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Survival of the Fittest?—Evolution and Human Health

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Overview and Rationale

Teach evolution in three days, bacteria and viruses in one day, and human body systems—if you have time to get to them—in four days. What are students supposed to learn about these major topics in biology on such a tight time schedule? And yet, that's exactly what biology teachers are asked to do with the pacing guide we are given to follow in teaching high school Biology I classes in my school district. The only way to accomplish this is to integrate these topics into one cohesive unit rather than teaching each one separately. In addition, the integration of the topics should help students understand how these sometimes seemingly disparate topics are connected. It has been said that nothing makes sense in biology except in relation to evolution. With this unit, I will be using evolution to help students understand how their bodies work and why they sometimes don't seem to work so well. By bringing in some of the ideas about evolutionary medicine, I hope to help my students see that evolution is not just about the past, but that it is happening all around us, and in us, and affects our everyday lives.

This two week unit will begin with an introduction to the theory of natural selection and how natural selection causes changes in populations. Since the previous unit will be on genetics, I will pose the question, "If individuals with unfavorable characteristics, like genetic disorders, would have been unlikely to survive in an environment with no doctors or medicines, then why are people still being born with these disorders today?" The class will then participate in an activity that simulates how the sickle cell allele might increase or decrease in frequency, depending on the type of environment. At the end of the activity, students will learn about the disease's connection to malaria, and the life cycle of the *Plasmodium* parasite and the *Anopheles* mosquito vector. They will observe normal and sickle-shaped red blood cells on prepared slides and investigate the effect of blood cell shape on the function of the circulatory system using models of sickle and normal red blood cells to help them visualize how the shape of the cells leads to the symptoms of sickle cell anemia.

Other systems—digestive, respiratory and nervous systems—will be described in terms of their evolutionary adaptations and examples of genetic disorders of those systems which have persisted in populations in spite of their costs to the individual. Students will study the effects of obesity and diabetes on the digestive system, and their link to our ancestors' diets and climate change. I will have students look at their own diets and analyze how they might be setting themselves up for problems with obesity and diabetes and what they could do to eat a diet that takes into account their evolutionary history. They will study the nervous system and the

effects of phenylketonuria (PKU) and Huntington's chorea and why these conditions remain at such relatively high frequencies in certain populations. Finally they will look at the effects of cystic fibrosis on the respiratory and digestive systems and how heterozygote advantage or genetic drift can affect the frequency of diseases.

The final system we will cover is the immune system. We will begin with a lab on antimicrobial product resistance. Students will expose E. *coli* bacteria to various types of antimicrobial products and look for colonies of resistant strains. This will be followed by a discussion of the arms race we are in with infectious microbes through the use of antibiotics, vaccines, and our own immune systems, and how we might avoid an arms proliferation, whereby microbes become even more virulent. Students will learn about how our immune system works and how it develops as we grow, in response to our environment. They will look at a variety of infectious diseases and their agents—HIV, Influenza, Smallpox, and Streptococcus—and how the viruses and bacteria that cause these diseases have adapted to survive and reproduce so successfully.

Background Information

The Immune System

The human immune system is an amazingly complex network of organs, tissues and specialized cells that function together in intricate ways to protect our bodies from disease and injury. There are three levels of defense: first, the skin and mucous membranes, which provide a barrier for infection, our innate or nonspecific immunity, which is our second line of defense if the invading pathogens breach the skin, and third, specific immunity that targets pathogens not taken care of by the innate immune system.

First Line of Defense

Our first line of defense, the skin, and the mucous membranes of our respiratory, digestive, and urogenital tracts, provide a physical and chemical barrier to infection. Cells in the outer layer of the epidermis of the skin are constantly shed, along with microbes that may have attached to those cells. These cells also produce the protein keratin which helps form a tough, water resistant and microbe resistant barrier. Oil and sweat glands in the dermal layer of the skin secrete their products onto the surface of the skin. This keeps the skin flexible and reduces the chance of cracks forming which might allow the introduction of microbes. The secretions also create a slightly acidic environment (pH 3 to pH 5) which inhibits the growth of microbes [1] . Pathogens can also enter the body through the respiratory, digestive and urogenital tracts, as well as the eyes. These areas have mucosal cells among the epithelial cells lining these tracts. Just like the skin, the epithelial cells of these areas are constantly shed. The mucous that covers the cells traps microbes so they can be eliminated. Microbes ingested with our food may be destroyed by enzymes in the saliva, by strong stomach acid, or be out-competed by the normal microbial population of our intestines. Cilia in the bronchial tubes sweeps microbes trapped in mucous up to the esophagus where they are swallowed and destroyed by stomach acids. Acidic urine and vaginal secretions create a less than favorable environment for invading microbes and help wash them out [2] . However, all microbes are not completely inhibited. There are numerous species of bacteria and fungi, both mutualistic and commensalistic, which inhabit our bodies. These include *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Escherichia coli*. A good source of information and pictures of the various microbes that inhabit our skin and mucous membranes is at http://www.textbookofbacteriology.net/normalflora.html. Under normal conditions, these microbes help to

protect us from pathogenic microbes which attempt to colonize or invade our skin. However, some of them may become pathogenic if introduced into the skin or if the immune system becomes compromised [3] .

Second Line of Defense

Our second line of defense is innate or nonspecific immunity. This system attacks any invaders without specificity. It is composed of several types of cells, complement proteins and the immune response. Several types of leukocytes—white blood cells—are involved. Monocytes mature into macrophages—phagocytic cells similar to amoeba, which engulf their prey and then digest them with the aid of lysosomal enzymes. These cells can be found patrolling the interstitial fluid around cells. Langerhans cells are macrophages that live in the skin. Neutrophils make up 50 to 70% of all leukocytes, but live only about one day. They use chemotaxis to find foreign invaders and then phagocytosis to engulf them. Hydrogen peroxide and enzymes are used to destroy the invader, which leads to death of the neutrophil. Pus is an accumulation of dead neutrophils and other remnants of an infection. Eosinophils attack parasites, and basophils release histamines, causing an inflammatory response to infection [4] . Natural Killer (NK) cells kill cells of the body that have been infected by viruses. The NK cells bind to the infected cell and release vesicles filled with perforin proteins and granzymes. The perforins form pores in the cell membrane of the infected cell, allowing entry to the granzymes which trigger apoptosis in the cell. As the cell is broken down, macrophages clean up the debris. Of course, the NK cells must find the infected cell and destroy it before viruses are assembled, otherwise it will be releasing viruses that can go on and infect other cells [5] . In addition to these cells, several chemicals are produced. About thirty different kinds of complement proteins are produced which become activated by antibodies during an inflammatory response and insert themselves into a pathogen's membrane, forming a membrane attack complex, which creates pores in the cell. The cell is destroyed as extracellular fluid diffuses in, bursting the cell. Complement proteins can also trigger the release of histamine from mast cells and basophil cells, dilating capillaries. Interferons are proteins that are released by viral-infected cells to stimulate nearby cells to block virus production [6] .

