DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

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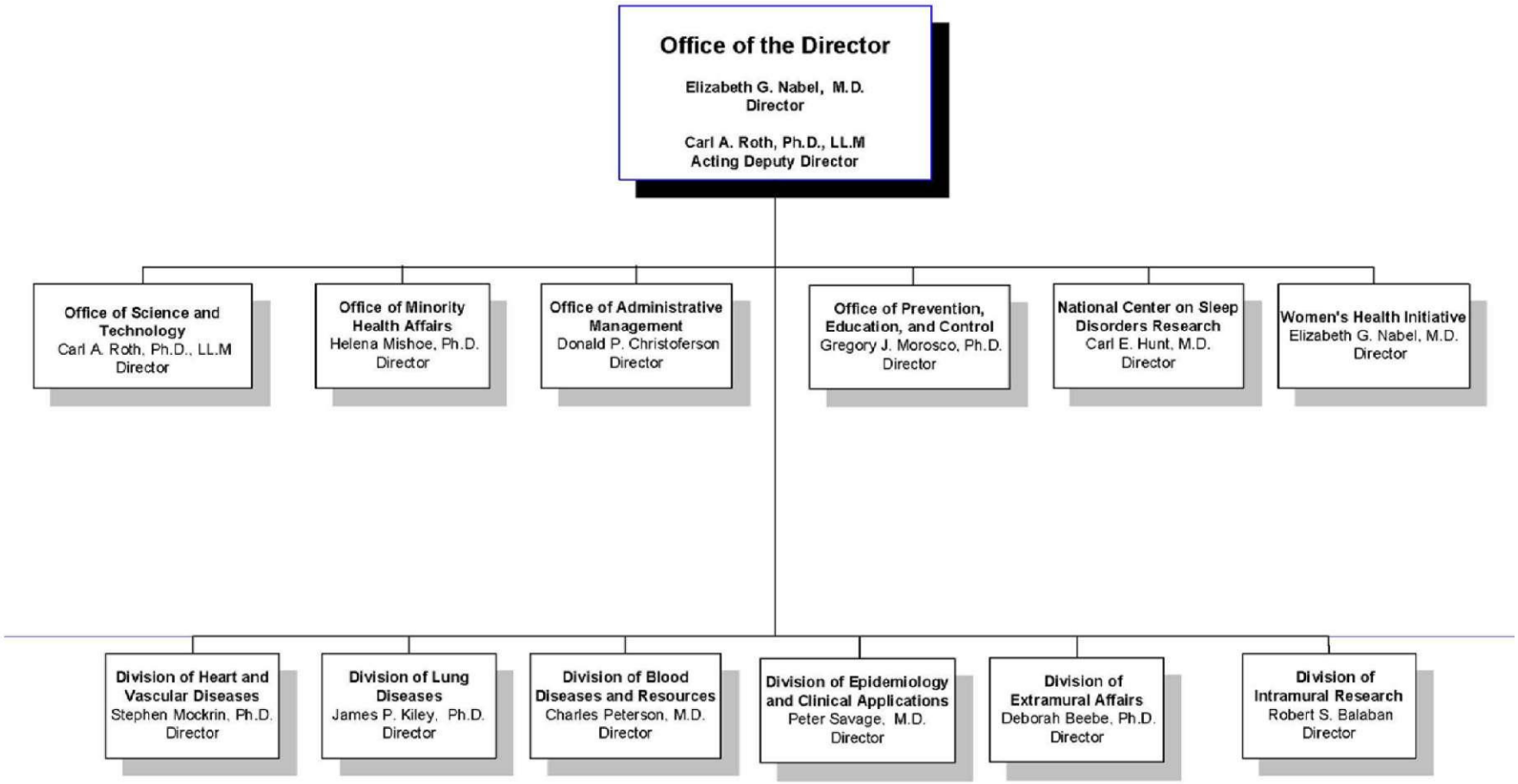


NHLBI-2

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

For carrying out section 301 and title IV of the Public Health Service Act with respect to cardiovascular, lung, and blood diseases and blood products, [$2,951,270,000] *$2,901,012,000.*

[Departments of Labor, Health and Human Services, Education and Related Agencies Appropriations Act, 2006, as enacted by Public Law (109-149)]

National Institutes of Health
National Heart, Lung, and Blood Institute

Amounts Available for Obligation 1/

Source of Funding	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Appropriation	$2,965,453,000	$2,951,270,000	$2,901,012,000
Enacted Rescissions	(24,252,000)	(29,513,000)	0
Subtotal, Adjusted Appropriation	2,941,201,000	2,921,757,000	2,901,012,000
Real transfer under NIH Director's one-percent transfer authority for Roadmap	(18,594,000)	(26,109,000)	0
Comparative transfer from OD for NIH Roadmap	18,594,000	26,109,000	0
Subtotal, adjusted budget authority	2,941,201,000	2,921,757,000	2,901,012,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	2,941,201,000	2,921,757,000	2,901,012,000
Unobligated balance lapsing	(34,000)	0	0
Total obligations	2,941,167,000	2,921,757,000	2,901,012,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2005 - $8,763,000 FY 2006 -$20,000,000 FY 2007 - $20,000,000
Excludes $1,200,000 in FY 2006 and $1,200,000 in FY 2007 for royalties.

Justification

National Institute of

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended.

Budget Authority:

FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
796	$2,941,201,000	801	$2,921,757,000	805	$2,901,012,000	4	-$20,745,000

This document provides justification for the Fiscal Year 2007 activities of the National Heart, Lung, and Blood Institute (NHLBI), including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2007 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)." Detailed information on the NIH Roadmap for Medical Research may be found in the Overview section.

INTRODUCTION

The NHLBI provides leadership for a national program in diseases of the heart, blood vessels, lungs, and blood; sleep disorders; and blood resources. It plans and conducts—through work in its own laboratories and through grant- and contract-supported activities in extramural scientific institutions—an integrated and coordinated program of basic research, clinical investigations and trials, observational studies, and demonstration and education projects related to the causes, prevention, diagnosis, and treatment of the diseases under its purview and to the clinical use of blood and all aspects of the management of blood resources. Since FY 1993, the Institute has been the home of the National Center on Sleep Disorders Research and, since FY 1998, it has had responsibility for the NIH Women's Health Initiative. The NHLBI supports research training and career development of new and established investigators in fundamental sciences and clinical disciplines to enable them to conduct research relative to its mission. In addition, it conducts educational activities, including development and dissemination of materials for health professionals, patients, and the general public, with a strong emphasis on prevention.

The following material summarizes recent scientific progress, promising future opportunities, and other activities of interest.

SCIENCE ADVANCES

Heart and Vascular Diseases

New Kidney Function Test Helps Predict Cardiovascular Disease (CVD) Risk

A blood test used to detect kidney dysfunction also may help doctors identify elderly patients who are at elevated risk for CVD. Although small decreases in kidney function can double an individual's likelihood of developing CVD, the standard measure of kidney dysfunction—the creatinine clearance test—cannot reliably detect such small changes, particularly in elderly patients. Researchers from the Cardiovascular Health Study determined that another FDA-approved test of kidney dysfunction—this one measuring blood levels of a protein called cystatin C—was a much better predictor of CVD than the creatinine clearance test for elderly patients. At present, the cystatin C test is used infrequently in clinical practice. However, studies are under way to confirm the results and to investigate the clinical use of cystatin C as an improved prognostic tool for the evaluation and management of kidney disease and CVD.

Scientists Make Progress on Engineering Blood Vessels from Human Cells

Researchers recently overcame a major barrier to production of human blood vessels in the laboratory. Scientists have been interested for many years in engineering human blood vessels for use in coronary and vascular surgeries, but previous attempts to create blood vessels from isolated human blood vessel cells have been hampered by the cells' limited ability to multiply and survive in the laboratory. Under normal conditions, every time a cell divides, its telomeres —long sequences at the end of the chromosomes—erode until eventually they become so short that the cell can no longer divide. In recent experiments, scientists were able to increase the lifespan and replication potential of human blood vessel cells by engineering them to turn on the gene for a protein that maintains the length of the telomeres. Cells producing the protein were much more effective than untreated cells at forming blood-vessel like tubes, and the artificial vessels produced using the altered cells were more durable than those formed using untreated cells. Although more work is needed to develop functional veins and arteries, the results bring researchers closer to the goal of producing an alternative source of replacement blood vessels for patients with vascular disease.

Free-Breathing Magnetic Resonance Imagine (MRI)

A new method for performing cardiac MRI could prove very useful in patients who have trouble undergoing conventional MRI. Cardiac MRI can be used to assess myocardial damage after a heart attack, but patients must hold their breath during the scan—a maneuver that is difficult for many people with cardiorespiratory ailments. Intramural scientists at the NIH have developed a new technique that allows patients to undergo cardiac MRI while breathing freely. The method uses an innovative motion-correction computer algorithm to remove respiratory motion artifacts before averaging several motion-corrected images of the heart to create a single image. When the researchers compared the conventional breath-held imaging method with their free-breathing method, they found that the new approach produced images of comparable quality in the same amount of time. Moreover, when used to measure the size of an area of damaged heart muscle caused by a heart attack, the two methods gave similar results. The new technique shows promise for making cardiac MRI available to a wider range of patients.

Promising Medical Uses for Sodium Nitrite

Sodium nitrite, a compound that occurs naturally in the body, has proven useful as an antidote for cyanide poisoning, and recent studies suggest it may someday be used to prevent or reduce cardiac damage after a heart attack. Under certain conditions, sodium nitrite can be converted into the potent vasodilator nitric oxide, which theoretically could not only restore blood flow after a heart attack by relaxing blood vessels, but also protect heart tissue from the damage ("reperfusion injury") that often occurs when blood flow is restored. Researchers tested this theory by experimentally inducing heart attacks in mice and then injecting them with sodium nitrite. The investigators found that sodium nitrite prevented irreversible tissue damage. Although extensive clinical studies remain to be done, the newly demonstrated ability of sodium nitrite to protect against cell death holds promise for preserving cardiac function following a heart attack.

Women's Health Study Reports Findings on Low-Dose Aspirin and Vitamin E Supplements

Despite promising results of observational studies, new findings from a large trial indicate that low-dose aspirin and vitamin E supplements play a minor role, if any, in protecting women from CVD. The Women's Health Study—a 10-year randomized, double-blind, placebo-controlled study conducted among nearly 40,000 healthy women ages 45 and older—found that aspirin did not prevent first heart attacks or death from CVD. The stroke rate, however, was 17 percent lower in those taking aspirin, and in women ages 65 and older, aspirin reduced the overall risk of major CVD events by 26 percent. The study also showed that vitamin E supplementation had no effect on heart attacks, strokes, or total deaths and—with regard to another hypothesized benefit—did not reduce rates of breast, lung, colon, or other cancers. The NIH continues to recommend that women focus on the well-proven approaches for reducing their risk of heart disease and stroke: eating for heart health; getting regular physical activity; maintaining a healthy weight; not smoking; and controlling high cholesterol, high blood pressure, and diabetes.

ACE Inhibitors May Not Be Needed by All Cardiac Patients

Many heart disease patients who are receiving state-of-the-art therapy may not need angiotensin-converting enzyme (ACE) inhibitors in their drug regimens. Although ACE inhibitors are widely prescribed for heart disease patients, the Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) trial showed that the drugs may be unnecessary for the many cardiac patients who are relatively healthy, have normal or near-normal heart function, and follow recommended treatment for their specific heart conditions. Researchers observed almost 8,300 cardiac patients with these characteristics who took either the standard dose of the ACE inhibitor trandolapril or an inactive placebo. After almost 5 years, the ACE inhibitor was no better than placebo in preventing death from CVD, or in reducing the occurrence of heart attack or the need for revascularization. Although recent results of two other highly regarded trials support the widespread use of ACE inhibitors for heart disease patients, differences in patient population (e.g., the PEACE participants were a lower CVD risk group) may explain the opposing findings. The PEACE findings suggest that large numbers of relatively low-risk heart disease patients who do not need ACE inhibitors for another indication (e.g., high blood pressure) may be able to avoid the side effects and expense of these drugs.

Antibiotics Do Not Prevent Second Cardiac Events

Taking antibiotics weekly for one year did not reduce the risk of heart attack or other cardiac event for patients with stable coronary artery disease (CAD), according to recent clinical trial results. Based on prior studies that had detected the bacterium *Chlamydia pneumoniae* in arterial plaques of patients with CAD, investigators hypothesized that antibiotics would reduce the risk of future cardiac events. They randomly assigned patients who had stable CAD to receive either once-weekly doses of the antibiotic azithromycin or placebo for one year. After following the patients for almost 4 years, researchers found no significant reduction in death, heart attack, unstable angina, angioplasty, bypass surgery, or stroke among those receiving the antibiotic compared with those given placebo. The findings were corroborated by results published at the same time from an industry-supported trial. Although antibiotics were not found to be effective in preventing second cardiac events in patients with *existing* coronary disease, investigation into the role of *Chlamydia pneumoniae* and other infectious agents in the early, perhaps still asymptomatic, stages of coronary disease development holds promise for identifying therapeutic approaches useful earlier in disease progression.

Protecting Babies after Heart Surgery

Hospital staff soon may be able to better monitor infants who are recovering from cardiac surgery—and possibly avert neurological damage and future developmental difficulties. Although medical and surgical advances over the past decade are saving lives of babies born with heart defects, many go on to develop neurobehavioral abnormalities that may have been caused or exacerbated by impaired blood flow during the post-operative period. Building on previous efforts to develop non-invasive techniques for measuring oxygenation, blood flow, and metabolic status of the brain, researchers used a technology known as near-infrared spectroscopy (NIRS) to monitor infants (aged 2 days to 7 months) after heart surgery. They determined that NIRS data correlated well with information obtained by transcranial Doppler, a common method of measuring cerebrovascular blood velocities. NIRS has several advantages: it is easier to use than transcranial Doppler as a long-term monitoring tool and it provides information not available from transcranial Doppler about factors affecting cerebral blood flow. Since NIRS allows for "real-time" analysis of blood flow measurements, problems can be detected as they begin to develop and steps taken to prevent or reduce long-term damage.

Story of Discovery: Treatment of Hypertension—Newer Is Not Always Better

In our quest for better medical therapies we tend to believe that newer equals better. For treatment of hypertension, however, a comparison of new drugs with an old tried-and-true therapy has challenged that notion.

The twentieth century ushered in an era of great interest in blood pressure with the development of a practical method to measure it. Accumulating actuarial data documented a relationship between high blood pressure and premature death, and physicians began to note associations between hypertension and risk of heart failure, stroke, and kidney failure. Although scientists had yet to prove that blood pressure lowering could ameliorate health risks, some approaches were attempted during the 1930s and 40s: sympathectomy (a surgical procedure that involved cutting nerves to blood vessels), pyrogen therapy (induction of a high fever), and strict low-sodium diets. Case studies suggested that each of the treatments was effective in lowering blood pressure and improving outcomes, but the drawbacks—ranging from discomfort to life-threatening complications—were substantial. During the 1940s and 50s, several antihypertensive drugs, such as hexamethonium, hydralazine, and reserpine, were developed but they, too, were not without side effects.

In 1958, a diuretic called chlorothiazide became available as the first safe, effective, orally administered therapy for hypertension. Diuretics work by stimulating the kidneys to excrete more urine. Increased removal of water and sodium reduces the volume of blood in the circulatory system and causes blood pressure to go down.

Throughout the 1960s and 70s the results of observational studies further strengthened the causal relationship between high blood pressure and cardiovascular disease, and clinical trials provided unequivocal evidence for the benefits of lowering blood pressure. As the public health significance of hypertension gained attention, renewed emphasis was focused on finding new, more effective treatments.

During the mid 1970s, two classes of drugs made their debut as treatment options for hypertension: ACE inhibitors and alpha blockers. Another class of drugs, calcium channel blockers (CCBs), was first used clinically to treat hypertension in 1980. The newer drugs became popular with physicians and patients. Diuretic use fell from 56 percent of antihypertensive prescriptions in 1982 to 27 percent in 1992.

In 1994 the NHLBI began the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). Its hypertension component addressed the question of whether the newer, more expensive blood pressure-lowering drugs were superior to the older, cheaper diuretics. The trial enrolled a diverse group of over 42,000 patients, aged 55 years and older, through 623 clinics and centers across the United States, Canada, Puerto Rico, and the U.S. Virgin Islands. Participants were randomly assigned to begin treatment with the diuretic chlorthalidone, the CCB amlodipine, the ACE inhibitor lisinopril, or the alpha blocker doxazosin, and then followed for an average of 5 years.

