DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

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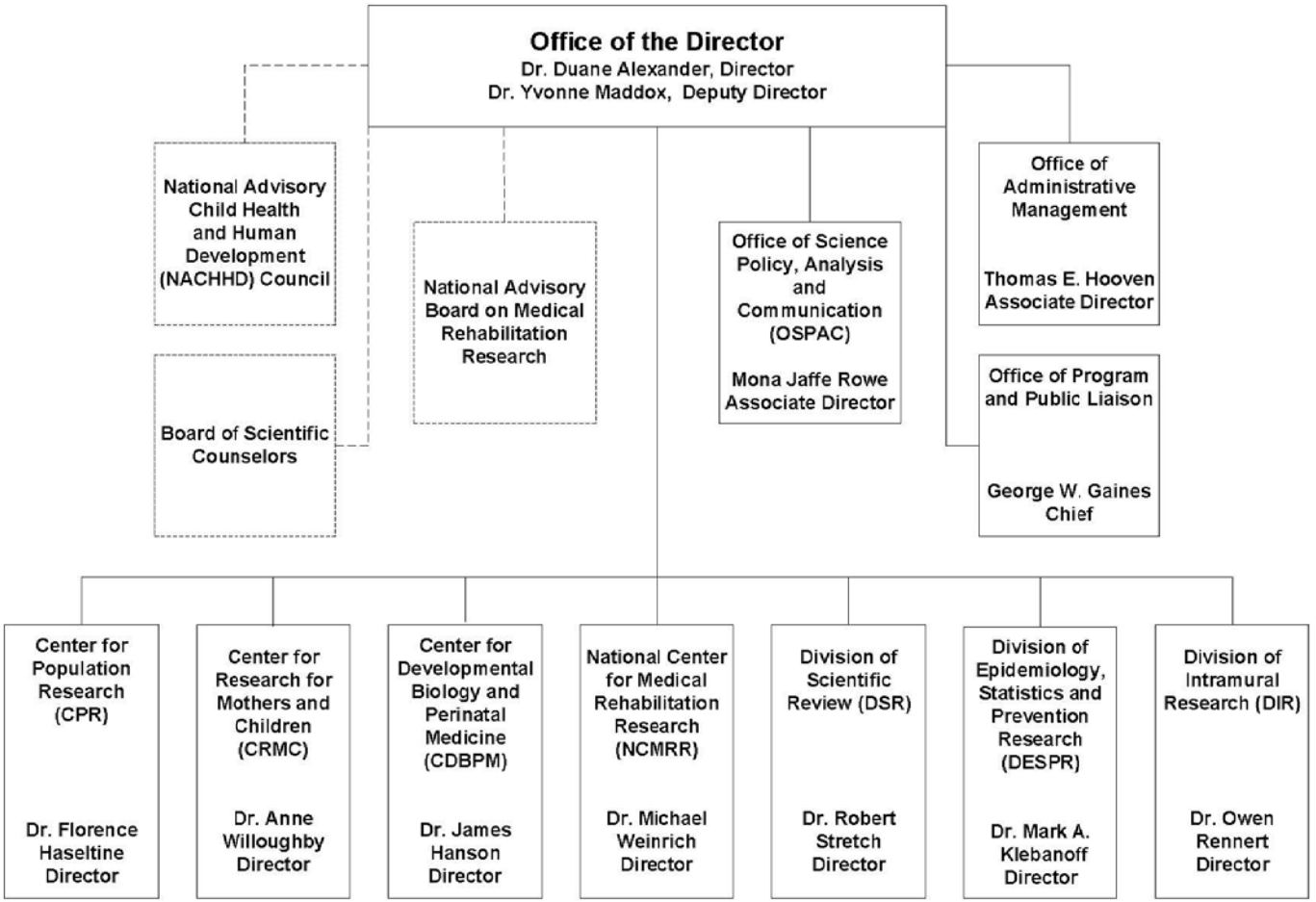


NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

For carrying out Section 301 and title IV of the Public Health Service Act with respect to child health and human development, [$1,277,544,000] *$1,257,418,000*.

[Department of Health and Human Services Appropriations Act, 2006]

**National Institutes of Health**
**National Institute of Child Health and Human Development**

**Amounts Available for Obligation 1/**

| Source of Funding | FY 2005 Actual | FY 2006 Appropriation | FY 2007 Estimate |
|---|---|---|---|
| Appropriation | $1,280,915,000 | $1,277,544,000 | $1,257,418,000 |
| Enacted Rescissions | (10,594,000) | (12,775,000) | 0 |
| Subtotal, Adjusted Appropriation | 1,270,321,000 | 1,264,769,000 | 1,257,418,000 |
| Real transfer under NIH Director's one-percent transfer authority for Roadmap | (8,031,000) | (11,302,000) | |
| Comparative transfer from OD for NIH Roadmap | 8,031,000 | 11,302,000 | |
| Subtotal, adjusted budget authority | 1,270,321,000 | 1,264,769,000 | 1,257,418,000 |
| Unobligated Balance, start of year | 0 | 0 | 0 |
| Unobligated Balance, end of year | 0 | 0 | 0 |
| Subtotal, adjusted budget authority | 1,270,321,000 | 1,264,769,000 | 1,257,418,000 |
| Unobligated balance lapsing | (17,000) | 0 | 0 |
| Total obligations | 1,270,304,000 | 1,264,769,000 | 1,257,418,000 |

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2005 - $46,223,000 FY 2006 - $52,000,000 FY 2007 - $52,000,000
Excludes $759,000 in FY 2005 and $800,000 in FY 2006 for royalties.

## Justification

## National Institute of Child Health and Human Development

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 |
| 548 | $1,270,321,000 | 523 | $1,264,769,000 | 526 | $1,257,418,000 | 3 | (7,351,000) |

This document provides justification for the Fiscal Year 2007 activities of the National Institute of Child Health and Human Development (NICHD), 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 mission of the National Institute of Child Health and Human Development (NICHD) is vital to the NIH goal of ensuring the overall health and well-being of the American people. Increasingly, research is confirming that lifelong health and well-being are strongly influenced by events occurring early in life.

Understanding human development evolves from understanding normative growth and change processes from pre-birth through adulthood. It begins at the most basic molecular and cellular levels and encompasses cognitive, behavioral, and social development. By understanding what goes "right," NICHD research provides clues as to what goes "wrong," laying the critical scientific foundation not only for understanding many disease processes, but also for preventing them altogether.

NICHD research is at the core of trying to unravel the longstanding mystery of nature versus nurture. This includes such exciting fields as epigenetics, where science is starting to explain factors that may influence heredity and the health of future generations. The NICHD is also home to research improving the rehabilitation of individuals when diseases, injuries, or chronic disorders intervene in the developmental process.

The NICHD's research spans the life cycle. Its underlying developmental science gives individuals and families *reasons for hope*, not only for beginning, but also for continuing to live long, productive, and healthy lives.

## Science Advances

**Prevention—*Reasons for Hope: Preventing viruses from entering cells/New way to protect families from type 1 diabetes***

*Blocking viruses.* Viruses, such as HIV, SARS, and avian flu, pose some of the most serious global health threats, and finding ways to prevent viral infections is a major biomedical challenge. Some viruses cause infection when they successfully attach to and fuse with the outer membrane of a healthy cell, enabling viruses to inject their own genetic material into the cell. Recently, NICHD researchers collaborated with other scientists to discover the mechanism by which viruses gain entry into healthy cells. The investigators learned that molecules called defensins appear to prevent viruses from entering cells by thwarting the fusion of the viral and cell membranes. Preventing viruses from entering cells enables the immune system to identify them for later destruction. Defensins are produced by cells that line the surfaces of many organs and tissues and are among the first cells to come into contact with viruses. This basic but elegant scientific discovery helps to explain how defensins work, allowing scientists to unravel the mystery of why some individuals are more resistant than others to certain types of viral infections. The finding also opens the door to new strategies for preventing viral illnesses. This is critical in an era of concern about pandemic viral infections and biological threats using viral agents.

*Preventing type 1 diabetes in family members.* Type 1 diabetes runs in families: siblings and offspring of someone with diabetes are 10 times more likely to develop the disease than the general public. Testing high-risk relatives of people with type 1 diabetes for genetic and autoimmune markers can identify with remarkable precision those most likely to develop diabetes within five years. No preventive therapy, however, is currently available to offer these high-risk relatives. NICHD-supported investigators found that some relatives identified by high levels of certain type 1 diabetes biomarkers could benefit from a daily dose of 7.5 mg of oral insulin. In fact, treated high-risk relatives were able to reduce their chance of developing diabetes by 43 percent, which is equal to delaying the onset of diabetes by 4.5 years. These findings imply that some relatives of patients with type 1 diabetes could prevent or delay the onset of the disease by simply swallowing a capsule every day. Considering that a diagnosis of type 1 diabetes means a lifetime of monitoring blood sugar levels, a carefully controlled diet, and increased risk of adverse health effects, this small preventative step may actually help to improve the health and quality of life of individuals at highest risk of developing type 1 diabetes.