The Inflammatory Response

When cells are damaged, they release chemicals—histamine, prostaglandins, and bradykinin— which dilate nearby blood vessels and increase the flow of blood to the area [7] . This causes several things to happen. The area will appear red from the increased flow of blood, bringing nutrients and oxygen to help heal the tissues. The warmth from the increased blood flow will help in the healing process as metabolism speeds up. Blood fluid leaking into the injured area causes swelling and pain as pressure builds up on nerve endings in the area. This increases the chance you will not use the injured area, giving it time to heal. Macrophages also enter the tissue from the blood, searching for bacteria that may have gained access. If they encounter bacteria, the macrophages release interleukin which travels to the brain, stimulating the hypothalamus to raise body temperature. Fever causes the liver and spleen to withhold iron from the blood. Because iron is an essential requirement for bacterial growth, this may be an adaptive response against the bacteria [8,9] . Taking medication to reduce the fever may make us feel better, but may prolong the infection by allowing the bacteria access to an essential nutrient. However, fever may also be a manipulation of the host by the pathogen to create a more ideal environment for growth. It just depends on the type of pathogen. At times, the cost of letting the fever run its course may be greater than its benefits—being unable to carry out necessary activities, a drain on the body's nutrient reserves and tissue damage due to an elevated temperature [10] .

Third Line of Defense—The Specific Immune Response

If invaders get past our innate immune system, then the specific immune system kicks in. It is sometimes called the adaptive immune system because it responds to specific types of pathogens that we come in contact with and it "remembers" them so that a return engagement is less likely to have dire consequences. For this to work, the system must be able to distinguish "self" from "non-self". The basis of this recognition system are antigens—molecules, often proteins, that may be fragments of a microorganism, surface proteins or glycoproteins on cell membranes, food items, pollen, or toxins. Antigens are also present on the cell surfaces of our own cells and are coded for by major histocompatibility complex genes (MHC). These genes are highly variable with hundreds of different alleles. The chance is rare that two people have exactly the same MHC alleles and therefore the same antigens. They are our label of "self". Recognition of the MHC proteins on our cell surfaces lets our immune system know what cells are friendly and which are not.

Two types of lymphocyte cells are involved in specific immunity and produce proteins which bind to foreign antigens—T cells and B cells. Both are formed by stem cells in the bone marrow. B-cells mature in the bone marrow; T cells mature in the thymus gland. B cells produce antibodies. Antibodies are made of 4 protein chains—2 longer heavy chains, and 2 shorter light chains that create a Y-shaped molecule. Both the heavy chains and the light chains have a variable region and a constant region. It is the variable regions which bind to antigens. During development of the B cells in the bone marrow, portions of the genes that code for these variable regions move around in the chromosome, rearranging themselves into different combinations in each B cell with the result that each B cell produces slightly different variable regions in these immunoglobin proteins. So at any one time, you have millions of different kinds of antibody-presenting B cells even though there are not millions of different genes for those antibodies. Then when an antigen comes along, the B cells that bind to that antigen with the right antibody (still on its surface) are partially activated. They take in the antigen and present fragments of it on their surface which helper T cells bind to. T cells finish the activation of the B cells by releasing cytokines which cause that B cell to start dividing; forming plasma cells which make the kind of antibodies that were first presented on the cell surface of the B cell—the ones that had the right variable region to bind to the antigen. So...no switching around of the variable gene segments this time; these clones will all make the same kind of antibodies which are now secreted from the cells.

If the maturing B cells in the bone marrow have made immunoglobin proteins which bind to self antigens on bone marrow stromal cells, they will self-destruct. Only about 10% will survive the cull. T cells go through a similar process in the thymus. When T cells migrate to the thymus, T cell receptor (TCR) proteins are produced by gene rearrangement that results in an enormous variety of different T cells—similar to the gene rearrangement that occurs with the B cells. TCRs are similar to the immunoglobins made by B cells but they are composed of only two protein chains, each with a constant region and a variable region. Like the immunoglobins, the variable region of the TCR binds to a self-MHC and peptide complex. Unlike immunoglobins, they remain in the cell membrane of the T cells and are not secreted. If they bind too tightly, or fail to bind at all to MHC antigens on specialized epithelial cells or to dendritic cells in the thymus, apoptosis is triggered. Only about 2-5% will have just the right amount of binding to MHC proteins and be released from the thymus [11] .

T cells are the stars of cell-mediated immunity—one form of specific immunity. The two types of T cells are cytotoxic T cells and helper T cells. Most often, activation of cytotoxic T cells occurs when they encounter a non-self antigen presented on an MHC molecule on the surface of a dendritic cell in the lymph nodes. If the T cell has the right TCRs, it will bind to the MHC-peptide complex. This induces the T cell to begin dividing, creating more cytotoxic T cells with the same kind of TRCs, and memory cytotoxic T cells which will remain

after the immune response. Activated cytotoxic T cells will induce apoptosis in any cell they find displaying the same MHC-peptide complex, in the same manner that natural killer cells do, using perforin proteins to rupture the cell membrane of the infected cell. Helper T cells are activated when macrophages that have engulfed some microbe, release interleukin-1, attracting the Helper T cells, which then bind to MHC-peptide complexes on macrophages. The Helper T cells begin dividing and producing more helper T cells and memory cells with identical TCRs to the first cell. They also release interleukin-2, which stimulates cytotoxic T cells to multiply. When the infection is under control, suppressor T cells turn off the response. Each variant of helper T cell releases a specific type of cytokine that binds to receptors on target cells of the immune system. The cytokine interferon stimulates and attracts macrophages. Interleukin-2 is also released when helper T cells bind to antigen presenting B cells, and activates the humoral response in B cells. [12,13]

