Lesson 2: HIV — Genetic Variation
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Overview
The science and social science related to HIV and AIDS continues to evolve. As the "Why Us" Project was taking place, researchers made new discoveries about genetic variation and HIV/AIDS. Though race is a social construct, racial groups were often established by geographic areas. Racial groups have long histories in diverse geographic areas that in turn made exposure to certain diseases more likely. Often this exposure and other geographic factors caused the development of genetic traits unique to specific racial groups. The "Genetic Variation" video module introduces viewers to the scientists and their findings.

Key Concepts
- Genetic traits and predisposition to a disease
- Health is a complex interaction of genetics, environment and experiences
- Importance of health history of family
- Differences in health challenges and disparities by gender, race, ethnicity, and age
Continuation Page: Genetic Variation

Materials for Activities and Educator Background Knowledge

Reading 2.1
Daily University Science article on human adaptation to malaria
http://www.unisci.com/stories/20012/0626011.htm

Reading 2.2
New York Times article on prevalence of hepatitis among Asians

Reading 2.3
Prevalence of diabetes in Native Americans
http://vltakaliseji.tripod.com/Vtlakaliseji/id2.html

Reading 2.4
Genetic Home Reference article on prevalence of cystic fibrosis in whites

Reading 2.5
Piedmont hospital article on prevalence of cardiovascular disease in Hispanic/Latino women http://www.piedmonthospital.org/diw/Content.asp?PageID=DIW008878

Additional Educator Resources (if desired/needed)

Unnatural Causes resource – ask the experts transcript on genetics, race, and disease

National Coalition for Health Professional Education in Genetics frequently asked questions about genetics, race, and disease
http://www.nchpeg.org/index.php?option=com_content&view=article&id=142&Itemid=64

(Copies of each reading can be found at the end of this lesson module. The additional reading can be found as a PDF in the Educator Resources Appendix.)
Procedure

Part I

View the “Genetic Variation” video module. After viewing the module use the following questions to facilitate group discussion or give the questions as prompts for journal entries.

Discussion/Journal Questions

1) What new information did you gather from the video module?

2) How does genetic variation contribute to the high rates of HIV/AIDS in African and African American Communities?

3) What other questions or comments do you have?

Part II

Background: Health is a complex interaction of genetics, environment, and experiences. For some diseases, the cause is purely genetic – we are born with the disease, and there is nothing we can do to change our genes. However, understanding our genetic traits can help us mitigate our risks. For other diseases, there is an interaction between genetics, environment, and experience – we can have a predisposition to the disease, but our environment, experiences and behavior can increase or decrease the chances of contracting the disease. For other diseases, genetics plays little role, and contracting the disease is entirely dependent on our environment, experiences and behavior.

Activity 2.1: Let’s examine how genetic variation affects susceptibility to HIV.

1) Give a brief overview of the history of human adaption to Malaria or have students/workshop participants read the history of human adaptation to Malaria (Reading 2.1)
Part II (continued)

Activity 2.1 (continued):

2) Make note of the fact that this adaptation is more due to geography and the environments than the actual genes related to racial features (hair color, eye color, skin color, etc.)

3) This adaptation, so helpful for protection against malaria, is making Africans and African Americans more susceptible to HIV. Because it is a new disease (in the scope of human history), humans have not adapted to this virus, and a previous adaptation is proving harmful.

4) One of the scientist used a coffee cup with and without a lid as an analogy for the differences in a gene from one group of people to another—in this case, between African American to non-African Americans. Did everyone in your class/workshop understand the concept that the analogy explained? Ask students/participants to come up with other analogies that could be used to explain the same gene phenomenon. Share and compare the analogies.

Activity 2.2: Having examined HIV’s prevalence in Africans and African Americans, examine other diseases that have larger prevalence in certain racial groups.

Divide into four groups. Each group reads one of the four articles: prevalence of Hepatitis B in Asians and Asian Americans (Reading 2.2), prevalence of diabetes in Native Americans (Reading 2.3), prevalence of cystic fibrosis in Whites (Reading 2.4), and prevalence of cardiovascular disease in Hispanic/Latino women (Reading 2.5).

Is the prevalence genetic, environmental, due to personal actions and experiences, or a combination of these factors?

Have each group present, explaining some of the statistics, some of the hypothesized reasons for the prevalence, and prevention and screening care each population is advised to take.
Part II (continued)
Activity 2.2 (continued):
After the group presentations, discuss the following questions:
1) Do all people from a specific racial group automatically have the disease?
2) Can people from other racial groups develop the diseases that have prevalence in a certain racial group?
3) How do social conditions like income, access to health care, access to healthy food, etc. contribute to the prevalence in different groups?
4) What are the opportunities of identifying disease prevalence by racial groups? What are the dangers?

