December 7 and 8, 1998
Broadcast live via satellite and the Web from the Howard Hughes Medical Institute in Chevy Chase, Maryland, USA

FOUR EXCITING LECTURES BY
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Presented as a public service by the Howard Hughes Medical Institute Office of Grants and Special Programs
Howard Hughes Medical Institute Programs

The Howard Hughes Medical Institute was founded in 1953 by aviator-industrialist Howard R. Hughes. Its charter, in part, reads:

The primary purpose and objective of the Howard Hughes Medical Institute shall be the promotion of human knowledge within the field of the basic sciences (principally the field of medical research and medical education) and the effective application thereof for the benefit of mankind.

Biomedical Research Program
The Howard Hughes Medical Institute (HHMI) is a nonprofit medical research organization dedicated to basic biomedical research and education. Its principal objectives are the advancement of fundamental knowledge in biomedical science and the application of new scientific knowledge to the alleviation of disease and the promotion of health.

Through its program of direct conduct of medical research, HHMI employs more than 330 independent investigators based at 72 medical schools, universities, and research institutes located throughout the United States. HHMI conducts research in five broad areas: cell biology, genetics, immunology, neuroscience, and structural biology.

To assist these research efforts, HHMI is involved in the training of graduate and postgraduate students in its investigators’ laboratories, has given substantial support to the international genome mapping program, provides research training to medical students through the Research Scholars Program (conducted jointly with the National Institutes of Health), and organizes scientific conferences, workshops, and program reviews.

Grants and Special Programs
To complement its research activities, HHMI instituted a grants program committed to strengthening education in the biological and related sciences at all levels—from kindergarten through postgraduate training. Other important objectives of the Institute’s grants programs are to advance public understanding and appreciation of science and to increase science education opportunities for women and underrepresented minority groups.

HHMI grants, administered by the Office of Grants and Special Programs, focus on two major areas: 1) undergraduate and precollege science education and 2) graduate science education and research.

Grants for Undergraduate and Precollege Science Education. These grants are intended to stimulate young people’s interest in science and the pursuit of scientific research and education careers. HHMI initiatives in this area comprise the undergraduate, precollege, and local (i.e., Washington, D.C., metropolitan area) programs. The grants reach a wide range of institutions involved in formal and informal science education, including elementary and
HOW TO USE THIS GUIDE

Joseph G. Perpich, M.D., J.D.,
Vice President for Grants and Special Programs

Each year the Howard Hughes Medical Institute presents the Holiday Lectures on Science, a lecture series created to raise awareness, especially among high school students, of current developments in science relevant to the public. The aim of the series is to increase students' knowledge about the biological sciences and to generate interest in the scientific process.

This teacher and student guide is designed to help students and their instructors take full advantage of the 1998 lecture series, entitled “Of Hearts and Hypertension: Blazing Genetic Trails.” The guide provides background on the lectures, lists useful publications and websites, summarizes the lecture topics, and indicates areas that are relevant to the Advanced Placement (AP) Biology Curriculum.

“Meet the Presenters” is a glimpse into the lecturers’ lives in science, offering insights into their career choices and illuminating the challenges they faced as they pursued their research. The biographies are meant to reveal the person behind the science and help students better understand the scientific method and appreciate the many satisfactions of a science career.

The “Classroom Connections” section provides a summary and list of key concepts for each of the four lectures. Teachers can use the concept lists to correlate lecture content with classroom curriculum. The lists should also focus student interest and stimulate questions.

The wealth of useful publications and websites listed in this guide can direct students to valuable resources and avenues for further exploration. These publications and websites are rated both by level of difficulty and relevancy to the content of the lectures. The guide also lists websites that are more generally related to the lecture topics: the heart, the kidney, hypertension and cardiovascular disease, and human genetics.

For the first time, the lectures are connected to the AP Biology Curriculum offered in many high schools across the country. The “Themes and Concepts Related to Advanced Placement Biology” sections in this guide are designed to help teachers and students use the lectures to enrich select areas of the AP curriculum.

The guide also describes the many features of the holiday lectures website (www.holidaylectures.org). For example, “Ask a Scientist” allows Web visitors to ask scientists questions via e-mail about the current lecture topic and also about a wide range of biology topics, all year long. Other features include demonstrations and virtual laboratories that will appear on the website to make this year’s lectures more interactive.

We hope this guide will help teachers and students get more from our holiday lecture series and gain insight into the exciting, challenging world of science.
Howard Hughes Medical Institute Holiday Lectures on Science

In 1993 the Howard Hughes Medical Institute established the Holiday Lectures on Science, an annual lecture series especially for high school students, to add depth to their science education and to generate enthusiasm for the pursuit of science. The Holiday Lectures on Science give students and teachers the opportunity to experience presentations by some of the world’s leading biomedical scientists. While the content is contemporary, the format of the lectures builds on traditions established in 1827 by the British scientist Michael Faraday and on science lecture series offered annually by colleges and universities around the world.

The scientists who deliver the annual lectures are HHMI investigators who have made significant contributions to biomedical research. Their work has been published in major medical and scientific journals and frequently described in general interest publications. In addition, the lecturers take seriously their charge to present complex concepts in ways that effectively reach a high school audience. “It was a tremendous privilege to be given the opportunity to interact with all those students, either directly or indirectly, and to think about what we really consider was valuable for them to learn,” says immunologist Philippa Marrack, Ph.D. She, together with John Kappler, Ph.D., delivered the 1996 holiday lectures on the immune system.

The lecture series has several complementary components:

- **A live event.** About 200 students from 80 high schools in the metropolitan Washington, D.C., area attend the lectures, which are held for two days in December at Institute headquarters in Chevy Chase, Maryland. Department chairs and principals at each school nominate participants on the basis of their demonstrated interest in science.

- **A broadcast event.** The original on-site lectures for an in-house audience have evolved into a multi-media event broadcast live via satellite and over the Web, reaching thousands of students in the United States and, now, worldwide. An interactive Holiday Lectures Chat with the lecturers is held on our website at [www.holidaylectures.org](http://www.holidaylectures.org). A January rebroadcast over Channel One Connection is another venue for bringing the lectures into the classroom. The videotaped versions of the lectures are also popular with teachers for classroom use.
An exhibit. A museum-quality exhibit is created each year to complement the lectures topic. It includes historical and modern artifacts, some of which have never been displayed before, live demonstrations, and a biography kiosk with videotaped interviews with the lecturers. This exhibit later appears on the Institute’s Holiday Lectures on Science website in a “virtual” format, allowing students across the nation and the world to tour the exhibit.

Holiday lectures website. Not only are the lectures broadcast live over the Web, but they are also available “on demand” at any time after the lectures. Previous lectures are also on the website. In addition, the website contains a virtual laboratory, complete with interactive laboratory tools and a notebook, as well as a host of demonstrations that enable students to gain “hands-on” experiences with the scientific concepts discussed in the lectures.

Teacher and student guide. This guide, which contains biographies of the lecturers and summaries and key concepts for each lecture, helps teachers and students use the lectures in the classroom to supplement AP Biology or other science curricula. An extensive list of relevant publications and websites for teachers and students opens new avenues for exploring the topics.

Many components of the lecture series are developed with the advice and assistance of the HHMI Holiday Lectures Teacher Resource Group, which is composed of high school educators from the Washington, D.C., area, and the HHMI Holiday Lectures Museum Resource Group, consisting of curators from Washington, D.C., area museums. Student interns from Washington, D.C., area high schools help create demonstrations and laboratories that appear on the website and offer a student perspective on the materials that are designed to enhance the lectures.

The lectures are an important component of the Institute’s grants program, which complements the Institute’s research activities. Through its grants, the Institute is a major contributor to the enhancement of science education for students from their earliest years through graduate or medical school and beyond. HHMI grant awards have supported science education at colleges, universities, medical schools, research institutes, science museums, and elementary and secondary schools.
Of Hearts and Hypertension: Blazing Genetic Trails

This year the lectures will focus on a topic of interest to people of all ages. “Of Hearts and Hypertension: Blazing Genetic Trails” will consider the functions of the heart and the kidneys and the diseases affecting these organs and explore the genetic and molecular bases of these diseases.

Two HHMI investigators, who are both physicians and human geneticists, will present the lectures. They are Richard P. Lifton, M.D., Ph.D., director of the Program in Genetics in Medicine and professor of medicine, genetics, and molecular biophysics and biochemistry at Yale University School of Medicine, and Christine E. Seidman, M.D., director of the Cardiovascular Genetics Service at Brigham and Women’s Hospital and a professor at Harvard Medical School.

Two presentations will be made on the first day of the series. Dr. Seidman will begin by discussing the complexities of the heart and the research that is yielding new understanding about the mechanisms by which genes, environment, and lifestyles can help or hurt the most important muscle in the body. Dr. Lifton will then discuss the current explosion of information in human genetics, fueled in part by the revolution in molecular biology and biotechnology and the massive government-sponsored human genome project, an international effort to map and sequence all the DNA in the human chromosome set.