**Technology—*Reasons for Hope: Technology brings scientists closer to understanding Lyme disease in humans/High-tech models can help to improve surgical outcomes for children with cerebral palsy/Measuring progress for stroke victims***

*A unique way to understand Lyme disease.* The organism (*Borrelia burgdorferi)* that causes Lyme disease is tricky and elusive once it enters human tissue, making diagnosis difficult. In the past, scientists lacked a laboratory model to examine how the bacteria behave once they invade the body. NICHD scientists overcame this obstacle by creating a medium for successfully studying *Borrelia burgdorferi* in a research setting. Unlike a classical two-dimensional medium often used to study microorganisms—such as that contained in a Petri dish—the investigators

simulated a three-dimensional human environment by placing tonsillar tissue in a rotating bioreactor that maintained the tissue's structure. Then, using light and electron microscopic analysis and a very sensitive technique called polymerase chain reaction (PCR), the researchers confirmed that the system can successfully find and study the bacteria after invading human tissue. This creative "tissue environment" provides scientists with a unique way to observe the invasive nature of Lyme disease bacteria at the molecular level and to explore how they genetically adapt to the human host. Just as importantly, the system allows researchers to study the process by which the bacteria cause disease under a variety of controlled laboratory conditions, many of which could be difficult to replicate in human beings. With 16,000 new Lyme disease cases reported in the United States each year,[1] this new technology should help researchers discover how untreated infections can thrive undetected for long periods of time, leading to such complications as arthritis, cardiac abnormalities, meningitis, and serious neurological conditions.

*A child's ability to walk.* Each year, parents of about 8,000 infants and 1,500 preschool-age children will learn that their child has cerebral palsy (CP), a condition that can impair a child's ability to walk.[2] Children with CP cannot control their muscles normally, and some muscles, such as the hamstrings, become too short or too tight to move properly. Surgery to lengthen the hamstrings can dramatically improve some children's gaits, but other children may receive little or no benefit. In fact, for some children, their walk actually worsens after surgery to a point where they can walk only with their knees and hips continuously bent. To identify which children with CP would benefit from hamstrings-lengthening surgery, researchers developed a three-dimensional computer model to simulate the musculoskeletal system, allowing them to study the underlying causes of abnormal gait in children with CP. This powerful new model is 100 times faster than previous means of studying human movement. The new computerized approach, which can be applied to other muscle and bone disabilities, allows clinicians to predict more accurately if surgery or an alternative treatment is best for improving an affected child's gait. Enabling clinicians to pinpoint the best time in a child's development at which to perform surgery should reassure parents that they are making the best decision to improve their child's health.

*Evaluating stroke patients.* A key step in planning any large national clinical trial is to ensure that researchers have robust and valid tools with which to collect and analyze data about observed health outcomes. This step ensures the validity and reliability of data collected at multiple sites by different investigators. To that end, researchers recently assessed the Wolf Motor Function Test (WMFT) as a means of accurately measuring change in subacute stroke patients- those who experienced a stroke only three to nine months earlier. The WMFT is a laboratory-based evaluation instrument that previously had been used to measure progress in regenerating neural function in patients who had sustained chronic strokes; it had never been used to test function in the subacute stage after a stroke. This period is particularly important—while outside the window of most current rehabilitation services, it is still within the timeframe when it is possible to influence changes in neural cells and pathways. The WMFT proved to be reliable and accurate when used to measure change in subacute stroke patients. With this rigorous tool in hand, the researchers were able to plan and execute a large clinical trial that could change current rehabilitative practice and outcomes for stroke patients.

**Women's Health—*Reasons for Hope: Identifying potential targets to treat fibroids/Reducing concerns related to hormones***

*Using gene regulation to treat uterine fibroids*. Each year, more than 200,000 women in the United States undergo a hysterectomy to treat the chronic pain and abnormal bleeding caused by fibroids.[3] NICHD-supported scientists are exploring alternative ways to treat fibroids without surgery. Previously, these researchers identified a multifunctional molecule called transforming growth factor beta (TGF-β) that acts as a major regulator of several processes that lead to the growth of uterine fibroids. Using gene microarray technology—a powerful new tool that allows multiple genes to be examined simultaneously—the researchers identified the different genes targeted by TGF-β action in normal and fibroid cells. Armed with this knowledge, the researchers then tested a gene therapy that appeared to block production and action of TGF-$\beta$. TGF-$\beta$ has potential implications in other aspects of women's reproductive health, including endometriosis. Ongoing research to discover the function of genes in uterine fibroids may provide further insight into developing novel, non-surgical therapeutic approaches, not only to prevent uterine fibroid growth, but also to treat other reproductive conditions. Successful non-surgical therapies for these conditions would eliminate surgical risk and the need for anesthesia, reduce recovery times, and help to lower health care costs.

*Popular contraceptive's effect on bone loss is reversible*. Understanding the potential impact of taking hormones is one of the many factors that influence a woman's choice of contraceptive method. To provide women and clinicians with more reliable information on which to base these decisions, the NICHD is funding several studies to evaluate the impact of Depo-Provera (depot medroxyprogesterone acetate or DMPA) on bone density in women of various ages and racial groups. Depo-Provera is an injectable hormonal contraceptive that lasts for three months. In this study, researchers compared the bone densities of healthy adolescent females who were already using DMPA to the bone densities of a matched group not using the product. The researchers focused on younger women because approximately 10 percent of adolescents (compared to 3 percent of women overall) use DMPA as a contraceptive, and because women develop most of their bone mass during their adolescent years. The researchers found that, although bone loss occurs while using Depo-Provera, the young women fully regained their bone density after discontinuing use of the product. DPMA is more than 99 percent effective and is the only injectable contraceptive available in the United States. This research should help women choose reliable, practical contraceptives with assurance that they need not increase their future risk of osteoporosis or bone fractures.

**Infertility and Fertility—*Reasons for Hope: Potential new uses for adult stem cells/New targets for treating male infertility/Another key to preventing miscarriage***

*Growing sperm stem cells in culture.* To help combat male infertility, NICHD-supported researchers are studying spermatogonal stem cells (SSCs), precursors to mature sperm. In the past, researchers had difficulty studying SSCs because the cells were unable to grow or thrive in a laboratory setting. Recently, the scientists overcame these technical barriers and developed a culture medium that contained the precise combination of cellular growth factors needed for mouse SSCs to reproduce themselves outside of the body. The researchers then successfully transplanted the newly grown cells into infertile mice, enabling the animals to produce sperm

and father offspring with the genetic traits of donor mice. This technique holds promise for future application in humans and has the potential to result in exciting new treatments for some types of infertility, such as in males who undergo chemotherapy. Moreover, successfully growing human SSCs in culture could provide a ready source of more versatile adult stem cells for future study and for replacing diseased or injured tissue in patients with spinal cord injury or disorders like Parkinson's or heart disease.

*Enzymes and motile sperm.* Many married couples dream of having a baby when they are ready, but some are unable to fulfill that dream. A recent study of infertile men showed that more than 81 percent of the time their sperm did not reach the egg,[4] encouraging researchers to focus attention on sperm motility. Two separate teams of NICHD-supported researchers have identified enzymes that are critical for sperm movement. In one study, researchers found that the enzyme GAPDS plays a key role in sperm movement and contributes to a process within the cell that produces fuel for the cell. In another collaborative study, researchers joined forces to discover that sperm also need an enzyme called sAC to move. These findings may lead to new therapies to help couples plan the families they want. For example, developing therapies that can help to restore one or both of these enzymes may help infertile men become fathers. Conversely, by interfering with the function of sAC or GAPDS in fertile men, researchers may be able to design safe and reversible male contraceptives.

*Preventing miscarriage.* Infertility affects about 6.1 million women in the United States.[5] One potential cause of infertility and a primary cause of miscarriage is an error in meiosis, the complex process that halves the number of chromosomes in eggs and sperm to prepare for conception. Errors in meiosis can lead to the death of the affected egg or miscarriage of a resulting embryo that contains an incorrect number of chromosomes. Recently, a team of researchers confirmed the identity of a receptor on the egg, Gpr3, which ensures that the egg waits for the proper signal before it divides its chromosomes in preparation for meeting a sperm. If the egg is missing Gpr3 or unable to activate the Gpr3 receptor, it cannot receive the signal and starts splitting early. With this knowledge, there is now a firm base to discover the corresponding inhibitory signal from the surrounding granulosa cells, and how that signal is regulated by hormones throughout the menstrual cycle. Identifying Gpr3 adds another piece to the puzzle surrounding human reproduction and suggests new ways for treating female infertility and for preventing miscarriages.