If T cells are the stars of the cell-mediated response, B cells rule the humoral response. They do not actively kill infected cells or invading microbes, but mark them for destruction by other members of the immune team. When a B cell encounters an antigen from an invading microbe that fits its surface immunoglobins (antibodies), it will phagocytize the antigen and present fragments of it on MHC proteins on its surface. Then a helper T cell will bind to the antigen-MHC complex and activate the B cell to start multiplying. In addition, the binding of free antigen alone can stimulate the B cells to divide. Some of these B cells will become memory B cells for future encounters with the pathogen, the rest become plasma cells, which begin producing and secreting antibodies which will bind to the foreign antigens, neutralizing them until macrophages or cytotoxic T cells can finish them off. There are five typesof antibodies. IgM, IgG, and IgD antibodies are surface receptors for antigens. IgM antibodies are the first type released in an immune response. They are composed of five Y-shaped immunoglobin proteins arranged in a ring. Both IgM and IgG antibodies, which are released in secondary responses, bind to antigens, causing agglutination. In the case of IgM antibodies, this attracts complement proteins which will perforate and kill the invading pathogen. IgG antibodies are more likely to attract macrophages which phagocytize the cell. IgA antibodies are found in secretions such as saliva and breast milk. IgE antibodies promote the release of histamine and are to blame for the overreaction of an allergy attack. [14]

Diabetes

When food is digested, starch and other carbohydrates are broken down by enzymes into monosaccharides and pass from the cells lining the small intestines into the bloodstream. Beta cells in the islets of Langerhans in the pancreas detect the increasing levels of glucose in the blood as it passes through the pancreas and release insulin which stimulates liver and skeletal muscle cells to take up glucose from the blood stream and store it in the form of glycogen, and adipose cells to store the glucose as fat. When a person has not eaten for a while, or is exercising and cells are using up their supply of glucose, blood sugar levels drop and the hormone glucagon is released from alpha cells in the islets of Langerhans, stimulating liver cells to convert stored glycogen into glucose and release it into the bloodstream [15] .

Diabetes mellitus is a disease that affects the body's ability to take up glucose sugar from the blood and into cells, either because of a lack of insulin or because the cells have reduced sensitivity to insulin. Without insulin, the body's cells are deprived of glucose, and blood sugar levels rise. There are two types of diabetes. Type 1, or juvenile diabetes, is an autoimmune disease in which the immune system attacks the beta cells in the pancreas which produce insulin. Type I diabetes is found in only 5 to 10 percent of all diabetics. It is only treatable with careful monitoring of blood sugar levels and diet, and insulin injections. Type 2 diabetes occurs most often in adults, and is associated with overeating. It is increasingly being diagnosed in children who are obese. Insulin is produced, but tissues in the body may be resistant to it. It is often treated simply by careful

monitoring of the diet, exercise, and weight loss and rarely requires injections of insulin [16,17] .

With either type of diabetes, when glucose levels in the bloodstream increase because glucose is not being taken up by the cells, damage can occur leading to dehydration, coma, and death. Glucose in the blood vessels reacts with proteins, causing vessel walls to thicken and the vessels to narrow. Nerve cells are damaged. Even when treated, the results of diabetes can be blindness, high blood pressure, heart disease, strokes, and tissue damage that leads to amputation. One of the first symptoms of diabetes is the production of *high amounts of sugary urine*[18] . So what possible selective advantage could there have been in having such a disease?

In his book *Survival of the Sickest*, Dr. Sharon Moalem proposes a possible scenario for how having Type 1 diabetes might have given a survival advantage. First he describes the interesting case of two very different organisms and their rather similar reaction to cold temperatures. In the first case, a German vintner had a crop of grapes which were hit by frost. He went ahead and made wine from them anyway and it turned out to be an extraordinarily sweet wine—now called ice wine. The grapes had responded to the cold weather by getting rid of excess water, increasing their sugar concentration. This higher sugar concentration effectively acted as antifreeze, lowering the freezing point and protecting the grape cells from being ruptured by the ice crystals which would have formed [19] .

The second story was about a small wood frog, *Rana sylvatica*, which survives the winters of North America by freezing. Its heart stops beating, it does not breathe and its brain does not appear to function. And yet, in the springtime, it thaws out and is perfectly fine. Its trick is that when the skin of the frog senses that the temperature is nearing the freezing point, water is moved out of its organs and blood and is collected in the abdomen. The liver releases large amounts of glucose into the blood, lowering the freezing point. The ice that forms, as the water in the abdominal cavity freezes, keeps the frog's organs on ice, without the dire consequences of ice crystal formation in the tissues. Large amounts of a clotting factor, fibrinogen, are also produced by the frog which will help protect it from any damage that occurs from being frozen [20] .

The empty promises of cryogenics aside, humans do not have this capability. Or do we? Just after the last Ice Age, another brief period of cold weather occurred from about 13,000 years ago until 12,000 years ago [21] . The humans who had migrated to northern Europe prior to this would have been tested by this fairly rapid climatic change. Many would have frozen to death, and yet many also survived. How? Some adaptations for living in cold environments have been observed in populations such as the Inuit and Norwegian fishermen. Hunter's response is the periodic re-dilation of blood vessels in the extremities that reduces the chance of frostbite in extremely cold weather. People who live in very cold conditions often have higher levels of brown fat—fat that contains a high concentration of mitochondria. It does not function in the same way that regular fat tissue does. Brown fat in the body does not require insulin to absorb glucose from the blood and it converts glucose into heat immediately, rather than storing it away. In babies, brown fat burns glucose to regulate body temperature until the baby is older. It is also active when a person is exposed to cold temperatures for a certain amount of time [22] . Finally, people often have to urinate when exposed to the cold. This may be partially due to a rise in blood pressure due to the constriction of blood vessels in the extremities, which signals the kidneys to get rid of excess fluids. Dr. Moalem suggests that it may also be the same reason that the grapes and frogs rid themselves of water—to concentrate sugars in the blood and lower the freezing point [23] .