On day two, Dr. Seidman will discuss the work she has done using genetics to identify the molecular basis of hypertrophic cardiomyopathy, a rare but leading cause of death in young athletes. Dr. Lifton will conclude the 1998 series by describing his research on the genetics of hypertension and other diseases affected by the kidney’s ability to regulate salt.

The 1998 lectures will be available live December 7 and 8 via satellite in the United States and Canada and worldwide via webcast from www.holidaylectures.org. Lectures one and two will be rebroadcast January 13, 1999, and lectures three and four will be rebroadcast January 20, 1999, over Channel One Connection, formerly known as The Classroom Channel.
During its six-year history, the Holiday Lectures on Science have covered a wide range of subjects.

Visit our website at www.holidaylectures.org to explore past lecture topics.

• The 1997 lectures—“Senses and Sensitivity: Neuronal Alliances for Sight and Sound”—featured A. James Hudspeth, Ph.D., M.D., HHMI investigator at The Rockefeller University, and Jeremy H. Nathans, M.D., Ph.D., HHMI investigator at The Johns Hopkins University. Their lectures discussed how two highly specialized organs, the eye and the ear, enable humans and other animals to see and hear.

• In 1996 John W. Kappler, Ph.D., and Philippa Marrack, Ph.D., HHMI investigators at the National Jewish Center for Immunology and Respiratory Medicine, explored “The Immune System: Friend and Foe.” They described how the immune system functions and, on rare occasions, malfunctions.

• The 1995 lectures focused on “The Double Life of RNA.” Thomas R. Cech, Ph.D., HHMI investigator at the University of Colorado at Boulder, described the discovery of a catalytic function for RNA that may help fight viruses, cancer, and genetic disease.

• In 1994 the topic was “Genes, Gender, and Genetic Disorders.” Shirley M. Tilghman, Ph.D., HHMI investigator at Princeton University, and Robert L. Nussbaum, M.D., of the National Human Genome Research Institute at the National Institutes of Health, presented the latest findings on sex determination in mammals and other animals.

• The 1993 lectures—“DaVinci and Darwin in the Molecules of Life”—featured Stephen Burley, M.D., D.Phil., and John Kuriyan, Ph.D., both HHMI investigators at The Rockefeller University. These lectures discussed the three-dimensional structure of biologically important molecules and their role in health and disease.
CROSS CONNECTIONS

HHMI has worked with several organizations that offer science education materials to a broad public audience. These organizations reach teacher and student networks to complement and extend the current holiday lectures audience.

Channel One Connection
Channel One Connection (formerly the Classroom Channel) has the ability to reach 8.2 million teenagers at 12,000 secondary schools in the United States via direct cable. For the past several years, the Holiday Lectures on Science have been rebroadcast via Channel One Connection. In addition, the lectures have been promoted in the “Channel One Educator’s Guide”—seen by more than 20,000 teachers—and on its high-traffic website (www.channelone.com).

Discover Magazine
Discover Magazine and its website (www.discover.com) reach a broad audience of parents, students, teachers, and other members of the public interested in science. The magazine, a subsidiary of the Walt Disney Company, reaches nearly 7 million readers each month. Its website is one of the most successful science sites, with an estimated 1 million visits per month. This year HHMI will promote the Holiday Lectures on Science in the magazine, in an educator’s guide that is available to high school science teachers, and on the magazine’s website. Discover’s website will feature video highlights of the holiday lectures, biographies and photographs of the lecturers, and curricular materials. It will also contain a tour of the top sites directly related to the lecture topics and a special feature that will link the content of the lectures to Discover Magazine’s own content, available on the Web.

Discovery Channel
Discovery Communications produces a wide variety of educational materials for all ages via Discovery Channel, The Learning Channel, Animal Planet, and other channels. Discovery’s School House produces print and Web features that help teachers use Discovery’s programming in classrooms. HHMI is working with Discovery to develop curricular materials tied to the holiday lectures and to make the lectures available to the Discovery School House audience (http://school.discovery.com).

South Carolina and Maryland Public Television and other PBS Affiliates
Local affiliates of the Public Broadcasting System have been granted the rights to a segment of the cable bandwidth to deliver educational content directly to schools. In addition, many local PBS affiliates have strong community ties and a network of educational contacts. Taking advantage of those connections, South Carolina Public Television has turned the Holiday Lectures on Science broadcast into a community event, where students, teachers, and parents attend the broadcast and discuss the lecture topic. HHMI is pursuing the expansion of this use of the lectures with Maryland Public Television and other PBS stations.
Christine E. Seidman, M.D., Howard Hughes Medical Institute investigator, director of the Cardiovascular Genetics Service at Brigham and Women’s Hospital, Boston, and professor at Harvard Medical School.

Richard P. Lifton, M.D., Ph.D., Howard Hughes Medical Institute investigator, director of the Program in Genetics in Medicine, and professor of medicine, genetics, and molecular biophysics and biochemistry at Yale University School of Medicine.

Matters of the Heart
Although they grew up in different parts of the country, attended different universities, and work on different diseases in different laboratories, both Christine Seidman and Richard Lifton pursued a life in science because they wanted to help people. “Few things in life are more rewarding,” says Lifton. But both researchers were interested in doing more than seeing patients in the clinic: they wanted to understand the molecular defects that underlie human disease. Now, using the tools of modern molecular biology and genetics, Seidman is dissecting the biology of heart disease, and Lifton is pursuing the roots of hypertension.

Seidman, director of the Cardiovascular Genetics Service at Brigham and Women’s Hospital, has identified several genes that, when mutated, can cause familial hypertrophic cardiomyopathy. The disease, which results in a thickening of the heart muscle, is a leading cause of death in young athletes. Lifton, director of the Program in Genetics in Medicine, at Yale University School of Medicine, studies the molecular defects responsible for hypertension and has identified several genes that regulate blood pressure. In their HHMI holiday lectures, on December 7 and 8, Seidman and Lifton describe how pinpointing genetic defects can lead to better understanding and treatment of human disease.

Christine E. Seidman
“I’ve been a science person since I was a little kid,” says Seidman, known by friends and colleagues as Kricket. “I’ve always been interested in how things happen and why they happen.” As a child, Seidman collected butterflies in jars and experimented with anesthesia. “I almost killed myself trying to find the right dose of ammonia and cleanser to anesthetize those animals,” she laughs.

As an intern at Johns Hopkins Medical School, Seidman focused her scientific interest on medicine and disease. She had attended Harvard University as a pre-med student and there met Jonathan Seidman, the man who would become her husband and close collaborator. After completing a B.S. in biochemistry in 1974, Seidman enrolled in medical school at George Washington University. She found the traditional “name that body part” style of learning unsatisfying. “We had to memorize what this nerve is and what that bone was,” says Seidman. “It was not particularly thought-provoking.”
Seidman also felt her medical school training was not bringing her any closer to her goal of really helping people. “We kept seeing the same diseases walk through the door,” says Seidman. “But we weren’t making any fundamental progress in understanding why a disease occurred or what we could do to make an important difference in a person’s life.” Her perception changed when she became an intern and then a resident at Johns Hopkins University and met Victor McKusick, an accomplished geneticist and the chief of medicine. “He showed me that you could bring science to medicine,” she says. McKusick, who was studying a variety of genetic disorders found in Amish people, would spend time with residents, talking about patients and about the latest scientific discoveries. Seidman says that McKusick impressed her with his love of science, especially genetics. “It was terrific to have a world-class geneticist not only willing to help you understand scientific manuscripts but also dedicated to having you apply new concepts to the practice of medicine,” she adds.

Rainy Day Revelations

For Seidman, it all came together one rainy Sunday afternoon in the early 1980s. She was sitting on the sofa, thumbing through Science, when she came across a paper that described the isolation of atrial natriuretic factor (ANF)—a peptide hormone secreted by the heart that appeared to regulate blood pressure. Seidman was inspired. “I realized that the heart is more than just a pump that squeezes—it’s a smart pump,” she says.

So she and her husband set out to clone the gene for ANF, by no means a simple task. “In the old days,” says Seidman, “many of the techniques now used routinely to isolate and purify genetic material were still considered ‘witchcraft’—as much art as science.” And though the ANF peptide is small—only 21 amino acids long—the researchers ended up synthesizing more than 400 different bits of DNA to fish the ANF gene out of genetic material isolated from rat hearts.

By 1984, Seidman and her husband had cloned the ANF gene. “Nothing could have made me happier,” says Seidman, who then became convinced that she could apply molecular biology to the study of the heart and the diseases affecting its structure and function.

