the safety of the participant protected? (*from* ClinicalTrials.gov)

The ethical and legal codes that govern medical practice also apply to clinical trials. In addition, most clinical research is federally regulated with built in safeguards to protect the participants. The trial follows a carefully controlled protocol, a study plan which details what researchers will do in the study. As a clinical trial progresses, researchers report the results of the trial at scientific meetings, to medical journals, and to various government agencies. Individual participants' names remain secret and are not mentioned in these reports.

Every clinical trial in the U.S. must be approved and monitored by an Institutional Review Board (IRB) to make sure the risks are as low as possible and are worth any potential benefits. An IRB is an independent committee of physicians, statisticians, community advocates, and others that ensures that a clinical trial is ethical and the rights of study participants are protected.

What should people consider before participating in a trial? (*from* ClinicalTrials.gov)

People should know as much as possible about the clinical trial and feel comfortable asking the members of the health care team questions about it, the care expected while in a trial, and the cost of the trial. The following questions might be helpful for the participant to discuss with the health care team.

• What is the purpose of the study?
• Who is going to be in the study?
• Why do researchers believe the experimental treatment being tested may be effective? Has it been tested before?
• What kinds of tests and experimental treatments are involved?
• How do the possible risks, side effects, and benefits in the study compare with my current treatment?
• How might this trial affect my daily life?
• How long will the trial last?
• Will hospitalization be required?
• Who will pay for the experimental treatment?
• Will I be reimbursed for other expenses?
• What type of long-term follow up care is part of this study?
• How will I know that the experimental treatment is working?
• Will results of the trials be provided to me?
• Who will be in charge of my care?
• What happens if I'm injured because of the study?

GLOSSARY

Blind — A clinical trial is "Blind" if participants are unaware on whether they are in the experimental or control arm of the study; also called masked.

Control group — In many clinical trials, one group of patients will be given an experimental drug or treatment, while the control group is given either a standard treatment for the illness or a placebo (See Placebo).

Double-blind study — A clinical trial design in which neither the participating individuals nor the study staff knows which participants are receiving the experimental drug and which are receiving a placebo (or another therapy). Double-blind trials are thought to produce objective results, since the expectations of the doctor and the participant about the experimental drug do not affect the outcome; also called double-masked study.

Efficacy — The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed.

Expanded access — Refers to any of the FDA procedures that distribute experimental drugs to participants who are failing on currently available treatments for their condition and also are unable to participate in ongoing clinical trials.

Food and Drug Administration (FDA) — The U.S. Department of Health and Human Services agency responsible for ensuring the safety and effectiveness of all drugs, biologics, vaccines, and medical devices. The FDA also works with the blood banking industry to safeguard the nation's blood supply.

Inclusion/exclusion Criteria — The medical or social standards determining whether a person may or may not be allowed to enter a clinical trial. These criteria are often based on age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Inclusion and exclusion criteria are not used to reject people personally, but rather to identify appropriate participants and keep them safe.

Informed consent — The process of learning the key facts about a clinical trial before deciding whether or not to participate. It is also a continuing process throughout the study to provide information for participants.

Peer review — Review of a clinical trial by experts chosen by the study sponsor. These experts review the trials for scientific merit, participant safety, and ethical considerations.

Phase I trials — Initial studies to determine the metabolism and pharmacologic actions of drugs in humans, the side effects associated with increasing doses, and to gain early evidence of effectiveness; may include healthy participants and/or patients.

Phase II trials — Controlled clinical studies conducted to evaluate the effectiveness of the drug for a particular indication or indications in patients with the disease or condition under study and to determine the common short-term side effects and risks.

Phase III trials — Expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide and adequate basis for physician labeling.

Phase IV trials — Post-marketing studies to delineate additional information including the drug's risks, benefits, and optimal use.

Placebo — An inactive pill, liquid, or powder that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness. In some studies, the participants in the control group will receive a placebo instead of an active drug or treatment. No sick participant receives a placebo if there is a known beneficial treatment.

Protocol — A study plan on which all clinical trials are based. The plan is carefully designed to safeguard the health of the participants as well as answer specific research questions. A protocol describes what types of people may participate in the trial; the schedule of tests, procedures, medications, and dosages; and the length of the study. While in a clinical trial, participants following a protocol are seen regularly by the research staff to monitor their health and to determine the safety and effectiveness of their treatment.