One key to the answer, suggests Dr. Moalem, is to look at the rates of Type I diabetes. It is most common in

people of Northern European descent—Finland, Sweden, the United Kingdom, and Norway—the area where this brief climatic cold spell occurred [24] . A coincidence? Or is it the result of natural selection acting on a population living under extreme conditions? Could having diabetes have been a survival advantage in the extreme conditions of this area 13-12,000 years ago? Dr. Moalem says yes. Hunter's response might have helped them in gathering food. In this population, people who had inherited the genes that would increase blood sugar levels and eliminate water might have had an advantage in being able to withstand the cold conditions. Although in today's environment a rise in blood sugar might be fatal, they would have had so little food that blood sugar levels would already be low. The presence of more brown fat because of the cold would have helped them maintain body temperature, but also would have burned away some of the blood sugar (no insulin required) and the symptoms of these Ice-age diabetics might not have been so detrimental. If the diabetes-like condition was temporary, perhaps triggered by temperature, these individuals might have been able to survive long enough to reproduce. In fact, one of the possible triggers for Type 1 diabetes today may be cold weather. Most cases of Type 1 diabetes are diagnosed as temperatures start to drop and many diabetics observe seasonal changes in their blood glucose levels. Even levels of fibrinogen—the same protein that helps repair frog tissues when frozen—rise in humans in the winter months [25] .

This theory has been given little support from other scientists. However, it does suggest how such diseases might give some selective advantage in a particular environment. Another theory proposed by University of California physiologist Jared Diamond suggests that one of the many genes for Type 1 diabetes (gene DR3) might confer a reproductive advantage—reducing the chances of miscarriage if the baby has inherited one copy of the DR3 gene [26] . Inheriting one copy of this gene often results in late onset of Type 1 diabetes—when the person could have already reproduced [27] .

Obesity

For millions of years our hominid ancestors were hunter-gatherers whose diet consisted of complex carbohydrates and very lean meat sources. Grains were rarely consumed. Then with the advent of farming and the domestication of animals about 10,000 years ago, the human diet started changing. Today our diets are largely dependent on highly processed grains and refined sugars. These grains are deficient in many important nutrients. The meat that we consume today from domesticated animals is much fattier than that of wild game. However, without this menu change brought about by the advent of agricultural practices, the human population would long ago have reached the carrying capacity of the earth for a hunter-gatherer type of diet based on wild food sources [28] . Today, people rarely grow their own food, relying instead on highly processed food sources. We barely recognize where our food comes from. In wealthy countries like the U.S., the easy availability of food year round and the cultural push to buy more and eat more, coupled with a decrease in activity levels, have resulted in an increase in the incidence of obesity. When compared with the diet of a foraging population, the American diet consists of much less protein and much higher levels of simple carbohydrates and refined grains. These kinds of carbohydrates cause rapid increases in blood glucose levels, and a prolonged diet of these kinds of foods can lead to insulin resistance and the development of Type 2 diabetes. [29] Salt, sugar, and fats would have been in short supply for our Stone Age ancestors. It would have been an adaptive feature for them to eat as much of these things as possible when they had the chance. Today, when these items are available in great quantities, all the time, this adaptive craving causes us to overindulge. [30]

Strategies and Lesson Plans

The objectives for this unit are ambitious—teach evolution, microbes, body systems and disease with an integrated approach. If successful, I believe this will not only solve the problem of never having enough time to teach each of these subjects separately, but will also help my students make better connections about how they are all related. During the course of the semester, students will be maintaining a biology journal which will include not only lab work and observations, but also their thoughts, reflections, and responses to pre- and post-instructional questions. The journals will be assessed both formatively and formally. A very good website on keeping science notebooks is at http://www.sciencenotebooks.org/. Also, Google the topic "interactive notebooks" for a variety of sites that show how to organize science notebooks.

Day 1—The students will have just completed a unit on genetics, and will have an understanding of how traits are inherited, different patterns of inheritance, and an introduction into some genetic diseases. I will begin the unit by asking students to reflect on the following question in their journals: "If individuals with unfavorable characteristics, like genetic disorders, would have been unlikely to survive in an environment with no doctors or medicines, then why are people still being born with these disorders today? Why haven't these genes disappeared from the population?" After giving them some time to think and write about this question, I will have them work in pairs to discuss their answers, change partners and share what they heard. I will then call on a few students to share what they heard in either of their groups. Students can make additions to their journals from the discussions.

In order to provide students an example that might help them discover answers to this question, I will then have students work in pairs to complete an activity that models natural selection against a recessive allele. This is another modified version of the popular Teddy Graham lab. A copy can be found in the Appendix. After reading the story of the bears, students will propose a hypothesis, complete the activity, and record a summary of the results in their journals. This activity allows students to observe a population with variation in phenotypes, environmental selection against one phenotype, and an increase in the frequency of one phenotype over time, showing that the population has evolved. After a discussion of each group's results, I will introduce Charles Darwin's theory of natural selection and have students compare what they just observed in the activity to this theory by responding in their journals.

Day 2—A second activity will model the effects of the heterozygote advantage with sickle cell anemia and malaria, but without revealing the name of the disorder. Reading the instructions before coming to class will be part of the previous day's homework assignment. Students are told to record questions about the lab's purpose or procedures in their journals for discussion before the activity begins. A copy of the activity can be found in the appendix. Students will again keep a record of the activity in their journals. What they should observe is that the individuals who survived in this activity were those who were heterozygous for the recessive allele that was lethal when an individual was homozygous for that allele. Following a discussion of the consequences of this type of selection, I will reveal that the disease demonstrated by this activity was sickle cell anemia, and that the selective agent was malaria. Many of my students are familiar with sickle cell anemia, and a few have told me they, or a family member, either have "the trait" or have sickle cell.