Probing the Pump

Seidman was interested in understanding how the heart responds to stresses such as valvular heart disease and high blood pressure. In these disease states, the heart swells, or hypertrophies, taxing the heart and decreasing its pumping efficiency. In the case of some inherited diseases, such as familial hypertrophic cardiomyopathies, heart muscle may thicken spontaneously, in the absence of occlusion, hypertension, or other outside factors, implicating an inherited problem. Seidman set out to identify the genes that signal the heart to hypertrophy.

Family Reunion

To identify genes that cause hereditary hypertrophic cardiomyopathy, Seidman first hit the phones, calling physicians all over the country to help her track down large families affected by the disease. In the extended Canadian family she first chose to work with, so many members had died of sudden cardiac arrest that family members referred to the disease as the Coaticook curse, for the place they lived. Seidman organized a family reunion, complete with a picnic, to gather the relatives for blood samples and to determine—using physical examination, electrocardiograms, and echocardiograms—which members showed the thickening of the heart muscle that was indicative of the disease.

To identify the chromosomal location of the mutant gene, DNA was extracted from a small blood sample obtained from each family member. The DNA was analyzed for genetic markers called polymorphisms, variations
from individual to individual. Scientists have found the locations of hundreds of genetic markers, which are used to identify specific places along all of the human chromosomes, just as zip codes can be used to identify where in the country a person lives. By identifying a marker sequence that is present in affected but not in unaffected members of a family, the chromosomal location of the disease gene can be pinned down. Using this approach, Seidman determined that a gene form causing cardiomyopathy in this family was located on chromosome 14.

From there, finding the gene was not difficult, says Seidman, because chromosome 14 happens to house the gene that encodes cardiac myosin—the major protein that makes muscles contract. Sure enough, when Seidman sequenced the cardiac myosin gene from affected family members, she found a mutation that causes familial hypertrophic cardiomyopathy.

**Sarcomere Disease**

But myosin isn’t the whole story. In some families with cardiomyopathies, the myosin gene is normal. That finding sent Seidman looking for mutations in other genes. So far, she has found dozens of mutations in seven different genes that can cause hypertrophic cardiomyopathy. The genes all encode proteins that form the sarcomere—the highly structured assembly of fibrous proteins that are the muscle cells’ contractile machinery.

Seidman is now exploring how mutations in different genes—and different mutations in the same gene—affect disease severity. For example, families that have a mutation in the myosin gene show a high incidence of sudden death at an early age. But in an Icelandic family that has a mutation in the gene that encodes cardiac myosin binding protein C, affected individuals don’t develop enlarged hearts until they are 40 or 50 years old.

**Turning to Mice**

Why do the mutations cause heart cells to hypertrophy or die? And why are some mutations more severe than others? To answer these questions, Seidman has used genetic engineering to make strains of mice with these disease-causing mutations. Researchers can manipulate and examine genetically engineered mice in ways they can’t do with human subjects. The mice are genetically much more similar to one another than any two humans are to each other (except identical twins, of course); using genetically engineered mice, researchers can tease apart the role of environment or habits and the direct consequences of a mutation. By examining mutant mice, Seidman hopes to determine whether exercise worsens or alleviates hypertrophy—and whether the results differ for males and females. Studying mice should also allow Seidman to identify drugs that might eventually reduce hypertrophy and perhaps prevent the arrhythmias that cause sudden cardiac arrest in humans.

**Richard P. Lifton**

For Richard Lifton, the space race and moon landing incited an early interest in science. By the age of 10, Lifton was regularly dredging water from the local pond so he could watch euglena and paramecia swim across the visual field of his hand-me-down microscope.

But Lifton was also interested in giving something back to the community. “I was a product of the idealism of the 1960s,” he says. So his thoughts turned to becoming a physician. Although Lifton found medicine compelling, he wasn’t sure that a career in the clinic would suit him. “It seemed that we were unable to do anything for so many people,” he says. “There were just so many cases where all you could do was watch.”

Lifton changed his tune during his junior year as an undergraduate at Dartmouth College, when he accepted a summer internship working in a research laboratory with Larry Kedes, then an HHMI investigator at Stanford University. “It was a great experience for me,” he says. “Larry was doing exactly what I wanted to do: he was a wonder-
ful physician and was making outstanding contributions to science—basic things that in the long run were going to relate to the biology of human disease.”

His summer internship turned into a six-month fellowship that inspired Lifton to enroll in the combined M.D.-Ph.D. program at Stanford, where he could learn the latest techniques in molecular genetics and biochemistry. “At that time,” Lifton says, “our tools were so primitive that I didn’t seriously consider working on anything as complex as a human disease.” Instead, Lifton started studying how genes are organized in the fruit fly *Drosophila melanogaster*. Working with molecular geneticist David Hogness and fellow graduate student Michael Goldberg, Lifton made a major discovery: the TATA box—a short DNA sequence that regulates the transcription of genes in all higher organisms.

After finishing medical school, Lifton returned to the clinic and completed four years of training at the Brigham and Women’s Hospital in Boston. When he finished his clinical rotation, he realized that things had changed. “While I was doing my residency, new tools were being developed that would permit us to study the causes of human disease like we dissect the genetics of *Drosophila,*” he says. For example, researchers had published the first maps that indicated where different genes were located on human chromosomes.

At the time, many researchers were studying diseases such as cancer and diabetes. But Lifton was interested in hypertension. “Nobody was looking into the genetics of hypertension,” he says, although hypertension contributes to hundreds of thousands of deaths annually, and the care of patients with hypertension is one of the largest expenses in the U.S. health-care budget. “Tackling such a difficult problem was viewed as impractical,” he recalls. So he set up a collaboration with Jean Marc Lalouel, a Hughes investigator at the University of Utah who was studying cardiovascular genetics. Lifton then spent three years in Utah, where he discovered the first known gene affecting the regulation of human blood pressure.

**High Pressure, Low Pressure**
Like Seidman with her studies of cardiomyopathy, Lifton identified a large family with severe high blood pressure. One woman had been hospitalized five times in unsuccessful efforts to control her blood pressure, and many of her relatives had died at young ages from cerebral hemorrhages due to hypertension. By looking at genetic markers present in the DNA of the woman and her siblings and their children, Lifton identified the gene and mutation responsible for the hypertension in the family.

By painstakingly searching through DNA from hundreds of individuals in dozens of large families, Lifton has mapped more than a dozen genes that, when mutated, change blood pressure in humans. But not all of these gene mutations cause high blood pressure. Some mutations actually cause life-threatening forms of low blood pressure in newborns. Over the past seven years, Lifton has identified mutations in three genes that raise blood pressure, eight genes that lower blood pressure, and two genes that can increase or decrease blood pressure, depending on whether the mutation activates the gene or shuts it down. The most intriguing aspect of these findings, says Lifton, is that all the mutations affect how the kidney handles salt.

**Importance of Salt**
An important function of the kidney is to control the volume of circulating blood and the concentration of salts in the blood. Control of blood volume is required for maintaining proper blood flow and delivery of nutrients to tissues, and tight control of the concentrations of sodium and other ions is necessary for the normal activity of...
many types of cells. The kidney controls blood volume by regulating the amount of salt it returns to the bloodstream and separately regulates ionic composition by reabsorbing more or less water from the blood.

In a sense, the pressure in the cardiovascular system—the arteries and veins that carry blood from the heart around the body—is like a hose clamped at both ends, says Lifton. Increasing the volume of fluid in the hose increases the pressure. Similarly, when the kidneys increase the return of salt and water to the bloodstream, blood pressure rises.

The genes that Lifton has identified encode channels, or transporters—proteins embedded in the cell membrane that control the flux of salt into the bloodstream. In the kidney, these proteins help regulate blood pressure. Mutations that cause hypertension increase the activity of these channels, causing the kidney to reabsorb more salt, while mutations that cause low blood pressure tend to block or reduce the activity of these channels.

**The Search Continues**

In the future, Lifton will continue to search for additional genes that play a role in controlling blood pressure and determining the clinical outcomes of patients with hypertension. Lifton suspects that just as there are genes that predispose people to hypertension, there are other genes that help determine whether a patient with hypertension will go on to develop a heart attack, stroke, or kidney failure, or will remain free of complications of hypertension. Understanding how these genes contribute to disease may also lead to the development of new treatments for heart failure and high blood pressure.

For Lifton, being able to find the answers to such questions is the greatest joy of science. "In science, you have a tremendous freedom to pursue what you're really interested in, the ability to discover something new about how nature works, and the opportunity to improve human health," he says. "How much more fun can you have?"
From humming birds to whales, all vertebrates have a muscular organ that pumps life-sustaining blood throughout the body. The human heart is roughly the size of a fist and contracts more than 2 billion times in a lifetime, pumping enough blood to fill a backyard swimming pool every week. How does this powerful muscle accomplish this amazing feat of strength and endurance day after day, and what happens when things occasionally go wrong?