**Pregnancy—*Reasons for Hope: Safe and less costly alternative to surgery after miscarriage/ First steps in better predicting preeclampsia/"Delivering" good news about vaginal births after Cesarean section***

*A safe nonsurgical treatment for miscarriage.* About one out of every seven pregnant women will need medical help this year because her pregnancy failed in its early stages.[6] Previously, doctors relied on dilatation and curettage (D&C) to prevent complications and clear the uterus following miscarriage. In seeking a less invasive treatment, some doctors began using misoprostol, a drug originally approved to reduce the risk of stomach ulcers in people who take aspirin or similar drugs, but that also can cause uterine contractions. No large-scale trials, however, had evaluated the safety and effectiveness of misoprostol as a follow-up to miscarriage until NICHD researchers collaborated in a study with four U.S. university hospitals. The study

demonstrated that misoprostol was nearly as effective as D&C and was well accepted by the women who used it. Misoprostol is appropriate for use on an outpatient basis as an effective, safe, acceptable, and economical alternative to surgery after a miscarriage. Misoprostol also offers hope for improving the health of women in developing countries where financial resources and access to medical facilities are limited, making medical treatment after a miscarriage difficult to obtain.

*First steps in better predicting preeclampsia*. Preeclampsia causes 15 percent of premature births in developed countries and kills 50,000 women worldwide each year.[7] Preeclampsia, which strikes pregnant women without warning, is identified by a rise in blood pressure and protein in the urine. It can progress quickly to life-threatening seizures and kidney failure in the mother and premature birth of her baby. Compared to whites, black women are 2.4 times more likely to develop preeclampsia and twice as likely to die from its complications.[8,9] NICHD researchers, collaborating with extramural colleagues, discovered a more specific method to identify women at risk. Noting that a urinary protein called placental growth factor (PlGF) normally increases during the first two trimesters of pregnancy, the researchers found that, in some women, PlGF levels become abnormally low and that preeclampsia develops in these women about five weeks later. The researchers hope to translate these findings into a simple urine test to identify earlier and more accurately women at risk of developing preeclampsia. This would allow high-risk women to receive specialty care as early as possible, further reducing maternal and neonatal complications and deaths.

*Risk with vaginal delivery after a Cesarean birth is low.* In 2002, one of every four American infants was delivered by Cesarean section, a marked difference from 1970, when only one of every 20 infants was a Cesarean birth.[10] This increase in Cesarean deliveries, however, highlights an important medical question faced by millions of women each year: Once a woman has delivered by Cesarean, what procedure is best for her for future births? Anecdotal accounts of uterine rupture and other problems frightened expectant mothers away from attempting vaginal births for subsequent pregnancies, but were they making the best decision? To answer this question, NICHD scientists studied the records of more than 30,000 women and found that the risks from a vaginal delivery after a prior Cesarean delivery are low. This large-scale study provides important information for women and their physicians when deciding whether to have a vaginal or repeat Cesarean delivery. The U.S. Public Health Service (PHS), in its *Healthy People 2010* report, proposed a target rate of increasing vaginal births after Cesarean delivery by 12.5 percent. This study may help the nation meet this important public health goal.

## Infant Mortality and Morbidity—*Reasons for Hope: Improved way to prevent brain damage and death in newborns/New target to help keep premature infants alive/Preventing infection can reduce later developmental impairments*

**Story of Discovery: Research to Prevent Brain Damage in Newborns**

The journey of hope to improve the lives of infants born with oxygen deprivation has taken 65 years. Loss of oxygen to the brain may result in death or a lifetime of blindness, mental retardation, or cerebral palsy. In October 2005, Seetha Shankaran and her colleagues in the NICHD Neonatal Research Network reported that lowering a newborn's body temperature a few degrees could reduce the likelihood of death or disability associated with depleted oxygen.

### Complications of Birth

Oxygen deprivation, or hypoxia, typically occurs as a complication of birth. For example, if the umbilical cord becomes trapped between a baby's head and the wall of the uterus, pressure on the cord may cut off the baby's oxygen supply. Hypoxia may also result from blood loss, perhaps when the placenta tears free of the uterine wall, or the uterus ruptures. Blood loss or hypoxia at birth may lead to hypoxic ischemic encephalopathy (HIE), a condition experienced by up to 1 in every 1,000 newborns.

In 1949, James A. Miller first reported in *Science* that lowering body temperature could increase survival in newborn animals deprived of oxygen. He cooled newborn guinea pigs by wetting them with rubbing alcohol and placing them in front of an electric fan. When deprived of oxygen, the guinea pigs whose body temperatures had been lowered by as few as 4 degrees survived significantly longer than did littermates that had not been cooled. Miller undertook the study because he questioned the then routine practice of warming babies who were deprived of oxygen at birth. Chemical reactions, including those needed to sustain life, occur progressively faster as temperature increases. Miller hypothesized that reducing the speed of those reactions by reducing body temperature could increase survival. Between 1959 and 1972, several reports appeared about using a cooling treatment—by then known as hypothermia—for infants who had not responded within five minutes to standard resuscitation techniques. Typically, an infant was placed in a cold-water bath, with only its nose, eyes, and mouth above water. Although infants treated with hypothermia appeared to be more likely to survive and less likely to have permanent disabilities, most of these early studies were too small to allow statistically valid conclusions. By the early 1970s, however, several research teams had shown that preterm infants were more likely to survive if they were cared for in warmer environments, and clinical interest in hypothermia waned.

### Rebirth of a Field

It took 17 years before researchers began to reconsider hypothermia as a potential treatment for HIE. In 1987, Raul Busto and his coworkers found that lowering body temperatures in adult rats that had undergone a surgical technique designed to mimic stroke could lessen brain damage. Encouraged by this finding, researchers resumed testing hypothermia in oxygen-deprived newborn animals. Most of these studies conducted in the mid-1990s showed that cooling immediately after hypoxia reduced the severity of brain damage. Earlier research showed that while the loss of oxygen damaged brain tissue, the initial damage started a chain of reactions that worsened the original injury with each passing hour. It seemed that early cooling might blunt the secondary damage and preserve brain tissue.

### Finding the Window of Opportunity

Immediate cooling, however, was often impractical in the delivery room. Efforts to stabilize the heart rate and other vital functions of newborns could take several hours, delaying when cooling could begin. Thus, researchers sought to discover whether benefits could still be gained if cooling the infant was delayed. Working with lambs, researcher Alistair Gunn and his coworkers found that the cooling treatment could be delayed for 5 ½ hours and still effectively reduce the extent of brain injury. In their research, the scientists used a special cooling cap, which circulates water around the head, lowering brain temperature while maintaining normal temperatures in the rest of the body. After showing that the cold cap was safe for newborn infants with HIE, the researchers later found that it could reduce the effects of moderate brain injury in newborns.

**Uniform Brain Cooling**

At the same time, Abbot Laptook was also searching for a more effective means to provide cooling therapy. An earlier study of adult stroke patients demonstrated that a cooling blanket could lower brain temperature. Like the cold cap, the blanket's temperature was controlled by circulating water and was used to effectively lower body temperature. However, when comparing head cooling to the cooling blanket in newborn swine, Laptook and his coworkers found that head cooling most effectively lowered temperatures in brain areas nearest the skull, while inner brain areas remained warm. By comparison, the blanket cooled the entire brain uniformly. Shortly thereafter, the researchers demonstrated the blanket's safety in newborns with oxygen loss.

In July of 2000, Laptook, Shankaran, and other colleagues in the NICHD Neonatal Research Network began enrolling oxygen-deprived term newborns in a large-scale study of the cooling blanket. In October 2005, the researchers published their findings, showing that using the blanket to lower body temperature to about 92°F within the first six hours of life reduced the chance for disability and death among full-term infants with HIE. Unlike earlier cold cap findings, however, this study showed that the blanket's more uniform cooling could reduce the extent of death and disability resulting from *both* severe and moderate brain injury.

**Continuing the Journey to Success**

Currently, the NICHD is consulting with the American Academy of Pediatrics as the organization develops practice recommendations to treat hypoxia at birth. Three ongoing hypothermia treatment studies will provide additional information on the most effective ways to provide the treatment. These continuing refinements should accelerate access to the therapy for all infants who could benefit from its use.

