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Human Health: Correlation, Causation, and Evolution

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Overview

Growing up as the son of immigrant parents on the streets of Brooklyn, Isidor Rabi may not have seemed to be leading a life that was particularly out of the ordinary. But he went on to become an extraordinary scientist, helping to invent radar and the atomic clock and winning the 1944 Nobel Prize in physics. When asked why he pursued a career in science rather than medicine or law like the other kids he grew up with, Rabi replied: "My mother made me a scientist. Every other Jewish mother in Brooklyn would ask her child after school: "So? Did you learn anything today?" Not my mother. She always asked me a different question. "Izzy," she would say, "did you ask a good question today?" That difference made me a scientist."

The seemingly slight difference in his mother's question caused Rabi to see the world through a vastly different lens than his classmates. Teaching science students to question information, rather than simply absorb it, cultivates curiosity, prompts students to delve deeper into the material, and helps them identify their unique personal interests. By teaching students to question the world around them, we teach them to think for themselves. Questioning opens the door to discovery, innovation, understanding, and, of course, further questioning.

Questions aren't just important in science, though—they're a vital component to success in many careers. Questions are asked in the legal system to determine guilt and innocence, they are asked by physicians to determine how to treat their patients, they are asked by architects to create the most appropriate design of structures, and so on and so forth. Of course, it's not simply about asking any question, it's about asking *good* questions. Asking the right questions can make the difference between winning and losing a lawsuit, or saving and killing an ailing patient. So, what makes a good question? And how can you teach students to ask good questions?

The aim of this unit is to teach students how to develop and analyze questions and hypotheses through the lens of evolutionary medicine. More specifically, the skills I want students to have at the end of this unit are the ability to: formulate testable questions, generate proximate and ultimate explanations for phenomena, and draw conclusions from data. The main concepts my students will understand by the end of the unit are that: evolution does not have a direction or plan, our bodies are a result of evolutionary compromises, there are both proximate and ultimate explanations to every human health issue, and correlation does not equal causation.

To provide some context for this unit, I teach biology and health at a small Chicago high school where 93% of the students are from low-income households. The majority of the students are Black (93%), while the second most common demographic is Hispanic (5.7%). My health classes have an average of 18 students enrolled, although class sizes may soon increase significantly.

This unit is designed with the students in my tenth grade Topics in Health Science class in mind. Since it is framed around formulating questions and hypotheses, it can easily apply to a high school biology course or a science class at the elementary level. My students do not have much background in data analysis or experimental design, so this unit is meant to build their skills in these areas. I am allotting four weeks to cover this information, but it can be adapted to fit a shorter time span for teachers whose students already have a foundation in experimental design.

Rationale

In the beginning of this past school year I asked my students to describe a scientist. The general consensus in each of my classes was that scientists are balding, nerdy men with glasses and lab coats. I then showed them a series of pictures of scientists running the gamut of ethnicity, age, gender, and religious background. I asked them again to describe a scientist, and after some class discussion we eventually decided that a scientist is someone who asks questions about the world, and then searches for answers to these questions through experimentation.

Since science is about asking questions, students in a science classroom must be encouraged to ask questions and be taught how to ask good questions. My experience thus far has been that students initially walk into my classroom reluctant and unsure about how to ask questions. I discovered this during the first unit we covered in biology: evolution. As a first year teacher I wasn't exactly sure how my students would react to learning about evolution, but I expected difficult questions about God and religion, and I was nervous about how to field such questions. Instead, I was met with a more disturbing issue. Not one student questioned a word I said. I asked them why they weren't asking any questions, and they said they didn't have any. I probed further, asking if what I was telling them conflicted with their views about the world, but I received no response. Frustrated, I finally said, "If I told you that grass is neon orange, would you question me then?" A few students shrugged, and one student said "well, I'd call you crazy." I proceeded to go on a rant about unreliable sources and how you have to question everything you read and hear, and how there'd be no such thing as iPods or antibiotics or TVs if people hadn't asked questions and sought the answers to those questions. That was all well and good, but it didn't bring my students any closer to learning how to question the world. This year I want to make a more focused effort to teach my students about the importance of questioning, and teach them how to ask *good* questions.

Evolutionary medicine is a perfect framework for teaching these skills, as it has a useful body of readily available data, and yet still has so many unanswered questions. Using evolutionary medicine will also be helpful because it is a field of science that students can relate to. As the intersection of evolutionary biology and human health, evolutionary medicine will allow students to ask questions about their bodies, their ancestors, and what it means to be human.