ALLHAT demonstrated that the diuretic was at least as good as the comparison drugs in preventing CVD events. Results were consistent in men and women, younger and older patients, and individuals with and without diabetes. Among black study participants, the diuretic was far superior to the ACE inhibitor in preventing strokes.

ALLHAT results prompted investigators to suggest that diuretics should be the initial therapy for patients with hypertension. The recommendations were included in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, which was published in 2004 by the National High Blood Pressure Education Program to guide physicians in treating hypertension. Thus, the older, inexpensive diuretic—a drug that had lost popularity due to development of newer medications—has regained its place as primary therapy for hypertension.

Newly Identified Stem Cells Hold Promise for Failing Hearts

Researchers have isolated a type of stem cell from human bone marrow that may be useful for reversing heart damage and preventing heart failure following a heart attack. When injected into the hearts of rats that had undergone experimentally induced heart attacks, the newly discovered cells incorporated into the damaged heart muscle, differentiated into several types of cells essential for the development of tissue, and formed new functional heart muscle. In addition, the transplanted cells secreted molecules that prevented cell death and induced proliferation and preservation of the rats' own heart tissue. Moreover, for the first time, these adult human bone marrow stem cells appeared to regenerate both blood vessels and heart muscle cells after a heart attack. Although additional studies must be conducted in large animal models before large-scale clinical studies can begin, this discovery provides hope that a patient's own bone marrow could be used to provide restorative therapy following a heart attack.

Molecules Produced by Stem Cells May Provide Protection after Heart Attack

Findings from a recent study suggest that molecules secreted by bone marrow-derived mesenchymal stem cells (MSCs) may help protect cardiac tissue after a heart attack. Earlier experiments in rats with induced heart attacks found that when MSCs that had been genetically engineered for enhanced survival were injected into the heart, tissue damage was limited and function was improved. Although the researchers did not know how the stem cells achieved this protective effect, they suspected that factors produced and secreted by the cells might be involved. To test their hypothesis, they grew the cells in the laboratory and collected the liquid in which the cells were growing. When injected into rat hearts, the liquid itself was found to reduce cardiac damage after a heart attack. Scientists are now working to identify and isolate the secreted factors responsible for this phenomenon. The factors might one day have important applications for the prevention of tissue damage after a heart attack.

Understanding the Regulation of Cholesterol Synthesis May Lead to New Therapies

Recent work by scientists studying cholesterol synthesis may lead to the development of new cholesterol-lowering drugs that would benefit patients who do not respond well to statins—the current drugs of choice. Statins lower blood cholesterol levels by blocking the enzyme HMG CoA reductase, which is needed to produce cholesterol. However, in some individuals, the body reacts to statin-induced inhibition of HMG CoA reductase activity by producing more of the enzyme, thereby causing blood cholesterol levels to rise even further. When this happens, the dose of statin must be increased to achieve cholesterol-lowering, which raises the risk of side effects. Researchers now have found that the body has a natural method to decrease levels of HMG CoA reductase. A molecule called lanosterol can signal the body to destroy HMG CoA reductase when it is not needed. Scientists hope that a better understanding of how lanosterol triggers the destruction of HMG CoA reductase may lead to the development of more effective and safer methods for treating elevated serum cholesterol.

Insufficient Sleep Related to Obesity and Metabolic Disorders

Two recent studies have shed light on the relationship of abnormal sleep patterns to obesity and to metabolic disorders associated with CVD. Researchers studying the role of the "Clock" gene, which helps regulate circadian rhythm (the daily rhythm of biological activities such as sleeping and eating), found that mice with a mutant form of the gene—already known to sleep less than normal mice—also ate more and gained more weight than normal mice. The mutant mice had abnormal levels of hormones that help regulate appetite, and a range of metabolic abnormalities such as high levels of blood cholesterol, triglycerides, and glucose. Results from a second study, conducted in human volunteers, also suggest that the system that controls sleep participates in regulating metabolism. Researchers found that people who usually sleep 6 hours a night or less, or 9 hours or more, were more likely to have diabetes or impaired glucose tolerance (a precursor to diabetes) than those who sleep 7 to 8 hours a night. Although studies are needed to clarify the specific mechanisms that relate circadian rhythm, sleep, obesity, and metabolism, the recent findings suggest that the current trend of sacrificing sleep to gain more time for work or play may be placing individuals at heightened risk for obesity and CVD.

Understanding Vioxx®

Scientists are beginning to discover how anti-inflammatory pain medications increase risk of heart attacks and strokes. Evidence that use of Vioxx® (rofecoxib) and related drugs is associated with CVD events recently made headlines in newspapers across the country and led to withdrawal of two drugs from the U.S. market. The pain relievers—a class of non-steroidal anti-inflammatory drugs (NSAIDs) called cyclooxygenase (COX)-2 inhibitors, or coxibs—initially were touted as being safer than traditional NSAIDs because coxibs were less likely to cause stomach ulcers and bleeding. Scientists now suspect that the drugs trigger CVD events by suppressing biosynthesis of a compound called prostacyclin—a hypothesis supported by experiments in mice demonstrating that coxib-mediated suppression of prostacyclin production triggers changes in the blood vessel walls, increases blood pressure, and causes clotting. Additional experiments showed that chronic inhibition of COX-2 also may reduce the atheroprotective effects of estrogen, thereby potentially increasing the risks of CVD complications for premenopausal women (who ordinarily are unlikely to suffer heart attacks or strokes) if they take coxibs for extended periods. Knowing that extended use of coxibs may increase the likelihood of heart attacks and strokes even in low-risk patients is important when evaluating the risks and benefits of coxib use. Research in this area is particularly important now because CVD complications are being associated with some traditional NSAIDs and companies are seeking FDA approval for new coxib family members.

Lung Diseases

Gene Therapy Success in Rat Models of Pulmonary Hypertension (PH)

Two recent studies in rats have demonstrated the potential of gene therapy to inhibit and reverse PH, a lung disease that leads to vascular constriction, right ventricular failure, and death. The molecular basis of PH is a defective cell-signaling pathway that culminates in increased production of a protein called survivin. Survivin inhibits cell death and, in excess, leads to unrestrained cell proliferation. In one study, investigators found that administering a gene for a key protein that interferes with the PH pathway and reduces survivin levels prevented disease in two of three rat models tested. Researchers in another study gave rats a mutant gene to suppress survivin levels either before or after inducing PH. When given prior to induction, the gene inhibited disease development; when given after PH had already developed, it reversed the disease. The studies demonstrate that halting runaway cell proliferation can have a dramatic effect on the course of PH, and may even reverse it, thus providing a basis for the development of new treatments.

Mechanisms of Apoptosis in Emphysema Identified

Alveolar apoptosis (programmed death of cells that form the lung air sacs) is strongly implicated in the pathogenesis of emphysema, but the biochemical pathways that mediate this phenomenon have been poorly defined. In concept, inhibiting alveolar apoptosis in patients with emphysema could arrest or reverse deterioration of lung function and markedly improve quality of life, exercise ability, and life expectancy. However, development of suitable interventions awaits an understanding of the underlying pathways and mechanisms involved. Using mouse or rat models, investigators from four separate projects found several key mediators, including oxidants, autoantibodies, proteases, and intracellular lipids that lead to apoptosis and emphysema. When the actions of the mediators were blocked, emphysema development was either halted or substantially diminished. Additional research is needed to demonstrate the relevance of the pathways to human emphysema, but the studies support the possibility that prevention and treatment may be achievable through pharmacological inhibition.

New Technique Offers Possibility of Stem Cell Therapy for Cystic Fibrosis (CF)

Patients with CF may someday benefit from a new combination of gene and stem cell therapies that could eliminate the adverse immune system reactions currently associated with gene therapy. CF is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, which leads to defective chloride ion secretion in lung airway epithelial cells. Researchers delivered functional copies of the CFTR gene to stem cells taken from the bone marrow of patients with CF. When grown in a newly developed air-liquid-interface system, the gene-corrected stem cells acquired the characteristic shape and biological markers of normal airway cells and, more important, secreted chloride ions. The results suggest that CF patients' own bone marrow stem cells could be removed, genetically repaired, and transplanted into the lungs to improve lung function.

Increased Immune Response Contributes to Development of Childhood Asthma

Recent studies of the complex interplay of genetic and environmental factors that lead to allergic responses may provide a basis for developing new medications to prevent the onset and progression of asthma. A recent study in mice demonstrated that a pre-existing allergic response mediated by an immune system component, called a Th2 cell, against a specific allergen can prime an individual to produce additional Th2 responses to other, newly encountered allergens. This phenomenon enhances allergic sensitization and may be a key event that contributes to development of asthma. Investigators discovered that giving the mice a class of compounds called immunostimulatory oligodeoxynucleotides (ISS-ODN) prevented sensitization. The results suggest that clinical use of ISS-ODN during early childhood could offer a means to prevent asthma, thereby reducing a significant public health burden.

Researchers Identify Genetic Profiles in Childhood Asthma

New research is shedding light on the role of genetic factors in childhood asthma. In the first study to link clusters of genes to specific asthmatic states, researchers compared gene expression in airway epithelial cells from non-asthmatic children, children with controlled (stable) asthma, and children presenting in the emergency room with an acute asthma attack. The investigators sifted through over 34,000 genes for each child studied. They found more than 300 genes that were differentially expressed between non-asthmatic and asthmatic children. Moreover, they found eight distinct gene clusters that were differentially expressed between children with stable and acute asthma, demonstrating that the gene expression profile of children with an active asthma exacerbation is clearly different from that seen with controlled asthma. These observations hold promise for precise genetic classification of asthma states, which could lead to therapies tailored specifically to patients experiencing acute attacks.

Blood Diseases and Resources

Assessing Transfusions' Risks and Benefits for the Premature Newborns

New results from a randomized clinical trial to determine when preterm infants should be given red blood cell (RBC) transfusions may cause neonatal intensive care units to reevaluate how they care for their most vulnerable patients. Newborns with low RBC concentrations need supplemental transfusions, but clinicians, wary of exposing babies to blood from multiple donors, have become increasingly conservative about ordering the procedure. In a recent study to determine whether the current, conservative approach to transfusions is advisable, investigators randomly assigned preterm infants to receive transfusions at either higher or lower RBC-concentration thresholds. Infants who received transfusions at the lower level were more likely to experience adverse neurological events or to have breathing difficulties than those whose transfusions were started at a higher level. The results suggest that current conservative practices should be reevaluated and that a more aggressive transfusion approach may provide a greater benefit.

NHLBI Story of Discovery: Building a Hemoglobin-Based Blood Substitute

The search for a compound that can improve oxygen delivery to tissues and organs has entered a new phase with the start of clinical trials of "next generation" hemoglobin-based blood substitutes. Despite improvements in blood safety, transfusions of blood and blood products have limitations that substitutes could circumvent. Storage constraints, for example, make blood impractical for emergency use on the battlefield or in ambulances. Even in hospitals, supply can be an issue (and is likely to become more of a concern as the U.S. population ages and requires an increasing number of invasive surgeries). Fluids that restore lost volume and deliver oxygen, therefore, could be acceptable blood substitutes in acute trauma situations or could supplement existing blood resources during surgery. Even with these limited objectives, blood substitutes could not be developed until researchers overcame several obstacles.

Because the oxygen-carrying hemoglobin protein is relatively easy to isolate from blood, clinicians were able to infuse hemoglobin solutions into patients as early as a century ago. Although some recipients appeared to benefit, others died; sometimes death was attributed to allergic reactions (anaphylaxis) or kidney failure, but researchers could only speculate as to the underlying causes. By the late 1940s, researchers had observed repeatedly that infusions could improve blood oxygen levels and increase blood pressure, had determined that fatal episodes of anaphylactic shock were attributable to contamination, and were beginning to understand that free hemoglobin behaves very differently from hemoglobin in the cell. It binds more tightly to oxygen, for example, and is not particularly effective at delivering oxygen to tissues. Furthermore, free hemoglobin rapidly breaks into fragments that are flushed from the body, destroying the kidney's delicate filtering mechanism along the way.

In the thirty-year period after World War II, researchers developed purification schemes that removed all life-threatening contaminants. With support from the NIH and elsewhere, they explored methods of chemically crosslinking hemoglobin subunits so that the protein would not break into kidney-damaging fragments. They sought to alter the purified protein so that it bound, carried, and released oxygen like it does when encapsulated in red blood cells.

Another problem became evident in the 1980s and 1990s, however, as researchers were developing and testing new hemoglobin-based oxygen carriers (HBOCs). The increase in blood pressure that initially had been thought to be a favorable sign of restored circulation actually was caused by blood vessel constriction and impaired blood flow through the smallest arteries and capillaries. Patients died, trials were stopped, and researchers turned their attention to understanding how free hemoglobin causes vasoconstriction and how it can be prevented.

Researchers had known for decades that hemoglobin binds to nitric oxide (NO), but they did not focus much attention on this interaction until others began to characterize NO's role in mediating vascular tone. By the mid-1990s, experts in the field were convinced that free human hemoglobin caused vasoconstriction by latching onto NO molecules found between cells lining the blood vessels, as well in the blood itself. Researchers pooled this new knowledge with findings from earlier efforts to stabilize hemoglobin and ultimately determined that enlarging the hemoglobin molecule to a point where it could not "fit" between the cells and access stored NO could reduce the problem of vasoconstriction.

All three HBOCs currently in clinical trials are based on polymerized hemoglobin or other chemical modifications to enlarge the protein. Hemopure® (Biopure Corp., Cambridge, MA) and PolyHeme® (Northfield Laboratory, Evanston, IL) are being tested in trauma patients, while Hemospan® (Sangart, San Diego, CA) is being tested for surgery patients. It is not yet clear which, if any, of the "next-generation" HBOCs will revolutionize surgical practices or save otherwise doomed trauma patients, but their development has greatly expanded our understanding of the importance of maintaining an adequate volume of fluid in the circulatory system, the regulation of blood flow through small vessels, and the mechanisms that control the oxygen delivery to hypoxic tissues. Even if none of the current options proves to be effective, the research that led to them has brought the scientific community ever closer to its goal of developing a safe and useful HBOC blood substitute.

Using Genomic Research to Solve a Clinical Dilemma

New results from the NHLBI Programs for Genomic Applications may change prescribing practices of clinicians who order blood thinners to prevent dangerous blood clots. Warfarin has been prescribed for patients since the 1950s, but physicians have had to rely on a trial-and-error approach to determine the appropriate dose. In search of a way to predict the amount of warfarin that would adequately protect a patient from excessive blood clotting without causing uncontrolled bleeding, investigators analyzed blood samples from patients who were being treated with the drug. They identified genetic markers that correlated with whether a patient responded best to a low, intermediate, or high dose of the drug. This observation may enable development of a blood test to guide physicians in prescribing safe and effective doses of blood thinners.

Finding Alternative Therapies for Chronic Myeloid Leukemia (CML)

Researchers are one step closer to developing a new class of drugs for people who suffer from the myeloproliferative disorder CML. Imatinib mesylate (Gleevec®) has prolonged the lives of many CML patients by inhibiting Bcr/Abl (the protein that causes CML). The drug is not effective, however, in patients who have mutations in the region of Bcr/Abl that interacts with it. To overcome this limitation, researchers are developing and analyzing compounds that could impair Bcr/Abl activity by binding to other parts of the protein. A compound called PD166326, tested in mice with a CML-like disorder, was found to provide better control of the illness than imatinib mesylate. The compound also was effective against imatinib-resistant forms of the mouse disease. These promising findings suggest that a drug based on PD166326 or a similar compound might lead to an effective therapy in patients.

Improving Peripheral Blood Stem Cell Transplantation Safety

Researchers have developed a method of stem cell transplantation for patients with blood cancers that appears to reduce complications while retaining the benefits of the procedure. Graft-versus-host disease (GVHD), which occurs when transplanted cells launch an immune response against the recipient, once was thought to be inseparable from the cells' graft-versus-leukemia (GVL) effect against the cancer itself. Now, after more than a decade of laboratory, animal, and clinical experiments on peripheral blood stem cells, scientists have developed a method of separating donor cells that trigger acute GVHD from those that produce the GVL effect. Researchers tested the approach, called selective T-cell depletion, in older patients with advanced leukemia and found it to be at least as safe as a standard regimen. It did not impair engraftment, the GVL effect, or recovery of immune function. As a next step, scientists hope to increase the technology's efficiency and to determine long-term effects of selective T-cell depletion on the development of chronic GVHD, disease recurrence, and survival.