*Small protein provides target to help prevent potentially lethal condition.* Each year, a serious intestinal disease—necrotizing enterocolitis (NEC)—affects about 9,000 premature infants in the United States, and 20 percent to 40 percent of those infected die.[11,12] Preemies develop NEC when their immature intestines cannot process nutrients, and intestinal cells start to die. Currently, no treatment effectively prevents this disease, and surgery is often the only hope. NICHD researchers, in a study using rat pups, showed that a small protein called epidermal growth factor (EGF) helps the intestines to grow, mature, and heal. Coincidentally, premature babies with NEC have very low EGF levels. By identifying EGF as a potential target for treating or preventing NEC, new hope exists for eliminating it as the most common gastrointestinal disease afflicting premature infants. This discovery could save the lives of 1,800 to 3,600 children in the United States annually. And in less-developed countries, where supportive care is less available and surgery is rarely an option, the number of lives saved could be even greater.

*Early infections are linked to developmental problems in the tiniest infants.* The tiniest surviving newborns, those weighing less than 2.2 pounds, are much more likely to develop problems with their immature brain and central nervous system, such as cerebral palsy, delayed mental development, or impaired vision or hearing. NICHD researchers confirmed this likelihood in an analysis of more than 6,000 medical records of extremely low birth weight (ELBW) infants. Just as importantly, the researchers found that these fragile preemies are highly susceptible to infections: The majority of the ELBW infants (65 percent) had at least one infection during their hospital stay, and nearly half of these infected infants suffered developmental impairments. This study is the first to document the extent of mental injury in ELBW babies and to link the occurrence of infection in these newborns with the increased risk for developmental impairments. The findings should stimulate research on how infections injure the brain tissue and nervous systems of fragile infants, improving ways to prevent lifelong developmental disabilities in the almost 30,000 ELBW babies born each year.[13]

**Child Development—*Reasons for Hope: Understanding critical brain functioning in autistic children/An approach to closing the literacy and reading gap for language minority students/ Reduced need to perform ear surgery on toddlers/Reducing poverty among immigrant children***

*Teaching parts of the brain to work together in autistic children.* "Can't see the forest for the trees" is a good description of children with autism, who often excel at details but cannot see the big picture. Researchers, exploring a theory that autism results from a failure of the various parts of the brain to work together, measured the brain activity of a group of high-functioning autistic volunteers while they performed a simple memory task involving letters of the alphabet. Using a brain imaging technique known as functional magnetic resonance imaging (*f*MRI), the researchers found that the autistic volunteers showed different brain activation patterns compared to non-autistic controls. For example, the volunteers with autism used the right hemisphere of their brain, which processes shapes and visual information, to recognize letters, as opposed to the left hemisphere, which normally processes letters and words. Also, the imaging showed that the different brain areas of the autistic volunteers were less likely to work together. Such synchronization is necessary for many kinds of higher-level thinking and analysis that prove difficult for those with autism. These findings support the theory that autistic brains have defects in their neurological wiring, forcing the various parts to work independently. This discovery could help change the way autistic children are taught, placing more emphasis on activities that stimulate problem-solving skills and activate multiple brain areas simultaneously. The societal cost of autism is around $43 billion each year.[14] Improving behavioral and educational therapies for autistic children may not only lessen these costs but also improve quality of life.

*Teaching Spanish-speaking children to read English*. As of 2000, nearly one in five Americans spoke English as a second language,[15] reflecting the fact that Hispanics comprise the most rapidly growing and the largest minority group in the United States.[16] In addition, the number of students designated by their schools as having limited proficiency in English increased by 72 percent over the last decade.[17] Together, these and other trends led the National Research Council, the National Reading Panel, and subsequent legislation (Reading Excellence Act, 1998; No Child Left Behind Act, 2001) to call for educators to use evidenced-based methods when teaching reading in U.S. schools. Given these facts, researchers asked, what are the best methods to use when teaching Spanish-speaking children to read in English? The researchers found that Spanish-speaking students initially instructed in Spanish and then in English outperform students instructed in only one language, whether it was Spanish or English. This study of 135 Spanish-speaking 4th-graders demonstrated the value of applying a bilingual approach to teaching reading to students for whom English is not their first language. The data showed that, when students were allowed to gain literacy skills initially in their native language and then transfer these reading skills to English, the children became more proficient in both languages. These findings provide an important, evidenced-based foundation upon which to design new reading programs for English-language learners, providing a critical step to help reduce the educational gap and increase lifelong success for these children.

*Reducing unnecessary surgeries for children.* Three-fourths of all children have a middle ear infection by the age of three.[18] These infections often result in fluid in the ear (effusion) that can temporarily impair hearing and language development. To prevent this, physicians began inserting drainage tubes in the middle ears of these children (tympanosotomy), making the

procedure the most common pediatric operation in toddlers; however, no evidence existed to verify its effectiveness. Researchers recently completed a large, longitudinal study to provide the empirical evidence needed to determine if the timing of tympanosotomy, early or delayed, made a difference in children's development. The researchers found that the earlier placement of tympanosotomy tubes does not appear to benefit language, speech, behavior, or intellectual development in children at ages three, four, or six years. These data support a more conservative treatment approach of "watchful waiting" and only inserting ear tubes for more serious circumstances, saving children from the pain and any adverse consequences associated with surgery while helping to reduce health care costs.

*Poverty among immigrant children*. The number of immigrant children in the United States—those who are either foreign-born or have at least one foreign-born parent—is increasing rapidly. Thirty-five years ago, immigrant families had lower poverty rates than U.S.-born families; now the poverty rates for immigrant families are two-thirds higher. In addition, the number of immigrant children living in poverty increased steadily, from about 12 percent in 1970 to about 21 percent in 2000.[19] Traditional explanations for overall poverty rates in the United States, however, fail to explain the causes of economic decline in immigrant families. To better understand the roots of the problem, researchers determined in a large demographic study that the key variables contributing to increased poverty rates among immigrant children include the facts that their parents are 1) less educated, 2) more likely to be unemployed, and 3) more likely to be recent immigrants. This study highlights possible factors leading to poverty among immigrant families, which can influence a child's ability to grow, learn, and become a self-sustaining adult.

**Adolescence—*Reasons for Hope: Defining pre-diabetes factors in obese youth/Detailing teenage driving habits to reduce crash rates***

*Hormonal protection from type 2 diabetes*. About 9 million children over the age of six are considered obese, and this number is rising.[20] As teenagers are becoming fatter, they are beginning to develop diseases once seen only in adults, such as type 2 diabetes and cardiovascular disease. One of the early warning signs of impending type 2 diabetes is insulin resistance, or the body's reduced ability to use insulin to process blood sugars. However, not all overweight teens with equal levels of body fat develop insulin resistance, leading researchers to question if something other than body fat triggers this condition. In a recent study, NICHD-supported researchers found that overweight teens who had not developed insulin resistance were different in two ways: 1) they stored less fat around the body organs and in muscle cells, and 2) they had higher levels of adiponectin, a hormone secreted by fat cells and appears to protect against type 2 diabetes. These findings provide important new insights about key factors that may determine insulin sensitivity and how insulin resistance develops as children become overweight. Such knowledge should help to refine prevention and intervention strategies that target the physiological factors associated with the epidemic of childhood obesity and its associated rise in type 2 diabetes.

*Gender of teen passenger can increase risky teen driving behaviors.* Motor vehicle crashes end more young lives than any other cause of death for 15 to 20 year olds.[21] Teen drivers are involved in three times as many crashes,[22] and crash rates among teens increase when teenage

passengers are in the car.[23] Despite these facts, few rigorous studies clarify the specific factors that contribute to these grim statistics. NICHD researchers examined how having other teens in the car could influence two factors—speed and following distance—that contribute to risky driving behaviors. Using video and a laser-assisted radar device, the researchers recorded and studied 3,000 vehicles as they left 10 different high school parking lots and again a short distance away. Of the vehicles, 471 were driven by teens. The researchers found that, overall, teens drive faster and closer to the car in front of them than does general traffic. Moreover, the teen drivers' speed increased significantly with a male passenger in the car: a quarter of the drivers exceeded the speed limit by at least 15 miles per hour when accompanied by teenage males. Conversely, male teens were less likely to tailgate or speed with a female teen passenger. These findings provide data that can help parents to set limits that could save teen lives.