The second component to scientific inquiry is that once you ask a question, you must conduct an experiment.

In order to search for answers to their own questions, students must develop the ability to read data. Regardless of where my students go in life, they need to know how to read, create, and analyze data tables and graphs. Graphs are powerful tools for persuasion, and they are used by politicians, advertisers, lawyers, doctors, journalists, and countless other professions. If students can read graphs and tables, they will better navigate themselves through the world and be more aware of when people are trying to manipulate them. In this unit, the content about evolution and health will be woven into graphs for students to analyze. During the labs they will also gather and interpret their own data.

This unit is aligned with many College Readiness Standards in each of the three science strands, including SI 20-23.2 (understand a simple experimental design) and EMI 20-23.1 (select a simple hypothesis, prediction, or conclusion that is supported by a data presentation or a model). It also covers Illinois Learning Standards 11A, 12A.5, and 13B.1. A more complete description of alignment with CRS skills and ISBE standards can be found in the appendix.

General Strategies

We will start the unit by reading an excerpt from Voltaire's *Candide* where the character Dr. Pangloss marvels at how the human body came to be the way it is (e.g. our faces are shaped the way they are in order to accommodate eyeglasses). Pangloss's assertion that we live in the "best of all possible worlds" reflects a common misconception about evolution and how the human body works: it makes the assumption that evolution aims for perfection, having some sort of ultimate plan. Pangloss also continuously confuses cause with effect, and vice versa. When discussing proximate and evolutionary causes with my students, I will frequently refer back to Pangloss and have them explain their reasoning behind the causation scenario they have identified.

Students will then be presented with a series of questions about the human body that they must generate answers for. Examples of these questions are: If fatty foods are so unhealthy, why do we crave them? Why is morning sickness an evolutionary advantage? Why hasn't Huntington's disease been weeded out? Why do we feel pain? Why do babies cry? Students will keep a sheet of their hypotheses for the entire unit, and we will address one question per day. At the beginning of each class period, students will generate three possible answers for that day's question: a proximate explanation, an ultimate (evolutionary) explanation, and a Panglossian explanation (they will become better at developing these answers over time, after extensive modeling and peer review). They will discuss their hypotheses for the day via "Think, Pair, Share," and will keep track of their notes on a graphic organizer. They will use the same graphic organizer format each day, which is a sheet of paper bisected by two columns: one for proximate causes and one for ultimate causes for the phenomenon we will be discussing that day.

Students will then analyze data on each topic to determine which of the answers is most supported by the evidence, and draw conclusions based on that. A series of labs will be woven into the curriculum (e.g. growing bacteria on agar in Petri dishes when discussing antibiotic resistance), and by the end of the unit students will be expected to write their own question about human health and design an experiment to test a hypothesis.

In addition to learning how to ask questions, it is important for students to make a hypothesis. This helps them to activate their prior knowledge of the topic, as well as to identify any preconceptions they might have.

People often fall into the trap of paying attention only to data that confirms what they already think is true, which can prevent them from achieving true understanding.

I also want instill in my students the understanding that it's okay to be wrong. Many discoveries were direct results of scientists making errors. For instance, we have mistakes to thank for pacemakers, penicillin, Teflon, Viagra, microwave ovens, Coca-Cola, rubber, and fireworks. We'll talk about this in class to begin removing the stigma of being wrong, as well as doing the "Wrong Answer" activity several times throughout the unit. In this activity, the teacher poses a question and actually asks students to give an *incorrect* answer. This makes giving a wrong answer the right answer. Teachers can use this to dispel misconceptions about a topic. For example, if a teacher asks, "How does the circulatory system work?" a student may respond that the stomach pumps blood throughout the body. The teacher's response might be, "That's a perfect wrong answer, since the stomach doesn't pump blood-the heart does." Once students get the hang of this activity, other students can (politely) start identifying why the wrong answers are wrong.

The approach to this unit will incorporate two vital components of science education: science content and science skills. Students will use the content knowledge they gain to question the "what" and the "why" of human health and disease. Students will also analyze data through those same lenses: the what (what is the relationship between two variables?) and the why (why are the two variables related in this way?). I want my students to develop the ability to approach a situation from multiple viewpoints, and then compare those viewpoints to draw conclusions.

Proximate vs. Ultimate Questions

In science, the distinction between the proximate and ultimate is a temporal one. The proximate deals with what is happening now, during an organism's lifetime. The ultimate deals with what happened before the organism was born, during its evolutionary history.