Historically, philosophers and physicians have tried to understand how the heart works in terms of its anatomy and functional properties, whether real or imagined. In the opening lecture of the series, Dr. Christine Seidman will describe, based in part on her own work, how our understanding of the heart has progressed to the cellular and molecular levels. The heart is not just a pump, but a pump that can run on autopilot as well as respond to a variety of stimuli. A collection of specialized heart muscle cells called the pacemaker generate an endogenous rhythm for contraction that spreads electrically to the rest of the heart. But the rhythm that originates with the heart is influenced by many factors, including hormones, other blood-borne signals, and the nervous system. Given the heart’s intricate form, complex regulation, and essential task, it’s no surprise that things can go wrong. The heart can develop tears and holes, valves can malfunction, and more subtle cellular defects of the muscle can occur.

Dr. Seidman will emphasize in particular an often fatal condition of the heart known as cardiomyopathy, which she has researched extensively. She will further discuss how the disorder can arise from environmental and inherited conditions. Whether cardiomyopathy is induced or inherited, the contractile proteins of the muscle are defective at a subcellular level, leading to dysfunction and visible swelling. In extreme cases the heart eventually fails and death ensues. However, molecular genetics research and other advances in cell biology hold the promise of vastly improved treatments for heart disease.

**Key Concepts**

- The heart consists of four chambers: right and left atria receive blood from veins, and right and left ventricles pump blood into the arteries. A system of one-way valves prevents the back flow of blood.
- During a single cardiac cycle, the atria and ventricles rhythmically relax and contract, which forces blood from the heart and through the body.
- The pacemaker region of the heart generates rhythmic electrical impulses that are conducted all over the heart, causing muscle fibers to contract in synchrony.
- The pacemakers themselves are under neural and hormonal control. The heart rate can be affected by such factors as fear, anger, physical exercise, and change in body temperature.
- The basic contractile element of the heart is the cardiac muscle cell, or myocardium. Structurally and functionally, cardiac muscle has properties that are similar to both voluntary and visceral muscle types. Cardiac muscle is striated like voluntary (“skeletal”) muscle but, like visceral (“smooth”) muscle, is controlled by the autonomic nervous system.
At the ultrastructural level, the myocardium is arranged into a highly organized structure called the sarcomere. There are many proteins that compose the sarcomere, and chief among the contractile proteins are actin and myosin. The physical act of contraction depends on these proteins sliding past one another when energy is released in the cells.

The heart can suffer from injuries and diseases that impede its normal functions. Valves can become physically damaged and cause a back flow of blood, for example, or the pacemaker or the conducting apparatus may become damaged, causing a problem with the synchronization of the rhythmic pumping. There are also many cellular defects that adversely affect the muscle cells.

In cardiomyopathy, the cardiac muscle cells become unusually thick and cause a distension of the heart itself, leading to reduced pumping volume and, in turn, escalating structural damage.

Themes and Concepts Related to Advanced Placement Biology
An outline to help teachers incorporate relevant portions of this lecture into the Advanced Placement (AP) Biology curriculum is presented below. This outline is based, first, on the Topic Outline from the Educational Testing Service (ETS) that organizes biology into subject areas. Second, information for each of the ETS-selected subject areas has been organized by the kinds of headings used in ETS-recommended textbooks on biology. The headings are intended to reflect only the relevant themes and information introduced in the lecture for each subject area and are not intended to cover the specific subject area comprehensively. For more information about AP Biology, visit [www.collegeboard.org](http://www.collegeboard.org).

Lecture 1—Brave Heart: Circle of Life—focuses on the structure and function of the heart and its physiological role in maintaining the body's circulation. The contractile apparatus of cardiac muscle cells, with special emphasis on dysfunction, will also be discussed.

I. Structural adaptations of the body
   A. Tissues
      1. Muscle
      2. Nerve
      3. Connective
   B. Organs
      1. Heart
      2. Lungs
      3. Kidneys

II. Physiological adaptations of the body
   A. Homeostasis
   B. Circulation
      1. Evolution of circulatory systems
      2. Function of circulatory systems in vertebrates
      3. Cardiovascular system
      4. Evolution of the vertebrate heart
      5. The human heart
   C. Respiration
      1. Where our oxygen comes from
      2. Structure and mechanics of the respiratory system
Resources for Teachers and Students

These resources are listed roughly in order of relevance to the lectures.

Selected Websites

The Cardiac Center: Research: Basic Science. Connected with the Brigham and Women's Hospital, this site offers information on Dr. Christine Seidman's laboratory and her research on cardiomyopathy.

Difficulty Level: 2–3  
Content Level: 5

www.bwheart.org/research_basicscseidman.html

The Heart: An Online Exploration. Provides information on the heart's structure and function, a student-designed heart project, a movie of the heart, the blood, the body's circulation, and heart monitoring, including actual sounds of a beating heart.

Difficulty Level: 1–2  
Content Level: 3–4

sln2.fi.edu/biosci/heart.html

Your Heart and How It Works. Examines how the heart, circulatory system, collateral system, and myocardium function when healthy and diseased.

Difficulty Level: 2–3  
Content Level: 4–5

www.amhrt.org/Heart/Heart_How/index.html

Human Anatomy Online. Provides information and graphic presentations of the anatomy of the heart and blood vessels.

Difficulty Level: 2–3  
Content Level: 4–5

www.innerbody.com/indexbody.html

The Heart: The Engine of Life Educational Software. Provides an animated, interactive tutorial program on the human heart. The program is available as shareware at a nominal cost.

Difficulty Level: 3–4  
Content Level: 4–5

www.animatedsoftware.com/ascodesc/theheart/hrtguide/hrtguide.htm

Selected Publications

Scientific


Difficulty Level: 5  
Content Level: 5


Difficulty Level: 3  
Content Level: 3–4


Difficulty Level: 5  
Content Level: 4

1 Refers to the estimated subject knowledge needed by a high school student to understand the information contained in a publication or other media reference. Rank is based on a scale of 1 (lowest) to 5.

2 Refers to how directly relevant the information in a publication or other media reference is to extending the information being presented by the lecturers. Rank is based on a scale of 1 (lowest) to 5.

Difficulty Level: 3–4  
Content Level: 4–5


Difficulty Level: 3–4  
Content Level: 3–4


Difficulty Level: 4  
Content Level: 4


Difficulty Level: 3–4  
Content Level: 4


Difficulty Level: 3–4  
Content Level: 4

**Popular**


Difficulty Level: 2–3  
Content Level: 3–4


Difficulty Level: 1–2  
Content Level: 3–4


Difficulty Level: 1–2  
Content Level: 3–4


Difficulty Level: 1–2  
Content Level: 3
LECTURE TWO — Telltale Genes: Charting Human Disease

We are in the midst of one of the great revolutions in the history of medicine. This revolution is revealing how the forms of genes we have inherited influence our susceptibility to disease. In this second lecture of the series, Dr. Richard Lifton will briefly review our current understanding of the human genome and the effort to sequence the 3 billion base pairs of DNA and map the 100,000 genes organized along the human chromosomes.

Until recently, tools to make direct links between changes in specific genes and the causes of specific diseases have been lacking. The recent explosion of knowledge about the human genome, fueled by the tools of molecular biotechnology and data from the human genome project, have enabled Dr. Lifton and many other investigators to unravel the genetic underpinnings of human disease more rapidly. In the past five years, astonishing progress in the understanding of human disease—including heart disease, cancer, stroke, and other common causes of death in the United States—has occurred across all fields of medicine.

Dr. Lifton will explore how new methods—based on pinpointing the location of disease genes on chromosomes, followed by molecular cloning—now permit the identification of disease genes. The steps involved in this main approach to studying human genes, called positional cloning, include 1) a study of families to determine which relatives have an inherited disease, 2) a comparison of the inheritance of the disease with the inheritance of molecular markers on the human chromosomes to determine the location of underlying disease genes, and 3) the use of a gene’s location on the chromosome to identify the disease genes themselves. Dr. Lifton will explain how understanding genetic influences on specific human diseases can suggest new tests to identify individuals with these inherited susceptibilities before disease has developed and can also lead to new approaches to treatment.

Key Concepts

• Deoxyribonucleic acid, or DNA, consists chemically of four types of building blocks, or bases, that make up the genetic material of all organisms from bacteria to humans.
• Differences in the sequence of these building blocks account for small differences between individuals and larger differences between species.
• The human genome contains 3 billion base pairs of DNA and approximately 100,000 genes, located on chromosomes. The human genome project aims to determine the entire 3 billion base pair sequence.
• Genes come in different forms called alleles. Differing alleles arise by mutation. Some mutations are advantageous, but most are not and can sometimes lead to disease or a propensity for disease.
• Positional cloning involves the identification of disease-causing genes by determining the exact position of these genes on chromosomes. This approach does not require prior knowledge about the function of the disease gene.
• Identification of disease genes leads to an understanding of the biological causes of disease. Either the gene or its protein product can serve as the basis of a diagnostic test or a potential target for therapy.