**HIV/AIDS—*Reasons for Hope: Reassurance that breast-feeding can be safe for HIV-infected mothers/Reducing mother-to-child transmission/Protecting the growth of children with HIV***

*Breast-feeding and maternal mortality*. Several years ago, a small-scale clinical trial in Kenya raised concerns that the simple act of breast-feeding her baby could increase an HIV-infected woman's risk of dying within two years of giving birth. Since this finding proved counter to those from other studies, NICHD-supported scientists analyzed data from clinical trials involving more than 4,000 HIV-infected women to resolve the concern. The researchers found *no* evidence of an increased risk of death in HIV-infected mothers who breast-fed their infants. In addition to laying to rest concerns about premature death, the study found that women who breast-fed for longer time periods actually *lowered* their risk of dying. These results and other important factors should reassure HIV-infected women that they can safely breast-feed their infants without increasing risk to their own health.

*HIV transmission through breast milk.* Although breast-feeding may be safe for HIV-infected mothers, it is a major source of transmission from HIV-infected mothers to their babies. In fact, without antiretroviral treatment, 40 percent of all HIV transmissions from mothers to their breast-fed infants may occur through breast milk.[24] Two studies, however, now show that treating HIV-infected lactating mothers with highly active antiretroviral therapy (HAART) helps to prevent the transfer of the virus to their children. One study found that the three drugs that comprise HAART therapy passed into the mothers' breast milk in significant concentrations, and one of these drugs made its way into the infants' blood at high enough levels to be protective. In the other study, researchers found that HAART effectively reduced the level of one form of the virus in breast milk. Together, these studies underscore how HAART can help to prevent HIV transmission through breast milk, providing hope for HIV-infected mothers that breast-feeding does not have to lead to infecting their babies. This is especially important in developing countries where HIV infection rates are high and formula feeding can be problematic because of expense, lack of clean water, and social acceptance.

*Growing up with HIV*. Children with HIV are often shorter and weigh less than their uninfected peers. Researchers studying HIV-infected children, as part of the Pediatric AIDS Clinical Trials Group, found that HAART treatment helped these children attain a normal rate of growth (height and weight) compared with uninfected cohorts. This research shows that HAART does more

than slow disease progression in HIV-infected children—the therapy also helps to ensure the steady growth and development of these children. The World Health Organization reported in 2004 that approximately 640,000 children were newly diagnosed with HIV worldwide.[25] HAART can help these children to develop and lead healthier, more productive lives.

## NIH Roadmap

### Careers in Clinical Research—*Reasons for Hope*: *Creating tomorrow's clinical research workforce will ensure that the nation benefits from today's research investments*

The NICHD continues to expand its role in the NIH Roadmap initiative, leading efforts to develop a new cadre of highly skilled and versatile clinical researchers. Five new K12 grants were added to the seven already funded under successive RFAs entitled "Multidisciplinary Clinical Research Career Development Programs." This program supports the early career development of doctoral-level health professionals from a variety of disciplines engaged in all types of clinical research, including patient-oriented research, translational research, small- and large-scale clinical investigations and trials, and epidemiologic and natural history studies. When finished with training, these individuals should be able to design and oversee high-quality research in multidisciplinary team settings as they become leaders in fields essential to reinvigorating the clinical research enterprise.

In addition, 10 T32 grants were awarded under a new RFA entitled "Predoctoral Clinical Research Training Programs." These grants will promote clinical research training among predoctoral medical, dental, nursing, and allied health students and provide efficient entry into clinical research careers. The programs are flexible enough to provide students access to a level of clinical research training that is appropriate to their career stage and degree of interest, while also accommodating their changing training needs over time. Each intensive training core will support the equivalent of 10 to 12 full-time trainees enrolled in a year-long, non-degree program; in an M.S. program (with a concurrent doctoral degree); or in a Ph.D. program. At a minimum, programs must include core educational components, summer or short-term research experiences, an intensive clinical research training program, a faculty core, and an administrative core.

Together, these two programs capture trainees at key points in their career development when they are most likely to nurture an interest in clinical research. The multidisciplinary emphasis reflects the changing approach to clinical research, particularly to the design and implementation of clinical trials. Thus, the NIH hopes to fill a well-documented void in developing the next generation of clinical researchers.

## Accomplishments

*Improving drugs for pregnant women.* The NICHD Obstetric-Fetal Pharmacology Research Network, which was established with support from the Office of Research on Women's Health to provide the expert infrastructure needed to test therapeutic drugs during pregnancy, is completing one of its first translational studies. Here, the research examines the safety and efficacy of glyburide, which is used to control the blood sugar of pregnant women who have

developed gestational diabetes. Gestational diabetes complicates about 4 percent of pregnancies in the United States and, if untreated, can lead to stillbirth or to poor birth outcomes for infants and to infections, high blood pressure, and preeclampsia in mothers. The Network is also set to launch a new clinical trial of 17-alpha-hydroxyprogesterone caproate (17-αOHPC), a promising therapy for high-risk pregnant women. Past studies showed that weekly injections of the drug could reduce the risk of preterm birth by approximately one-third in women with a history of preterm birth; however, more data are needed on appropriate dosage, how the drug is metabolized during pregnancy, and the drug's impact on the ability to monitor pregnancy by using a variety of biomarkers. The Network has a strong start, allowing researchers to conduct a whole new generation of safe, technically sophisticated, and complex studies that will help clinicians protect the health of women while improving birth outcomes and reducing infant mortality.

*Improving drugs for children.* The NICHD Pediatric Pharmacology Research Unit Network has expanded its innovative and translational trials on drugs for children. This year, the Network started new, multisite protocols to study a variety of drugs used to manage pain in children. At the same time, under the Best Pharmaceuticals for Children Act, the Institute has expanded its partnerships with other Institutes to develop clinical and preclinical studies of drugs such as methotrexate, daunomycin, lithium, hydroxyurea, and methylphenidate, which are commonly used to treat a variety of health conditions, including cancer, depression, and attention disorders. Additional studies have begun on three more drugs (baclofen, azithromycin, and meropenem) also commonly used to treat children. Finally, the NICHD has started an initiative to bring together scientists from government, industry, and academia to discuss the challenges associated with developing pediatric formulations. This is an excellent example of how the NIH can form a public-private partnership to improve the safety of all medications given to children.

*Newborn screening: The hope of early identification and treatment.* The NICHD Newborn Screening Initiative is moving forward in its effort to develop and employ the latest technology for improving the availability, accessibility, and quality of genetic and other diagnostic laboratory testing for rare diseases and conditions affecting newborns. Ultimately, this research could help identify at-risk infants as early as possible and provide the data needed to develop therapies for many of these conditions. As a cornerstone activity, the NICHD has funded a major grant for developing and refining a newborn screening test for spinal muscular atrophy (SMA), a common fatal neuromuscular disease in children. The NICHD will soon be funding other grants to increase understanding of the underlying causes of and, ultimately, new treatment targets for conditions such as SMA or other currently, or soon-to-be, screened genetic conditions.

*NIH Neuroscience Blueprint: Developing a new national resource on child development.* Significant progress continues on a magnetic resonance imaging (MRI) study to create the first database of normal brain growth and development in children ranging from birth to 18+ years of age. The NICHD leads this effort with the full partnership of the NIMH, NINDS, and NIDA. Currently, no single standardized and comprehensive source of information exists on MRI measurement of normal brain development over time in children and teens in the United States. These standardized data—when coupled with a variety of medical, cognitive, and behavioral information—will provide the foundation needed to determine how variations in normal brain development may be related to a range of developmental disorders and brain-related diseases and

conditions. In conjunction with the NIH Neuroscience Blueprint initiative, the study will expand its use of diffusion tensor imaging (DTI). This new technology will permit scientists to measure myelinated fiber tracts, known as "white matter," which allow different parts of the brain to connect and communicate with each other. Additional children are being recruited to the study, while more technologically sophisticated DTI analytic tools and software are being developed.

*Reducing health disparities: Outreach to American Indian/Alaska Native (AI/AN) and Mississippi Delta communities.* The NICHD has just contracted Native American Management Services, Inc. (NAMS), to work with community members, NICHD staff, and other federal partners to develop SIDS risk-reduction and educational resources for five Indian Health Service Areas (in Aberdeen, Alaska, Bemidji, Billings, and Portland). The partnership will allow the Institute to work closely with local representatives to develop an array of interactive media containing targeted prevention messages. NAMS will also train local outreach workers to help them use these materials and better meet the needs of their individual communities.

Some of the highest infant mortality and SIDS rates in the nation are in the Mississippi Delta. Under a new contract with Service Specialists, Ltd., the NICHD will target its successful SIDS outreach campaign to the families and communities in the Delta region. The local group will work with a variety of public and private organizations to teach them how to use NICHD-developed risk-reduction materials. The goal is to augment existing community networks and resources to help them reach pregnant women, parents, extended families, and other caregivers of infants under one year of age with scientifically based but "user-friendly" information.