Proximate questions, then, center on how an organism develops and functions. They tend to be "how?" and "what?" questions. For instance: How do songbirds learn to sing the right song? How do animals regenerate limbs? What is happening inside of people when they have appendicitis? How does Alzheimer's disease affect the brain? What causes Alzheimer's disease?

Ultimate questions, on the other hand, focus on the evolutionary reasons for why organisms have the traits they do. They are "why?" questions. For instance: Why do songbirds sing while other birds do not? Why can't humans regenerate limbs? Why do people have an appendix when they can live without one? Why hasn't Alzheimer's disease been weeded out of the population by natural selection? If trees and tortoises can live hundreds of years, why isn't the maximum human lifespan longer?

Neither type of question is better than the other; both proximate and ultimate questions must be asked about an organism's trait in order to gain a full understanding of that trait. This is similar to the moral of the tale about a group of blindfolded men that encounter an elephant. One blindfolded man runs his hand along the elephant's trunk and declares the creature is like a snake. Another man feels the elephant's leg and says the elephant is like a pillar, while another man feels the ear and decides the elephant is like a hand-fan, and so on. The men argue endlessly about who is correct, until a wise man declares that they are all partially correct. They each have a piece of the puzzle and need to combine their knowledge to get the full picture. Like the blindfolded men, biologists have long argued about the cause of various traits. Oftentimes, both sides were right-they just needed to realize that one side was looking at the proximate cause and the other was looking at the ultimate cause. [1]

The History of the Proximate and Ultimate Approach

Depending on whom you ask, the birth of the proximate-ultimate distinction happened anywhere from 2,300 years ago to 50 years ago. Some go all the way back to Aristotle, pointing to his system of separating causation into four distinct categories: material cause, formal cause, efficient cause, and final cause. The point was that something can be the result of different types of causes, and that these causes should be analyzed separately and together to understand the bigger picture. [2]

Other scholars trace the origins of the proximate-ultimate distinction to William James's *1890 Principles of Psychology*, where he touched upon the double-layered causation for instinctual actions. James gave the example of a man who is eating dinner: if you ask the man why he is eating dinner, he might say it's because the food tastes good. But there is another reason beyond that: the man is also eating dinner because he needs food to survive. [3]

In a 1961 paper, Ernst Mayr popularized the proximate-ultimate distinction and applied it specifically to biology. He gave four types of causes: ecological, genetic, intrinsic physiological, and extrinsic physiological cause. Mayr illustrated the differences between these types of causes with an example question: Why did the warbler at Mayr's New Hampshire summer home begin migrating south on the night of August 25th? [4] An ecological cause would be that the warbler had to fly south because it would otherwise starve during the harsh winter. A genetic cause would be that the warbler has adaptive genes that cause it to migrate when certain environmental stimuli signal the approach of winter. An intrinsic physiological cause would be that the bird's migration is linked to photoperiodicity, and the bird migrates as soon as day length drops below a certain number of hours. An extrinsic physiological cause would be that the bird, which was already generally prepared to fly south, left on that particular day because a cold front came in.

Mayr called the ecological and genetic explanations "ultimate" causes, which directed the change in DNA sequence of an organism over time. The intrinsic and extrinsic physiological explanations were termed "proximate" causes, which controlled an organism's reaction to its immediate surroundings.

Two years later, Niko Tinbergen presented four types of viewpoints from which an organism's trait should be examined to fully understand it: ontogeny, causation, survival value, and evolution. The first two are proximate viewpoints, while the latter two are ultimate viewpoints—although this terminology was not applied until later. Tinbergen defined causation as events leading up to the occurrence of a behavior. The cause of a behavior can be examined from the viewpoint of ontogeny, which explores how a specific trait develops in an organism (e.g. How are behavioral changes controlled? What causes a behavior to differ with age or by gender?). A second way of looking at a behavior is from the causation viewpoint, which is gained by dissecting a behavior's process: What sensory and motor mechanisms are involved in this behavior?

The cause of a behavior can also be investigated from more distant viewpoints. The survival-value view examines why a particular behavior is adaptive. As an example, Tinbergen asks: Is the size and shape of a blackbird's beak best suited to its environment? [5] The fourth and final way of looking at the cause of a behavior is from an evolutionary standpoint, which studies the evolutionary history of a trait (e.g. How does this behavior compare in closely and distantly related species?)

Tinbergen's four viewpoints and Mayr's four types of causation have since merged, forming our current proximate and ultimate approaches to causation. [6] Researchers use these approaches to gain a more complete understanding of traits, behavior, and what it means to be human.