Closure

Though our individual choices and actions can determine much about our health, there are conditions outside our control that can affect us, sometimes even more than our choices and actions. It is important to know the health concerns that affect our families, our communities, and our groups so that we can take precautionary actions to maximize our health.

Discuss or journal the following:

1) Are you aware of the health history of your family members? Who can you ask to find out more?
2) Are there any health issues that are prevalent in your local community? How might you find out what these are?
3) What are your group identities (gender, race, ethnicity, age, ability, etc.)? What are the health issues that are prevalent for your groups? How might you find out more?
4) Does understanding the interactions between genes, environment, and experience change your thoughts about how you might act? Why or why not?
Activities and Educator Keys

The five activities for this lesson and video module are embedded in the procedures. There are links to five different articles that are used in the activities. These links take you to longer articles. Usually, the articles can be found in the Educator Resources Appendix in PDF form. For the purposes of these activities, five adapted and shortened documents follow in this lesson plan. Since the activities are reading and dialog, there are no keys for the five activities for this lesson.
The Archaeology And Genetics Of Malaria Resistance

(adapted from http://www.unisci.com/stories/20012/0626011.htm)

Between 7,000 and 12,000 years ago, a dramatic climate change increased temperature and humidity in Africa, creating new lakes and pools of water. At about the same time, in the Middle East and northeast Africa, the advent of agriculture resulted in forest clearing and an increase in sunlit pools of water.

These developments combined to create suitable conditions for malaria-carrying mosquitoes to breed and infect growing populations settling in one spot to raise crops instead of moving about in small groups as hunter-gatherers.

Sarah Tishkoff and an international team of collaborators show that the history of mutations of the G6PD gene, which appears to provide resistance to malaria, the leading cause of death in humans, runs along the same time line as the history of the disease itself.

"In regions where malaria is prevalent, naturally occurring genetic defense mechanisms have evolved for resisting infection by malaria. We looked at variations of the mutation that have appeared independently in several areas of the world where the incidence of malaria is high," Tishkoff says. "In each region we studied, the mutations at G6PD that provide protection against malaria appear to have arisen at about the same time that history tells us malaria became prevalent.

"The genetic history tells us these malaria resistant mutations arose very recently. Those individuals who have these mutations are more likely to survive and to pass on their genes to their offspring, and therefore these mutations spread rapidly through populations."

All humans have the G6PD gene -- it's a general housecleaning agent, helping with glucose metabolism. Some people are born with a mutation of the G6PD gene, which, when reacting to certain triggers, such as infection (or some foods such as fava beans), can cause anemia, itself a serious and even deadly condition. But those same people also seem more able to resist the worst effects of malaria, a mosquito-borne parasite that annually infects 500 million people and kills 2 million.

"In most cases, a genetic mutation is eventually eliminated by natural selection," says Tishkoff. "But by giving its carriers increased resistance to malaria, this G6PD mutation has been perpetuated." Tishkoff's team studied the genetic histories of people with the mutated form of the G6PD in areas of Africa, the Middle East and the Mediterranean that have a high incidence of malaria.
Different variations of the gene appear in the different areas and seem to have evolved independently of each other, likely as a response to selection resulting from malarial infection.

"One mutation found throughout Africa arose within the past 3,840 to 11,760 years," says Tishkoff. "This estimate is consistent with archeological and historical documents that show malaria has had a significant impact on humans only within the past 10,000 years, since the origination of agriculture."

Another G6PD variant found in areas of the Mediterranean, the Middle East and India originated much more recently. According to Tishkoff's study, that variant developed within the past 1,600 to 6,640 years, a time frame that parallels historical Greek and Egyptian reports of the spread of a more severe form of malaria in those regions.

Tishkoff proposes that this mutation, which spread rapidly across a broad geographic region in a short time, may have been introduced by Greek migrations throughout the area. She speculates that it could have been spread by the army of Alexander the Great, which conquered regions throughout the Mediterranean, India, the Middle East and North Africa during the 4th century B.C.

"This is an excellent example of how we can combine genetics, archeology and history to study recent human evolution," says Tishkoff. "This study demonstrates how the environment, culture, genes and history interact to shape patterns of variation in the modern human genome."

The study was funded by an NSF Sloan fellowship, a Burroughs Wellcome Fund Career Award, an NSF grant to Sarah Tishkoff and another NSF grant awarded to Andrew Clark.