Measuring Iron Levels in Patients with Transfusion-Dependent Hemoglobin Disorders

A new, noninvasive approach for measuring iron deposits in human tissue may lead to better clinical care and new therapies for thousands of patients who regularly receive blood transfusions as treatment for sickle cell disease or beta-thalassemia. Such patients must undergo chelation therapy to prevent iron-induced organ damage, and their iron levels are monitored regularly with liver biopsies and blood tests. However, heart failure caused by toxic amounts of iron remains a significant, often fatal, consequence of regular blood transfusions. The new approach, which relies on magnetic resonance imaging (MRI), can accurately measure iron accumulation in the liver, and possibly in other organs such as the heart. The MRI screening method is expected to allow clinicians to detect toxic iron accumulation before heart tissue is irreversibly damaged and, because it is non-invasive, to be better tolerated by patients. It also has value as a research tool: the NHLBI Thalassemia Clinical Research Network plans to use the technique when evaluating a new chelation regimen that may better prevent iron toxicity in cardiac tissue.

Transfusions for Stroke-Prone Children with Sickle Cell Anemia

A clinical trial has provided important—and unexpected—information about stroke prevention in children with sickle cell anemia. An earlier study demonstrated the value of periodic blood transfusions in high-risk patients, aged 2–16 years, but whether the therapy, which carries its own risks, could be discontinued after a certain age was unknown. The Stroke Prevention Trial II (STOP II) began in 2000 with an expected recruitment of 100 patients age 2 to 18. It was stopped two years early with only 79 patients enrolled because 14 of the 41 patients who had been randomly assigned to discontinue transfusions reverted to a high risk of stroke as measured by a special ultrasound technique, and 2 patients suffered strokes. These adverse events did not occur in the group that continued with transfusions. The NHLBI issued a clinical alert advising physicians who treat children with sickle cell anemia not to discontinue transfusions in susceptible patients. It also urged physicians to discuss with patients and their families the stroke prevention benefits of continuing periodic transfusions and the risks associated with them.

Unraveling Malaria's Mysteries

Scientists have uncovered a potential new target for anti-malaria drugs. The life cycle of malaria-causing parasites such as the deadly *Plasmodium falciparum* includes a "blood stage" during which the parasites mature within red blood cells of a human host. The parasites essentially commandeer the cells, releasing proteins that render the host environment hospitable for reproduction and protected from immune system attack. Researchers recently found a short protein segment common to over 300 *Plasmodium* proteins that are essential for the parasite's proliferation and survival. The discovery, which has been corroborated by other investigators, raises the possibility that a single therapeutic agent could be developed to interfere with multiple aspects of malaria-causing infection by specifically disrupting the segment common to the many proteins.

NIH ROADMAP

The NHLBI has taken the leadership role in the Re-engineering the Clinical Research Enterprise Initiative of the NIH Roadmap. One of its components is the Inventory and Evaluation of Clinical Research Networks (IECRN), the primary objectives of which are (1) to identify a broad range of clinical research networks and provide a web-based clinical research network inventory database for researchers to identify and collaborate with other clinical research networks, (2) to describe and assess network practices, (3) to identify and examine clinical research network practices that allow achievement of their goals through operating efficiently, promoting successful interactions within the network and with other networks, and (4) to conduct a National Leadership Forum for researchers to discuss the study findings. The National Leadership Forum will engage clinical research network leaders in building a common framework for dialogue on the NIH Roadmap initiative, present candidate "best practices," support cross-network exchange in the clinical research networks, and provide a springboard for ongoing dissemination of information and practice models to the clinical research network community. Sharing clinical research network information and best practices will open opportunities to address research questions across the NIH.

The NHLBI also is leading the Clinical Research Networks and National Electronics Clinical Trials and Research Network (NECTAR) Initiative. The goal is to explore the feasibility of expanding and integrating clinical research networks at academic centers and community-based health care providers that care for sufficiently large groups of well-characterized patients. Implementing this vision will require new ways to organize how clinical research information is recorded, new standards for clinical research protocols, modern information technology, and new strategies to strengthen the clinical research workforce. This initiative seeks to promote and expand clinical research networks capable of rapidly conducting high-quality clinical studies that address multiple research questions. The 12 network feasibility projects that are now under way address a range of medical specialties (heart, cancer, critical care, psychiatry, transplantation), over multiple ages and populations/settings (primary care, rural, minority, HMO), using varied information systems and informatics tools. For example, one of the feasibility projects is defining common data elements and cardiovascular vocabulary used in clinical research. Another is studying and defining the common data elements and vocabulary definitions used in tuberculosis clinical research. A third is looking at how to facilitate the integration of primary physicians and their practice populations into the existing clinical research enterprise. The development of common infrastructure elements (e.g., informatics, governance, terminology) will facilitate cooperation among research groups and networks to address research questions of mutual interest and across disciplines. The outcome and objectives of both the NIH Roadmap Inventory and Feasibility initiatives address areas relevant to the scientific mission of the NHLBI.

NEW INITIATIVES FOR FY 2007

Cardiovascular Cell Therapy Clinical Research Network

The NHLBI plans to establish a network to conduct phase I and II clinical protocols of cell therapies for CVD. Studies suggest that cell therapy may be able to improve cardiac function and replace damaged or diseased tissue. In animal models of acute myocardial infarction, bone marrow mononuclear cells, endothelial progenitor cells, and mesenchymal stem cells all have

shown an ability to improve ventricular function. Early clinical studies suggest that transplantation of bone marrow cells may improve cardiac function in human disease as well. Examples of research topics that the network might investigate include evaluating cell-based strategies to treat patients with significantly depressed left ventricular function following myocardial infarction, determining which patients with chronic heart failure would derive the greatest benefit from cell therapy, developing screening methods to monitor cell therapy treatment in individual patients, elucidating the mechanisms responsible for functional benefit resulting from cell therapy, and developing standards for sample collection from patients. Knowledge gained from network studies will facilitate the clinical implementation of cell-based therapies for CVD to improve patient outcomes.

Network for Cardiothoracic Surgical Investigations in Cardiovascular Medicine

A network will be developed to evaluate new surgical techniques, technologies, devices, and bioengineered products through rigorous phase I and II clinical trials. Despite the lifesaving nature of cardiac surgery, the large number of patients who undergo it, and its major impact on health care resources, few cardiac surgery patients participate in clinical studies or trials. New surgical procedures and devices are often incorporated into clinical practice without objective evaluation of their relative benefit compared with established therapies. The network will standardize methods and measures for investigators, coordinate multidisciplinary teams, and facilitate recruitment of sufficient numbers of patients, particularly those with rare conditions, to yield meaningful study results. Anticipated research topics include new surgical techniques for mitral valve repair, robotically assisted cardiac surgery, next-generation ventricular assist devices, neuroprotective strategies in patients undergoing cardiopulmonary bypass, minimally invasive surgical techniques, and cell therapy as an adjunct to surgery.

Specialized Centers of Clinically Oriented Research on Host Factors in Chronic Lung Diseases

Centers will be established to promote multidisciplinary basic and clinical research related to the role of altered host defense mechanisms in immune and pulmonary dysfunction that leads to development and progression of chronic lung diseases. The incidence and prevalence of such diseases—asthma, COPD, fibrotic lung disease, interstitial lung disease—continue to rise. Prevention and treatment present formidable challenges due to the complexity of the respiratory tract and its unique relationship with the external environment as it responds to numerous environmental insults including bacteria, viruses, allergens, and other inhaled particulates. Although not problematic for healthy people, such encounters may initiate or exacerbate disease if host defense functions are absent or dysfunctional. This program will support research to understand the host defense and immune mechanisms at the cellular and molecular levels. Anticipated research topics include the characterization of innate host responses, the role of missing or aberrant immune responses, the mechanisms by which immune systems influence disease, the role of infection, and the role of genetic and environmental factors that predispose an individual to develop chronic lung disease.

Specialized Centers of Clinically Oriented Research on Chronic Obstructive Pulmonary Disease (COPD)

This new program will foster multidisciplinary basic and clinical research related to COPD, enable more rapid translation of basic research to clinical application, and speed progress in the diagnosis, prevention, and treatment. Although most cases of COPD could be prevented by lifelong avoidance of cigarette smoking, tens of millions of Americans have a substantial smoking history and are at risk. In addition, about two million nonsmokers have COPD that is due to other causes. Research topics to be investigated under this initiative are expected to include evaluation of pulmonary immune system activity in subjects with COPD, correlation of disease severity with phenotypes, studies of the systemic manifestations of COPD, identification of genetic factors associated with susceptibility, identification of risk factors for development of COPD in nonsmokers, characterization of cellular and molecular mechanisms related to COPD, and characterization of common pathways involved in the development of COPD and lung cancer.

Specialized Centers of Clinically Oriented Research in Pulmonary Vascular Disease

This program will support multidisciplinary research centers to apply innovative state-of-the-art approaches, including genomics and proteomics, to clinical issues in pulmonary vascular disease. Primary pulmonary hypertension (PPH) is an aggressive, devastating disease with a poor prognosis. Basic research on lung endothelial biology and analysis of lung tissue from patients with PPH and other forms of severe pulmonary arterial hypertension are changing concepts of pathogenesis. Genetic mutations for PPH have been found, although the mechanisms by which mutations contribute to pathogenesis remain incompletely understood. Progress in identifying a gene for PPH is leading to new animal models of the disease. Additional efforts are needed to link genomics and proteomics to etiologies and mechanisms of hypertensive pulmonary vascular disease. Anticipated approaches to this problem include gene array and proteomic studies; phenotypic characterization of endothelial cells from patients with pulmonary vascular disease; studies exploring the role of endothelial progenitor cells in pathogenesis; innovative clinical studies to evaluate new treatment agents; studies of the association of pulmonary hypertension to systemic sclerosis, emphysema, and interstitial pulmonary fibrosis; investigation of innovative approaches to imaging, diagnosis, and treatment; studies of right ventricular size and function in pulmonary thromboembolism and pulmonary hypertension; investigations of the pulmonary sequelae of congenital heart disease in neonates and adults; and studies to determine the relationship between abnormal lung vascular development and chronic lung disease in neonates and children.

OTHER ITEMS OF INTEREST

Coordination of Obesity Research at the NIH

Obesity is a topic of great concern to the NHLBI because many diseases and conditions under the Institute's purview are caused or exacerbated by excess body weight. In addition to supporting its own extensive portfolio of obesity-related research, the Institute is leading efforts to oversee obesity research activities across the NIH. The directors of the NHLBI and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) co-chair the NIH Obesity Research Task Force (ORTF), a trans-NIH group formed in 2003 that includes 26 NIH components. In 2004, the ORTF published the *Strategic Plan for NIH Obesity Research* to guide coordination of NIH obesity research activities and enhance the development of new efforts based on identification of areas of greatest scientific opportunity and challenge. The plan emphasizes four scientific themes: *Research Toward Preventing and Treating Obesity Through Behavioral and Environmental Approaches To Modify Lifestyle*; *Research Toward Preventing and Treating Obesity Through Pharmacologic, Surgical, or Other Medical Approaches*; *Research on Understanding the Relationship between Obesity and its Associated Health Conditions*; and *Research on Cross-cutting Topics* (e.g., health disparities, technology, multidisciplinary/interdisciplinary research teams, translational research, training, education and outreach). In FY 2005 the ORTF fostered trans-NIH collaboration on the development and funding of several obesity initiatives recommended in the strategic plan. The NHLBI, in cooperation with four other ORTF member institutes, co-sponsored an issue of the journal *Nature Neuroscience*, which focused on the neurobiology of obesity. In September 2005, the directors of the NIH, the NHLBI, and the NIDDK attended the National Science and Technology Council Committee on Science meeting at the White House to discuss the NIH's role in providing a scientific evidence base for federal efforts to address obesity and to identify ways in which various federal agencies can collaborate to slow and reverse the rise in obesity in the United States.

We Can! (Ways to Enhance Children's Activity and Nutrition)

Since the *We Can!* program was launched in June 2005, more than 40 communities throughout the United States have begun to implement its activities to prevent overweight and obesity among youth. The program, which was developed by the NHLBI in collaboration with the NIDDK, the National Institute of Child Health and Human Development, and the National Cancer Institute, serves as a one-stop source for practical tools to help 8–13 year-old youngsters maintain a healthy weight. *We Can!* provides resources and community-based programs that focus on behaviors to encourage healthy eating, increase physical activity, and reduce sedentary time. Its messages are reaching parents through partners that include the American Academy of Family Physicians, Action for Healthy Kids, Parents' Action for Children, and the President's Council on Physical Fitness and Sports. Other avenues for reaching American homes have been established through partnerships with Univision Communications, Inc., and the Black Entertainment Television Foundation. *We Can!* resources and activities for parents, caregivers, and youth are suitable for use by local civic groups, parent organizations, or churches, and materials can be downloaded from the Internet at wecan.nhlbi.nih.gov.

Therapy for Pulmonary Hypertension (PH) in Patients with Sickle Cell Disease (SCD)

A clinical trial will test whether treatment with sildenafil (Viagra®) is beneficial for SCD patients who have PH, a common and often fatal complication of SCD. Evidence that sildenafil may be a useful therapy comes from recent observations in a small study showing that the drug improved exercise capacity and pulmonary artery pressure in patients who had both SCD and PH. To verify the initial study's findings and to gather evidence needed by the US FDA before sildenafil can be approved for such patients, the NHLBI is awarding contracts for a double-blinded, randomized, placebo-controlled study of 180 patients from around the country. Participants will be randomly assigned to receive the drug or a placebo for 16 weeks, during which time investigators will assess exercise capacity, pulmonary blood pressure by echocardiography, and overall health. Following successful completion of the main trial (the first 16 weeks), patients will be eligible to participate in a 52-week follow up study to compare the effects of low and high doses of sildenafil on exercise capacity and pulmonary blood pressure.

Clinical Trial of New Approach to Improving Serum Lipid Levels in Patients with CVD

The NHLBI is supporting a new investigator-initiated clinical trial, known as AIM-HIGH (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides and Impact on Global Health Outcomes), to compare two treatment strategies for preventing CVD events in patients with existing CVD. Lowering blood levels of LDL cholesterol has long been known to reduce the risk of coronary heart disease, but recent studies suggest that therapy to modify two other blood lipid risk factors—low HDL cholesterol and high triglycerides—may reduce CVD risk even further. All participants in AIM-HIGH will be given the drug simvastatin to lower LDL cholesterol, and half will be randomly assigned also to receive extended-release niacin to raise HDL cholesterol and lower triglycerides. Participants will be followed for an average of 4 years to determine whether the combination drug therapy provides greater CVD protection than the statin drug alone.

Stress Management to Reduce CVD Risk

The NHLBI is seeking to expand its portfolio of research on the interactions between mental stress and risk of various forms of CVD. A number of studies have provided evidence that stress can influence cardiovascular functioning (e.g., blood pressure, heart rhythm) or acute events (e.g., heart attack, stroke). However, it is uncertain whether clinical treatment of stress can reduce manifestations of CVD or whether stress-management approaches should be incorporated into clinical practice. To stimulate research on these issues, the NHLBI is soliciting grant applications via a program announcement. As part of the new program, the Institute hopes to fund randomized clinical trials in patients with coronary artery disease to determine whether stress reduction improves risk factors or measures of disease progression. Another objective of the program will be to compare different stress management approaches (e.g., meditation, cognitive–behavioral therapy) to determine whether some are more effective than others for reducing coronary artery disease manifestations.

Long-Term Oxygen Therapy (LTOT) for COPD

Concerns have arisen about the effectiveness of LTOT in patients who have COPD but only moderate hypoxemia (low blood oxygen level). Although LTOT is well known to be beneficial for COPD patients who experience severe hypoxemia when resting, little evidence is available to guide treatment of patients with less serious disease. Indeed, an analysis of data from the National Emphysema Treatment Trial indicated that LTOT may even be associated with increased mortality risk in COPD patients without severe hypoxemia. Many physicians routinely prescribe LTOT for COPD patients regardless of their hypoxemia severity and COPD patients with moderate hypoxemia may represent the majority of the 1 million patients in the United States who receive LTOT. The NHLBI is initiating a randomized trial to determine whether LTOT prolongs—or possibly even shortens—life expectancy in COPD patients with moderate hypoxemia. Results of the trial will provide a scientific basis for clinical management of COPD and could result in a substantial decrease in expenditures for LTOT.

Research on Muscular Dystrophy (MD)

The NHLBI has joined other NIH components to support research that could explain the pathogenesis of MD and lead to therapies for affected patients. A multi-institute program announcement, for example, has provided a new opportunity for the NHLBI to encourage research on cardiac abnormalities and respiratory muscle weakness that cause much of the morbidity and mortality associated with certain forms of MD. Grants awarded by the NHLBI under the new program are expected to complement an ongoing effort with the NIH Office of Rare Diseases (ORD) to encourage scientists interested in diseases such as MD to apply for research support even if they lack extensive preliminary data. In 2005, the NHLBI and the ORD further strengthened their combined efforts to address MD by cosponsoring a workshop to solicit suggestions from clinicians, scientists, and patient advocates about research needs and opportunities related to cardiomyopathies that affect children who have MD or other rare diseases. The NHLBI is now collaborating with workshop participants to disseminate recommendations to the extramural research community and, through the NIH MD Coordinating Committee and the new NIH MD Scientific Working Group, staff are continuing to look for opportunities to encourage researchers to study cardiac and pulmonary complications of MD.