An applied example is a 2001 study of infant crying conducted at Vassar College. [7] Humans are the only primates that cry, and human infants are the only animals that may continue crying even when a caregiver is in physical contact with them. Crying is adaptive in the sense that it alerts a caregiver that the baby needs something, but on the other hand this same noise draws attention to predators as well. So why do babies cry? This question can be answered from each of Mayr and Tinbergen's viewpoints.

From a proximate standpoint, the external causes to crying are pain (such as during vaccination), hunger (babies tend to cry every 3 to 3.5 hours after being fed), discomfort (such as when feeling cold, since crying generates heat through increased movement) and—most importantly—babies cry when they are left alone. Internal causes of crying might be that babies are giving off excess energy to regulate their internal environments, or they are responding to changes in their maturing central nervous system. Crying is thought to be controlled by the hypothalamus and limbic system (the emotional center of the brain).

If we take a step back, we can explore ultimate causes for baby crying. From the viewpoint of survival value and evolution, babies cry because it elicits attention from their caregivers. If crying really is an adaptation for inducing care giving, it is expected that females of childbearing age have evolved to respond accordingly to this signal. It turns out that this is indeed the case. The female response to an infant crying is the same across cultures: when babies cry, women hold and feed them. When a mother hears her baby cry, the temperature of her breasts increases and her breasts get heavier, making her feel an urge to breastfeed. Additionally, when a mother listens to a tape recording of her baby crying, her heartbeat slows down and then speeds up, preparing her for action. When listening to the cries of multiple babies, both mothers and fathers can accurately identify their own baby's cry (although only mothers correctly interpreted if the cry was for hunger, pain, or pleasure). Historically, birth cries may have also been used by parents to gauge whether or not they should invest their time and energy into raising the baby. For example, infants with Down's syndrome, neonatal asphyxia, cru du chat syndrome, and brain damage have cries that are much higher or lower-pitched than those of normal newborns [8] . In the harsh environments our ancestors lived in, abandoning a baby with an abnormal cry could increase parents' fitness by giving them a chance to have other babies that were more likely to survive and reproduce.

From the viewpoint of ontogeny, the reasons for crying change as babies get older. Regardless of parenting style, infants cry at an increasing rate until they are 6 weeks old, and then cry less and less until they reach 4 months old, when crying rates level out. Between the ages of 7 to 9 months, infant crying becomes more intentional, since they direct their crying toward specific caregivers and show signs of what results they expect (for instance, they quiet down as their caregiver comes closer). At around the time babies learn to crawl, they become fearful of strangers and cry when they perceive an oncoming separation from their caregiver. This fear makes sense evolutionarily, since the ability to crawl increases the baby's chances of meeting strangers and accidently becoming separated from their caregivers. At this point, the cause of crying shifts from a proximate one to a future one: a foreseen separation event.

Crying is an evolutionary compromise, since it benefits the baby by alerting caregivers, while at the same time it can also attract predators, annoy caregivers, and is energetically expensive. To gain a fuller understanding of why babies cry, it is necessary to analyze both the proximate and the ultimate causes.

Proximate and Ultimate Questions in Evolutionary Medicine

The partnership between proximate and ultimate causation is particularly beneficial in evolutionary medicine. Evolutionary medicine is the application of evolutionary theory to the field of human health and medicine. [9]

Our bodies function by processes and behaviors that have been shaped over millions of years of evolution. And yet, when doctors are trying to cure a patient, they generally look for a proximate cause of the symptoms, neglecting the evolutionary cause. For instance, doctors may treat a patient with low iron levels by giving them more iron to alleviate their symptoms. The doctors would be assuming that the patient's suffering was due to a proximate cause: an iron deficiency. The doctors may find, however, that their patient actually worsens after their treatment. They must then consider the ultimate causes for the patient's symptoms. Perhaps the patient is infected with a parasite, and the body has evolved an immune response that lowers its own iron in order to deprive such a parasite from obtaining this rare nutrient it needs to continue reproducing. [10]

Evolutionary medicine raises many ultimate questions: Why might morning sickness be an evolutionary adaptation? If fatty foods are so unhealthy, why do we crave them? Why do so many people have allergies? Why do we sleep? I will focus on five main topics in this unit: fatty foods, aging, infant crying, sickle cell anemia, and HIV immunity. The last two will be discussed in depth below.