Themes and Concepts Related to Advanced Placement Biology

An outline to help teachers incorporate relevant portions of this lecture into the Advanced Placement (AP) Biology curriculum is presented below. This outline is based, first, on the Topic Outline from the Educational Testing Service (ETS) that organizes biology into subject areas. Second, information for each of the ETS-selected subject areas has been organized by the kinds of headings used in ETS-recommended textbooks on biology.
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Lecture 2—Telltale Genes: Charting Human Disease—is concerned with human genetics, molecular biology, and the human genome project. The use of human pedigrees to trace the inheritance of disease in families as a means of mapping and cloning genes by position is emphasized.

I. DNA structure and function
   A. Where cells store hereditary information
   B. Chromosome components that contain the hereditary information
   C. Chemical nature of nucleic acids
   D. Three-dimensional structure of DNA
   E. How DNA replicates
   F. Genes: the units of hereditary information

II. Patterns of inheritance
   A. Chromosomes: the vehicles of Mendelian inheritance
   B. The science of genetics

Resources for Teachers and Students

These resources are listed roughly in order of relevance to the lectures.

Selected Websites

Program in Genetics and Development: Richard P. Lifton. This website, associated with the Yale University School of Medicine, describes Dr. Lifton’s current research and contains links to several recent representative publications.

   Difficulty Level: 2–3          Content Level: 5
   info.med.yale.edu/bbs/gendev/faculty/lifton.html

Positional Cloning. This site provides an overview of the experimental methods used for conducting positional cloning studies and uses the identification of the Huntington’s disease gene as an example.

   Difficulty Level: 3–4          Content Level: 5

The Natural History of Genes. This site provides science education tools for teachers, activities, experiments, and ideas for preparing low-cost equipment.

   Difficulty Level: 2–3          Content Level: 3–4
   raven.umnh.utah.edu

Genetics Information. This site offers extensive information and answers to questions concerning the human genome project.

   Difficulty Level: 2–3          Content Level: 3–4
   www.ornl.gov/TechResources/Human_Genome/resources/info.html

Making Maps. This site offers a look at how genetic linkage maps are prepared with the help of different chromosomal markers.

   Difficulty Level: 3–4          Content Level: 5
A Feast for the Future (A Transgenic Feast for Your Students). Access Excellence is a teacher-oriented website that provides an “activities exchange” including this one on transgenics for students in grade levels 9–12.

Difficulty Level: 2–3  
Content Level: 3–4


Transgenics. Offers a discussion of plant, animal, and microorganism transgenics, an overview of techniques used, and numerous links to related sites.

Difficulty Level: 2–3  
Content Level: 3–4

osms.otago.ac.nz/bur_tran.htm

Selected Publications

Scientific


Difficulty Level: 2–3  
Content Level: 3–4


Difficulty Level: 2–3  
Content Level: 4–5


Difficulty Level: 2–3  
Content Level: 3–4


Difficulty Level: 2–3  
Content Level: 4


Difficulty Level: 2–3  
Content Level: 3–4


Difficulty Level: 2–3  
Content Level: 2–4


Difficulty Level: 2–3  
Content Level: 3–4

Popular


Difficulty Level: 2–3  
Content Level: 3–4


Difficulty Level: 1–2  
Content Level: 4


Difficulty Level: 1–2  
Content Level: 4


Difficulty Level: 2  
Content Level: 3


Difficulty Level: 1–2  
Content Level: 3

Heart disease is the leading cause of death in the United States and, while it typically occurs after middle age, even seemingly fit and healthy young people can die suddenly from unrecognized heart disease. As Dr. Seidman will point out in the third lecture of the series, considerable media and medical attention has been focused on athletes who suffer cardiovascular collapse while participating in sports. These dramatic events are usually caused by hypertrophic cardiomyopathy, a disorder characterized by thickening (hypertrophy) of the ventricular muscle, sometimes leading to fatal irregular heart rhythms (arrhythmias).

Dr. Seidman specializes in genetic studies of cardiomyopathies, a disorder known to run in families. She and other researchers have successfully conducted genetic studies to identify the molecular basis of the disorder. A mutation in one of several genes that encode sarcomere proteins (the contractile apparatus of muscle cells) can cause hypertrophic cardiomyopathy. Distinct mutations are associated with different outcomes—only some gene defects predispose affected individuals to sudden death, while others predispose their bearers to more subtle forms of disease.

Dr. Seidman has augmented her studies on human families with research on genetically engineered mice to better understand what influence factors such as exercise may have on cardiomyopathies. Ultimately, these studies can illuminate differences between the sexes in susceptibility to heart disease and guide physicians and scientists in recommending improved treatments, including diet and lifestyle changes.

**Key Concepts**

- Abnormal, or mutated, genes, as well as infection, toxins, and poor dietary choices, can result in damage to the heart. However, there are mutations that have the opposite effect and appear to protect the heart from disease.
- Hereditary heart disease may have an underlying abnormality involving several genes (polygenic) or a single gene (monogenic).
- Hypertrophied hearts that are characteristic of hypertrophic cardiomyopathy contain larger rather than more cells.
- Mutations affecting heart muscle contractile proteins cause hypertrophic disease. The multiplicity of genes and mutations involved results in the variety of signs and symptoms of disease.
- The expression of genetic defects in an individual is typically influenced by other genes, lifestyle, and environment.
- Mice that have been genetically engineered with heart disease mutations provide models for exploring how gender, exercise, and environment shape heart disease.

**Themes and Concepts Related to Advanced Placement Biology**

An outline to help teachers incorporate relevant portions of this lecture into the Advanced Placement (AP) Biology curriculum is presented below. This outline is based, first, on the Topic Outline from the Educational Testing Service (ETS) that organizes biology into subject areas. Second, information for each of the ETS-selected subject areas has been organized by the kinds of headings used in ETS-recommended textbooks on biology. The headings are intended to reflect only the relevant themes and information introduced in the lecture for each subject area and are not intended to cover the specific subject area comprehensively. For more information about AP Biology, visit [www.collegeboard.org](http://www.collegeboard.org).
Lecture 3—Heartbreak: Of Mutations and Maladies—explores how the inheritance of altered (mutated) genes that affect heart muscle can result in a variety of heart disorders.

I. Physiological adaptations of the body
   A. Muscle structure
      1. Cardiac
      2. Smooth
      3. Skeletal
   B. Muscle function
      1. The structure of myofilaments
      2. How myofilaments contract
      3. How cardiac muscle contracts
      4. How nerves signal muscles to contract

II. Mutation
   A. Gene Mutation
   B. The biological significance of mutation

Resources for Teachers and Students
These resources are listed roughly in order of relevance to the lectures.

Selected Websites
The Hypertrophic Cardiomyopathy Association. A Web page that provides patient information, physician education, and support services. The site includes graphics on the disease, information on diagnosis, current research, and complications of the condition.
   Difficulty Level: 3-4       Content Level: 4-5
   www.HCMA-heart.com

NHLBI, Cardiomyopathy. Facts about cardiomyopathy are presented by the National Heart, Lung, and Blood Institute of the National Institutes of Health in Bethesda, Maryland. The site also includes a glossary of terms.
   Difficulty Level: 2–3       Content Level: 4–5
   www.nhlbi.nih.gov/nhlbi/cardio/other/gp/cardiomy.htm

COHIS: Cardiovascular Diseases: Heart Diseases. Created by the Community Outreach Health Information System, this site provides answers to questions on the diagnosis and treatment of heart diseases, blood vessel diseases, and related illnesses.
   Difficulty Level: 2–3       Content Level: 4–5
   gopher1.bu.edu/COHIS/cardvasc/heart/heart.htm

The National Heart, Lung, and Blood Institute Information Center. Facts about the heart, high blood pressure, and the lungs are available as publications from this Institute, part of the National Institutes of Health in Bethesda, Maryland. Special publications on several of these topics as they pertain to women and minorities are also available separately.
   Difficulty Level: 2–3       Content Level: 4–5
   www.nhlbi.nih.gov/nhlbi/edumat/pub_gen.htm
Selected Publications

Scientific


Difficulty Level: 5
Content Level: 5


Difficulty Level: 4–5
Content Level: 5


Difficulty Level: 2–3
Content Level: 5


Difficulty Level: 2–3
Content Level: 5


Difficulty Level: 5
Content Level: 5


Difficulty Level: 3–4
Content Level: 5


Difficulty Level: 5
Content Level: 5


Difficulty Level: 3–4
Content Level: 5

Popular


Difficulty Level: 1–2
Content Level: 4


Difficulty Level: 1–2
Content Level: 3


Difficulty Level: 1–2
Content Level: 3
Each day, the human kidneys filter nearly 50 gallons of blood plasma and 3 pounds of salt. Blood courses through the kidney and other internal organs, driven by the heart pumping blood through arteries. The blood inside these arteries exerts pressure on the artery walls. In this final lecture of the series, Dr. Lifton will explain how high blood pressure, or hypertension, damages blood vessels, contributing to heart attacks, strokes, and kidney failure. The control of blood pressure seems deceptively simple, since it is determined by the amount of blood pumped by the heart and the resistance to blood flow provided by the arteries. However, since many factors regulate each of these processes, determining the causes of hypertension has been difficult.