Studies of the Lymphatic System

The NHLBI has recruited an internationally recognized clinical scientist to initiate lymphatic disease studies within the NHLBI intramural program and across the intramural and extramural programs of the NIH. The investigator, who will conduct a research protocol at the NIH Clinical Center, also will develop clinical care guidelines about lymphatic diseases. While recruitment of this investigator was under way, NHLBI intramural scientists began developing proposals for a translational program in lymphatic disease, and NHLBI and NIDDK investigators started collaborating on a study of the development of the lymphatic system. At least seven NIH components fund research relevant to lymphatics, and the growing interest in the topic is evidenced by the Clinical Center's decision to host a Grand Rounds session on "NIH-Trans-Institute Lymphatic Research Program: From Bench to Bedside" in March 2006.

Applying *Salud para su Corazón* to Other Countries, Cultures, and Health Conditions

An NHLBI program to reduce the burden of heart disease in Latinos has become a model for other efforts to improve health in underserved communities across the United States. *Salud para su Corazón* ("Health for Your Heart)," which the NHLBI launched more than a decade ago in the Washington metropolitan area, relies on *promotores* (lay health workers) who use culturally based approaches to link health care providers to communities. In partnership with the National Council of La Raza, the nation's largest Hispanic grassroots organization, the NHLBI developed a curriculum that has been used to train over 700 *promotores* nationwide. Collaboration with the U.S. Health Resources and Services Administration (HRSA) has expanded the program to community health centers in the U.S.–Mexico Border region, and *Salud para su Corazón* materials soon will be used to train *promotores* in other countries through a partnership with the Pan American Health Organization.

Salud para su Corazón resources also have been adapted for use by lay health workers from other underserved communities. When the NHLBI launched a program called Honoring the Gift of Heart Health, which it developed in conjunction with the Indian Health Service and tribal communities, *promotores* conducted the initial train-the-trainer session for the community health workers from Alaska Native and American Indian communities. In addition, materials for community health workers have been used in the NHLBI-funded Healthy Hearts in Public Housing program, and the *promotores* model will be the basis for NHLBI programs to raise cardiovascular health awareness in Asian American, Native Hawaiian, and Pacific Islander communities.

CVD is not the only health challenge that faces underserved communities, nor is it the only condition that can be addressed with the help of *promotores*. The NHLBI, therefore, is capitalizing on the success of *Salud para su Corazón* and the dedication of the *promotores* by developing a new program that will train a cadre of *promotores* to bring asthma education, prevention, and control messages and resources into their communities.

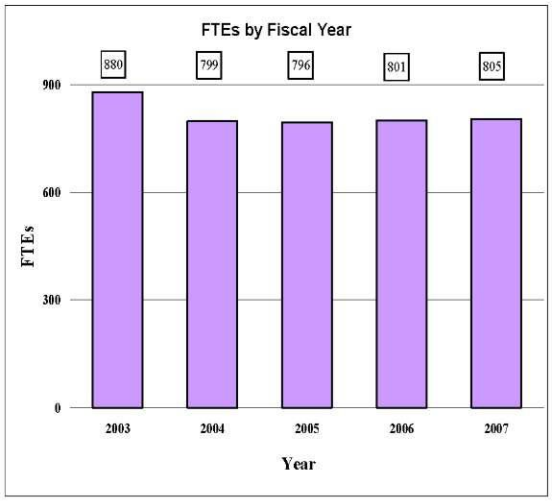
New Treatment Guidelines for Pregnant Women with Asthma

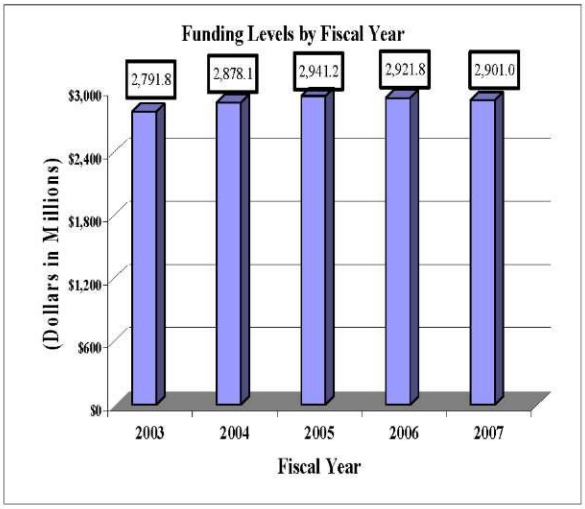
The National Asthma Education and Prevention Program (NAEPP) issued the first guidelines in more than a decade for managing asthma during pregnancy. The report, which includes discussion of medications that were not available when the last guidelines were published, updates treatment recommendations for pregnant women with asthma based on a systematic review of data on the safety of asthma medications during pregnancy. Because poorly controlled asthma can lead to serious medical problems for a pregnant woman and her fetus, the NAEPP concluded that it is safer for pregnant women to be treated with asthma medications than for them to have asthma symptoms and exacerbations. In addition to addressing pharmacologic options for controlling mild, moderate, and severe asthma and emergency treatment for women experiencing acute asthma exacerbations, the report emphasizes the importance of controlling asthma symptoms by identifying and limiting exposure to asthma triggers. It also reminds health care providers that several conditions often associated with asthma (such as rhinitis, sinusitis, and gastroesophageal reflux) are frequently more troublesome during pregnancy and that appropriate treatment of such conditions is an integral part of asthma management.

Budget Policy

The Fiscal Year 2007 budget request for the NHLBI is $2,901,012,000 a decrease of $20,745,000 and .7 percent decrease from the FY 2006 Appropriation. Included in the FY 2007 request is NHLBI's support for the trans-NIH Roadmap initiatives, estimated at 1.2% of the FY 2007 budget request. A full description of this trans-NIH program may be found in the NIH Overview.

A five year history of FTEs and Funding Levels for NHLBI are shown in the graphs below. Note that as the result of several administrative restructurings in recent years, FTE data is non-comparable.





NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. We estimate that the average cost of competing RPGs will be $493,000 in FY 2007. While no inflationary increases are provided for direct recurring costs in noncompeting RPGs, where the NHLBI has committed to a programmatic increase for an award, such increases will be provided.

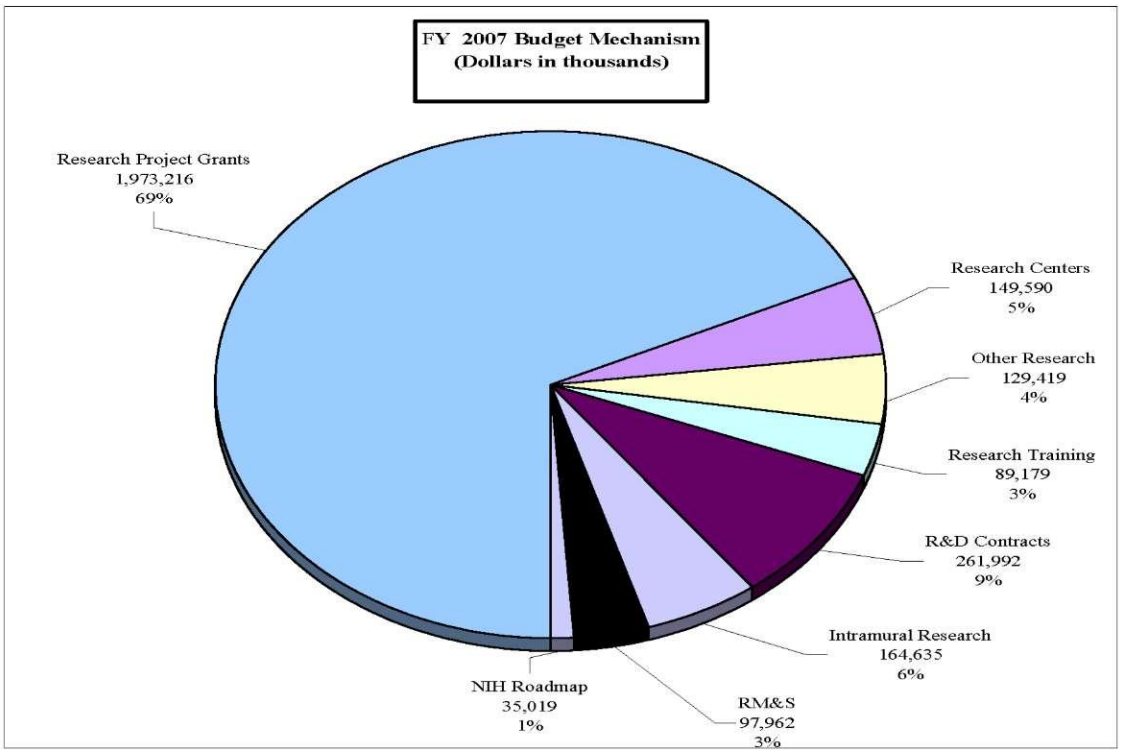
NIH must nurture a vibrant, creative research workforce, including sufficient numbers of new investigators with new ideas and new skills. In the FY 2007 budget request for NHLBI, $1.6 million will be used to support 18 awards for the new K/R "Bridges to Independence" program.

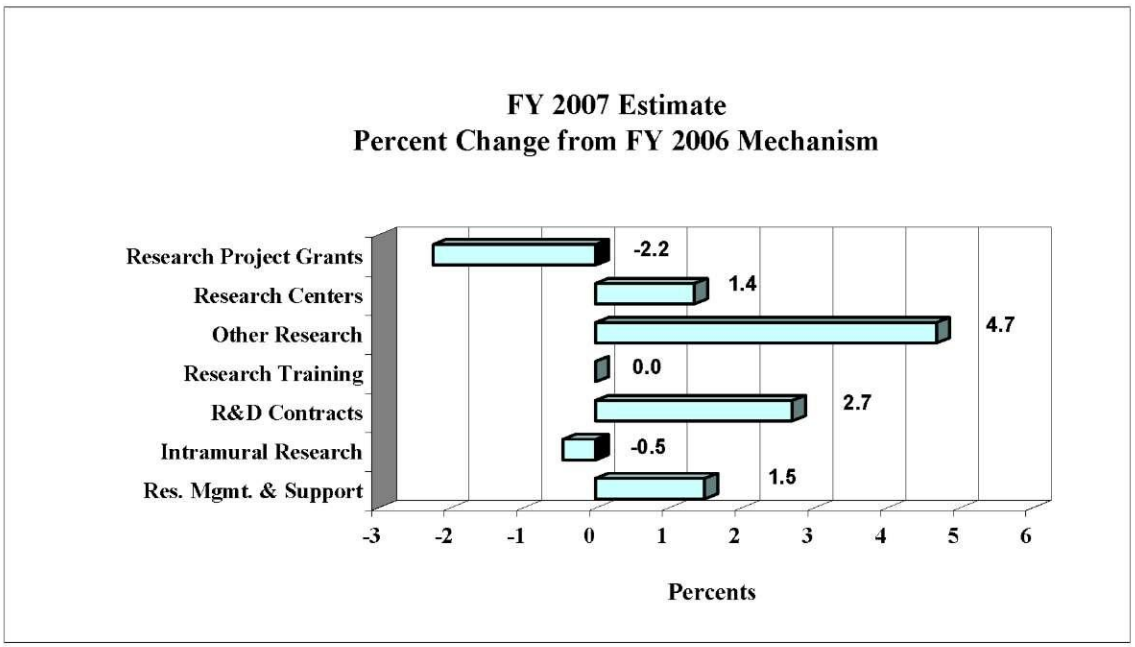
NHLBI will also support the Genes, Environment, and Health Initiative (GEHI) to: 1) accelerate discovery of the major genetic factors associated with diseases that have a substantial public health impact; and 2) accelerate the development of innovative technologies and tools to measure dietary intake, physical activity, and environmental exposures, and to determine an individual's biological response to those influences. The FY 2007 request includes $4,912,000 to support this project.

In the FY 2007 request, stipend levels for trainees supported through the Ruth L. Kirschstein National Research Service Awards will remain at the FY 2006 levels.

The FY 2007 request includes funding for 56 research centers, 660 other research grants, including 542 career awards, and 193 R&D contracts. Intramural Research decreases by 0.5 percent. Research Management and Support increases by 1.5 percent.

The mechanism distribution by dollars and percent change are displayed below:





NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Budget Mechanism - Total

MECHANISM	FY 2005 Actual		FY 2006 Appropriation		FY 2007 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	3,089	$1,508,085,000	3,054	$1,529,519,000	2,825	$1,458,640,000
Administrative supplements	(139)	11,895,000	(80)	5,335,000	(80)	5,500,000
Competing:						
Renewal	319	176,132,000	292	160,455,000	310	170,650,000
New	585	270,025,000	537	249,302,000	572	265,251,000
Supplements	5	1,673,000	5	1,665,000	5	1,675,000
Subtotal, competing	909	447,830,000	834	411,422,000	887	437,576,000
Subtotal, RPGs	3,998	1,967,810,000	3,888	1,946,276,000	3,712	1,901,716,000
SBIR/STTR	232	74,240,000	224	72,000,000	223	71,500,000
Subtotal, RPGs	4,230	2,042,050,000	4,112	2,018,276,000	3,935	1,973,216,000
Research Centers:						
Specialized/comprehensive	68	151,065,000	60	147,265,000	56	149,265,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	0	0	0	0	0
Comparative medicine	0	450,000	0	321,000	0	325,000
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	68	151,515,000	60	147,586,000	56	149,590,000
Other Research:						
Research careers	519	71,018,000	514	70,318,000	542	75,938,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	38	26,295,000	48	34,895,000	53	35,000,000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	1	2,428,000	0	2,403,000	0	2,475,000
Other	79	10,000,000	70	16,006,000	65	16,006,000
Subtotal, Other Research	637	109,741,000	632	123,622,000	660	129,419,000
Total Research Grants	4,935	2,303,306,000	4,804	2,289,484,000	4,651	2,252,225,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	202	9,665,000	200	9,958,000	200	9,958,000
Institutional awards	1,797	78,681,000	1,779	79,221,000	1,779	79,221,000
Total, Training	1,999	88,346,000	1,979	89,179,000	1,979	89,179,000
Research & development contracts	192	268,573,000	191	255,091,000	193	261,992,000
(SBIR/STTR)	(5)	(785,000)	(2)	(200,000)	(2)	(200,000)
	FTEs		FTEs		FTEs	
Intramural research	404	166,348,000	402	165,380,000	404	164,635,000
Research management and support	389	96,034,000	394	96,514,000	396	97,962,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Buildings and Facilities		0		0		0
NIH Roadmap for Medical Research	3	18,594,000	5	26,109,000	5	35,019,000
Total, NHLBI	796	2,941,201,000	801	2,921,757,000	805	2,901,012,000
(Clinical Trials)		(213,696,000)		(214,764,000)		(215,838,000)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2005 Actual FTEs	FY 2005 Actual Amount	FY 2006 Appropriation FTEs	FY 2006 Appropriation Amount	FY 2007 Estimate FTEs	FY 2007 Estimate Amount	Change FTEs	Change Amount
Extramural Research: Heart, Lung, Blood and Sleep Research		2,660,225		2,633,754		2,603,396		(30,358)
Subtotal, Extramural research		2,660,225		2,633,754		2,603,396		(30,358)
Intramural research	404	166,348	402	165,380	404	164,635	2	(745)
Res. management & support	389	96,034	394	96,514	396	97,962	2	1,448
Research	3	18,594	5	26,109	5	35,019	0	8,910
Total	796	2,941,201	801	2,921,757	805	2,901,012	4	(20,745)

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Summary of Changes

FY 2006 Estimate				$2,921,757,000
FY 2007 Estimated Budget Authority				2,901,012,000
Net change				(20,745,000)
	FY 2006 Appropriation		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$57,846,000		$875,000
b. Annualization of January 2006 pay increase		57,846,000		448,000
c. January 2007 pay increase		57,846,000		954,000
d. Payment for centrally furnished services		28,925,000		434,000
e. Increased cost of laboratory supplies, materials, and other expenses		78,609,000		1,682,000
Subtotal				4,393,000
2. Research Management and Support:				
a. Within grade increase		47,329,000		716,000
b. Annualization of January 2006 pay increase		47,329,000		367,000
c. January 2007 pay increase		47,329,000		781,000
d. Payment for centrally furnished services		15,415,000		231,000
e. Increased cost of laboratory supplies, materials, and other expenses		33,770,000		651,000
Subtotal				2,746,000
Subtotal, Built-in				7,139,000