[Contact: Dr. Sarah Tishkoff, Ellen Ternes ]
26-Jun-2001
Hepatitis Risk for East Asians

(adapted from http://www.nytimes.com/2006/05/11/nyregion/11hepatitis.html)

By RICHARD PÉREZ-PEÑA and MARC SANTORA
Published: May 11, 2006

Among East Asian immigrants in New York City, one person in seven carries the hepatitis B virus, a new study has found. The condition puts them at far greater risk than other Americans for deadly diseases like liver cancer and cirrhosis. Most of the people tested had no idea that they were infected, a fact that frustrates doctors who know that with proper screening and treatment, the disease can be controlled, if not cured. But three-quarters of the people in the study had no health insurance, and even those who did had trouble getting coverage for screening.

The study, led by researchers at New York University School of Medicine, found that 15 percent of East Asians in New York — as many as 100,000 people — are chronic hepatitis carriers, with the rate highest among immigrants from China. That infection rate is 35 times the rate found in the general population.

Because Hepatitis B is endemic in many Asian countries, growth in the number of Asian immigrants in New York and across the country has made the disease a broad, expensive, emerging health problem. In the 2000 census, there were 800,000 Asians in the city, with roughly half from China.

Hepatitis B, like hepatitis C, is generally contracted through the blood, and is not transmitted through casual contact with infected people. Hepatitis A, which is caused by a different virus, can be transmitted through food, but hepatitis B cannot, with very rare exceptions.

Since the development a generation ago of a vaccine that is given to nearly all children born in the United States and to many adults who are considered at risk, hepatitis B has become rare in this country. While doctors have long worried about the disease in immigrant groups who come from countries like China — which does not have a comprehensive national vaccination program — little has been done to raise awareness of the danger.

People can carry the hepatitis B virus for decades without showing any signs of illness, until it causes life-threatening diseases like cancer or cirrhosis. "That often is the first sign of trouble," said Dr. Pollack, an associate professor at the medical school.

Hepatitis B is prevalent in many poor countries, and there are an estimated 350 million cases worldwide. It is most common in China, but scientists do not understand why. In this country, hepatitis B is associated with transmission by sex and intravenous drug use. But in Asia, the disease most commonly passes from mothers who do not know they have it to their children in the womb. It may also be transmitted among children who have close physical contact.
Early detection and suppression of the virus can interrupt the cycle of mother-to-child transmission. An adult immune system can usually fight off a new hepatitis B infection, though a small number of cases become chronic. But, Dr. Pollack said, "If you get it when you're an infant, your chance of getting chronic hepatitis B is greater than 90 percent."

In the last decade, doctors have been able to use an array of new drugs to treat chronic infection, but they do not cure the disease. Rather, they often suppress the virus so that it causes little or no harm. The medication must be taken for life.

The researchers found that people from Fujian province — the biggest source of Chinese immigration to the United States in recent years — had the highest rate of infection, which corresponds to findings by the Chinese government. Men between the ages of 20 to 39 were also more likely than other groups to have the virus; overall, men were twice as likely as women to be infected.

Some 61 percent of the subjects, who volunteered for the screening, were born in China, and 30 percent were born in Korea. A small number were from other parts of Asia, and those groups had much lower rates of infection than the Chinese.

Over all, 24 percent of the people screened were found to carry the virus, but that included a large number of people who said they had been tested before, and may already have known that they were infected. Those people might have sought screening to obtain confirmation or treatment. Among those who had been tested previously, 40 percent were infected.

Among those who said they had never been tested, who were just over half the subjects, 15 percent, tested positive. The researchers concluded that this figure, not the higher number, reflected infection rates in the East Asian population as a whole.

Lawrence K. Altman contributed reporting for this article.
Native Americans and Diabetes - The Facts
(adapted from http://vltakaliseji.tripod.com/Vtlakaliseji/id2.html)

This information on Native Americans and Diabetes is taken from the American Diabetes Association.

What is Diabetes?

Diabetes is a disease that affects the body's ability to produce or respond to insulin, a hormone that allows blood glucose (blood sugar) to enter the cells of the body and be used for energy. Diabetes falls into two main categories: type 1, which usually occurs during childhood or adolescence, and type 2, the most common form of the disease, usually occurring after age 45.

Diabetes is a chronic disease that has no cure.

How Does it Affect Native Americans?

Prevalence of type 2 diabetes among Native Americans in the United States is 12.2% for those over 19 years of age. One tribe in Arizona has the highest rate of diabetes in the world. About 50% of the tribe between the ages of 30 and 64 have diabetes.