Randomized trial — A study in which participants are randomly (i.e., by chance) assigned to one of two or more treatment arms of a clinical trial.

Single-blind study — A study in which one party, either the investigator or participant, is unaware of what medication the participant is taking; also called single-masked study.

Information on this page was retrieved on April 28, 2005, from the National Library of Medicine's website, ***ClinicalTrials.gov****.*

EXPLORATION ACTIVITY: STRATEGIES FOR DELIVERING ANTI-HIV THERAPY IN SOUTH AFRICA

Sponsored by:	National Institute of Allergy and Infectious Diseases (NIAID)
Information provided by:	National Institute of Allergy and Infectious Diseases (NIAID)

PURPOSE

Providing effective anti-HIV therapy in developing countries is challenging. This study will evaluate new strategies for delivering anti-HIV medications to people in South Africa. These strategies include using specially trained nurses to administer therapy (rather than doctors), treating all HIV infected members of a household at the same time, and having community members observe patients taking their medications.

Condition	Treatment or Intervention
HIV infections	• Behavior: Monitoring by HIV-trained primary care nurses • Behavior: Community-based directly observed therapy (DOT) • Drug: stavudine • Drug: lamivudine • Drug: efavirenz • Drug: zidovudine • Drug: didanosine • Drug: lopinavir/ritonavir

- Study Type: Interventional
- Study Design: Treatment, Randomized, Open Label, Active Control, Factorial Assignment, Efficacy Study
- Official Title: Safeguard the Household: A Study of HIV Antiretroviral Therapy Treatment Strategies Appropriate for a Resource Poor Country

Further Study Details:

- Expected Total Enrollment: 1050
- Expected completion: December 2011

The benefit of antiretroviral therapy is well established but limited to wealthy nations. A predefined, simple sequence of treatment regimens focused on extending the durability of limited treatment options has the best potential to be implemented in resource poor countries. South Africa has 15% of the world's HIV/AIDS patients and a limited number of physicians to treat them (l per 1,600 and less than 5 infectious diseases specialists). HIV patient care in the primary care setting must therefore be delivered by personnel other than doctors. Further, treatment strategies should include entire households to ensure maximum adherence and minimize sharing of drugs.

This study will have two parts. The first part will compare a first-line antiretroviral therapy regimen administered and monitored by primary health care sisters (nurses) with the same regimen administered by doctors. The second part of the study will determine if community-based directly observed therapy (DOT) is significantly superior to continued clinic-based treatment support for patients who have failed first-line therapy, as measured by cumulative virology failure rate. The project will also evaluate the cost and economic impact of a predetermined schedule of antiretroviral therapy; treatment outcomes in terms of morbidity, opportunistic and endemic infections, and mortality; and factors contributing to treatment failure, including toxicity, resistance, compliance, and treatment interruption.

In Part 1, households will be randomly assigned to receive first-line antiretroviral therapy under the monitoring and care of either an HIV-trained medical doctor supported by adherence counselors or an HIV-trained primary health care sister (nurse with training in diagnosis and treatment prescription). Members of the household who are HIV infected will receive stavudine, lamivudine, and efavirenz (nevirapine or nelfinavir may be used for special populations).

Participants who fail first-line antiretroviral therapy in Part 1 of the study will be entered into Part 2 of the study. Participants in Part 2 will receive zidovudine, didanosine, and lopinavir/ritonavir. Saquinavir/ritonavir will be substituted for lopinavir/ritonavir if the participant is receiving treatment for active tuberculosis. Participants will be randomly assigned to have their treatment monitored through either a clinic-based treatment support group or through community-based directly observed treatment (DOT). For the DOT arm, a community member will observe therapy for at least one dose a day, five days a week, at the home or work of the participant.

HIV infected children age 3 months to 16 years who live in a participating household will also be included in the study. These children will receive first-line treatment with clinic visits monitored by either the assigned sister (nurse) or doctor along with their households. In Part 2, children will be provided with a second-line treatment regimen with continued daily monitoring of doses in the household.