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Summary of Changes--continued

CHANGES	FY 2006 Appropriation		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	3,054	$1,534,854,000	(229)	($70,714,000)
b. Competing	834	411,422,000	53	26,154,000
c. SBIR/STTR	224	72,000,000	(1)	(500,000)
Total	4,112	2,018,276,000	(177)	(45,060,000)
2. Research centers	60	147,586,000	(4)	2,004,000
3. Other research	632	123,622,000	28	5,797,000
4. Research training	1,979	89,179,000	0	0
5. Research and development contracts	191	255,091,000	193	6,901,000
Subtotal, extramural				(30,358,000)
	FTEs		FTEs	
6. Intramural research	402	165,380,000	2	(5,138,000)
7. Research management and support	394	96,514,000	2	(1,298,000)
8. Cancer control and prevention	0	0	0	0
9. Construction		0		0
10. Buildings and Facilities		0		0
11. NIH Roadmap for Medical Research	5	26,109,000	0	8,910,000
Subtotal, program		2,921,757,000		(27,884,000)
Total changes	801		4	(20,745,000)

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Budget Authority by Object

		FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Total compensable workyears:				
	Full-time employment	801	805	4
	Full-time equivalent of overtime & holiday hours	2	2	0
	Average ES salary	$157,510	$164,126	$6,616
	Average GM/GS grade	13.0	13.0	0.0
	Average GM/GS salary	$87,826	$91,515	$3,689
	Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$94,249	$98,207	$3,958
	Average salary of ungraded positions	$108,391	$112,943	$4,552
	OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
	Personnel Compensation:			
11.1	Full-Time Permanent	$49,038,000	$51,308,000	$2,270,000
11.3	Other than Full-Time Permanent	23,230,000	24,345,000	1,115,000
11.5	Other Personnel Compensation	2,605,000	2,730,000	125,000
11.7	Military Personnel	1,628,000	1,706,000	78,000
11.8	Special Personnel Services Payments	8,508,000	8,916,000	408,000
	Total, Personnel Compensation	85,009,000	89,005,000	3,996,000
12.0	Personnel Benefits	18,908,000	19,815,000	907,000
12.2	Military Personnel Benefits	1,206,000	1,264,000	58,000
13.0	Benefits for Former Personnel	52,000	55,000	3,000
	Subtotal, Pay Costs	**105,175,000**	**110,139,000**	**4,964,000**
21.0	Travel & Transportation of Persons	3,600,000	3,600,000	0
22.0	Transportation of Things	270,000	270,000	0
23.1	Rental Payments to GSA	0	0	0
23.2	Rental Payments to Others	60,000	60,000	0
23.3	Communications, Utilities & Miscellaneous Charges	1,400,000	1,400,000	0
24.0	Printing & Reproduction	1,000,000	1,000,000	0
25.1	Consulting Services	1,300,000	1,300,000	0
25.2	Other Services	16,000,000	16,000,000	0
25.3	Purchase of Goods & Services from Government Accounts	156,782,000	149,513,000	(7,269,000)
25.4	Operation & Maintenance of Facilities	5,000,000	5,000,000	0
25.5	Research & Development Contracts	190,091,000	200,000,000	9,909,000
25.6	Medical Care	2,300,000	2,300,000	0
25.7	Operation & Maintenance of Equipment	6,000,000	6,000,000	0
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**377,473,000**	**380,113,000**	**2,640,000**
26.0	Supplies & Materials	16,000,000	16,000,000	0
31.0	Equipment	12,000,000	12,000,000	0
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	2,378,663,000	2,341,404,000	(37,259,000)
42.0	Insurance Claims & Indemnities	0	0	0
43.0	Interest & Dividends	7,000	7,000	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**2,790,473,000**	**2,755,854,000**	**(34,619,000)**
	NIH Roadmap for Medical Research	**26,109,000**	**35,019,000**	**8,910,000**
	Total Budget Authority by Object	**2,921,757,000**	**2,901,012,000**	**(20,745,000)**

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Salaries and Expenses

OBJECT CLASSES	FY 2006 Appropriation	FY 2007 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$49,038,000	$51,308,000	$2,270,000
Other Than Full-Time Permanent (11.3)	23,230,000	24,345,000	1,115,000
Other Personnel Compensation (11.5)	2,605,000	2,730,000	125,000
Military Personnel (11.7)	1,628,000	1,706,000	78,000
Special Personnel Services Payments (11.8)	8,508,000	8,916,000	408,000
Total Personnel Compensation (11.9)	**85,009,000**	**89,005,000**	**3,996,000**
Civilian Personnel Benefits (12.1)	18,908,000	19,815,000	907,000
Military Personnel Benefits (12.2)	1,206,000	1,264,000	
Benefits to Former Personnel (13.0)	52,000	55,000	3,000
Subtotal, Pay Costs	**105,175,000**	**110,139,000**	**4,964,000**
Travel (21.0)	3,600,000	3,600,000	0
Transportation of Things (22.0)	270,000	270,000	0
Rental Payments to Others (23.2)	60,000	60,000	0
Communications, Utilities and Miscellaneous Charges (23.3)	1,400,000	1,400,000	0
Printing and Reproduction (24.0)	1,000,000	1,000,000	0
Other Contractual Services:			
Advisory and Assistance Services (25.1)	700,000	700,000	0
Other Services (25.2)	16,000,000	16,000,000	0
Purchases from Govt. Accounts (25.3)	77,103,794	69,097,302	(8,006,492)
Operation & Maintenance of Facilities (25.4)	5,000,000	5,000,000	0
Operation & Maintenance of Equipment (25.7)	6,000,000	6,000,000	0
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**104,803,794**	**96,797,302**	**(8,006,492)**
Supplies and Materials (26.0)	9,000,000	9,000,000	0
Subtotal, Non-Pay Costs	120,133,794	112,127,302	(8,006,492)
Total, Administrative Costs	**225,308,794**	**222,266,302**	**(3,042,492)**

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

SIGNIFICANT ITEMS IN HOUSE AND SENATE APPROPRIATIONS COMMITTEE REPORTS

FY 2006 House Appropriations Committee Report Language (H. Rpt 109-143)

Item

Innovative technologies for engineering small blood vessels -- The Committee understands that the supply of natural blood vessels for multiple grafts does not meet the demand for patients undergoing heart artery bypass surgery and that prosthetic grafts for children born with complex heart defects fail at an unacceptable rate. The Committee encourages NHLBI to conduct research to advance the development of substitutes for natural blood vessels. (p. 62)

Action taken or to be taken

In 2005, the NHLBI solicited grant applications for a 5-year program titled "Innovative Technologies for Engineering Small Blood Vessels." This initiative is designed to spur development of artificial vascular grafts that are less than 5.0 mm in internal diameter for use in patients with cardiovascular disease. Clinical evaluation will take place toward the end of the funding period. Applicants are encouraged to identify and refine criteria for evaluation and testing, including validation in animal models as may be required by the Food and Drug Administration. The NHLBI anticipates making awards in response to this solicitation during FY 2006.

Item

Specialized centers of clinically oriented research (SCCOR) for vascular injury, repair, and remodeling -- Vascular diseases result from clogged, weakened or otherwise damaged blood vessels. The Committee encourages NHLBI to consider initiating a new SCCOR program to conduct interdependent clinical and multidisciplinary basic research projects on the molecular and cellular mechanisms of vascular injury, repair, and remodeling. Such a program would promote patient-oriented research to improve prevention, detection, and treatment of vascular diseases. The SCCOR would provide an environment for new clinical investigators to develop skills and research capabilities to conduct relevant research in this area. (p. 62)

Action taken or to be taken

On August 17, 2004, the NHLBI published a request for applications for Specialized Centers of Clinically Oriented Research (SCCORs) in Vascular Injury, Repair, and Remodeling. The objective of this program is to stimulate formation of clinically relevant, multidisciplinary collaborations for conducting clinical and basic research on the health issues of people with vascular diseases. This patient-oriented research will enable scientists and clinicians to improve understanding of the underlying mechanisms of vascular diseases and, consequently, develop better diagnostic and therapeutic options for their management. Applications for grants were reviewed in September 2005, and funding is expected to start in April 2006.

Item

Cooley's anemia -- The Committee remains strongly supportive of the focused research effort that is being undertaken by the thalassemia clinical research network, which is comprised of the leading research institutions in the field of thalassemia, or Cooley's anemia. The Committee believes that this network is just beginning to meet its promise and urges NHLBI to continue it and support the research projects undertaken by it. (p. 62)

Action taken or to be taken

The NHLBI is pleased to report that the Thalassemia Clinical Research Network has been renewed for another 5 years, from 2005 to 2010. The network currently comprises 5 clinical centers in Boston, New York, Philadelphia, Toronto, and Oakland, and a data coordinating center at the New England Research Institute in Watertown, Massachusetts. Major satellite sites include Chicago, Los Angeles, and London (UK). The network currently is conducting a clinical intervention trial that hopes to provide better therapy for thalassemia patients who are suffering heart dysfunction due to iron overload. Several other protocols are under development.

Item

Cardiovascular advanced screening program -- The Committee encourages NHLBI to sponsor a workshop on advanced screening methods for cardiovascular disease. This workshop would incorporate the Cardiovascular Health Study data, expertise from the National Cholesterol Education Project, and input from the cardiology community. The proceedings from this workshop could be used in the development of a Federal plan to address barriers to access to these advanced screening methods. (p. 63)

Action taken or to be taken

Advanced screening methods for cardiovascular disease (CVD), using innovative biomarkers and imaging methods, constitute an area of great scientific opportunity and are the subject of intense NHLBI research activity. Data from the Cardiovascular Health Study, the Framingham Heart Study, the Atherosclerosis Risk in Communities Study, and the Multi-Ethic Study of Atherosclerosis have demonstrated the power of these advanced methods to identify persons at risk for developing overt CVD and the potential for reducing that risk. The NHLBI has convened several recent workshops and working groups in this area, including "The Vulnerable Patient" (December 2005), "Asymptomatic Left Ventricular Dysfunction in the Community: Prevalence, Risk Factors, and Prevention" (August 2005), "Oxidative Stress/Inflammation and Heart, Lung, Blood, and Sleep Disorders" (November 2004), and "Determining the Role of Subclinical Disease Testing in Patients at Intermediate Risk" (July 2004). In addition, the National Institute of Biomedical Imaging and Bioengineering co-sponsored a workshop on "Challenges and Opportunities in Managing High Risk/Vulnerable Atherosclerotic Plaque" (September 2005). Another NHLBI workshop, "Research Needs for C-Reactive Protein," is planned. As was the case with past meetings, we expect this upcoming workshop to incorporate data from the Cardiovascular Health Study, expertise from the National Cholesterol Education Program, and input from the cardiology community. Once the recommendations of these expert groups are available, the NHLBI will evaluate the need for additional workshops to address barriers to access of these advanced screening methods, as well as their appropriate and cost-effective utilization.

Item

Transmissible spongiform encephalopathies -- The Committee encourages the NHLBI to enhance its efforts to develop a diagnostic test for TSE that would be suitable for screening the blood supply. Currently, there is no suitable method for identifying TSE-infected blood. In addition, the Committee encourages the NHLBI to seek new technologies and procedures for inactivating blood-borne causative agents for human TSEs, further ensuring a safe blood supply. Human TSEs, for which there are no known treatments, include Creutzfeld-Jakob disease and new variant Creutzfeldt-Jakob disease. (p. 63)

Action taken or to be taken

The NHLBI and the National Institute of Neurological Disorders and Stroke (NINDS) are jointly supporting an extramural contract program to develop tests to detect TSE. The first two cases of variant Creutzfeld-Jakob disease linked to blood transfusion were reported in the United Kingdom during the past year. These observations align with previous studies in laboratory animals, which have shown that the TSE agents (abnormal prions) are present in blood, but in such low concentrations that current tests are not sensitive enough to detect them. Hence, investigators in the NHLBI/NINDS sponsored program are developing procedures to concentrate TSE agents to levels that can be detected with current assays. A variety of different concentration approaches are being tried. The NHLBI is also supporting a small business grant to develop a methodology that will allow fast and efficient detection of infectious prion proteins prior to the onset of clinical symptoms. The major goal of all these programs is to develop tests that can detect TSEs in asymptomatic individuals and would be suitable for screening the U.S. blood supply.

The NHLBI also acknowledges the need for procedures to inactivate and/or remove abnormal prion proteins from blood and blood components. The Institute is supporting studies in which investigators are developing methods using gamma-irradiation to inactivate prions in plasma-derived protein products while preserving the integrity and function of the products. In addition, the concentration procedures that are being developed for use in combination with TSE assays are also being evaluated as a means of removing or separating infectious prions from blood and blood products.

Item

Scleroderma – The Committee is encouraged by NHLBI's growing interest in scleroderma, a chronic and progressive disease that predominantly strikes women. Scleroderma is disfiguring and can be life-threatening, affecting multiple systems including the heart and lungs. The Committee is pleased that NHLBI funded the Scleroderma Lung Study, a large multi-center trial whose focus is to find a therapy that may alter the course of the inflammation of the lungs that occurs in approximately 40 percent of those diagnosed with the systemic scleroderma. The Committee also commends NHLBI for its commitment to finding a cause and improved therapies for pulmonary arterial hypertension. Pulmonary arterial hypertension occurs in approximately 50 percent of those diagnosed with systemic scleroderma. More research is needed to identify the causes of the complications of scleroderma that include pulmonary fibrosis, pulmonary hypertension, myocardial fibrosis, cardiac arrhythmias, pericarditis, and Raynaud's Phenomenon. (p. 63)

Action taken or to be taken
The NHLBI, in collaboration with the National Institute of Arthritis and Musculoskeletal and Skin Diseases, supported a multi-center clinical trial to evaluate the efficacy of oral cyclophosphamide, an anticancer drug, in stabilizing or improving lung function in scleroderma patients who have active lung inflammation (alveolitis). Thirteen U.S. medical centers enrolled 162 patients. The trial showed that administration of oral cyclophosphamide for one year to patients with systemic scleroderma-interstitial lung disease and evidence of active alveolitis had a modest beneficial effect on lung function, shortness of breath, skin thickening, and health-related quality of life. The results were presented at the international meeting of the American Thoracic Society, May 23, 2005, in San Diego.

The NHLBI continues to support investigator-initiated research on molecular mechanisms that contribute to the development of pulmonary fibrosis in scleroderma patients and also supports an extensive research program in pulmonary hypertension. Moreover, the Institute funds research to elucidate the molecular basis of myocardial fibrosis formation and the role that fibrosis plays in the development of cardiac arrhythmias and heart failure.

Item
National COPD education and prevention program -- The Committee is pleased that NHLBI held a preliminary workshop to formulate strategies towards implementing a national chronic obstructive pulmonary disease (COPD) education and prevention program. Since COPD is the fourth leading cause of death in the United States, the Committee urges NHLBI to continue its education efforts to bring advances in medical care to the public. Early identification of those at-risk for or who have COPD is essential in the effort to stem the growth of the population with COPD. The Committee encourages NHLBI to continue its efforts in this area, working with national lung organizations to develop a national education campaign for providers and the public about COPD. (p. 63)

Action taken or to be taken
As a result of the 2004 workshop, the NHLBI has initiated a 3-year COPD Awareness and Education Campaign. This effort was undertaken to address the top recommendation that emerged from the workshop, namely, to increase knowledge of COPD among people at risk of developing the disease, people who already have the disease, and health care providers. The campaign will highlight the seriousness of COPD, and it will encourage those at risk and those experiencing characteristic signs and symptoms to talk with their health care providers about COPD. The campaign also will educate providers about the rising prevalence of COPD, methods for risk assessment and early detection, and treatment options.

The NHLBI will continue to work with relevant stakeholders—including COPD patients and caregivers, members of advocacy groups, clinicians, representatives of national organizations and coalitions, and federal government representatives—to plan and execute this national effort.

In tandem with the education campaign, the NHLBI will continue to disseminate new advances in COPD research so that they may be applied rapidly by the public and health care providers.