HIV Immunity

The Human Immunodeficiency Virus (HIV) went from being unheard of to a worldwide pandemic seemingly overnight. As of 2008 there were 33.4 million people living with HIV worldwide, and more than 25 million have died from the virus since people became aware of it in 1981. [11] The virus attacks a person's white blood cells, destroying these cells of the immune system, leading to the disease Acquired Immunodeficiency Syndrome (AIDS). This process can result in night sweats, chronic diarrhea, blurred vision, weight loss, swollen lymph nodes, and shortness of breath, among other symptoms. With a deteriorating immune system, people with AIDS can easily be killed by opportunistic infections that would normally only cause mild discomfort, such as many bacteria and virus illnesses.

Although patients can be given a cocktail of antiretroviral medications to help control the progression to AIDS in HIV-infected persons, there is no cure. The virus mutates too quickly for therapies and the immune system to completely destroy the virus in an infected person. Researchers have recently become aware, however, of a special form of the CCR5 gene that appears to give people natural immunity to HIV.

Proximate: How is the CCR5 gene involved in HIV?

The CCR5 (C-C chemokine receptor type 5) gene encodes for a protein of the same name that is found in the membranes of T cells and macrophages, two types of immune system cells. The CCR5 protein is a receptor for chemokines, and is thought to be involved in fighting off infections through inflammation. [12] It also happens to play a role in HIV infection.

When people are exposed to HIV, the virus attaches itself to their T-cells. HIV injects its genetic information into a T-cell and causes that cell to use its own machinery to build new HIV particles. Those new HIV particles then burst through the cell, killing it, and finding more T-cells to attack. HIV can't inject its genetic information into just any cell, though. It needs to latch onto specific receptors on the cell membrane first. That's where the CCR5 protein comes into play. HIV binds mainly to the CD4+ protein, but to latch on properly it needs the help of the CCR5 receptor. Once the virus binds to these receptors, it can enter the cell and start replicating.

Some people have a recessive mutation in their CCR5 gene. This Δ32 mutation is a 32-basepair deletion in the CCR5 gene, which produces a CCR5 protein receptor that does not function for HIV attachment. As a result, people with two copies of this defective gene have T-cells that do not function normally. Although not ideal, as far as scientists understand, people with this mutation seem to be fairly healthy. However, they also happen to be resistant to HIV, because without the CCR5 receptor the virus cannot enter and replicate in their T-cells.

Ultimate: Why is there such a high prevalence of the CCR5 allele in Europe?

The defective CCR5 gene is surprisingly common in Europe and people of European-descent. In North America, 21.7% of Caucasians had one copy of the Δ32 allele, while it was found in only 5.8% of African Americans, 6.9% of Hispanics, and 0.6% of Asians. [13] The frequency of the Δ32 allele is highest in Nordic countries like Sweden and Norway, and it decreases the further south you go. The question is, why?

HIV is a problem all over the world, but the pandemic is worst in Sub-Saharan Africa. Although HIV immunity is beneficial for someone living in Europe, it would seem even more advantageous and urgent for someone living in a country such as Swaziland, where more than one-third of the adult population is infected with HIV. [14] Why hasn't natural selection caused Swazis to evolve the "32 mutation so they can be immune to HIV too? The answer is that HIV is too new of an environmental challenge for humans, and too few human generations have happened since the onset of the HIV pandemic for spontaneous mutations to occur in human populations and to spread to high frequency.

So why does anyone have the Δ32 version of the CCR5 gene? HIV has not been around long enough to result in such a high prevalence of this allele. Thus, there must be some other explanation for why this mutation is already so common in Europeans before HIV ever became a pandemic problem. Scientists have a couple of hypotheses to explain this phenomenon.

One explanation is that this allele helped people survive during the Black Death that wiped out about one-third of Europe's population in the 1300s. [15] This pandemic caused such a high death toll that any mutation conferring resistance would have been strongly selected. Thus, if the allele protected people from the plague, it would have been passed on at a greater frequency to the next generation. Since the plague didn't reach Africa, there wouldn't be a cause for evolutionary forces to select for the Δ32 allele, especially since it produced T-cells that didn't function properly. However, this explanation is incomplete because the plague is caused by a bacterium, *Yersinia pesti*s, and it is not clear why a mutation protecting against a bacterial infection would be effective at protecting against the virus HIV. It is possible that an unknown virus actually caused the high death toll in Europe during the plague years, and that this virus is closely enough related to HIV that the same mutation protects against it.

Regardless of the disease agent, some researchers argue that the Black Death didn't kill enough people or last long enough to be a strong enough selective force to result in such high frequencies of the Δ32 allele. They argue instead that the Δ32 allele protects against the well-known disease smallpox, caused by variola virus. [16] Although smallpox didn't kill as many people at once as the Black Death did, it killed far more people over a longer period of time. Smallpox also tended to kill younger people, before they were old enough to reproduce. This would have created an intense selective pressure for an allele that provided natural immunity against the smallpox virus. More research must be conducted to resolve this debate.