Evidence that hypertension may be inherited has led investigators to study blood pressure variations using genetic approaches. Cases have been discovered where mutations in a single gene can account for large differences in blood pressure between patients with and people without the mutation. Dr. Lifton will discuss how his laboratory has identified mutations for three genes that cause high blood pressure and eight genes that cause low blood pressure. Interestingly, these mutations all affect how the kidney regulates salt. The kidneys remove metabolic wastes and also regulate blood volume by regulating salt balance. Mutations that increase the amount of salt and water retained by the kidney increase intravascular volume and cardiac output, thereby increasing blood pressure; the converse is also true.

Dr. Lifton will explain how these findings confirm the key role that the control of renal salt plays in the regulation of blood pressure in humans. He will discuss opportunities for new tests for hypertension and potential targets for new or improved medications to treat high blood pressure.

Key Concepts
• New genetic evidence shows that variation in blood pressure is attributable to the combined effects of inherited and environmental factors.
• Although the primary causes of hypertension remain unknown in the vast majority of subjects, mutations in certain genes appear to be involved in specific types of hypertension.
• Molecular genetic approaches have led to the identification of single genes on specific chromosomes that, when mutated, can lead to elevated blood pressure.
• So far, all genes that have been found to affect blood pressure alter the activities of ion channels used by the kidney to regulate salt.
• Mutations have already been identified in 11 genes that can either raise or lower blood pressure.

Themes and Concepts Related to Advanced Placement Biology
An outline to help teachers incorporate relevant portions of this lecture into the Advanced Placement (AP) Biology curriculum is presented below. This outline is based, first, on the Topic Outline from the Educational Testing Service (ETS) that organizes biology into subject areas. Second, information for each of the ETS-selected subject areas has been organized by the kinds of headings used in ETS-recommended textbooks on biology. The headings are intended to reflect only the relevant themes and information introduced in the lecture for each subject area and are not intended to cover the specific subject area comprehensively. For more information about AP Biology, visit www.collegeboard.org.
Lecture 4—The Kidney’s Tale: Of Salt and Hypertension—examines the structure and function of the kidney and its role in helping maintain stability in the body’s internal environment. The inheritance of genetic mutations that affect blood pressure is also discussed.

I. Physiological adaptations of the body
   A. Kidneys and water balance
      1. Osmoregulation
      2. Organization of the vertebrate kidney
      3. How the mammalian kidney works
      4. Excretion of nitrogenous wastes
      5. The kidney as a regulatory organ
   B. Circulation
      1. Blood
      2. Regulation of blood pressure

II. Mutation
   A. Gene mutation
   B. Biological significance of mutation

Resources for Teachers and Students
These resources are listed roughly in order of relevance to the lectures.

Selected Websites

Blood Pressure, High. The website presents an overview of high blood pressure, including common causes ranging from medications to syndromes and diseases.
   Difficulty Level: 1–2
   Content Level: 3
   www.healthanswers.com/database/ami/converted/003082.html

Glomerulus. This site provides information and graphics on the structure and function of the specialized components that make up the kidney.
   Difficulty Level: 2–3
   Content Level: 4–5
   hms.medweb.harvard.edu/ihp/IHP_Renal/Ren_Tex/glom.htm

Hypertension Network. This site offers information on new research findings and recommendations for people with hypertension.
   Difficulty Level: 2–3
   Content Level: 4–5
   www.bloodpressure.com/index.html

National Kidney Foundation Web Site—Kidney Facts. This site provides information on kidney structure and function, symptoms and causes of kidney failure, and treatments for kidney failure.
   Difficulty Level: 2–3
   Content Level: 4–5
   www.nkf.org.sg/newnkf/facts.htm

National Institute of Diabetes and Digestive and Kidney Diseases. NIDDK, part of the National Institutes of Health, offers a variety of publications, links to other resource organizations, literature searches, newsletters, and other items through the NIDDK website and the National Kidney and Urologic Diseases Information Clearinghouse.
   Difficulty Level: 2–3
   Content Level: 4–5
   www.niddk.nih.gov/health/kidney/nkudic.htm
**Tutorials on Urinalysis and Renal Cystic Disease.** Two tutorials concisely discuss in easy-to-follow language how urine is examined and evaluated and how renal cystic diseases are diagnosed. Each tutorial is amply illustrated.

Difficulty Level: 2–3  
Content Level: 4–5  
www.medlib.med.utah.edu/WebPath/TUTORIAL/TUTORIAL.html#3

**Selected Publications**

**Scientific**

Difficulty Level: 4  
Content Level: 5

Difficulty Level: 3–4  
Content Level: 5

Difficulty Level: 4–5  
Content Level: 5

Difficulty Level: 3–4  
Content Level: 5

Difficulty Level: 4–5  
Content Level: 5

Difficulty Level: 4–5  
Content Level: 5

Difficulty Level: 4–5  
Content Level: 5

Difficulty Level: 5  
Content Level: 4

**Popular**

Difficulty Level: 1–2  
Content Level: 3

Difficulty Level: 1–2  
Content Level: 3
ADDITIONAL RESOURCES

SELECTED WEBSITES TO VISIT

Exploring the Heart

CADl: Heart Sounds. Sounds made by the heart, including abnormal sounds that arise from mitral valve stenosis, are explained and illustrated.

Difficulty Level: 3–4  
Content Level: 4–5

cs-www.uchicago.edu/~fensterm/CADI/heart-sounds.html

The Heart and the Circulatory System. Part of the Activities Exchange for Access Excellence, this website provides useful information on the anatomy of the heart, heart activities for the classroom, other resources for subject matter on the heart, and a glossary of terms.

Difficulty Level: 2  
Content Level: 4–5

www.gene.com/ae/AE/AEC/CC/heart_background.html

The Heart Preview Gallery. This site provides activities such as listening to heartbeats, images and movies about the heart, and teacher resource materials about the heart.

Difficulty Level: 2  
Content Level: 3–5

www.fi.edu/biosci/preview/heartpreview.html

Heart Care. This site provides information on prevention and treatment of heart disease with links to such topics as invasive and noninvasive diagnostics, medical treatment, surgery, and risk reduction.

Difficulty Level: 2–3  
Content Level: 3–5

www.advocatehealth.com/binder/binderx2.html

HeartInfo–Heart Information Network. Featured at this heart information site are current news, a very extensive glossary of terms, a search engine, a Question & Answer Library, HeartInfo Resources, and other features.

Difficulty Level: 2–3  
Content Level: 3–5

www.heartinfo.org

MedWeb: Cardiology. A large number of links ranging from academic departments to sites related to telemedicine and transplantation provide information on cardiology.

Difficulty Level: 3–5  
Content Level: 3–5

www.gen.emory.edu/medweb/medweb.cardiology.html

North American Society of Pacing and Electrophysiology. This site focuses on irregular heartbeats through press releases, information on scientific research, and other features.

Difficulty Level: 3–5  
Content Level: 3–5

www.naspe.org
Exploring the Kidney

The Basics of the Kidney. Featured on this site is information on the parts and workings of the human kidney and on polycystic kidney disease.

Difficulty Level: 2–3 Content Level: 4–5
www.clark.net/pub/nhp/med/kidney/basics.html

KDF: About Kidney Disease and Dialysis. Answers to various questions concerning kidney dialysis, together with a short self-test assessment, are provided in text and drawings.

Difficulty Level: 2–3 Content Level: 2–3
www.kdf.org.sg/know-right.html

Kidney: Outline. Outlines kidney structure and function. Includes gross and microscopic images.

Difficulty Level: 3–4 Content Level: 4–5
www.mc.vanderbilt.edu/~alemanma/kidney-outline.html

How the Kidney Works. Features demonstrations detailing how the kidney works, its function, and specific diseases involving kidney function. Take a tour through the kidney and its components using software that you can download right from the site.

Difficulty Level: 3–4 Content Level: 3–4
nephron.com/fkgl.html

The Kidney Quiz. This site allows visitors to take an online quiz on kidney knowledge, answer eight questions, and check out their scores.

Difficulty Level: 2 Content Level: 3
www.thriveonline.com/health/dyngames/gen/health.kidney.html

Kidney, Gross Specimen. This site contains gross and microscopic images of kidneys and features questions and answers concerning specimen pathology.