Item

Sleep disorders -- The Committee continues to recommend that the National Center on Sleep Disorders Research partner with other Federal agencies, such as the Centers for Disease Control and Prevention, as well as voluntary health organizations to develop a sleep education and public awareness initiative to serve as an ongoing, inclusive mechanism for public and professional awareness on sleep and sleep disorders. (p. 63)

Action taken or to be taken

The National Center on Sleep Disorders Research (NCSDR) has successfully developed and disseminated programs to expand and enhance its sleep education and public awareness activities. Patients and the public can easily obtain timely information about sleep disorders via the new NHLBI web-based Diseases and Conditions Index (http://www.nhlbi.nih.gov/health/dci). A summary on sleep apnea is now available, and materials on insomnia, restless legs syndrome, and narcolepsy will be posted by spring 2006. A new book for patients and the public, "Your Guide to Healthy Sleep" (NIH Publication Number 06-5271), was recently released. It provides comprehensive information about the importance of sleep across the age span and the health costs of insufficient sleep, tips on how to obtain adequate sleep, and an easy-to-read overview of the four common sleep disorders mentioned above. In June 2005, the NCSDR coordinated a state-of-the-science NIH conference on the diagnosis and management of chronic insomnia. Participants formulated comprehensive treatment recommendations to improve sleep health and quality of life for adults who suffer from this common disorder.

The NCSDR is also collaborating with other federal agencies such as the Center for Disease Control and Prevention (CDC), and with voluntary sleep health organizations such as the National Sleep Foundation (NSF), to enhance sleep literacy and increase public awareness of sleep and sleep disorders. These partnerships are being supported in part through the federal, scientific, and public affiliations of the Sleep Disorders Research Advisory Board (SDRAB). In addition, the NCSDR is working with representatives from the SDRAB (including the CDC) and the major voluntary sleep organizations (including the NSF) to develop a comprehensive education and dissemination program for improving sleep health and awareness. In conjunction with a strategic planning process now under way in the NHLBI, the collaborating partners will establish goals and priorities for new public and professional sleep awareness initiatives in the upcoming several years.

Item

Marfan syndrome -- Marfan syndrome is characterized by aortic aneurysms, painful orthopedic issues, pulmonary issues and ocular manifestations that can result in blindness. The Committee commends NHLBI for its support of research opportunities to study this life threatening, degenerative genetic disorder. Recent advances in basic research are ready to be translated into promising clinical trials. The Committee suggests that NHLBI collaborate with other institutes to support a clinical trial for drug therapies to potentially reverse the cardiovascular and pulmonary manifestations of this disorder. (p. 64)

Action taken or to be taken

The NHLBI recently awarded a contract to establish and maintain a national registry of patients with Marfan syndrome and other connective tissue diseases who are receiving treatment for cardiovascular complications. This registry resulted from discussions with the National Institute

of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) and the National Marfan Foundation and an NHLBI-convened working group to review the current status of thoracic aortic aneurysms related to Marfan syndrome and other genetic disorders. The working group agreed that establishing a registry was a critical initial step in stimulating investigator-initiated research to elucidate pathogenesis and improve treatment for cardiovascular complications of Marfan and other connective tissue diseases. The registry will gather information about patients, care providers, hospitals, and clinical interventions; collect blood and tissue specimens; and maintain a repository of tissue and blood, family pedigrees, and data on extra-cardiac complications. The NHLBI will collaborate with the NIAMS, the National Eye Institute, the National Institute of Dental and Craniofacial Research, and the National Human Genome Research Institute in monitoring the work of the registry to permit development of standardized reporting of patient characteristics, indications for surgical intervention and other treatments, and adverse events. This approach is expected to facilitate clinical evaluation and patient management. The resulting resource should also enhance future research on improving fundamental understanding, treatment, and management of genetic aortic aneurysms and other cardiac and extra-cardiac complications.

The NHLBI Pediatric Heart Network (a multi-center, collaborative clinical research group) is in the process of developing a trial to evaluate pharmacological agents that may slow the process of aortic root enlargement in children and young adults with Marfan syndrome. The trial is expected to start enrolling patients in 2006.

Item

Alpha-1 antitrypsin deficiency -- The Committee is aware that Alpha-1 antitrypsin deficiency is often misdiagnosed as asthma or Chronic Obstructive Pulmonary Disease (COPD). Alpha-1 is a major cause of liver transplantation in adults and children. The Committee recommends the establishment of an inter-institute coordinating committee to facilitate cooperation between NHLBI, NIDDK, NHGRI, and other institutes to enhance the NIH research portfolio, encourage targeted detection, raise public awareness about Alpha-1 and provide appropriate information to health professionals. (p. 64)

Action taken or to be taken

Alpha-1 antitrypsin deficiency (AATD) is one of many diseases for which several NIH institutes and centers share interest and common goals. For best advancement of the science and the most advantageous use of resources, the relevant NIH components with shared interests essentially work together as an inter-institute committee by communicating frequently. This has resulted in a strong and steady history of collaboration.

The NHLBI, the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and the Office of Rare Diseases (ORD) have co-sponsored many activities in areas relevant to AATD. Examples include the conference grants "Therapy for Alpha-1 Antitrypsin Deficiency Conference," "Alpha-1 Antitrypsin Deficiency Conference," and "Alpha-1 Antitrypsin Deficiency: the Challenge of a Genetic Condition"; the workshop "Protein Processing and Degradation in Pulmonary Health and Disease"; and the request for grant applications "Genetic Modifiers of Single Gene Defect Diseases." The workshop on protein processing resulted in a program announcement, TPA-05-190 "Protein Interactions Governing Membrane Transport in Pulmonary Health and Disease"; during its development the draft announcement was shared via the NIH Early Notification System with other NIH components who might be interested in

participating. The NIDDK and the ORD recently supported the expansion of The Biliary Atresia Research Consortium network to include the Cholestatic Liver Disease Consortium, which includes AATD.

In addition, each NIH component with an interest in AATD sponsors activities related to its own mission. Even these activities are strongly interrelated, since particular laboratories or investigators often receive support from both the NHLBI and the NIDDK to study different aspects of the disease. Examples include laboratories at the University of Pittsburgh in Pittsburg, Pennsylvania and at the University of Florida in Gainesville, Florida.

The NHLBI and the NIDDK recognize the need for improved understanding, awareness, and treatment of this condition, and both work with the Alpha One Foundation on public awareness and education. The Institutes will continue their cooperation with investigators, clinicians, patient advocates, and other components of the NIH to improve detection and treatment of AATD.

Item

Duchenne muscular dystrophy(DMD) -- The Committee is pleased that NLHBI has enhanced its research and related activities surrounding pulmonary complications associated with DMD and urges the Institute to continue to enhance its work in this area. The Committee hopes that NHLBI will become more involved with NIH muscular dystrophy activities by joining the Muscular Dystrophy Coordinating Committee. (p. 64)

Action taken or to be taken

The NHLBI continues to support basic studies on cardiac abnormalities associated with Duchenne muscular dystrophy (DMD) and other familial cardiomyopathies. The Institute also supports pulmonary research on respiratory muscle weakness in muscular dystrophy, including studies of how force is generated by muscle cells, how regulatory molecules (e.g., oxygen, nitric oxide, tumor necrosis factor alpha) control the contractile ability of respiratory muscles, and how inflammation causes loss of muscle proteins and weakness.

In concert with other NIH components, the NHLBI recently participated in a number of activities to foster research on the myopathic diseases:

- The National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Institute of Neurological Disorders and Stroke, the National Institute of Child Health and Human Development, and the NHLBI issued a program announcement to study pathogenesis of the muscular dystrophies and explore therapeutic approaches. An application proposing to investigate respiratory muscle physiology has resulted.
- The Office of Rare Diseases (ORD) and the NHLBI solicited applications for exploratory and developmental research grants to investigate rare diseases. At least one grant application to study muscular dystrophy has been submitted.
- In March 2005 the NHLBI, in cooperation with the ORD, brought together scientists and clinicians involved in research on childhood cardiomyopathies associated with rare diseases, such as DMD, to provide advice on research opportunities that may lead to better understanding and treatment. A summary of the working group meeting is posted on the NHLBI Web site.

NHLBI staff participated in meetings of the NIH Muscular Dystrophy Coordinating Committee and helped develop the new NIH Muscular Dystrophy Scientific Working Group. NHLBI director Dr. Elizabeth Nabel will participate in future meetings of the Coordinating Committee.

Item

Novel targets and therapy development for clot-based stroke -- The Committee recognizes that an urgent need exists to develop new therapies to reduce bleeding risk and minimize brain damage and loss of function from stroke. The Committee encourages NHLBI to consider initiating a collaborative effort to identify new molecular targets, explore promising agents, and develop innovative therapies to quickly restore blood flow to the brain to limit stroke damage. (p. 64)

Action taken or to be taken

The NHLBI is committed to the search for new therapies to improve the management of clot-based (ischemic) stroke. In fiscal year 2005 the NHLBI, in collaboration with the National Institute of Neurological Disorders and Stroke (NINDS), solicited grant applications for a new program titled "Novel Targets and Therapy Development for Ischemic Stroke." In addition, in March, 2005 the NINDS and the NHLBI, in partnership with the Canadian Stroke Network (CSN), organized a workshop to address the roles of inflammation and immunity in stroke and to identify anti-inflammatory strategies for stroke prevention and treatment. Expert recommendations from the workshop will help guide future efforts in stroke. The NHLBI and the NINDS participate in the ongoing Trans-NIH Stroke Working Group to foster better communication and collaboration on
stroke. The NHLBI is actively pursuing with the NINDS and the Trans-NIH group additional efforts to improve knowledge of brain hemostasis, understand stroke in patients with sickle cell disease, and develop therapeutic options for preserving brain function without triggering serious bleeding complications.

Item

Nontuberculous mycobacteria [NTM] -- Mycobacteria are environmental organisms found in both water and soil that can cause significant respiratory damage. The Committee is aware of the increasing incidence of nontuberculous mycobacteria [NTM] pulmonary infections in women, particularly involving rapidly growing mycobacteria, an inherently resistant subspecies. The Committee encourages NHLBI to collaborate with NIAID and other institutes leading to a better understanding of NTM and enhancing diagnostics and treatment and promoting appropriate education of health care providers. (p. 64)

Action taken or to be taken

NHLBI and NIAID staff have established an ongoing communication regarding NTM research. A joint meeting is scheduled with NTM Info and Research, Inc., an advocacy group, and interested investigators from the tuberculosis and pulmonary communities to discuss issues associated with NTM research. In addition, the NHLBI is planning a workshop, "Research Needs in Bronchiectasis," in fiscal year 2006. (NTM is often associated with bronchiectasis, a chronic widening of the bronchial tubes that can lead to serious lung damage.) The workshop will bring together experts in the fields of pulmonology, mycobacterial and other infectious diseases, immunology, and basic sciences to summarize the state of the field and identify research needs and priorities. NHLBI staff also serve as liaisons to the NIH Rare Diseases

Clinical Research Network program, which included a rare lung disease consortium on ciliary dyskinesia, a condition that predisposes to bronchiectasis associated with NTM and other chronic bacterial infections.

Item

Lymphangioleiomyomatosis (LAM) -- The Committee remains very interested in efforts to find a cure for LAM, a progressive and often fatal lung disease of women with no effective treatment. The Committee understands that very recent scientific findings have presented new treatment approaches for clinical testing, and that experimental trials with the drug sirolimus have begun. The Committee encourages NHLBI to explore opportunities for funding clinical treatment trials through both intramural and extramural means and to use all available mechanisms as appropriate, including support of state-of-the-science symposia, request for applications, and facilitating access to human tissues, to stimulate a broad range of clinical and basic LAM research. (p. 65)

Action taken or to be taken

The National Heart, Lung, and Blood Institute (NHLBI) intramural program continues to support the collection, processing, and distribution of LAM tissue. NHLBI-supported basic research into the origins of LAM cells is providing insights that might someday lead to blocking their development. Furthermore, success has been achieved in growing cells from a LAM-associated kidney tumor in cell culture, which conserves scarce lung LAM cells. LAM cells have also been grown from LAM lung and from the skin tumors found in patients with tuberous sclerosis complex (TSC). Proteins have been identified that promote the growth and movement of these LAM cells, and this knowledge may improve understanding of why LAM cells can spread among different organs, including the lungs, kidneys, and lymphatics. More is being learned about the role of estrogen and why LAM affects women almost exclusively. Since the pathways affected in LAM are important in most human tissues, such as in the proliferation of smooth muscle in atherosclerosis and in some cancers, the knowledge gained by studying LAM may also help in understanding and treating other diseases. NHLBI intramural investigators have been able to isolate LAM cells from blood and other body fluids, facilitating the genetic diagnosis of the disease.

NHLBI-funded scientists elucidated the cellular pathways affected by genetic abnormalities in TSC and LAM cells and found that a protein needed to control cell size and growth was missing or misshapen. This discovery quickly led to a potential target for the treatment of LAM when it was discovered that sirolimus (rapamycin) mimics the function of the missing protein. A promising pilot study of sirolimus treatment for TSC and LAM, sponsored by the National Cancer Institute through the Quick Trial Initiative, has led to development of a larger, more definitive multicenter trial under the auspices of the Rare Lung Diseases Consortium supported by the Office of Rare Diseases and the National Center for Research Resources. In addition, laboratory studies of LAM cell lines derived from patients show that cells from different individuals appear to vary in their sensitivity to sirolimus. This suggests that some patients might respond to treatment better than others, emphasizing the need to understand the causes of LAM and to identify other possible treatment targets.

In LAM lung, there is increased production of proteins called matrix metalloproteinases (MMPs), which cause the destruction of the lung. A collaborative extramural-intramural clinical trial is being planned to test whether inhibition of MMPs is safe and improves lung function in patients with LAM.

Information on LAM research is exchanged and discussed at trans-NIH TSC coordinating committee meetings, organized by the National Institute of Neurological Diseases and Stroke.

FY 2006 Senate Appropriations Committee Report Language (S. Rpt 109-103)

Item

Bleeding and Clotting Disorders -- The Committee commends NHLBI for its leadership in advancing research on bleeding and clotting disorders and their complications. The Committee encourages NHLBI to maintain its work in this area and applauds the Institute for its efforts, in cooperation with the National Hemophilia Foundation, to support research on improved and novel therapies for these disorders. (p. 97)

Action taken or to be taken

During fiscal year 2005 the NHLBI, in collaboration with the National Hemophilia Foundation (NHF), implemented a new program titled Improved Therapy for Hemophilia and Hereditary Bleeding Disorders, which was designed to stimulate innovative research in this area. The Institute plans to continue to work with the NHF to identify and address the needs of the bleeding and clotting disorders community.

Item

Bone Marrow Failure Diseases -- The Committee encourages NHLBI to expand its research efforts into bone marrow failure diseases, including aplastic anemia (AA), myelodysplastic disorders (MDS), and paroxysmal nocturnal hemoglobinuria (PNH). Each year, in some cases, MDS, the most prevalent of these diseases, can progress over time to become acute leukemia. More research is critically needed to understand the causes of these diseases, to develop effective treatments and cures, and to prevent the progression of certain cases into leukemia. (p. 97-98)

Action taken or to be taken

Three recent NHLBI-initiated research programs are seeking to uncover critical genetic, biochemical, and molecular pathways that operate in the development of bone marrow failure diseases and to identify the mechanisms of disease mutagenesis, evolution, and progression. During fiscal year 2005, nine research grants were funded via the request for applications (RFA) "Myelodysplastic Syndrome: Seeking Cure through Discovery on Pathogenesis and Disease Progression," and eight awards were made under a second RFA, "Cellular and Genetic Discovery toward Curative Therapy in Myeloproliferative Disorders." Some of the grants comprise studies of basic stem cell biology, which may uncover the mechanisms of stem cell mutagenesis, abnormal proliferation, and deregulated cellular physiology. Others propose to identify biomarkers for these diseases in the expectation that this knowledge will enable improved disease characterization, early diagnosis, and identification of molecular targets that may be exploited for preventative or therapeutic intervention. In fiscal year 2004, 16 research grants were awarded in response to an NHLBI solicitation on congenital bone marrow failure

syndromes. These awards focus on diseases such as Diamond-Blackfan anemia, dyskeratosis congenital, severe congenital neutropenia, Shwachman-Diamond syndrome, and congenital amegakaryocytic thrombocytopenia, thus increasing NHLBI's portfolio of investigations on rare bone marrow deficiency disorders.

The NHLBI, in conjunction with the NIH Office of Rare Diseases and the National Cancer Institute, jointly sponsored the Bone Marrow Failure Scientific Symposium in October 2005 in Washington, D.C. This conference was organized by the Aplastic Anemia and MDS International Foundation, and it focused on aplastic anemia, paroxysmal nocturnal hemoglobinurea, and myelodysplastic syndrome. The agenda provided an opportunity for researchers from around the world to discuss the etiology, genetics, pathophysiology, and immunological mechanisms of bone marrow failure, as well as the most current treatment approaches.