Sickle Cell Anemia

Sickle cell anemia is a genetically inherited disease that interferes with the ability of a person's blood cells to carry oxygen. This causes people to have episodes of extreme pain in their arms, legs, chest, and back. These episodes can last from hours to days, and occur throughout the patient's lifespan. People with sickle cell anemia often die of organ failure, usually before the age of 40, although an improved understanding of the disease has increased life expectancy slightly.

Proximate: How does sickle cell anemia affect the body?

Red blood cells contain hemoglobin, a molecule that is composed of two A subunits and two B subunits. Hemoglobin contains iron, which accounts for the color of our blood because iron is red in the presence of oxygen.

Our cells need oxygen to do their jobs, and we would quickly die without it. The hemoglobin in red blood cells carries oxygen throughout our bodies, and then returns to the lungs to get replenished with oxygen before making another trip. Red blood cells are normally shaped like circles, but the HBB (hemoglobin B) mutation makes the deoxygenated B subunits stick together, resulting in blood cells that are shaped like sickles, or crescents.

Sickle cell anemia is caused by a point mutation in the HBB gene on chromosome 11. The mutation causes just one amino acid change—a glutamic acid becomes a valine—but this small mutation results in a greatly misshapen protein. This has to do with glutamic acid being hydrophilic (meaning it "loves" water), while valine is hydrophobic (meaning it "fears" water).

When hemoglobin is carrying oxygen, the change to valine is not noticeable—it's the deoxygenated form that causes problems. A normal B hemoglobin subunit would have a glutamic acid on its outside, since it is attracted to the watery environment of the cell. The hemoglobin changes shape when it lets go of the oxygen molecule, which exposes the valine to a hydrophobic region on its neighboring hemoglobin. A normal B hemoglobin subunit would have a hydrophilic glutamic acid there, which would be repelled from that hydrophobic region. But, as like is attracted to like, the hydrophobic valine sticks to the hydrophobic region. The hemoglobin molecules all stick together, distorting the membrane of the red blood cell and causing it to take on a sickle shape. [17]

The sickle-shaped cells can clog vessels and block blood flow, preventing oxygen from reaching the body's organs. This causes the painful sickle cell episodes and can eventually lead to organ damage.

Ultimate: Why is there such a high frequency of the sickle cell allele in populations of African descent?

Sickle cell anemia is clearly a terrible disease—so why hasn't natural selection weeded it out? Well, in most regions of the world the frequency of the sickle cell allele is very low or non-existent, as expected. However, the allele is surprisingly common in tropical and subtropical regions, such as Sub-Saharan Africa, India, and South America. The disease malaria is also very common in these same regions. It turns out that this is not a coincidence.

There are between 300 and 500 million cases of malaria each year, resulting in more than 1 million deaths annually. [18] Malaria is most commonly caused by a parasite from the *Plasmodium* genus. Anopholes mosquitoes carry *Plasmodium* larvae, which can be unwittingly transmitted to humans via a female mosquito bite. The larvae replicate in a person's liver and then eventually invade the red blood cells as they enter the next phase of their lifecycle and reproduce.

When people carry one copy of the sickle cell HBB allele and one normal copy, they have the sickle cell trait. Their red blood cells are the correct shape unless they are in a low oxygen situation, such as when exercising in high altitudes. The body's immune response is to identify the sickle cells and destroy them. When P. *vivax* parasites enter a person's red blood cells, they use a significant amount of oxygen. This causes the red blood cells to become sickle shaped, and the body targets just the those blood cells (which happen to be the blood cells carrying the malaria parasite) for destruction. This greatly increases a person's chance of surviving a malarial infection, since the parasite population is kept under control.

If both parents are heterozygous for the sickle cell (meaning they have one copy of the normal allele and one copy of the sickle cell allele), their children have a 25% chance of having sickle cell anemia, a 50% chance of having sickle cell trait (they might pass sickle cell anemia to their own children, but they will be resistant to malaria), and a 25% chance of having two normal copies of the gene (putting them at much greater risk of dying from malaria). Because of this heteroyzgote advantage, it is not surprising that the sickle cell allele has not been weeded out of human populations in the tropics. Natural selection favors sickle cell heterozygotes because they can best survive malaria.