Difficulty Level: 2 Content Level: 3
icarus.med.utoronto.ca/digidoc/diginp4a.html

Exploring Hypertension and Cardiovascular Disease

Food and Drug Administration (FDA) Home Page. In addition to acting as a search engine, this site offers access to a range of FDA papers, press releases, and reports on drugs, medical devices, public policy, and other issues of importance to the investigation of heart disease.

Difficulty Level: 3–5 Content Level: 4–5
www.fda.gov

Healthfinder Guided Tour—Heart Disease and Stroke. Topics range from general questions and tests to warning signs of disease and ways to prevent and treat heart disease and stroke.

Difficulty Level: 2–3 Content Level: 3–5
www.healthfinder.gov/tours/heart.htm
Health Index. Articles on health that have appeared in USA Today are featured, and a search engine is provided. Blood pressure, the latest research on heart disease, and genetics are among the topics covered.

   Difficulty Level: 2–3    Content Level: 3–4
   www.usatoday.com/life/health/lh99.htm

Ivanhoe’s Medical Breakthroughs. This site presents information on medical breakthroughs from Ivanhoe Broadcast News Service, a television news service. A search engine is also provided for key words or categories of related reports.

   Difficulty level: 2–3    Content Level: 3–5
   www.ivanhoe.com/docs/backissues.html

American Society of Hypertension. This website offers news and articles, editorials, and reports on hypertension as well as links to other sites.

   Difficulty Level: 3–5    Content Level: 3–5
   www.ash-us.org/body1.html

Medical Matrix. This site provides online forums, pathology images, learning modules, major resources, a search engine, and other features. Information on the heart, as well as on hypertension and the kidney, can also be obtained.

   Difficulty Level: 3–5    Content Level: 3–5
   www.medmatrix.org/Index.asp

How to Keep Your Blood Pressure under Control. Provides information on the basics of blood pressure and the causes and symptoms of high blood pressure, including the effects of high salt, and a checklist of things people can do to help keep blood pressure under control.

   Difficulty Level: 2–3    Content Level: 3
   www.coolware.com/health/medical_reporter/hypertension.html

HealthBeat—Hypertension. Provides general information about blood pressure, including how it is measured, appropriate levels, and causes of prevention of hypertension.

   Difficulty Level: 2–3    Content Level: 3
   www.idph.state.il.us/public/hb/hbhype.htm

Doctor’s Guide. This site provides to physicians and patients medical news, Internet medical resources, details of new drugs, and other information related to a variety of cardiovascular topics.

   Difficulty Level: 2–4    Content Level: 3–4
   www.pslgroup.com/dg/3cd16.htm

Cardiovascular Institute of the South. This site offers a range of reports on prevention, diagnosis, and surgical and nonsurgical treatments of cardiovascular problems, including articles on women and heart disease.

   Difficulty Level: 2–3    Content Level: 3–4
   www.cardio.com

Mayo Clinic Health Oasis: Daily News on Disease, Treatment, Drugs, Diet. This website provides numerous health-related articles on hypertension as well as cardiology. Self-test quizzes, “ask a physician,” reference articles, and links to related sites are some of the site’s features.

   Difficulty Level: 2–3    Content Level: 3–5
   www.mayohealth.org/mayo/common/htm/index.htm
Exploring Human Genetics

Primer on Molecular Genetics (Department of Energy). This website provides text and figures on the preparation of physical maps of the human genome, sequencing technologies, model organism research, and data collection and interpretation.

Difficulty Level: 2–3  
Content Level: 3–5  
www.bis.med.jhmi.edu/Dan/DOE/intro.html

Disorders Studied by the Center for Human Genetics. In addition to early-onset cardiovascular disease and kidney disease, the center is also studying various inherited genetic disorders ranging from age-related macular degeneration to tuberous sclerosis.

Difficulty Level: 2–4  
Content Level: 3–5  
www2.mc.duke.edu/depts/medicine/medgen/dx.html

Gene Almanac. This website has been developed and maintained by the Cold Spring Harbor Laboratory, an HHMI grantee, and includes online instructional resources; publications, texts, laboratory kits, and other products; and information about student and teacher workshops, field trips, and school membership programs.

Difficulty Level: 2–4  
Content Level: 4–5  
vector.cshl.org

Understanding Gene Testing. This site provides easy-to-understand answers to frequently asked questions about gene testing in patients. A search engine to facilitate use of the site and a glossary of terms are also provided.

Difficulty Level: 2–3  
Content Level: 3–4  

Gene Letter. Offers articles on a range of scientific, medical, and other issues related to genetic testing and includes a search engine.

Difficulty Level: 2–3  
Content Level: 2–4  
www.geneletter.org/mainmenu.htm

ONLINE PUBLICATIONS

Selected Science and Medical Publications

American Heart Association. This site provides access to five online journals: Atherosclerosis, Thrombosis, and Vascular Biology; Circulation; Circulation Research; Stroke; and Hypertension.

Difficulty Level: 5  
Content Level: 4–5  
www.edoc.com/amhrt

Annals of Internal Medicine. This site maintains a search function that allows location of relevant articles through the use of key words.

Difficulty Level: 5  
Content Level: 4–5  
www.acponline.org/journals/annals/annaltoc.htm

CHEST—The Cardiopulmonary and Critical Care Journal. This Web page provides access to articles on the heart and hypertension through the site’s search engine.

Difficulty Level: 4–5  
Content Level: 4–5  
www.chestnet.org
Heart Web. This online, peer-reviewed cardiology journal includes original manuscripts, multimedia presentations, news releases, and a search engine.

Difficulty Level: 3–5  
Content Level: 4–5  
www.heartweb.org

Journal of Clinical Investigation. Categories for this site include molecular medicine/genetic disorders and atherosclerosis/thrombosis/vascular biology, among others.

Difficulty Level: 4–5  
Content Level: 4–5  
www.jci.org

Journal of Experimental Medicine. This website provides a search engine as well as links to related publications through PubMed.

Difficulty Level: 4–5  
Content Level: 4–5  
www.jem.org

Journal of the American College of Cardiology. Full-text articles as well as abstracts are accessible through the site's search engine.

Difficulty Level: 4–5  
Content Level: 4–5  
www-east.elsevier.com/jac

Journal of the American Medical Association. In addition to current and past articles in the Journal of the American Medical Association, the Association's Archives journals are accessible.

Difficulty Level: 4–5  
Content Level: 4–5  
www.ama-assn.org/sci-pubs/pubsrch.htm

The Lancet. This website provides limited access to The Lancet once a registration page has been filled out.

Difficulty Level: 3–4  
Content Level: 4–5  
www.thelancet.com

Nature. This site provides information on science articles and science news appearing in Nature, an international weekly journal of science. The home page contains an update on science topics, as well as links to coverage of genetics, medicine, structural biology, and biotechnology.

Difficulty Level: 3–5  
Content Level: 3–5  
www.nature.com

Science. Offered on this website for a paid subscription is a full text of the journal Science as well as news and information articles on research advances, a search engine, and education programs.

Difficulty Level: 3–5  
Content Level: 2–4  
www.aas.org

The New England Journal of Medicine. A search engine, articles appearing in this week's issue, and an “images in clinical medicine” quiz are available on this site.

Difficulty Level: 4–5  
Content Level: 4–5  
www.nejm/org
**GENERAL INTEREST PUBLICATIONS**

**Discover Magazine.** Viewers can access current articles, a soon-to-be-completed collection of scientific images, links to related sites, and school programs linked to the magazine. A search engine is also available.

  Difficulty Level: 2–3  
  Content Level: 3–4  
  www.discover.com

**NOVA Online.** A search engine enables the viewer to use key words to access transcripts of NOVA television shows and related articles.

  Difficulty Level: 2–3  
  Content Level: 3–5  
  www.pbs.org/wgbh/nova

**ScienceNews On-Line.** This site provides selected full-text articles, other online features, and a search engine for Science News.

  Difficulty Level: 2–3  
  Content Level: 3–4  
  www.sciencenews.org

**Scientific American.** This page contains links to quick article summaries, selected articles, news and analysis, interviews, an “ask the experts” section, and other features. The search engine capability is limited.

  Difficulty Level: 2–3  
  Content Level: 3–5  
  www.sciam.com

**The New York Times.** Free registration allows access to articles from the current day’s edition as well as a search engine.

  Difficulty Level: 1–2  
  Content Level: 3  
  www.nytimes.com
HOLIDAY LECTURES ON SCIENCE ON THE WEB

The holiday lectures website is an integral part of the Institute’s efforts to engage teachers and students in “mindson” learning that enriches the lecture content. The website is continually updated with new curricular materials. Please continue to check our site, www.holidaylectures.org, for new information.

Webcast
In addition to their availability via satellite broadcast and cable rebroadcast, the 1998 Holiday Lectures on Science are simultaneously broadcast live over the Web. Using a Web browser, students, teachers, and other visitors around the world can view the lectures with full-motion video and audio. The 1998 lectures are also available “on demand” from the website any time following the broadcast. Past lectures are also on the Web.