Today, diabetes has reached epidemic proportions among Native Americans. Complications from diabetes are major causes of death and health problems in most Native American populations. Of equal concern is the fact that type 2, or adult-onset diabetes, is increasingly being discovered in Native American youth.

Diabetes Rapidly Increasing Among Native Americans, Alaskans

Reported in the December, 2000 issue of Diabetes Care: Diabetes has been growing in prevalence among Native Americans and Alaskan Natives, according to a recent study by the federal Centers for Disease Control and Prevention. The study found a nearly 30 percent increase in diabetes diagnoses among these populations between 1990 and 1997. During this time period prevalence among women was higher than among men, but the rate of increase was higher among men than women (37 percent v. 25 percent). The increase in prevalence was highest in Alaska, where it rose 76 percent during the 1990s, and lowest in the Northern Plains region of the United States, where it rose by 16 percent during this time period.

According to the National Institute for Diabetes and Digestive and Kidney Diseases, the "thrifty gene" theory proposes that African-Americans, Hispanic-Americans, Asian Americans and Native Americans inherited a gene from their ancestors which enabled them to use food more efficiently during "feast and famine" cycles. Today there are fewer such cycles; this causes certain populations to be more susceptible to obesity and to developing type 2 diabetes.
Native Americans and Diabetic Complications

The serious complications of diabetes are increasing in frequency among Native Americans. Of major concern are increasing rates of kidney failure, amputations and blindness.

Ten to twenty-one percent of all people with diabetes develop kidney disease. In 1995, 27,900 people initiated treatment for end stage renal disease (kidney failure) because of diabetes. Among people with diabetes, the rate of diabetic end stage renal disease is six times higher among Native Americans.

Diabetes is the most frequent cause of non-traumatic lower limb amputations. The risk of a leg amputation is 15 to 40 times greater for a person with diabetes. Each year 54,000 people lose their foot or leg to diabetes. Amputation rates among Native Americans are 3-4 times higher than the general population.

Diabetic retinopathy is a term used for all abnormalities of the small blood vessels of the retina caused by diabetes, such as weakening of blood vessel walls or leakage from blood vessels. Diabetic retinopathy occurs in 18% of Pima Indians and 24.4% of Oklahoma Indians.

What is Needed?

In ideal circumstances, Native Americans with diabetes will have their disease under good control and be monitored frequently by a health care team knowledgeable in the care of diabetes.

Patient education is critical. People with diabetes can reduce their risk for complications if they are educated about their disease, learn and practice the skills necessary to better control their blood glucose levels, and receive regular checkups from their health care team.

People with diabetes, with the help of their health care providers, should set goals for better control of blood glucose levels, as close to the normal range as is possible for them. Health care team education is vital. Because people with diabetes have a multi-system chronic disease, they are best monitored and managed by highly skilled health care professionals trained with the latest information on diabetes to help ensure early detection and appropriate treatment of the serious complications of the disease. A team approach to treating and monitoring this disease serves the best interests of the patient.
Cystic Fibrosis Among Whites
(adapted from http://ghr.nlm.nih.gov/condition/cystic-fibrosis)

Reviewed January 2008

What is cystic fibrosis?

Cystic fibrosis is an inherited disease of the mucus glands that affects many body systems. The disorder's most common signs and symptoms include progressive damage to the respiratory system and chronic digestive system problems.

Mucus is a slippery substance that lubricates and protects the linings of the airways, digestive system, reproductive system, and other organs and tissues. In people with cystic fibrosis, the body produces mucus that is abnormally thick and sticky. This abnormal mucus can obstruct the airways, leading to severe problems with breathing and bacterial infections in the lungs. These infections cause chronic coughing, wheezing, and inflammation. Over time, mucus buildup and infections result in permanent lung damage, including the formation of scar tissue (fibrosis) and cysts in the lungs.

Most people with cystic fibrosis also have digestive problems because thick, sticky mucus interferes with the function of the pancreas. The pancreas is an organ that produces insulin (a hormone that helps control blood sugar levels). It also makes enzymes that help digest food. In people with cystic fibrosis, mucus blocks the ducts of the pancreas, preventing these enzymes from reaching the intestines to aid digestion. Problems with digestion can lead to diarrhea, malnutrition, poor growth, and weight loss. Some babies with cystic fibrosis have meconium ileus, a blockage of the intestine that occurs shortly after birth.

Cystic fibrosis used to be considered a fatal disease of childhood. With improved treatments and better ways to manage the disease, many people with cystic fibrosis now live well into adulthood. Adults with cystic fibrosis experience medical problems affecting the respiratory, digestive, and reproductive systems. For example, most men with cystic fibrosis are unable to father children (infertile) because the tubes that carry sperm (the vas deferens) are blocked by mucus and do not develop properly. This condition is known as congenital bilateral absence of the vas deferens (CBAVD). Infertility is also possible, though less common, in women with cystic fibrosis.