Item

Cardiothoracic Surgery – The Committee recognizes the contributions of cardiothoracic surgery to the improvement in cardiac health in this country and looks forward to the advances that will come from further clinical research in the field. The Committee is encouraged by the steps the Institute is taking to establish a network for cardiothoracic surgical investigations, and urges rapid implementation of this plan with sufficient funding to continue the progress being made in the treatment of heart disease. (p. 98)

Action taken or to be taken

The NHLBI will release a Request for Applications for funding in FY 2007 to develop a network to evaluate new surgical techniques, technologies, devices, and bioengineered products through rigorous phase I and II clinical trials. The network will coordinate multidisciplinary teams and facilitate recruitment of sufficient numbers of patients, particularly those with rare conditions, to yield meaningful study results. Anticipated research topics include new surgical techniques for mitral valve repair, robotically assisted cardiac surgery, next-generation ventricular assist devices, neuroprotective strategies in patients undergoing cardiopulmonary bypass, minimally invasive surgical techniques, and cell therapy as an adjunct to surgery.

Item

Cardiovascular Diseases -- The Committee continues to strongly urge the Institute to place the highest priority on research for heart disease, stroke and other cardiovascular diseases. Therefore, the Committee urges the NHLBI to expand its research portfolio and increase its resources into the causes, cure, prevention and treatment of cardiovascular diseases. The Committee remains concerned that funding over the years for cardiovascular disease research has not kept pace with the scientific opportunities available, the number of Americans afflicted with cardiovascular diseases, or their economic toll. The Committee urges NHLBI to expand existing studies and to invest in promising initiatives. (p. 98)

Action taken or to be taken

The NHLBI supports clinical, epidemiological, and basic research in the causes, prevention, and treatment of cardiovascular diseases (CVDs), including large clinical trials involving patients with coronary artery disease, heart failure (HF), arrhythmias, and sudden cardiac death. Three major ongoing trials address ways to prevent and treat CVD in patients with type 2 diabetes (BARI-2D, ACCORD, and the FREEDOM trial). Other ongoing trials include STICH

(assessing the benefits of coronary artery bypass surgery and surgical reshaping of the heart in selected HF patients), ACES (investigating use of an antibiotic to prevent coronary events in patients with coronary artery disease), Heart Failure-ACTION (testing the effect of aerobic exercise training in patients with HF). A new trial TOPCAT will evaluate aldosterone agonist therapy in HF patients who have preserved systolic cardiac function a large and heretofore understudied group of patients. In collaboration with the Department of Defense, the NHLBI recently established a network for research on improving resuscitation outcomes. Additional networks for research in HF, cardiovascular surgery, and cell-based therapy are planned for 2006 and beyond. The NHLBI has recently expanded its programs into an effort to understand and remedy the cardiovascular health disparities that are manifest in higher prevalence of hypertension and other cardiovascular conditions, less effective treatment and poorer outcomes among African Americans. A new initiative has funded research partnerships between academic institutions and minority-serving clinics to develop strategies to improve cardiovascular health outcomes in African Americans and other minorities. Ongoing epidemiologic studies to document CVD risk in population subgroups are the Framingham Heart Study, the Multi-Ethnic Study of Atherosclerosis (in whites and Americans of African, Hispanic, and Chinese heritage), the Strong Heart Study of American Indians, the GOCADAN study of Alaskan Natives, and the Jackson Heart Study of African Americans in Mississippi. A new program is investigation risk of CVD in Mexican Americans, Puerto Ricans, Cubans, and Central Americans.

Lifestyle and behavioral interventions to prevent CVD are a major focus, and research includes development of strategies to enhance delivery of guideline-based therapy for CVD risk factors and improve patient adherence to treatments, clinical trials to evaluate weight control methods in various populations and settings, assessment of a school-community linked approach to prevent the decline in physical activity that girls experience during adolescence, and testing of health promotion methods for Native American communities.

The NHLBI also remains at the forefront of expansion into new promising areas using advanced technologies. The NHLBI's basic CVD research addresses innovative therapies for transfer of cells and genes; new circulatory assist devices for infants; improved imaging methods to diagnose CVD more reliably, less invasively, and at earlier stages; application of nanotechnology to diagnose and treat CVD; proteomics to identify biomarkers of CVD; tissue engineering to produce small-diameter, functional, blood vessels; genome-wide association studies on CVD; advanced computational tools to study the biology of complex systems; and exploration of the role of nutrition and diet in the causation and treatment of heart failure.

Item

Cardiovascular Disease, Hypertension, and Kidney Disease -- The Committee is aware that chronic kidney dysfunction is an important risk factor for the development of cardiovascular disease. Additionally, hypertension, or high blood pressure, is the second leading cause of end-stage renal disease [ESRD], accounting for 23.6 percent of ESRD patients. ESRD and kidney dysfunction together affect millions of Americans and is especially prevalent among elderly persons, African-Americans and patients with diabetes. Given the significant morbidity and mortality associated with cardiovascular disease among patients with kidney disease, the Committee recognizes the urgency to examine the relationship between cardiovascular disease and kidney disease. The Committee encourages NHBLI and NIDDK to work together to develop appropriate basic and clinical research initiatives addressing the pathogenesis of

cardiovascular events in patients with kidney disease, while exploring therapeutic and preventive interventions. The Committee also encourages NHBLI to work with the renal community to support ongoing educational programs directed to health professionals, patients and the public to raise the awareness of the relationship between cardiovascular disease, hypertension and kidney disease. (p. 98)

Action taken or to be taken

The NHLBI and the NIDDK have long worked together on the relationship between kidney disease and cardiovascular disease (CVD). Representatives of both institutes participated in the National Kidney Foundation Task Force on CVD, which published its report in 1998. The institutes co-sponsored in 2003 a "Workshop on CVD in Chronic Kidney Disease (CKD): Options for Intervention,"which led to intensified scientific interest in the interactions between kidney disease and CVD. Since this meeting, senior staff of the two institutes met to address progress and directions in this research arena, and they will continue to meet in the future. The NHLBI and the NIDDK also coordinate basic research activities via the federal Kidney, Urologic, and Hematologic Diseases Interagency Coordinating Committee, which is led by the NIDDK with active participation of the NHLBI. Over the past few years, the NHLBI has, with NIDDK representation, convened working groups designed to further understanding of heart–kidney interactions in CVD. The active interaction has ensured that oversight of studies of cardiovascular disease, sponsored by NHLBI, and studies of kidney disease, sponsored by NIDDK, utilize expertise in both disease areas, and that both renal and cardiovascular endpoints are assessed. For example, the NHLBI has provided technical expertise in the design of NIDDK's Chronic Renal Insufficiency Cohort (CRIC) Study: this study will assess the impact of progressive renal insufficiency on the cardiovascular system. Measures of kidney function have been incorporated into a number of studies sponsored by NHLBI, such as the ACCORD study, which examines the effect of blood pressure, glycemic control and lipid management in a large sample of patients with Type 2 diabetes. An important current effort is a joint program announcement to encourage investigator-initiated proposals for conducting ancillary studies within such ongoing major clinical research studies, with one specific area of emphasis being clarification of the cardiovascular risk factors in the kidney disease population. The NHLBI is a cosponsor of a new NIDDK program announcement, "Pilot and Feasibility Program Related to the Kidney," designed to foster rapid testing of innovative approaches to problems in acute and chronic kidney disease. The NIDDK has an agreement with the NHLBI to co-fund the Hispanic Community Health Study, which will identify the prevalence of and risk factors for heart and kidney diseases. The NIDDK is cosponsoring an NHLBI program announcement that encourages small businesses to develop a practical, non-invasive, rapid screening test for abnormal increases in blood pressure subsequent to salt ingestion.

Since the inception of the National High Blood Pressure Education Program (NHBPEP) the relationship of hypertension to CKD has been a focus, and several actions have been developed to promote the message that controlling hypertension prevents or slows the progression of kidney disease. The NHBPEP Coordinator serves as a member of the National Kidney Diseases Education Program (NKDEP) and as a consultant to NKDEP staff regarding their education and outreach activities. The NKDEP Director, in turn, serves on the NHBPEP Coordinating Committee and has contributed substantially to NHLBI guidelines on prevention and management of high blood pressure and on hypertension and renovascular diseases. NKDEP materials for patients, providers, and the public are consistent with NLHBI messages and seek to

increase awareness of kidney disease risk factors, the importance of testing those at high risk, and the availability of reno-protective treatments. In addition, the NHLBI staff review the National Kidney Foundation (NKF) clinical guidelines on detection and management of renal disease, and the Web sites of the NKDEP, NKF and NHLBI are linked. These collaborative efforts ensure that one common message is being developed and translated to clinicians and the public.

Item

Cardiovascular Disease With Juvenile Diabetes -- The Committee commends NIDDK and NHLBI for their efforts in developing new opportunities for studies on the pathogenesis of cardiovascular disease complications among patients with juvenile diabetes, and to evaluate opportunities for intervention studies to reduce CVD complications among patients with juvenile diabetes. The Committee encourages the Institutes to closely monitor research progress in this field and to continue to promote the clinical translation of research findings into new therapies. (p. 98)

Action taken or to be taken

During fiscal year 2004, the NHLBI initiated a research program to investigate the effects of inflammation, hyperglycemia, insulin resistance, hypertension, and dyslipidemia on the early development and rate of progression of CVD in patients with type 1 (juvenile) diabetes. In March 2005, the NHLBI convened a meeting with the investigators funded under this program to report on research progress and to promote information exchange and scientific collaboration. Representatives from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and the Juvenile Diabetes Research Foundation (JDRF) also participated. This program is expected to produce research findings that will facilitate identification of the causes of CVD complications in patients with type 1 diabetes and provide a basis for development of more effective interventions to prevent or postpone CVD complications.

In January 2005, the NHLBI participated in a 2-day meeting convened by the NIDDK on the "Special Statutory Funding Program for Type 1 Diabetes Research." As a result of this meeting, the Diabetes Mellitus Interagency Coordinating Committee is developing a strategic planning effort for type 1 diabetes research. The NHLBI is part of the Executive Committee and a member of the working group on research to prevent or reduce complications of type 1 diabetes.

The NHLBI continues to work with the NIDDK on new programs to stimulate research on the CVD complications of type 1 diabetes. Recently, the NHLBI participated in two NIDDK initiatives: "Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) to Develop New Therapeutics and Monitoring Technologies for Type 1 Diabetes and its Complications" and "Mouse Metabolic Phenotyping Centers Consortium," which will characterize mouse models for studying obesity and diabetes.

The NHLBI is also working with other funding agencies. For instance, NHLBI scientists recently participated in a workshop sponsored by the American Diabetes Association (ADA) and the JDRF on "Delineating the Similarities and Differences Between the Complications of Type 1 and Type 2 Diabetes." Attendees were asked to identify new opportunities and key areas of need in research; the outcome of their deliberations is expected to assist the funding agencies in working together productively and in focusing their individual and collaborative research activities.

Item

Chronic Obstructive Pulmonary Disease (COPD) National Education and Prevention Program -- The Committee is pleased that NHLBI held a preliminary workshop to formulate strategies toward implementing a National Chronic Obstructive Pulmonary Disease (COPD) Education and Prevention Program. Since COPD is the fourth leading cause of death in the United States, the Committee urges the NHLBI to continue its education efforts to bring advances in medical care to the public.

Early identification of those at-risk for or who have COPD is essential in the effort to stem the growth of the population with COPD. The Committee encourages NHLBI to continue its efforts in this area, including working with national lung organizations such as the American Thoracic Society and the American Lung Association to develop a national education campaign for providers and the public about COPD. (p. 98/99)

Action taken or to be taken

Please refer to page NHLBI-35 of this document for NHLBI's response to this significant item regarding Chronic Obstructive Pulmonary Disease (COPD) National Education and Prevention Program.

Item

Cooley's Anemia -- The Committee remains strongly supportive of the focused research effort that is being undertaken by the Thalassemia Clinical Research Network, which is comprised of the leading research institutions in the field of thalassemia, or Cooley's anemia. The Committee believes that this network is just beginning to meet its promise and urges the Institute to continue it and support the research projects undertaken by it. (p. 99)

Action taken or to be taken

Please refer to page NHLBI-33 of this document for NHLBI's response to this significant item regarding Cooley's Anemia.

Item

Down Syndrome -- The Committee encourages NHLBI to review the causes of congenital heart disease in children with Down Syndrome. Studies should also be encouraged in analyzing the increased risk of leukemia in persons with Down Syndrome. (p. 99)

Action taken or to be taken

The NHLBI funds a variety of research on congenital heart disease in children with Down syndrome. During the past year, as part of its multicenter Pediatric Heart Network, the Institute supported a study of drug therapy after surgery for a specific type of heart disease (atrioventricular septal defect) that affects a significant number of children with Down syndrome. The NHLBI has also supported two research projects on the role of Down syndrome-associated genes in heart development and congenital heart disease, one of which is being conducted in a Specialized Center of Clinically Oriented Research. In addition, the NHLBI research portfolio includes over 100 grants to study heart development at the cellular and molecular levels, which should provide information about abnormal heart development in all

children, including those with Down syndrome. Research related to the risk of hematologic malignancies, including leukemia, in persons with Down syndrome is within the mandate of the National Cancer Institute.

Item

Duchenne Muscular Dystrophy -- The Committee is pleased that NLHBI has enhanced its research and related activities surrounding cardiac complications associated with DMD and urges the Institute to continue to expand and enhance this work going forward. The Committee urges NHLBI to become more involved with NIH Muscular Dystrophy activities by joining the Muscular Dystrophy Coordinating Committee. (p. 99)

Action taken or to be taken

Please refer to page NHLBI-38 of this document for NHLBI's response to this significant item regarding Duchenne Muscular Dystrophy.

Item

Heart Failure Clinical Research Network -- The Committee is concerned that, in spite of advances in treatment, both the number of newly diagnosed cases and the number of Americans suffering from heart failure continues to grow, while the long-term prognosis for patients still remains poor. The Committee urges the NHLBI to initiate a planned research network to conduct clinical studies using burgeoning new approaches to improve outcomes for heart failure patients, and provide an infrastructure to enable rapid translation of promising research findings into enhanced patient care. The network would have the capability of implementing multiple concurrent clinical studies that may show promise for new therapies and provide background for larger clinical trials. (p. 99)

Action taken or to be taken

Establishment of the NHLBI Heart Failure Clinical Research Network is well under way. The Network will consist of up to eight regional clinical centers in North America and one data coordinating center. Working in concert with each other and with the NHLBI, the Network participants will expedite clinical research to improve the diagnosis, management, and treatment of heart failure. The infrastructure will allow flexibility for exploring promising new avenues of clinical research on heart failure, as they become apparent, as well as for optimizing existing therapies. Moreover, emerging discoveries in basic science will be evaluated for their clinical usefulness. Examples of possible approaches include clinical trials of cell-based treatments and of novel biomarkers for early diagnosis and assessment of therapy. Five-year awards will be made to successful applicants in mid-2006.

Item

Hemoglobinopathies – Sickle cell anemia and thalassemia are inherited blood disorders caused by mutations in the genes for the hemoglobin molecule, the protein in red blood cells that carries oxygen to all parts of the body. These conditions cause many problems including moderate to severe anemia, chronic pain, iron overload with its associated diabetes, liver and heart failure, enlarged spleen, bone weakness, pulmonary hypertension, and stroke. The Committee recognizes NHLBI's continued commitment to invest in basic and clinical research in sickle cell anemia and thalassemia, and encourages NHLBI to sponsor a conference of experts to develop a report focused on the science and management issues that are common to these

hemoglobinopathies. The Committee supports a cooperative effort to identify areas of scientific collaboration and promising new research directions in sickle cell anemia and thalassemia. (p. 99-100)

Action taken or to be taken
On June 29, 2005, a panel of 18 scientific experts, along with representatives from the Sickle Cell Disease Association of America, the Cooley's Anemia Foundation, the National Institute of Diabetes and Digestive and Kidney Diseases, and the NHLBI, met to discuss scientific and management issues that are common to sickle cell disease (SCD) and thalassemia. Major areas of interest were the following:

- chronic transfusion therapy and management of iron overload
- treatment of pulmonary arterial hypertension
- development of agents that can increase fetal hemoglobin levels in the red cell
- creation of genotype/phenotype databases
- development of clinical registries for the diseases
- determination of the roles of zinc and other nutrients in the formation of bone mass.

In 2006 three major research networks will be in place to study SCD and thalassemia. Establishment of a Hemoglobinopathies Coordination Committee (HCC) is planned to oversee and facilitate, where appropriate, collaboration between the networks on clinical studies. The HCC will be composed of investigators involved in SCD and thalassemia research. Representatives from the network steering committees will also serve on the HCC and HCC members, in turn, will serve on the network steering committees. The NHLBI will provide guidance to the NCC and assist in its coordination activities.