## Innovations in Management and Administration

*NICHD Program evaluation: Supporting strong stewardship of federal research investments.* Ongoing evaluation is essential to the strong stewardship of federal research programs. The NICHD has taken a lead role in establishing the infrastructure and in conducting the studies needed to support such reviews. Already, with the help of NIH one-percent, set-aside evaluation funds, the NICHD has just completed, or will soon complete, the following internal evaluations:

- a multifaceted assessment of the National Cooperative Program in Infertility Research and the Specialized Cooperative Centers Program in Reproduction Research;
- a program review of the clinical and translational research of the Reproductive Medicine Network;
- a feasibility and design study of the Women's Reproductive Health Research program;
- a review of the trans-NIH, Extramural Associates Research Development Award program, administered by the NICHD;
- a feasibility and design study of the trans-NIH Roadmap K12 Multidisciplinary Clinical Research Career Development program;
- an evaluation of the Building Interdisciplinary Research Careers in Women's Health program, led by the Office of Research on Women's Health and administered by the NICHD; and
- an assessment of the Sudden Infant Death Syndrome Partnership.

The Institute plans to conduct surveys to obtain feedback from individuals who have a direct connection to the operations and outcomes of NICHD research programs or initiatives. The survey data will augment the NICHD's ongoing efforts to evaluate research-related activities. The NICHD is also distinct among NIH Institutes and Centers for dedicating a new contract solely to supporting a full range of evaluation activities that meet the urgent and ongoing needs of the Institute's leadership.

## Fiscal Year 2007 Initiatives

*Effects of infertility treatments on growth, and development to age three years.* In response to emerging concerns about the healthy development of children born with the aid of assisted reproductive technology (ART), the NICHD will support a study tracking such children from birth through age three. The weight of scientific evidence indicates that ART children are more likely to be premature and small for their gestational age. Scientists do not know whether these problems result from ART treatments or from the underlying cause(s) of the parents' infertility. Also unknown is whether ART children are at risk of developmental delays or disorders or, if so, whether these children "catch up" with normal developmental landmarks. It has been difficult to answer these questions because parental recall of infertility treatments may be imprecise and because, until recently, birth certificates did not include information about such treatments.

NICHD scientists now plan to take advantage of new standardized, electronic birth certificates that are being phased in by all states and that require ART information. The ART information will enable the researchers to accurately identify large cohorts of infants born with and without the aid of such treatments. Then, working with parents, the scientists will closely track the children's development over the first three years of life. The research should yield a better understanding of the origins of any growth and developmental problems, and may ultimately help infertile couples and clinicians make more informed choices among possible therapies. A more immediate benefit is that any developmental delays or disorders in study children will be detected when they first emerge, and these children will be referred to appropriate early intervention programs.

This NICHD study responds to recommendations from the President's Council on Bioethics and the World Health Organization, for longitudinal studies of cognitive, developmental and health effects in children that may be associated with parental infertility treatments.

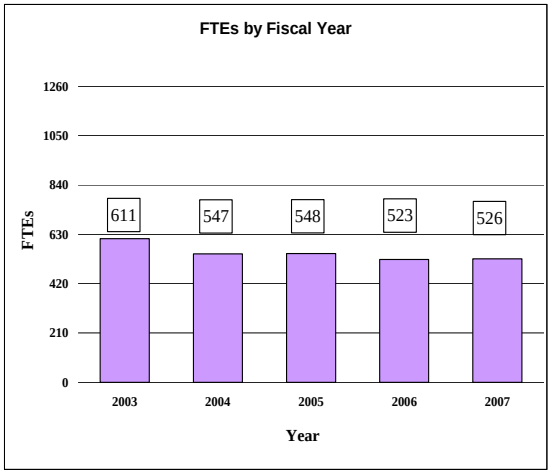
*Community-based rehabilitation intervention.* The aging of the baby-boom generation and expected pressures on the U.S. health care system make research into effective therapies in community settings a high priority. Clinical trials of rehabilitation therapies have demonstrated the efficacy of novel interventions in preventing or significantly lessening disabling conditions associated with stroke, traumatic brain injury, and other disorders and conditions. Little is known, however, about whether and how well such therapies will work in less-controlled community practice settings. Scientists do not know whether – or how -- efficacious rehabilitative therapies and even clinical trial design may need to be modified for community settings.

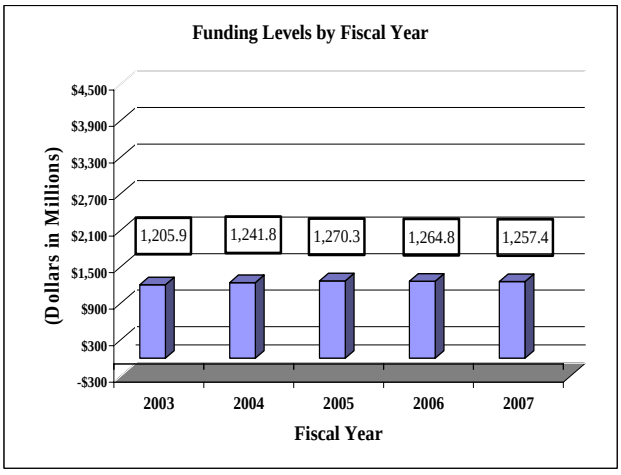
To address these critical questions, the NICHD will solicit applications for clinical trials by scientists partnering with persons with disabilities, practitioners, and others in the community. Investigators are encouraged to explore such critical questions as how to engage community partners in research design and how to motivate persons with disabling conditions and their clinicians to participate in rehabilitative therapy clinical trials. Other research questions include how to determine the extent of patient and clinician adherence to research protocols and how to define outcomes that are meaningful to persons with disabilities, clinicians, and scientists. Projects could range from studies of financing mechanisms and risk adjustment to trials of specific therapies.

## Budget Policy

The Fiscal Year 2007 budget request for the NICHD is $1,257,418,000, a decrease of $7,351,000 and -0.6 percent over the FY 2006 Appropriation. Included in the FY 2007 request is NICHD'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 NICHD 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 $283,269 in FY 2007. While no inflationary increases are provided for direct recurring costs in noncompeting RPGs, where the NICHD has committed to a programmatic increase for an award, such increases will be provided.

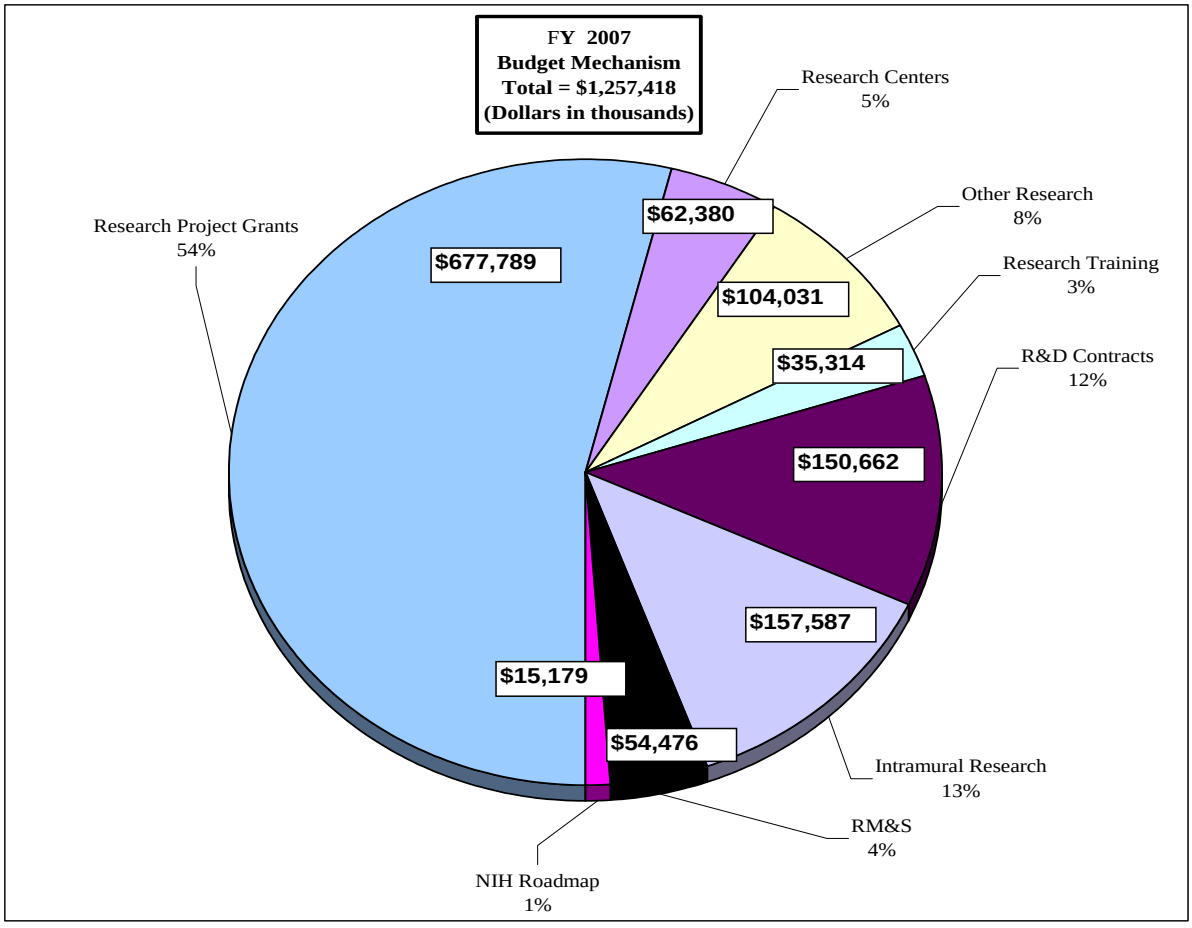
NIH must nurture a vibrant, creative research workforce, including sufficient numbers of new investigators with new ideas and new skills. In the FY 2007 budget request for NICHD, $720,000 will be used to support 8 awards for the new K/R "Pathway to Independence" program.