Students will learn more about sickle cell anemia, malaria and the circulatory system at rotating stations set up at lab tables for students to explore more about these two diseases. Station 1 will have microscopes set up with slides showing normal red blood cells and sickle cells for students to sketch into their journals. Information in the form of charts and diagrams of the components of the circulatory system will be available

for students to complete a foldable to place in their journal. I use Dinah Zike's Foldables frequently instead of normal notes, because students can use them much like flash cards for studying.

Station 2 will have a model of a capillary and normal and sickle cells that will allow students to visualize the problem that the change in red blood cell shape creates. The capillary will be represented by a piece of clear flexible plastic tubing, the normal red blood cell by round fabric red blood cell models and sickle cells will be made of stiffer material. The normal red blood cells should go easily, one by one through the tubing, while the sickle cells should jam up in the tubing, at least some of the time. Students will record in their journals their thoughts on why this might create problems. Also at this station will be diagrams and information on gas exchange between red blood cells, the lungs, and body tissues. Students will complete a worksheet to be folded and taped into their journals. They should be able to make the connection between the information about gas exchange and how a sickle crisis might cause problems.

At Station 3, students will compare the mRNA sequence for normal and sickle cell hemoglobin and translate a portion—the *beta*-globin gene—into amino acids. This is a good review of protein synthesis, and also shows how mutations can create traits that can be selected for. They will compare structural models of normal hemoglobin and sickle cell hemoglobin that show how the substitution of one amino acid affects the shape of the protein. Reflections will be recorded in their journals.

Station 4 will cover the symptoms and genetics of sickle cell. Students will complete a Punnett square showing the possible offspring of two individuals heterozygous for sickle cell anemia. They will relate the symptoms of the disease to the effects of the faulty hemoglobin using a cause and effect diagram.

At Station 5, students will look at the characteristics of the disease malaria. Here students will analyze a diagram of the *Plasmodium* and Anopheles mosquito life cycles, investigate the symptoms of malaria, and compare maps showing where malaria and sickle cell anemia occur.

Students will rotate through these stations. I have eight lab tables and will set up duplicates of four of the stations on each side of the room, with, either one of the stations at the rear of the room, or two stations set up on one lab table. All information collected by the students will be entered into their journals. A rubric for the work will be provided to the students before they begin. They will complete a self-assessment column and staple the rubric at the end of their responses.

Day 3,4, 5—This is another "survival of the sickest" day. One of the themes of the books *Why We Get Sick* and *Survival of the Sickest* is that harmful traits that have continued to be passed down must have provided some reproductive advantage. Students will by now have come to understand how sickle cell gave an advantage to individuals who were heterozygous for the trait in resisting malaria. The lessons on these days will cover several other diseases whose benefits can only be speculated on—diabetes, PKU, Huntington's and cystic fibrosis. We will begin first with an overview of the digestive system, including a discussion of whether or not the appendix should be considered a vestigial structure in light of recent evidence that it may be reservoir for beneficial bacteria. I will give them a brief overview of what the diet of early humans was like when we were hunter-gatherers, and how that diet changed with the advent of agricultural practices. They will watch excerpts from the movie Super Size Me about our country's addiction to fast food. Students will then record in their journals what they eat for a week on one side of their page and then what healthier choices they could have made beside the first list. Many of the students are familiar with diabetes, but they often do not know the difference between Type 1 and Type 2, so I will give them an overview of the disease. Then I will tell them the story of the ice wine and the wood frog. They will watch a video clip of the wood frog freezing and thawing—available at http://www.pbs.org/wgbh/nova/sciencenow/3209/05.html. I'll tell them the story of the

diabetics who may have survived the last ice age because of the anti-freeze effects of their high blood sugar. I will have students discuss why some people with certain ancestry might not be able to digest dairy products very well, while those with different ancestry still can and what the survival advantages might have been at one time to having each kind of digestive capability.

Students will have already heard about PKU, Huntington's and cystic fibrosis briefly in our genetics unit. I will demonstrate the effects of genetic drift and the founder effect on gene frequency in a population and we will discuss and evaluate the hypotheses that the relatively high proportion of these harmful diseases might be the result of genetic drift, or natural selection, and how they are being maintained in the population today. Students will construct a model of a neuron and will do an activity that demonstrates how a signal is passed along the axon of a neuron. They will look at how PKU and Huntington's affect this signaling in the nervous system. After looking at the various structures of the respiratory system, they will learn about the effects of cystic fibrosis on this system and view a video about a family who opted to use in *vitro* fertilization and genetic testing in an attempt to have a child free from the disease.

Day 6, 7, 8, 9—The Immune system and infectious diseases. There will be several labs for this part of the unit. The first will be on bacterial resistance to various antimicrobial products. Students will design an experiment to test the effects of a product or products on E. *coli* bacteria. I envision them doing comparison testing on several anti-microbial products—a fairly simple experiment, but the emphasis will be on experimental design and control of variables. I plan to cover bacterial structure in the cell unit, but will review the structure of bacteria and describe viral life cycles. After an introduction to the various components of the immune system, I will have students work in groups to develop skits and act out various things that go on in the immune system—the action of macrophages, the inflammatory response, and how T cells and B cells work. Once students understand about antigens and antibodies, they will do an experiment from Lab-Aids, Inc called "Immunology and Evolution". This simulation lab tests blood proteins of various animals using antibodies to human blood serum produced by rabbits. The idea is that the greater the degree of precipitation, the more closely related the test subject is to humans.

Outbreak!—As a final culminating project, each student will select one infectious disease to research and describe a scenario in which there is an epidemic associated with that disease. Their presentation may take many forms—a PowerPoint, video, newscast, or graphic novel. They must include information on historical outbreaks of the pathogen, its characteristics, how it is transmitted, its effects on the body, what factors might have led to the current outbreak being described, and what possible measures might be used to contain the outbreak today. Students will be required to write a 1000 to 1200 word essay that describes their research findings to be submitted one week prior to their presentation. This will allow me the chance to review their facts to be sure they have the science right before they present to the class.