Specific Teaching Strategies

Activity 1: Asking Questions

Give students a scenario about animal behavior. Have them write down any questions this scenario brings to mind. An example scenario is the following: Naked mole rats are nearly blind, and live in colonies in Africa. Only the queen has babies, while the rest of the naked mole rats in the colony help take care of them. They even help potty train the babies.

Discuss the questions that students had about the scenario, and if they didn't come up with very many, help guide them. Write the questions on the board in two columns: proximate and ultimate. Example questions might be: Why are the naked mole rats nearly blind? How do they get around and find food if they can't see? Why do they live in colonies instead of by themselves? How is the queen the only one that can have babies? Why don't the other naked mole rats start their own colonies so they can have babies too? Why do the babies get potty trained? How do the babies get potty trained?

Next, show students several online clips of animal behavior and for each clip have them jot down the answers to the following questions: 1) What is the animal doing? 2) Why is the animal doing this? The list below consists of a few example links that can be used for this activity:

1. African Dung Beetle: http://www.youtube.com/watch?v=I1RHmSm36aE (What: rolling a ball of dung. Why: to attract a mate)
2. Giraffe Battle: http://www.youtube.com/watch?v=C7HCIGFdBt8 (What: fighting each other. Why: competing for a mate)
3. Ladybug and Braconid Wasp: http://www.youtube.com/watch?v=tYcniJwbqoI&feature=related (What: wasp laying eggs in ladybug. Why: to give its eggs safety and nutrition) http://www.youtube.com/watch?v=vMG-LWyNcAs&feature=fvw (Information about parasitic wasp laying eggs in a caterpillar)
4. Bowerbirds: http://www.youtube.com/watch?v=GPbWJPsBPdA (What: making a nest. Why: to attract a mate)

Discuss the questions and behaviors, and then segue into the next activity. Give students an envelope with proximate and ultimate questions, and a worksheet that has two columns: one with the title "Proximate" and the other with the title "Ultimate." Ask the first question from the envelope and tell students to place it in the "Proximate" column. Ask a second question and tell students to place it in the "Ultimate" column. Ask a third question and have a student volunteer share which column they think it belongs in and why. Repeat this with a few more questions as a class, and then have students finish organizing the remainder of the questions on their own. Ask students to come up with their own definition about proximate and ultimate questions. Then discuss as a class the distinction between the two types questions. Have students write their own questions and add them to the list.

Close the class by discussing why it is important to ask questions in science and in life in general. For homework, have students write 10 proximate and 10 ultimate questions.

Activity 2: HIV Lecture

Give students the graphic organizer for today's topic: HIV. Ask students to generate three proximate (how?) questions about HIV, and three ultimate (why?) questions about HIV. Example questions might be: How is HIV transmitted? How do people die from HIV? How does HIV destroy the immune system? Why do humans get HIV? Why do some people seem to be immune to HIV? Why isn't everyone immune to HIV?

Once students have jotted their questions down on the graphic organizer, have them guess what the answers to their questions might be. Do a "Think, Pair, Share," activity, where students share their questions and hypotheses with a partner, and then share and discuss them as a class. Have students write down the two questions we will be focusing on for the day: What does the CCR5 gene do? Why is there such a high prevalence of the CCR5 deletion allele in Europe?

Give a lecture (using PowerPoint or other visuals) about the CCR5 gene and its connection with HIV. Students will take notes on a separate sheet of paper, and then choose the three most important pieces of information that help answer each of the focus questions for the day. They will analyze graphs of CCR5 allele frequencies and explain the trend using the information they learned about smallpox and the Black Death.

At the end of class, students will revisit the two focus questions from the day and concisely answer each of them as an exit ticket.

Activity 3: Bacteria lab

At the end of the unit, once students have had practice analyzing data and generating proximate and ultimate questions, they are ready to design their own lab. Give each lab group a jar of five termites, a paint brush, and three pens (one Papermate, one Bic, and one other brand). Have students draw a circle with the Papermate pen, and gently place the termite on top of it. The termite will follow the path of the pen.

Ask students to develop a list of proximate and ultimate questions about this behavior (Why does the termite follow the path of the pen? Does the termite prefer one pen over another?). Help students narrow down which one to make a hypothesis and design an experiment for. Students should carry out the experiment and complete a lab write up. Discuss the results as a class. Termites are attracted to the ink in Papermate pens because it is chemically similar to a pheromone that female termites give off.

Termites can be ordered from Carolina Biological Supply Company, and information about this lab can be found at: http://www.uky.edu/Ag/Entomology/ythfacts/resourc/tcherpln/termtrails.htm

Bibliography

Resources

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This is an excellent book that discusses the evolutionary reasons behind various human traits.