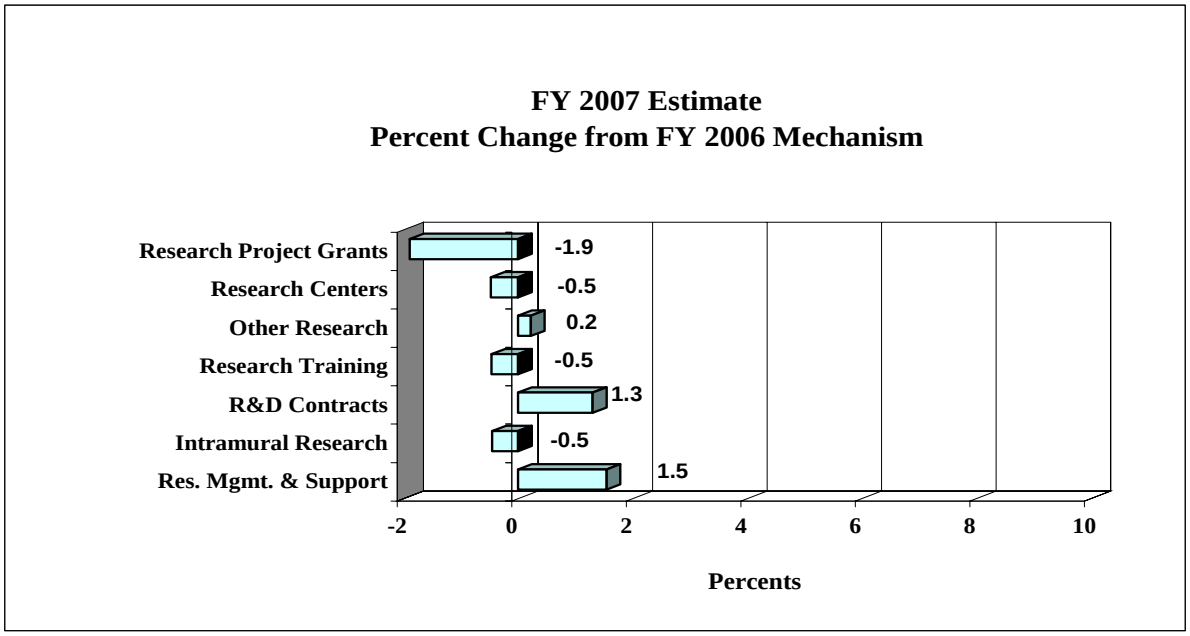
NICHD will also support the Genes, Environment, and Health Initiative (GEHI) to: 1) accelerate discovery of the major genetic factors associated with diseases that have a substantial public health impact; and 2) accelerate the development of innovative technologies and tools to measure dietary intake, physical activity, and environmental exposures, and to determine an individual's biological response to those influences. The FY 2007 request includes $1,942,000 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 44 research centers, 486 other research grants, including 257 career awards, and 213 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:



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**NATIONAL INSTITUTES OF HEALTH**

**National Institute of Child Health and Human Development**

Budget Mechanism - Total

| MECHANISM | FY 2005 Actual | | FY 2006 Appropriation | | FY 2007 Estimate | |
|---|---|---|---|---|---|---|
| Research Grants: | No. | Amount | No. | Amount | No. | Amount |
| Research Projects: | | | | | | |
| Noncompeting | 1,264 | $519,836,000 | 1,305 | $507,229,000 | 1,280 | $495,563,000 |
| Administrative supplements | (80) | 8,440,000 | (58) | 6,376,000 | (58) | 6,347,000 |
| Competing: | | | | | | |
| Renewal | 91 | 41,806,000 | 95 | 43,595,000 | 94 | 43,198,000 |
| New | 407 | 99,759,000 | 423 | 103,565,000 | 419 | 102,734,000 |
| Supplements | 7 | 1,367,000 | 7 | 1,366,000 | 7 | 1,368,000 |
| Subtotal, competing | 505 | 142,932,000 | 525 | 148,526,000 | 520 | 147,300,000 |
| Subtotal, RPGs | 1,769 | 671,208,000 | 1,830 | 662,131,000 | 1,800 | 649,210,000 |
| SBIR/STTR | 114 | 28,862,000 | 112 | 28,710,000 | 112 | 28,579,000 |
| Subtotal, RPGs | 1,883 | 700,070,000 | 1,942 | 690,841,000 | 1,912 | 677,789,000 |
| Research Centers: | | | | | | |
| Specialized/comprehensive | 43 | 62,281,000 | 44 | 62,430,000 | 44 | 62,133,000 |
| Clinical research | 0 | 0 | 0 | 0 | 0 | 0 |
| Biotechnology | 0 | 250,000 | 0 | 0 | 0 | 0 |
| Comparative medicine | 0 | 474,000 | 0 | 247,000 | 0 | 247,000 |
| Research Centers in Minority Institutions | 0 | 0 | 0 | 0 | 0 | 0 |
| Subtotal, Centers | 43 | 63,005,000 | 44 | 62,677,000 | 44 | 62,380,000 |
| Other Research: | | | | | | |
| Research careers | 249 | 40,176,000 | 249 | 39,734,000 | 257 | 40,255,000 |
| Cancer education | 0 | 0 | 0 | 0 | 0 | 0 |
| Cooperative clinical research | 85 | 38,677,000 | 85 | 41,589,000 | 85 | 41,401,000 |
| Biomedical research support | 0 | 0 | 0 | 0 | 0 | 0 |
| Minority biomedical research support | 0 | 0 | 0 | 0 | 0 | 0 |
| Other | 144 | 22,727,000 | 144 | 22,477,000 | 144 | 22,375,000 |
| Subtotal, Other Research | 478 | 101,580,000 | 478 | 103,800,000 | 486 | 104,031,000 |
| Total Research Grants | 2,404 | 864,655,000 | 2,464 | 857,318,000 | 2,442 | 844,200,000 |
| Research Training: | FTTPs | | FTTPs | | FTTPs | |
| Individual awards | 125 | 5,925,000 | 121 | 5,860,000 | 121 | 5,831,000 |
| Institutional awards | 710 | 29,947,000 | 687 | 29,618,000 | 687 | 29,483,000 |
| Total, Training | 835 | 35,872,000 | 808 | 35,478,000 | 808 | 35,314,000 |
| Research & development contracts | 240 | 149,348,000 | 212 | 148,723,000 | 213 | 150,662,000 |
| (SBIR/STTR) | (1) | (65,000) | (1) | (65,000) | (1) | (65,000) |
| | FTEs | | FTEs | | FTEs | |
| Intramural research | 354 | 159,036,000 | 369 | 158,302,000 | 371 | 157,587,000 |
| Research management and support | 189 | 53,379,000 | 152 | 53,646,000 | 153 | 54,476,000 |
| Cancer prevention & control | 0 | 0 | 0 | 0 | 0 | 0 |
| Construction | | 0 | | 0 | | 0 |
| Buildings and Facilities | | 0 | | 0 | | 0 |
| NIH Roadmap for Medical Research | 5 | 8,031,000 | 2 | 11,302,000 | 2 | 15,179,000 |
| Total, NICHD | 548 | 1,270,321,000 | 523 | 1,264,769,000 | 526 | 1,257,418,000 |
| (Clinical Trials) | | (210,945,000) | | (210,528,000) | | (208,982,000) |