Activities

Changes in a Teddy Graham Population—based on an activity by Bert and Lynn Wartski

Teacher notes: For a class of about 30 students, I will use about 2 boxes of Teddy Grahams. The new mini types will work as well, and will be less expensive. There are actually two types of bears in a box—one kind has their arms raised, the other kind has their arms by their sides. There are almost always more of the arms

down bears. I let students work in pairs, and I give each pair an initial population of bears, pouring them from the box onto a clean paper towel at their lab station. I don't count them, because it doesn't matter. Each group starts with about 15-20 bears. Have them count this initial population and record the data. Then tell everyone that the monsters are coming. The monster will eat only three Happy Bears. If there are not three Happy Bears, the difference will be made up by eating Sad Bears. Both partners are not eating! They can take turns, or save all the "eaten" bears until the end and split them up. Then I go around with the second box and pour out a few "baby bears"—about 7-10 in the first few generations until the population gets bigger. I don't count and I don't try to match up the characteristics of the survivor parents with the offspring—it will all work out. Then and only then do the students count the total number and types of survivors plus offspring and record that as generation 2. Each generation count will occur after the monsters have eaten and the bears have reproduced. As the population size increases, I tell them that the monster population has also increased, and by the 4 th and 5 th generations, the monsters are eating up to 6 bears—always eating Happy Bears first if available.

Background Information: *If you go out in the woods today, you're sure of a big surprise. If you go out in the woods today, you'd better go in disguise. For every bear that ever there was, will gather there for certain, because today's the day the (Teddy Grahams) have their picnic*—(Jimmy Kennedy) Teddy Grahams live in the remote Nabisco Forest of North America. There they roam freely, attending Teddy Graham picnics when they are not hiding from their main predator, the bear-eating monster, *Homo horribilis*. Teddy Graham bears appear in two different phenotypes. The "Happy Bear" variety often display with their arms raised skyward when startled, freezing into position in an attempt to avoid detection. Apparently they also have very sweet and tender flesh as a result of their more pronounced inactivity. The "Sad Bear" variety never raises their arms, and will run away at the first sight of a bear-eating monster. The rush of adrenaline released by the exertion of their muscles in avoiding capture, results in flesh that is tougher and less sweet. *Homo horribilis* shows a preference for eating the "Happy Bear" variety of Teddy Grahams if they have a choice. During the course of a year, one *Homo horribilis* will consume about three Teddy Grahams, and if it cannot find "Happy Bears", they will make up the difference in their diet by making do with "Sad Bears". Teddy Grahams breed once a year and a new crop of bear cubs are produced shortly thereafter. (It has not been confirmed, but it is believed that is the purpose of the "picnics".)

Assignment: Observe the population of Teddy Graham bears in your section of the Nabisco Forest for 5 generations and make note of the total population size initially and at the end of each breeding season. Also record the breakdown in the population of "Happy" and "Sad" phenotypes for each generation.

Results:

Generation:	Number of Happy Bears:	Number of Sad Bears:	Total Number of Bears:	Percentage of Happy Bears:	Percentage of Sad Bears:
Initial					
2					
3					
4					
5					

Analysis of Data:

1. Construct a graph showing the change in the percentage of Happy and Sad bears in each generation.
2. Which variation in the Teddy Graham population was least favorable in terms of survival?
3. How did this affect the population over time?

Conclusion:

1. At times there may be no surviving Happy Bears during the mating season, and yet there will almost always be some Happy Bear cubs born each year. How can this be explained?
2. Will the Happy Bear trait ever disappear from this population? Why or why not?
3. Did this population of bears change over time, and if so, what caused it to change, and in what way is the population different now?
4. How might the change in the population of Teddy Grahams affect the *Homo horribilis* population? In what ways might that population start to change over time?
5. What would happen if the Happy Bear trait became more favorable in this environment?
6. What might happen if it were favorable to be heterozygous rather than homozygous dominant or recessive?

After a discussion of Charles Darwin's theory of Natural Selection, students will relate the results of this activity to the main points of the theory, recording it in their Biology Journals:

A. There is variation in a population….(ex. There was variation in the traits of the Teddy Grahams. Some were easier for the monsters to catch.)
B. More offspring are born than will survive
C. There is competition for limited resources
D. Those born with favorable variations will get the limited resources, survive, reproduce and pass on those favorable variations.
E. Favorable variations accumulate in a population over time, changing the population.

With some classes, I might go further and have them calculate the frequencies of the alleles:

Analysis #2—The Hardy Weinberg Equation

Sexual reproduction shuffles genes in each generation so that the frequency of phenotypes is not always the most reliable way to measure whether or not certain alleles are being selected against. But it is also impossible to look at an individual with a dominant phenotype and determine whether it is homozygous dominant with two dominant alleles, or heterozygous, with a dominant and a recessive allele. The Hardy-Weinberg equation provides a statistically reliable way to estimate the frequencies of two alleles for a trait. If a population is at equilibrium and is not evolving, then the frequencies of the alleles should stay the same over time.

If the frequency of the *allele S* for the Sad trait is p and the frequency of the *allele H* for the Happy trait is q, then all the alleles for this trait in a population would be p + q=1. If some bears are homozygous for Sad then the frequency of that phenotype would be p^2. The frequency of homozygous Happy bears would be q^2. There would be two ways to get heterozygotes—pq or qp, so the frequency of heterozygotes is 2pq. Adding up the frequencies of the alleles for all possible phenotypes, you would have:

$p^2 + 2pq + q^2 = 1.0$

$p + q=1.0$

$p^2 =SS$

2pq=SH

q^2 =HH

If the Happy allele is recessive, then we can look at the percentage of Happy Bears in each generation and determine q^2. For example if the percentage of Happy Bears is 9% or 0.09, then $q^2 = 0.09$. Now solving for q—the frequency of the H allele would be 0.3, and if q is 0.3, then 1-q=p, so p, the frequency of S, is 0.7

1. Use your data to solve for the values of the Happy and Sad alleles in the initial population and in the 5 th generation. If they frequency of the alleles has changed, then the population has evolved—did it?

Generation	Frequency of HH (q^2)	Frequency of H (q)	Frequency of S (p)	Frequency of SS (p^2)	Frequency of SH (2pq)
1					
5					

2. How could you determine the rate at which the population has evolved?

The Mystery Trait

Teacher Notes: This activity is similar to the Advanced Placement Biology Population Genetics and Evolution Lab #8 that uses cards with alleles written on them that students use to represent their genotype. I will bring in a small wading pool to represent the "gene pool" of our population, and a trash can labeled "Evolutionary Trash Heap". Half of the cards will have "H" and half will have "h" to represent the dominant and recessive alleles for normal hemoglobin and the sickle cell version of hemoglobin. After the initial count of genotypes, students who are hh will "die" as well as a few who are HH.