Item
Hemophilia – The Committee commends the NHLBI for its leadership in advancing research on bleeding and clotting disorders and the complications of these disorders. The Committee encourages the NHBLI to maintain its work in this area and support research on improved and novel therapies. (p. 100)

Action taken or to be taken
The NHLBI is committed to advancing research in diagnosis and treatment of bleeding and clotting disorders and to reducing their associated medical complications. In collaboration with the National Hemophilia Foundation, the Institute has implemented a new RFA program titled Improved Therapy for Hemophilia and Hereditary Bleeding Disorders. The NHLBI and the National Institute of Neurological Disorders and Stroke have issued another RFA, Novel Targets and Therapy Development for Ischemic Stroke, and plan to fund several meritorious grants under this program in FY 2006. A Specialized Center of Clinically Oriented Research (SCCOR) program in Hemostatic and Thrombotic Disorders will be funded by the NHLBI in early FY 2006 to support clinical and basic research for improved prevention, diagnosis and treatment of thrombotic and bleeding disorders. The NHLBI plans to continue working with other organizations and NIH components on research to improve knowledge and therapeutic options for bleeding and clotting disorders.

Item

Innovative Technologies for Engineering Small Blood Vessels -- The Committee understands that the supply of natural blood vessels for multiple grafts does not meet the demand for patients undergoing heart bypass surgery, and that prosthetic grafts for children born with complex heart defects fail at an unacceptable rate. To advance the development of substitutes for natural blood vessels, the Committee urges the NHLBI to continue to invest in research to address this matter. (p. 100)

Action taken or to be taken

Please refer to page NHLBI-32 of this document for NHLBI's response to this significant item regarding Innovative Technologies for Engineering Small Blood Vessels.

Item

Lung Cancer -- Chronic Obstructive Pulmonary Disease [COPD] is the fourth leading cause of death in the United States. Lung cancer was the leading cancer killer in both men and women in 2005. The Committee understands that COPD may be a predictor of future onset of lung cancer. With 24 million people having decreased lung function, and in the face of an ever-aging population, the need to develop better treatment and prevention strategies to address this linkage will only increase over the coming decade. The Committee encourages NHLBI to collaborate more extensively with NCI to develop appropriate research initiatives that can be undertaken cooperatively, and encourages NHLBI to sponsor a workshop on COPD as it relates to lung cancer with input from the lung community. (p.100)

Action taken or to be taken

COPD and lung cancer are related conditions due, in the majority of cases, to long-term cigarette smoking. Decreased lung function, the primary manifestation of COPD, is associated with increased risk of lung cancer, and it is possible that the lung inflammation seen in COPD predisposes patients to develop lung cancer. In fact, lung cancer was the most common cause of death among study participants with COPD who were followed in the long-running NHLBI-sponsored Lung Health Study. It is conceivable that interventions to interrupt the inflammatory process might work to prevent both diseases.

The NHLBI is encouraging research in this area. Expert guidance regarding promising research directions was obtained from two working groups -- "COPD and Lung Cancer" and "Clinical Research in Chronic Obstructive Pulmonary Disease" -- convened by the NHLBI in March 2002. The latter group recommended basic research to identify common cellular and molecular mechanisms in COPD and lung cancer and clinical research to investigate possible similarities in genetic susceptibility and assess the efficacy of chemopreventive interventions. Since that time progress has been made in these areas. The Lung Tissue Research Consortium, recently established to collect and distribute lung tissue specimens for research use, will allow molecular comparisons of lung tissues from COPD patients who have or do not have lung cancer. With regard to clinical research, discussions are under way between staff of the NHLBI and the NCI regarding possibilities for chemoprevention trials that would include outcome measures related to both diseases.

Item

Marfan Syndrome -- The Committee commends the NHLBI for its support of research on this life-threatening, degenerative genetic disorder, which is characterized by aortic aneurysms and dissections, painful orthopedic issues, pulmonary issues and ocular manifestations that can result in blindness. Years of basic research are ready to be translated into a clinical trial for a drug therapy that may potentially prevent aneurysm development, which may benefit not only the Marfan population but thousands of people who are afflicted with genetically triggered aneurysms and others with similar connective tissue disorders. The Committee urges the NHLBI to support this effort through all available mechanisms, as deemed appropriate. (p. 100)

Action taken or to be taken

Please refer to page NHLBI-36 of this document for NHLBI's response to this significant item regarding Marfan Syndrome.

Item

Novel Targets and Therapy Development for Clot-based Stroke -- The Committee recognizes that an urgent need exists to develop new therapies to reduce bleeding risk and minimize brain damage and loss of function from stroke. The Committee encourages NHLBI and the National Institute of Neurological Disorders and Stroke to initiate a planned collaborative effort to identify new molecular targets, explore promising agents, and develop innovative therapies to quickly restore blood flow to the brain to limit stroke damage. (p. 100-101)

Action taken or to be taken

Please refer to page NHLBI-39 of this document for NHLBI's response to this significant item regarding Novel Targets and Therapy Development for Clot-based Stroke.

Item

Pulmonary Fibrosis -- The Committee urges the NHLBI to increase funding for lung research, particularly in the area of pulmonary fibrosis, a disease that is terminal and for which there is currently no effective treatment. (p. 101)

Action taken or to be taken

NHLBI funding for pulmonary fibrosis has grown to $14 million in fiscal year 2005, an increase of 94 percent since fiscal year 2003. This expansion was stimulated by recommendations from the NHLBI-sponsored workshop "Future Research Directions in Idiopathic Pulmonary Fibrosis," which provided impetus for two initiatives. First is a research program to discover and validate new molecular targets involved in fibrosis formation in idiopathic pulmonary fibrosis (IPF). Investigators are studying IPF patients or samples of human tissue to identify these targets and the agents that might interact with them to inhibit fibrosis formation. Five grants have been awarded for this work. Second is the IPF Clinical Research Network, consisting of 11 clinical centers and a data and coordinating unit, which will evaluate combinations of existing drugs that might attack the fibrosis process at multiple points and stabilize or reverse the disease. Protocol development is under way, and the Network expects to begin enrolling IPF patients into a multiple-drug placebo-controlled clinical trial in June 2006.

Item

Pulmonary Hypertension -- Pulmonary Hypertension [PH] is a rare, progressive and fatal disease that predominantly affects women, regardless of age or race. PH causes deadly deterioration of the heart and lungs and is a secondary condition in many other serious disorders such as scleroderma and lupus. The Committee continues to view research in this area as a high priority and commends NHLBI's efforts to promote PH related research. For fiscal year 2006, the Committee encourages the Institute to increase funding for basic research, gene therapy and clinical trials of promising pharmaceuticals, and to take appropriate measures to ensure the submission of high quality proposals in this area. (p. 101)

Action taken or to be taken

During fiscal year 2005, the NHLBI supported more than 80 projects on PH, including studies of basic cell and molecular biology, efforts to identify the gene(s) and gene mutations that influence development of PH, and multidisciplinary program projects combining basic and patient-based research. One such study is gathering genetic information on patients with PH in a search for causative gene–environment interactions. The intramural division of the Institute supports two clinical trials to examine the underlying mechanisms of PH in patients with sickle cell anemia. A working group was convened in October 2005 to discuss cellular and molecular mechanisms of right heart failure, a leading cause of death among PH patients. Participants considered strategies for determining how and why right heart failure develops, and they provided several recommendations for basic and clinical research to improve diagnosis and treatment.

A new program announced in 2005 will support Specialized Centers of Clinically Oriented Research (SCCOR) in Pulmonary Vascular Disease. These cooperative research projects will integrate basic science approaches to study disease mechanisms and clinical research for adult and pediatric PH.

The NHLBI continues to receive investigator-initiated basic and clinical grant applications on PH. Institute staff will actively encourage the submission of new applications in both basic and clinical research on PH and maintain its collaboration with the Pulmonary Hypertension Association to support young clinical investigators pursuing research careers in PH.

Item

Sleep Disorders -- The Committee continues to urge the National Center on Sleep Disorders Research to partner with other Federal agencies, such as the Centers for Disease Control and Prevention, as well as voluntary health organizations, such as the National Sleep Foundation to develop a sleep education and public awareness initiative to serve as an ongoing, inclusive mechanism for public and professional awareness on sleep and sleep disorders. (p. 101)

Action taken or to be taken

Please refer to page NHLBI-36 of this document for NHLBI's response to this significant item regarding Sleep Disorders.

Item

Specialized Centers of Clinically Oriented Research [SCCOR] for Vascular Injury, Repair, and Remodeling -- Vascular diseases result from clogged, weakened or otherwise damaged blood vessels. The Committee encourages the NHLBI to initiate a planned new SCCOR program to conduct interdependent clinical and multidisciplinary basic research projects on the molecular and cellular mechanisms of vascular injury, repair, and remodeling. This program

would promote patient-oriented research to improve prevention, detection, and treatment of vascular diseases, such as heart attack and stroke. The SCCOR would provide resources to enable new clinical investigators to develop skills and research capabilities to conduct relevant research in this area. (p. 101)

Action taken or to be taken
Please refer to page NHLBI-32 of this document for NHLBI's response to this significant item regarding Specialized Centers of Clinically Oriented Research [SCCOR] for Vascular Injury, Repair, and Remodeling.

Item
Thrombosis and Thrombophilia -- The Committee is very concerned about the basic science of thrombosis and thrombophilia, major cause of death and disability in this country. The Committee strongly urges the Institute to expand its support for basic research into their underlying causes in order to improve diagnosis and treatment for these conditions. The committee also strongly urges the Institute to support this research and urges collaboration with the thrombophilia centers funded by CDC. (p. 102)

Action taken or to be taken
The NHLBI recognizes the need to expand support for research in thrombophilia and thrombosis and, in June 2005, convened a working group of experts to discuss the state of the art and set research priorities. A representative from the CDC attended the meeting and described its thrombophilia program. After extensive discussion, the working group generated a set of recommendations addressing four topics: deep vein thrombosis and pulmonary embolism, multi-institute clinical studies, basic sciences studies, and future technology development for exploration of the genomic basis of risk of thrombosis. These expert recommendations will form a basis for future NHLBI action to expand research and pre-clinical studies in this area.

Item
Vascular Biology -- The Committee is very supportive of the Institute's research initiatives and encourages NHLBI to continue to advance the field of vascular biology, the study of blood and blood vessels and their interactions. Vascular biology research provides the foundation for understanding the underlying causes of atherosclerosis, angiogenesis, inflammation, and thrombosis. Venous and arterial thrombosis, blood clots that can lead to heart attacks, strokes, or respiratory dysfunction, are a particularly important and understudied area of vascular biology. Much remains to be learned about the basic mechanisms of pathologic thrombosis, but research has determined that age is one of the most important risk factors. The Committee encourages NHLBI, in collaboration with NIA, to develop a research agenda on thrombosis and its impact on the elderly, to improve the diagnosis and treatment of this potentially fatal complication of many diseases. (p. 102)

Action taken or to be taken
The NHLBI's extensive support for vascular biology research includes studies that address fundamental mechanisms controlling blood vessel formation; cellular and molecular mechanisms that contribute to the heterogeneity of coronary, peripheral, pulmonary, and lymphatic vessels; the role of the immune system, inflammation, and lipids in vessel wall biology; the effects of hemodynamics and hypertension on the vessel wall; characterization and stabilization of atherosclerotic plaques and aneurysms; and therapeutic and preventive approaches for

atherosclerotic arterial diseases. The NHLBI also supports basic and clinical research on venous and arterial thromboses. Other efforts address therapy for pulmonary hypertension in sickle cell disease and thalassemia and management of sickle cell disease patients at risk of vasoocclusive crises and stroke. The NHLBI also supports a number of programs in collaboration with the NIDDK to understand and prevent vascular complications of diabetes.

In FY 2005, the NHLBI established a "Career Development Program in Vascular Medicine"; convened working groups on "Computational Modeling Approaches to Vascular Biology," "Cerebrovascular Biology and Disease," "Blood Vessel Maturation," and "Thrombophilia and Thrombosis"; participated in development of the NIH Trans-Institute Angiogenesis Research Program Web site; and established a Vascular Medicine Branch in the Division of Intramural Research.

During fiscal year 2006, the NHLBI will initiate two programs of Specialized Centers of Clinically Oriented Research, one in Hemostatic and Thrombotic Diseases and another in Vascular Injury, Repair, and Remodeling, thus enhancing its strong support for vascular biology. The NHLBI will also collaborate with the NIA and professional organizations to develop a research agenda on thrombosis in the elderly population. The immediate plan is to convene a working group to identify needs and research priorities that will guide the future direction of NIH efforts on thrombotic disorders and their complications in older persons.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2006 Amount Authorized	FY 2006 Appropriation	2007 Amount Authorized	FY 2007 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	$2,832,578,000	Indefinite	$2,811,833,000
National Heart, Lung, and Blood Institute	Section 41B	42§285b	Indefinite		Indefinite	
National Research Service Awards	Section 487(d)	42§288	a/	89,179,000		89,179,000
Total, Budget Authority				2,921,757,000		2,901,012,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1998	1,404,770,000 2/	1,513,004,000	1,534,898,000 3/	1,531,061,000
1999	1,641,524,000 2/4/	1,720,344,000	1,793,697,000	1,793,697,000
Rescission				(1,188,000)
2000	1,759,806,000 2/	1,937,404,000	2,001,185,000	2,040,291,000
Rescission				(10,867,000)
2001	2,069,582,000 2/	2,321,320,000	2,328,102,000	2,299,100,000
Rescission				(875,000)
2002	2,567,429,000	2,547,675,000	2,618,966,000	2,576,125,000
Rescission				(3,063,000)
2003	2,778,728,000	2,791,411,000	2,820,011,000	2,812,011,000
Rescission				(18,278,000)
2004	2,867,995,000	2,867,995,000	2,897,595,000	2,897,145,000
Rescission				(18,454,000)
2005	2,963,953,000	2,963,953,000	2,985,900,000	2,965,453,000
Rescission				(24,252,000)
2006	2,951,270,000	2,951,270,000	3,023,381,000	2,951,270,000
Rescission				(29,513,000)
2007	2,901,012,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes procurement reform, rent, and salary and expense reductions of $1,118,000.
4/ Reflects a decrease of $5,161,000 for the budget amendment for bioterrorism.

NATIONAL INSTITUTES OF HEALTH

National Heart, Lung, and Blood Institute

Detail of Full-Time Equivalent Employment (FTEs)

OFFICE/DIVISION	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Office of the Director	9	12	14
Women's Health Initiative	4	4	4
Office of Science and Technology	37	37	37
Office of Prevention, Education, and Control	38	38	38
Office of Administrative Management	66	68	68
Office of Minority Health Affairs	5	5	5
Division of Heart and Vascular Diseases	58	58	58
Division of Epidemiology and Clinical Applications	61	61	61
Division of Lung Diseases	21	21	21
Division of Blood Diseases and Resources	23	23	23
Division of Intramural Research	376	376	378
Division of Extramural Affairs	95	95	95
National Center on Sleep Disorders Research	2	2	2
Total	796	801	805

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

FISCAL YEAR	Average GM/GS Grade
2003	11.4
2004	11.7
2005	12.2
2006	13.0
2007	13.0

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

Detail of Positions

GRADE	FY 2005 Actual	FY 2006 Appropriation	FY 2007 Estimate
Total - ES Positions	5	6	7
Total - ES Salary	$752,917	$787,552	$820,630
GM/GS-15	88	89	90
GM/GS-14	99	101	101
GM/GS-13	133	133	133
GS-12	92	92	92
GS-11	36	36	36
GS-10	5	5	5
GS-9	39	39	39
GS-8	44	44	44
GS-7	13	13	13
GS-6	4	4	4
GS-5	7	7	7
GS-4	0	0	0
GS-3	3	3	3
GS-2	0	0	0
GS-1	0	0	0
Subtotal	563	566	567
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	13	13	13
Senior Grade	4	4	4
Full Grade			
Senior Assistant Grade			
Assistant Grade			
Subtotal	17	17	17
Ungraded	224	225	227
Total permanent positions	629	633	636
Total positions, end of year	809	814	818
Total full-time equivalent (FTE) employment,end of year	796	801	805
Average ES salary	$150,583	$157,510	$164,126
Average GM/GS grade	12.2	13.0	13.0
Average GM/GS salary	$83,963	$87,826	$91,515

Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research

NATIONAL INSTITUTES OF HEALTH
National Heart, Lung, and Blood Institute

New Positions Requested

	FY 2007		
	Grade	Number	Annual Salary
Administrative Officer	GS 15	1	$126,974
Medical Officer	AD	3	$192,770
Total Requested		3	