How common is cystic fibrosis?

Cystic fibrosis is a common genetic disease within the Caucasian (white) population in the United States. The disease occurs in 1 in 2,500 to 3,500 Caucasian newborns. Cystic fibrosis is less common in other ethnic groups, affecting about 1 in 17,000 African Americans and 1 in 31,000 Asian Americans.
What genes are related to cystic fibrosis?

Mutations in the CFTR gene cause cystic fibrosis. The CFTR gene provides instructions for making a channel that transports negatively charged particles called chloride ions into and out of cells. The flow of chloride ions helps control the movement of water in tissues, which is necessary for the production of thin, freely flowing mucus.

Mutations in the CFTR gene disrupt the function of the chloride channels, preventing them from regulating the flow of chloride ions and water across cell membranes. As a result, cells that line the passageways of the lungs, pancreas, and other organs produce mucus that is unusually thick and sticky. This mucus clogs the airways and glands, causing the characteristic signs and symptoms of cystic fibrosis.

Other genetic and environmental factors likely influence the severity of the condition. For example, mutations in genes other than CFTR might help explain why some people with cystic fibrosis are more severely affected than others. Most of these genetic changes have not been identified, however.

How do people inherit cystic fibrosis?

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

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Hispanic women develop cardiac risk factors much earlier than Caucasian women, typically exhibiting the heart health status of a Caucasian woman 10 years older, according to a report from a recent Cardiovascular Disease Epidemiology and Prevention conference, sponsored by the American Heart Association.

The research suggests that being Hispanic may be an independent risk factor for heart disease, and that these women need to be identified and treated earlier.

"The tendency for medical practice is to assume that Hispanics have a delayed onset or less prevalence of cardiac disease, and our study shows that they have earlier onset and the same risk as Caucasians," says study author Dr. John Teeters, a cardiology fellow at the University of Rochester Medical Center.

"Physicians should be more aggressively targeting this population for identification of risk factors such as cholesterol and obesity and recognizing that a 20- or 30-year-old Hispanic may have the same risk factors as a 30- or 40-year-old Caucasian," he says.

The findings turn the so-called "Hispanic Paradox" on its head. This medical notion has long held that Hispanics have less heart disease than Caucasians do, despite having higher rates of risk factors.

But Dr. Teeters and his colleagues found that Hispanic women have earlier onset of disease, more risk factors, and an equal, if not higher, risk of cardiac disease.

"We did the study because the literature shows that the risk is less," he says. “But, in actual clinical practice, Hispanic patients are coming in with a lot of risk factors.”

In other words, there appeared to be a wide gap between theory and practice.

For this study, the researchers conducted a series of free community health screenings at churches, community centers, and outpatient clinics that primarily serve Hispanics.

Medical histories were collected for 79 Hispanic women, along with measurements of blood pressure, body mass index (BMI), waist circumference, lipid profiles, and blood sugar.

A group of 91 Caucasian women were compared. The average age of the Hispanic women was 53 versus 63 in the Caucasian group. Only 61 percent of the Hispanic women were postmenopausal, compared with 85 percent of the Caucasian women.
Despite age differences and differences in menopausal status, heart disease risk for the two ethnic groups was about the same.

Hispanic women had a higher rate of pre-hypertension (32 percent) compared with Caucasian women (19 percent).

Physical activity levels for Hispanic women were significantly lower and they had a slightly higher rate of metabolic syndrome, a cluster of risk factors that predispose a person towards cardiovascular disease.

Scores for hypertension, diabetes, high cholesterol, and waist circumference were similar between the two groups.

"I thought the findings were shocking," says Dr. Suzanne Steinbaum, director of women and heart disease and the Heart and Vascular Institute at Lenox Hill Hospital in New York City. "We have to find out what about Hispanic women is leading to this increased risk of heart disease."

"Hispanic women need to get checked earlier because their risk is earlier," adds Dr. Steinbaum. "Hispanic women in their 20s really need to have an exam. Pre-hypertension needs to be looked for and treated early."

What, then, explains the wide acceptance among clinicians of the Hispanic Paradox?

Dr. Teeters believes that the Hispanic Paradox may have resulted from incomplete data.

"Hispanic patients are less likely to come to care, so there's probably under-recognition of the degree of disease," notes Dr. Teeters.

"Many are immigrants and many go home when they become ill. There's also a higher degree of illegal alien status so there's probably underreporting," says Dr. Teeters.