Background Information: Evolution is defined as a change in the frequencies of alleles in a population over many generations. A population's gene pool is the total of all the alleles carried by all the individuals in that population. Because sexual reproduction shuffles alleles in each generation, the result is often a change in the frequencies of various phenotypes in the next generation, without necessarily a change in the frequency of each allele. But what happens if certain phenotypes are selected against? Would this change the frequency of one allele or the other? Complete the following hypothesis about the effects on a population's gene pool:

Hypothesis: If one phenotype is selected against in a population, then …

In this activity, the dominant alleles for a trait will be represented by the letter H and the recessive allele by the letter h. Possible genotypes could thus be _____, _____, or _____.

Procedure:

Note: It is important that during this activity, all students listen carefully when we are collecting the tallies of genotypes from each generation for our class data.

1. Each student will be given two "allele" cards from the class gene pool—and H and an h—so that everyone starts out as heterozygous genotypes.
2. To represent reproduction, each student will then pair up with another student. Holding the cards behind your back so that you do not know which card is which, you will hold out one of your cards—your

gamete—to your partner. These two cards represent one offspring. One person now takes on the genotype of the offspring, getting additional cards from the gene pool as necessary.
3. Selection now occurs...
4. individuals do not "survive", they will throw their cards into the Evolutionary Trash Heap (ETH) bucket and they sit out until they can take on the offspring's cards of two surviving parents. The teacher will conduct a count of each surviving student's genotype, HH, Hh, or hh, using hand counts and record the class tally on the board as generation 2.
5. Students pair up with someone else and steps two and three are repeated. If the offspring and both parents survive, a student who does not have cards will take on the offspring's genotype. Listen for the count! The new offspring and the remaining parents will represent the next generation.
6. We will continue this for several generations. At the end, copy the class data from the board into your journal, and answer the following questions in your journal:

Analysis of Data:

1. What might have been the favorable variation in this environment?
2. What was the favorable variation?
3. Explain the continued appearance of the unfavorable variation being born in the population, even though it does not survive.

Notes

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1. George B. Johnson, *Biology*, 8 th ed, 1040.
2. Ibid. 1040-1041.
3. Ethne Barnes, *Diseases and Human Evolution,* 20.
4. Brain, Marshall."Discovery Health "How Your Immune System Works"." Discovery Health "Health Guides". http://health.howstuffworks.com/human-body/systems/immune/immune-system11.htm# (accessed July 12, 2010).
5. Ethne Barnes, *Diseases and Human Evolution*, 23.
6. George B. Johnson, *Biology*, 8 th ed, 1043-1044.
7. Ibid, 1042.
8. Ibid, 1043
9. Kluger, Matthew, and Barbara Rothenberg. " Fever and Reduced Iron: Their Interaction as a Host Defense Response to Bacterial Infection ." *Science* Vol. 203, No. 4378 , no. Jan. 26, 1979 (1979): pp. 374-376 . http://www.jstor.org/sici?origin=sfx%3Asfx&sici=0036-8075%281979%29203%3A4378%3C374%3AFARITI%3E2.0.CO%3B2-5 (accessed July 13, 2010).
10. Scott Freeman and Jon C. Herron. *Evolutionary Analysis*, 560.
11. George B. Johnson, *Biology*, 8 th ed, 1047-1048.
12. Ibid.
13. George Johnson, *Biology*, 7 th ed, 1020-1021.
14. Ibid, 1023-1024.
15. Ibid, 1008
16. Ibid.
17. Sharon Moalem and Jonathan Prince. *Survival of the Sickest: A Medical Maverick Discovers Why We Need Disease*, 24-25.
18. Ibid, 24-25.

19. Ibid, 38-39.
20. Ibid, 41-44.
21. Ibid, 31-32.
22. Ibid, 36-37.
23. Ibid, 37.
24. Ibid, 26.
25. Ibid, 45-46.
26. Randolph Nesse and George C. Williams. *Why We Get Sick: The New Science of Darwinian Medicine*, 100-101.
27. "Genes Can Cause Type 1 Diabetes." Welcome to Genetic Health. http://www.geneticheath.com/dbts_genetics_of_type_1_diabetes.shtml#Anchor1 (accessed July 13, 2010).
28. Wenda Trevathan. *Evolutionary Medicine and Health : New Perspectives*, 19.
29. C. Koella and Stephen C. Stearns. *Evolution in Health and Disease*, 270-271.
30. Randolph Nesse and George C. Williams. *Why We Get Sick: The New Science of Darwinian Medicine*, 148-149.

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Barnes, Ethne. *Diseases and Human Evolution*. Albuquerque, NM: University of New Mexico Press, 2005. An excellent, interesting book written for a general audience. Great source for information on diseases and their effect on history for teachers and I would also give excerpts to my students.

Brain, Marshall. "Discovery Health "How Your Immune System Works"." Discovery Health "Health Guides". http://health.howstuffworks.com/human-body/systems/immune/immune-system11.htm# (accessed July 12, 2010). A website with good basic information on the immune system, as well as video clips and animations.

Freeman, Scott, and Jon C. Herron. *Evolutionary Analysis (4th Edition).* 4 ed. San Fransisco: Benjamin Cummings, 2007. A more advanced textbook on evolution.

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J., Trevathan Wenda R. Trevathan Wenda R. Smith Euclid O. McKenna Jim J. McKenna Jim. *Evolutionary Medicine and Health : New Perspectives.* Oxford: Oup, 2008. A collection of articles reviewing the latest research on the relation of evolution to disease. Use this if you want to go much deeper.

Janeway, Jr., Charles, Paul Travers, Mark Walport, and Mark Shlomchik. *Immunobiology*. 5 ed. Sacramento, CA: Garland Science, 2001. A college textbook on the immune system and how it works. If you have never had a course on the immune system, and want the details, then this is a great book for finding the answers to your questions.