The study will last 5 years.

ELIGIBILITY

Ages Eligible for Study: 3 Months and above,

Genders Eligible for Study: Both

Inclusion Criteria for the first person in the household who enters the study:

- HIV infected
- Older than 16 years of age
- History of a CDC Category C AIDS-defining illness or a CD4 cell count less than 350 cells/mm3 within 60 days prior to study entry
- Have not previously taken anti-HIV medications. People who have taken anti-HIV medications for post-exposure prophylaxis or prevention of mother-to-child transmission may be eligible if the previous exposure did not exceed 6 weeks of nucleoside reverse transcriptase inhibitors or protease inhibitors, or two doses of a non-nucleoside reverse transcriptase inhibitor.

Inclusion Criteria for children less than 16 years old in a household that has been entered in the study:

- HIV infected
- Live in house with an adult participating in the study
- History of severe CDC Category B or C AIDS-defining illness, with the exception of a single episode of bacterial sepsis or a single episode of Zoster; or one CD4% less than 20% (less than 25% for children 3 to 18 months) obtained within 60 days prior to study entry
- Have not previously taken anti-HIV medications. Children who have taken anti-HIV medications for post-exposure prophylaxis or prevention of mother-to-child transmission may be eligible if the previous exposure did not exceed 6 weeks of nucleoside reverse transcriptase inhibitors or protease inhibitors, or two doses of a non-nucleoside reverse transcriptase inhibitor therapy. Children who received 6 weeks of AZT or a single dose of nevirapine will be included in the study.
- Consent of parent or legal guardian
- Primary caregiver who is willing and able to administer anti-HIV medications

Exclusion Criteria:

- Newly diagnosed AIDS-defining (CDC Classification C) opportunistic infection or condition requiring acute therapy at the time of enrollment. A stable patient on therapy for more than 7 days may be enrolled.
- Use of medications with significant effect on bone marrow, nervous system, pancreas, or liver within 30 days prior to study entry
- Use of cytotoxic medications within 30 days prior to study entry
- Active alcohol or substance abuse
- Severe diarrhea (more than 6 stools/day for 7 consecutive days) within 30 days prior to study entry
- Acute hepatitis within 30 days prior to study entry
- Bilateral peripheral neuropathy of Grade 2 or greater at the time of screening
- Women in the first trimester of pregnancy
- Inability to tolerate oral medication
- Any clinical condition that, in the opinion of the investigator, would make the person unsuitable for the study or unable to comply with the dosing requirements

ClinicalTrials.gov processed this record on 2005-05-26

STUDENT ACTIVITIES

1. Visit the "Resources" page of ClinicalTrials.gov, and click on "Glossary of Clinical Trial Terms" (or, use the handout provided by your teacher). Using this glossary, write down definitions for each of the following words:

a. Randomized Trial

b. Control Group

c. Efficacy

d. Inclusion/Exclusion Criteria

e. Protocol

2. Answer the following questions:

a. What is the purpose of this study?

b. What are the two parts to this study?

c. What are the inclusion criteria for this study?

d. What are the exclusion criteria?

e. Who is sponsoring this trial?

f. What is the trial's protocol?

g. Why is protocol important?

3. On the front of the "Understanding Clinical Trials" handout, there is a list of questions that people should consider before participating in a clinical trial. Read over this list. (On the website, this list is under the question "What should people consider before participating in a trial?")

a. Using the information provided in the description of the "Strategies for Delivering Anti-HIV Therapy in South Africa" clinical trial, answer the list of questions that people should consider before participating in a clinical trial.

b. What questions can you not answer?

c. What could you do to find the answers?

4. What are the possible benefits of conducting this trial, both to the participants and to the general public?

EXPLORATION ACTIVITY: SAFETY OF AN IMMUNE RESPONSE TO A BIRD FLU VIRUS VACCINE (H9N2) IN HEALTHY ADULTS

Sponsored by:	National Institute of Allergy and Infectious Diseases (NIAID)
Information provided by:	National Institute of Allergy and Infectious Diseases (NIAID)

PURPOSE

Avian influenza (AI), or bird flu, has recently become a major health concern in Asia and other parts of the world. The purpose of this study is to test the safety of and immune response to a new AI vaccine in healthy adults.