Holiday Lectures Chat
An interactive Holiday Lectures Chat is another feature of the 1998 holiday lectures. Students will be able to type questions and see Drs. Lifton and Seidman on video on the computer screen as they respond to student inquiries. The Holiday Lectures Chat will take place from 1:30 p.m. to 2:30 p.m., EST, on December 7 and 8. Please continue to check the website for more information.

Online Exhibit
The on-site exhibit, described on page 36 of this guide, is available in a “virtual” format. QuickTime Virtual Reality technology is used to present objects and information from the exhibit. The technology, which uses embedded video, allows Web visitors to pan the exhibit hall and browse artifacts and explanatory text.

Interactive Web Laboratories and Demonstrations
“Virtual Lab ‘98: Genetics of Heart Disease.” This virtual laboratory will enable students to learn the principles of cardiac diagnostic tools and the rationale for genetic analysis.

Animated Demonstrations: Modules have been developed to illustrate facts about the heart and kidney. They include:
- Heart Size Simulator, which explores the relationship between animal size and heart rate
- Evolution of Vertebrate Circulation, a survey of how the circulatory system and the heart structure differ among species
- Effects of Altitude, which explores what happens to the heart rate at different altitudes and how the partial pressure of oxygen affects the heart rate
- Effects of Caffeine, Tobacco, and Alcohol on the Heart Rate

The Interactive Web is a multimedia storehouse that also contains previous lectures, dating back to 1995, as well as past laboratories, demonstrations, and exhibits.

Please visit the website often for frequent updates and additions.
Ask a Scientist

This key feature of the Holiday Lectures on Science series enables Web visitors to e-mail questions on the current lecture topic, and on a range of other biological topics, to teams of scientists associated with Institute-funded programs. These scientists are particularly interested in communicating scientific concepts to young adults. Every legitimate science question receives at least one personal response. Questions and answers of general interest are also posted on the site. The Ask a Scientist e-mail address is grantask@hhmi.org.

Related Links

Teachers and students can access a list of websites that are related to the lecture topics. A rating system allows Web visitors to determine which sites are most relevant.

Previous Lectures

Those who missed the 1997 lectures—“Senses and Sensitivity: Neuronal Alliances for Sight and Sound”—can order a free videotaped copy online. Web visitors can also view the complete 1997 lecture series “on demand” and can take advantage of the many interactive features of the site. A virtual neurophysiology laboratory allows visitors to explore the sensory system of the leech, while the virtual exhibit permits visitors to walk through the exhibit hall and explore the electric field of electric fish. These lectures are indexed by topic so Web visitors can go directly to the portions of the lectures that most interest them.
This year’s Holiday Lectures on Science features a museum-quality exhibit that complements the lecture series and provides an interactive experience for students. After the lectures are concluded, this on-site exhibit will continue to exist in a “virtual” format on the website, providing visitors with an experience that is almost as rich and compelling as being on site. A documentary of the exhibit will be broadcast via satellite and the Web during the breaks between the lectures.

The exhibit will explore the function of the heart and kidney, as well as heart disease and hypertension. Historical and modern artifacts and images will trace advances in understanding and treating heart disease and hypertension—from the time when autopsies were the only available source of information to the present and future, as molecular medicine offers new insights and suggests previously unforeseen possibilities for treatment and prevention.

Students will see real specimens of diseased and normal hearts, as well as some early microscopic images that revealed information about the heart and kidney. They will see how the development of new diagnostic tools made possible an understanding of circulatory function that had never before been revealed through anatomical studies. Advances in measuring the heartbeat and blood pressure will be traced through artifacts from the National Museum of Health and Medicine, the Stetten Museum of the National Institutes of Health, the Smithsonian Institution, and other contributing institutions.

Visitors to the exhibit will see and hear what can be learned by using a stethoscope and a sphygmomanometer (blood pressure cuff); find out how heart surgery developed and what it taught physicians; see artificial hearts and valves; and learn about the contributions of epidemiological studies and molecular research to the understanding and treatment of cardiovascular illness. They will be able to examine living zebrafish under a microscope to see normal fish and mutant fish, with abnormal hearts and kidneys.

The exhibit will also include multimedia stations featuring a virtual lab and other software, and a biography kiosk that features videos and photographs of each lecturer.

This is the third year that the Holiday Lectures on Science has included an exhibit, developed with the efforts and guidance of the HHMI Holiday Lectures Museum Resource Group, which is composed of curators from Washington, D.C., area museums.
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ACKNOWLEDGMENTS

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Adrienne Noe, Ph.D., director, National Museum of Health and Medicine, Washington, D.C.
Anne Whitaker, librarian, History of Medicine Division, National Library of Medicine, Bethesda, Maryland

Special thanks for their assistance with the exhibit is extended to Lenore Barbian, Ph.D., Walter Reed Army Medical Center; Alan Hawk, Walter Reed Army Medical Center; and Carol Garfinkel, exhibit developer.

With the guidance of Satoshi Amagai and Eric Keller, the following high school interns provided technical and graphics assistance in developing the Holiday Lectures on Science website:
Sunil Bhaskarla, Thomas Edison High School, Wheaton, Maryland
Mike Chelen, Sidwell Friends School, Washington, D.C.
Kyle Jaster, Sidwell Friends School, Washington, D.C.
Hassan Raza, Thomas Edison High School, Wheaton, Maryland
Alex Yesnik, Sidwell Friends School, Washington, D.C.

We also acknowledge the contributions of Cynthia Allen, Satoshi Amagai, Joan Guberman, Karen Hopkin, Tracy Kidd, Frank Portugal, and Judith Saks in preparing this publication to accompany the Holiday Lectures on Science.

This guide was prepared under the direction of Dennis WC. Liu, Ph.D., program officer, Public Science Education Program, Howard Hughes Medical Institute.

Photo Credits: Bill Geiger, pages 1, 4, and 34; Stanley Rowin, page 8; Harold Shapiro, page 10.

Design: AXIS Communications, Washington, D.C.

Printer: Beach Brothers Printing, Rockville, Maryland

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secondary schools, museums, zoos, botanical gardens, aquaria, colleges and universities, medical schools, and research institutes. The annual Holiday Lectures on Science, which feature presentations by distinguished biomedical investigators, are an important HHMI initiative for young people.

To date, the Undergraduate Biological Sciences Education Program has awarded $335 million to strengthen life sciences education at 220 public and private colleges and universities. These awards are intended to enrich educational opportunities for science majors and enhance the scientific competency of students who major in nonscience subjects. Funds are used to support student research, attract and train science faculty, and develop innovative approaches to undergraduate science education. Funds also support outreach to elementary and secondary schools and community colleges.

Through its Precollege Science Education Program, HHMI has awarded $29 million to 74 science museums, aquaria, botanical gardens, and zoos, and 42 biomedical research institutions to support innovative educational programs and to interest youngsters in science. Nearly 600,000 students, 40,000 teachers, and 77,000 adult family members have participated in HHMI-funded activities.

Through its Washington, D.C., Metropolitan Area Initiatives, the Institute has awarded more than $6 million to provide kindergarten, elementary, and high school students with "hands-on" experience in the science classroom and laboratory and to support teacher training activities.

Grants for Graduate Science Education and Research. These grants are intended to attract and train graduate and postgraduate students for careers in biomedical research, enhance the research capabilities of biomedical research organizations, and support promising foreign scientists.

The Graduate Science Education Program supports graduate students, medical students, and physician-scientists who show strong promise of becoming tomorrow's leading biomedical investigators as they move along the continuum from graduate education to junior faculty positions. Support is awarded through three fellowship programs: predoctoral fellowships in biological sciences, research training fellowships for medical students, and postdoctoral research fellowships for physicians. Since 1988 HHMI has provided $138 million in graduate fellowship support to almost 1,800 students and physician-scientists in the early stages of their careers.

Through its Research Resources Program, HHMI provides support to medical schools and to research organizations that serve the biomedical community as unique resource laboratories and teaching facilities. In 1995 HHMI awarded $80 million to 30 U.S. medical schools to help sustain their commitment to biomedical research, through strengthened research infrastructure and career development of junior faculty in the basic and clinical sciences. A new $90 million competition is planned for 1999.

Completing these initiatives is the Institute's International Program, which supports outstanding foreign scientists who are conducting fundamental biomedical research outside the United States. Since 1991 HHMI has awarded more than $53 million in five-year grants to 177 International Research Scholars.

HHMI also regularly gathers and analyzes data to evaluate its various grant initiatives and identify national trends relevant to science education and research. In addition, HHMI convenes meetings of educators, scientists, and policy experts to discuss these trends and issues relevant to public and private sector programs.

Complete information on all Grants and Special Programs initiatives is available on the website at www.bioeducation.org.