Johnson, George B, Jonathan Losos, Kenneth A. Mason, Peter H Raven, and Susan Singer. *Biology*. 8 ed. New York: McGraw-Hill Science/Engineering/Math, 2008. This is a basic AP Biology/entry level college textbook which I turned to for help understanding the higher level sources I was reading.

Johnson, George, Jonathan Losos, Kenneth Mason, Peter Raven, and Susan Singer. Biology. 7 ed. New York: McGraw-Hill Science/Engineering/Math, 2005.

Kluger, Matthew, and Barbara Rothenberg. " Fever and Reduced Iron: Their Interaction as a Host Defense Response to Bacterial Infection ." *Science* Vol. 203, No. 4378 , no. Jan. 26, 1979 (1979): pp. 374-376 . http://www.jstor.org/sici?origin=sfx%3Asfx&sici=0036-8075%281979%29203%3A4378%3C374%3AFARITI%3E2.0.CO%3B2-5 (accessed July 13, 2010). You must have access to the journal, Science, or access to it through JSTOR. This article describes research done that show that fever reduces levels of iron in the body, inhibiting bacterial growth.

Koella, C., and Stephen C. Stearns. *Evolution in Health and Disease.* 2 ed. New York: Oxford University Press, USA, 2008.

Linnemeyer, Paul A.. "The Immune SystemÃ, — An Overview - The Body." The Complete HIV/AIDS Resource - The Body. http://www.thebody.com/content/art1788.html (accessed July 26, 2010). This is an HIV website that has good basic information on the immune system suitable for both teachers and students. There is also a new section at the site profiling African-American men and women who are active in AIDS research and education.

Moalem, Sharon, and Jonathan Prince. *Survival of the Sickest: A Medical Maverick Discovers Why We Need Disease*. New York: William Morrow, 2007. A controversial, but very interesting and thought-provoking book about how diseases might have had selective advantages in certain environments.

Nesse, Randolph M., and George C. Williams. *Why We Get Sick: The New Science of Darwinian Medicine.* 1 ed. New York: Vintage, 1996. Get this book! Every page is a revelation about why our bodies work the way they do to fight off infections, the limitations we have inherited from our ancestors, how the development of culture and the changes in our society have affected our ability to fight disease, and why we age.

"The Normal Bacterial Flora of Humans." Online Textbook of Bacteriology. http://www.textbookofbacteriology.net/normalflora.html (accessed July 20, 2010). A great source for the types of bacteria that inhabit the body, with pictures of many of them.

Websites for Teachers

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http://www.youtube.com/watch?v=dZANKFxrcKU –Teddy Bear Picnic song

http://www.youtube.com/watch?v=6S_eKvc2PgQ&feature=fvw –Teddy Bear Picnic song with cartoon

http://mysciencespace.com/documents/InteractiveNotebook.pdf —science notebooks

http://www.pbs.org/wnet/secrets/previous_seasons/lessons/lp_plague.html —Mystery of the Black Death lesson plan

http://edtech.suhsd.k12.ca.us/inprogress/cvh/hhuckaby/bioweb/sicklecellgeneprofile.htm —sickle cell DNA, cells and hemoglobin images and info

http://www.bio.davidson.edu/courses/Bio111/Hemomut.html —interactive coding for hemoglobin/sickle cell gene

http://www.cdli.ca/~dpower/resp/co2.jpg —pics of CO2 transport

http://www.butler.org/healthGate/images/si55551170.jpg —O2 transport pics

http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=mmed&part=A512 —skin flora

http://www.textbookofbacteriology.net/normalflora.html —Normal Bacterial Flora of Humans Contains a chart of the skin microbes as well as pictures.

http://www.pbs.org/wgbh/nova/sciencenow/3209/05.html —video of freezing wood frog.

http://www.hhmi.org/biointeractive/disease/pdf/antibiotic_resistance/antibiotics_activities.pdf —activity for bacteria resistance.

http://www.scienceteacherprogram.org/biology/Webster02.html —antibiotic resistance inquiry lab.

Websites for Teachers and Students

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http://www.geneticheath.com/dbts_genetics_of_type_1_diabetes.shtml#Anchor1 —Genes that cause Type 1 diabetes. Genetic Health website

http://www.geneticheath.com/Diabetes_Home.shtml —good info on diabetes

http://www.nih.gov/about/researchresultsforthepublic/Type1Diabetes.pdf —info on type 1 diabetes

http://kidshealth.org/kid/htbw/htbw_main_page.html —contains cute video of how the immune system works.

http://www.actionbioscience.org/evolution/meade_callahan.html —good site for helpful harmful characteristics of bacteria.

http://evolution.berkeley.edu/evolibrary/home.php —discussion and examples of different topics in evolution. Includes discussion of antibiotic resistance and efforts to slow it down in hospitals.

http://health.howstuffworks.com/human-body/systems/immune/immune-system.htm —understandable info on the immune system

Appendix

Implementing District Standards

This unit addresses the following North Carolina goals and objectives for Biology I:

Objective 3.03 Interpret and predict patterns of inheritance. Students will identify the patterns of inheritance for recessive traits and for sickle cell anemia.

Objective 3.05 Examine the development of the theory of evolution by natural selection. Students will learn about Darwin's theory of natural selection and apply that theory to the results seen in the Teddy Graham and sickle cell activities. They will discuss and observe the selection for resistance to antimicrobial products by designing an experiment to test those products.

Objective 4.02 Analyze the processes by which organisms accomplish essential life functions. Objective 4.03 Assess, describe and explain adaptations affecting survival and reproductive success. Objective 4.04 Analyze

and explain the interactive role of internal and external factors in health and disease. Students will be comparing normally functioning systems to systems that are affected by disease, for example, in the Day 2 lab rotation on the circulatory system and how sickle cell anemia affects that system. They will learn how our bodies respond to these challenges using our immune system. They will learn about the various types of bacteria and viruses and how microbes have responded to that attack as they complete the culminating Outbreak activity. They will learn about the changes in human diets over time and how those changes affect the body which has adaptations for a very different kind of diet. Students will develop skits to interpret how the immune system responds to infectious disease.