Study hypothesis: Influenza A viruses are widely distributed in nature and infect a wide variety of birds and mammals. The direct transmission of avian influenza viruses from birds to humans has recently become a major health concern in Asia and other parts of the world, raising concern of a possible influenza pandemic in humans. This vaccine will evaluate the safety, infectivity and immunogenicity of Live Influenza A vaccine H9N2 (6-2) AA ca reassortant (A/chicken/Hong Kong/G9/97 x A/Ann Arbor/6/60 ca), a cold-adapted, live attenuated virus vaccine administered intranasally for the protection of humans against pandemic influenza viruses of the H9N2 subtype.

Condition	Treatment or Intervention
Influenza virus diseases	Vaccine: H9N2 (6-2) AA ca Reassortant (A/chicken/Hong Kong/G9/97 x A/Ann Arbor/6/60 ca)

- Study Type: Interventional
- Study Design: Prevention, Non-Randomized, Open Label, Dose Comparison, Single Group Assignment, Safety Study
- Official Title: Phase I Inpatient Study of the Safety and Immunogenicity of H9N2 (6-2) AA Ca Reassortant (A/Chicken/Hong Kong/G9/97 x A/Ann Arbor/6/60 Ca), a Live Attenuated Virus Vaccine Candidate for Prevention of Avian Influenza H9N2 Infection in the Event of a Pandemic

Further study details as provided by National Institute of Allergy and Infectious Diseases (NIAID):

- Primary Outcomes: Frequency of vaccine-related reactogenicity events and other adverse effects for each dose of the H9N2 G9/AA ca reassortant vaccine; immunogenicity and infectivity for each dose of the H9N2 G9/AA ca reassortant vaccine
- Expected Total Enrollment: 70

AI viruses in their natural reservoir in waterfowl are the source from which novel HA and NA subtypes are introduced into the human population, and have the potential to initiate an influenza pandemic. This study will evaluate the safety and immunogenicity of a live, attenuated, cold-adapted reassortant AI virus vaccine, H9N2 (6-2) AA ca Reassortant (A/chicken/Hong Kong/G9/97 x A/Ann Arbor/6/60 ca).

Patient participation in this study will be for at least 60 days, with patients followed for at least 42 days after vaccination. In this study, participants will be enrolled sequentially, from highest to lowest dose of vaccine, into one of three groups. At study entry at Day 0, participants will be admitted to the hospital in order to familiarize them with trial procedures. Blood and nasal wash samples will be collected prior to vaccination. On Day 2, participants will have a physical exam and will receive one dose of vaccine; the vaccine will be administered as nose drops. Participants will undergo directed physical examinations daily while they are in the hospital. Nasal washes will also be collected daily from the day of admission through the day prior to discharge to test for the presence of vaccine virus. Participants may be discharged from the hospital after 3 consecutive negative viral cultures, but not before Day 14. Additional blood collection will occur daily from Day 0 to Day 7 and again on Day 21. Participants will return for follow-up visits 28 to 32 days and 42 to 46 days after receiving the vaccine. Blood and nasal wash collection will occur at these 2 study visits, and participants will also have directed physical exams.

Depending on the immune response to the first dose of vaccine, some participants may be asked to return to the hospital one to two months after their first vaccination to receive an additional dose of vaccine at a lower concentration.

ELIGIBILITY

Ages Eligible for Study: 18 Years and above

Genders Eligible for Study: Both

Accepts Healthy Volunteers

Criteria
Inclusion Criteria:

- Born after 1968
- Good general health
- Available for the duration of the trial

Exclusion Criteria:

- Clinically significant neurologic, cardiac, pulmonary, hepatic, rheumatologic, autoimmune, or renal disease
- Behavioral, cognitive, or psychiatric disease that, in the opinion of the investigator, affects the ability of the volunteer to understand and cooperate with the study
- Liver, renal, or hematologic disease
- Alcohol or drug abuse within 12 months of study entry
- History of severe allergic reaction or anaphylaxis
- Current asthma or reactive airway disease
- History of Guillain-Barre syndrome
- HIV-1 infected
- Hepatitis C virus infected
- Positive for hepatitis B surface antigen (HBsAg)
- Known immunodeficiency syndrome
- Use of corticosteroids or immunosuppressive drugs within 30 days of study entry. Participants who have used topical corticosteroids are not excluded.
- Live vaccine within 4 weeks of study entry
- Killed vaccine within 2 weeks of study entry
- Absence of spleen
- Blood products within 6 months of study entry
- Current smoker
- Have traveled to the Southern Hemisphere or Asia within 30 days prior to study entry
- Have traveled on a cruise ship within 30 days prior to study entry
- Work in the poultry industry
- Investigational agents within 60 days prior to study entry, or currently participating in another investigational vaccine or drug trial
- Allergy to eggs or egg products
- Purified protein derivative (PPD) positive (positive tuberculosis [TB] test)
- Family member with immunodeficiency
- Other condition that, in the opinion of the investigator, would affect the participant's participation in the study
- Pregnant or breastfeeding

ClinicalTrials.gov processed this record on 2006-03-09

STUDENT ACTIVITIES

1. Visit the "Resources" page of ClinicalTrials.gov, and click on "Glossary of Clinical Trial Terms" (or, use the handout provided by your teacher). Using this glossary, write down definitions for each of the following words

a. Randomized Trial

b. Control Group

c. Phase 1 Trials

d. Inclusion/Exclusion Criteria

e. Protocol

2. Answer the following questions:

a. What is the purpose of this study?

b. What are the inclusion criteria for this study?

c. What are the exclusion criteria?

d. Who is sponsoring this trial?

e. What is the trial's protocol?

f. Why is protocol important?

3. On the front of the "Understanding Clinical Trials" handout, there is a list of questions that people should consider before participating in a clinical trial. Read over this list. (On the website, this list is under the question "What should people consider before participating in a trial?")

a. Using the information provided in the description of the "Safety of an Immune Response to a Bird Flu Virus Vaccine (H9N2) in Healthy Adults" clinical trial, answer the list of questions that people should consider before participating in a clinical trial.

b. What questions can you not answer?

c. What could you do to find the answers?

4. What are the possible benefits of conducting this trial, both to the participants and to the general public?

Germs in the Arts and Humanities

Tuberculosis. TB is featured prominently in music and literature, especially in the 19th and early 20th centuries. Many of the works listed below are classics that are regularly taught in English classes. Connecting several topics and activities from *Biological Bodyguards* with one of these works will enrich the students' learning of both science and humanities, providing context to what may otherwise seem to be abstract knowledge.

MUSIC

La Bohème — Giacomo Puccini
La Traviata — Giuseppe Verdi

AMERICAN LITERATURE

The Bell Jar — Sylvia Plath

BRITISH LITERATURE

Nicholas Nickleby — Charles Dickens

WORLD LITERATURE

An Anonymous Story — Chekhov
The Black Monk — Chekhov
Ivanov - Chekhov
Crime and Punishment — Fiodr Dostoevskii
Demons (The Possessed) — Fiodr Dostoevskii
The Idiot — Fiodr Dostoevskii
Camille (La Dame aux Camilias) — Alexandre Dumas
The Magic Mountain — Thomas Mann
Fathers and Sons — Ivan Turgenev

Syphilis. Literary references to syphilis aren't always as direct as those to tuberculosis, but hints do appear in many texts from previous centuries. A few examples are listed here.

A Tale of Two Cities — Charles Dickens
A Doll's House — Henrik Ibsen
Measure for Measure — William Shakespeare
Candide — Voltaire

Latin teachers may want to locate the original Renaissance poem that gave syphilis its name — "Syphilis sive morbus Gallicus" ("Syphilis, or the French Disease"). It was written by the physician Girolamo Fracastoro (1478-1553), a native of Verona. The disease is named after the hero of the poem, a shepherd named Syphilis. At the time, medical professionals were unsure about the origins and transmission of the disease. To quote the poem (translation by Nahum Tate, 1686):

Girolamo Frascastoro

> Since nature's then so liable
> to change
> Why should we think this late
> contagion strange?
>
> The offices of nature to define
> And to each cause a true
> effect assign
> Must be a task both hard
> and doubtful too.
>
> [But] nature always to herself
> is true.

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