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This is the journal article where Niko Tinbergen lays out his proximate and ultimate approaches to studying animal behavior.

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Illinois State Standards: Appendix A

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http://www.isbe.state.il.us/ils/science/stage_E/descriptor.htm

11A — Students who meet the standard know and apply the concepts, principles, and processes of scientific inquiry.

1. Formulate independent content-specific hypothesis referencing pertinent reliable prior research, or proposing options for appropriate questions, procedural steps, and necessary resources.
2. Design an inquiry investigation which addresses proposed hypothesis, determining variables and control groups, incorporating all procedural and safety precautions, materials and equipment handling directions and data-collection formatting preparations, or securing approval for all procedures, equipment use and safety concerns.
3. Conduct inquiry investigation, using technologies for observing and measuring directly, indirectly, or remotely, completing multiple, statistically-valid trials, or accurately and precisely recording all data.
4. Interpret and represent analysis of results to produce findings that support or refute inquiry hypothesis, evaluating data sets to explore explanations of outliers or sources of error and trends, or applying statistical methods to compare mode, mean, percent error and frequency functions.
5. Present and defend process and findings in open forum, generating further questions, explaining impact of possible sources of error, or reflecting on and evaluating peer critiques and comparable inquiry investigations for consolidation or refinement of procedures.

12A — Students who meet the standard know and apply concepts that explain how living things function, adapt, and change.

5. Apply scientific inquiries or technological designs to explain tests of evolutionary evidence, analyzing acceptance of geologic and fossil records, researching comparative anatomy, embryology, biochemistry and cytology studies of analogous and homologous structures.

13B — Students who meet the standard know and apply concepts that describe the interaction between science, technology, and society.

1. Analyze career and occupational decisions that are affected by a knowledge of science, associating scientific concepts considered in career-specific decisions (e.g., use of pesticides by farmers, choosing ink for printing), or explaining chemical/physical interactions in occupational settings (e.g., insect abatement programs, waste water treatment).
2. Analyze claims used in advertising and marketing strategies for scientific validity, collecting statements of purported scientific studies to evaluate mathematical validity, or researching scientific foundations use (or manipulation) in marketing and advertising strategies for target populations.

College Readiness Standards: Appendix B

Interpretation of Data 16-19

1. Select two or more pieces of data from a simple data presentation
2. Determine how the value of one variable changes as the value of another variable changes in a simple data presentation

Interpretation of Data 20-23

1. Compare or combine data from a simple data presentation (e.g., order or sum data from a table)
2. Translate information into a table, graph, or diagram

Scientific Inquiry 20-23

1. Understand a simple experimental design
2. Identify a control in an experiment
3. Identify similarities and differences between experiments

Evaluation of Models, Inferences, and Experimental Results 20-23

1. Select a simple hypothesis, prediction, or conclusion that is supported by a data presentation or a model
2. Identify key issues or assumptions in a model

Proximate and Ultimate Questions for Human Health Unit: Appendix C

HIV resistance

- What does the CCR5 gene do?
- Why is there such a high prevalence of the CCR5 allele in Europe?

Aging

- What causes us to age?
- Why do we age?

Fatty foods

- How do we digest fatty foods? How does the body crave fatty foods?
- Why do we crave fatty foods?

Sickle Cell Anemia

- How does sickle cell anemia affect the body?
- Why is there such a high frequency of the sickle cell allele in populations of African descent?

Huntington's Disease

- How does Huntington's disease affect the body?
- Why hasn't Huntington's disease been weeded out of the population?

Regenerating Limbs

- How do animals regenerate limbs?
- Why can't humans regenerate limbs?

Babies crying

- What makes a baby cry?
- Why do babies cry?

Type 1 Diabetes (Juvenile)

- What does diabetes do to the body?
- Why is Type 1 Diabetes more common in northern Europeans?

Notes

- 1 Mayr 1961, 1503
- 2 Dewsbury 1999, 189
- 3 Dewsbury 1999, 190
- 4 Mayr 1961, 1502
- 5 Tinbergen 1963, 419
- 6 Dewsbury1999, 191
- 7 Zeifman 2001, 265
- 8 Ibid.
- 9 Trevathan 2007, 140

- 10 Ness and Williams 1994, 7
- 11 UNAIDS
- 12 Weizmann Institute of Science
- 13 Lucotte 2002, 201
- 14 CDC
- 15 Hedrick and Verrelli 2006, 293-5
- 16 Galvani and Slatkin 2003, 15276-7
- 17 Sabeti 2008
- 18 World Health Organization 2007