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

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Budget Authority by Activity**
**(dollars in thousands)**

| ACTIVITY | FY 2005 Actual | | FY 2006 Appropriation | | FY 2007 Estimate | | Change | |
|---|---|---|---|---|---|---|---|---|
| | FTEs | Amount | FTEs | Amount | FTEs | Amount | FTEs | Amount |
| Extramural Research | | $1,049,875 | | $1,041,519 | | $1,030,176 | | ($11,343) |
| Intramural Research | 354 | 159,036 | 369 | 158,302 | 371 | 157,587 | 2 | (715) |
| Research Management & Support | 189 | 53,379 | 152 | 53,646 | 153 | 54,476 | 1 | 830 |
| NIH Roadmap for Medical Research | 5 | 8,031 | 2 | 11,302 | 2 | 15,179 | 0 | 3,877 |
| Total | 548 | 1,270,321 | 523 | 1,264,769 | 526 | 1,257,418 | 3 | (7,351) |

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

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Summary of Changes**

| | | | | |
|---|---|---|---|---|
| FY 2006 Estimate | | | | $1,264,769,000 |
| FY 2007 Estimated Budget Authority | | | | 1,257,418,000 |
| Net change | | | | (7,351,000) |
| | FY 2006 Appropriation | | Change from Base | |
| CHANGES | FTEs | Budget Authority | FTEs | Budget Authority |
| A. Built-in: | | | | |
| 1. Intramural research: | | | | |
| a. Within grade increase | | $60,668,000 | | $786,000 |
| b. Annualization of January 2006 pay increase | | 60,668,000 | | 471,000 |
| c. January 2007 pay increase | | 60,668,000 | | 1,022,000 |
| d. Payment for centrally furnished services | | 27,812,000 | | 417,000 |
| e. Increased cost of laboratory supplies, materials, and other expenses | | 69,822,000 | | 1,367,000 |
| Subtotal | | | | 4,063,000 |
| 2. Research Management and Support: | | | | |
| a. Within grade increase | | 23,328,000 | | 398,000 |
| b. Annualization of January 2006 pay increase | | 23,328,000 | | 181,000 |
| c. January 2007 pay increase | | 23,328,000 | | 394,000 |
| d. Payment for centrally furnished services | | 7,486,000 | | 112,000 |
| e. Increased cost of laboratory supplies, materials, and other expenses | | 22,832,000 | | 452,000 |
| Subtotal | | | | 1,537,000 |
| Subtotal, Built-in | | | | 5,600,000 |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Summary of Changes--continued**

| CHANGES | FY 2006 Appropriation | | Change from Base | |
|---|---|---|---|---|
| | No. | Amount | No. | Amount |
| B. Program: | | | | |
| 1. Research project grants: | | | | |
| a. Noncompeting | 1,305 | $513,605,000 | (25) | ($11,695,000) |
| b. Competing | 525 | 148,526,000 | (5) | (1,226,000) |
| c. SBIR/STTR | 112 | 28,710,000 | 0 | (131,000) |
| Total | 1,942 | 690,841,000 | (30) | (13,052,000) |
| 2. Research centers | 44 | 62,677,000 | 0 | (297,000) |
| 3. Other research | 478 | 103,800,000 | 8 | 231,000 |
| 4. Research training | 808 | 35,478,000 | 0 | (164,000) |
| 5. Research and development contracts | 212 | 148,723,000 | 1 | 1,939,000 |
| Subtotal, extramural | | | | (11,343,000) |
| | FTEs | | FTEs | |
| 6. Intramural research | 369 | 158,302,000 | 2 | (4,778,000) |
| 7. Research management and support | 152 | 53,646,000 | 1 | (707,000) |
| 8. NIH Roadmap for Medical Research | 2 | 11,302,000 | 0 | 3,877,000 |
| Subtotal, program | | 1,264,769,000 | | (12,951,000) |
| Total changes | 523 | | 3 | (7,351,000) |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Budget Authority by Object**

| | FY 2006 Appropriation | FY 2007 Estimate | Increase or Decrease |
|---|---|---|---|
| Total compensable workyears: | | | |
| Full-time employment | 523 | 526 | 3 |
| Full-time equivalent of overtime & holiday hours | 2 | 2 | 0 |
| Average ES salary | $156,320 | $162,104 | $5,784 |
| Average GM/GS grade | 11.7 | 11.6 | (0.1) |
| Average GM/GS salary | $83,735 | $86,833 | $3,098 |
| Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207) | $71,203 | $73,838 | $2,635 |
| Average salary of ungraded positions | 128,564 | 133,321 | 4,757 |

| | OBJECT CLASSES | FY 2006 Appropriation | FY 2007 Estimate | Increase or Decrease |
|---|---|---|---|---|
| | Personnel Compensation: | | | |
| 11.1 | Full-Time Permanent | $29,081,000 | $30,248,000 | $1,167,000 |
| 11.3 | Other than Full-Time Permanent | 19,751,000 | 20,544,000 | 793,000 |
| 11.5 | Other Personnel Compensation | 1,563,000 | 1,626,000 | 63,000 |
| 11.7 | Military Personnel | 1,720,000 | 1,789,000 | 69,000 |
| 11.8 | Special Personnel Services Payments | 16,367,000 | 16,811,000 | 444,000 |
| | **Total, Personnel Compensation** | 68,482,000 | 71,018,000 | 2,536,000 |
| 12.0 | Personnel Benefits | 14,009,000 | 14,572,000 | 563,000 |
| 12.2 | Military Personnel Benefits | 1,505,000 | 1,565,000 | 60,000 |
| 13.0 | Benefits for Former Personnel | 0 | 0 | 0 |
| | **Subtotal, Pay Costs** | **83,996,000** | **87,155,000** | **3,159,000** |
| 21.0 | Travel & Transportation of Persons | 3,760,000 | 3,727,000 | (33,000) |
| 22.0 | Transportation of Things | 533,000 | 530,000 | (3,000) |
| 23.1 | Rental Payments to GSA | 1,000 | 1,000 | 0 |
| 23.2 | Rental Payments to Others | 31,000 | 31,000 | 0 |
| 23.3 | Communications, Utilities & Miscellaneous Charges | 1,448,000 | 1,437,000 | (11,000) |
| 24.0 | Printing & Reproduction | 1,253,000 | 1,242,000 | (11,000) |
| 25.1 | Consulting Services | 1,051,000 | 1,043,000 | (8,000) |
| 25.2 | Other Services | 15,499,000 | 15,383,000 | (116,000) |
| 25.3 | Purchase of Goods & Services from Government Accounts | 123,470,000 | 124,056,000 | 586,000 |
| 25.4 | Operation & Maintenance of Facilities | 2,364,000 | 2,347,000 | (17,000) |
| 25.5 | Research & Development Contracts | 117,951,000 | 117,066,000 | (885,000) |
| 25.6 | Medical Care | 1,576,000 | 1,564,000 | (12,000) |
| 25.7 | Operation & Maintenance of Equipment | 2,627,000 | 2,607,000 | (20,000) |
| 25.8 | Subsistence & Support of Persons | 0 | 0 | 0 |
| **25.0** | **Subtotal, Other Contractual Services** | **264,538,000** | **264,066,000** | **(472,000)** |
| 26.0 | Supplies & Materials | 12,925,000 | 12,828,000 | (97,000) |
| 31.0 | Equipment | 8,774,000 | 8,696,000 | (78,000) |
| 32.0 | Land and Structures | 0 | 0 | 0 |
| 33.0 | Investments & Loans | 0 | 0 | 0 |
| 41.0 | Grants, Subsidies & Contributions | 876,196,000 | 862,514,000 | (13,682,000) |
| 42.0 | Insurance Claims & Indemnities | 0 | 0 | 0 |
| 43.0 | Interest & Dividends | 12,000 | 12,000 | 0 |
| 44.0 | Refunds | 0 | 0 | 0 |
| | **Subtotal, Non-Pay Costs** | **1,169,471,000** | **1,155,084,000** | **(14,387,000)** |
| | **NIH Roadmap for Medical Research** | **11,302,000** | **15,179,000** | **3,877,000** |
| | **Total Budget Authority by Object** | **1,264,769,000** | **1,257,418,000** | **(7,351,000)** |

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

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Salaries and Expenses**

| OBJECT CLASSES | FY 2006 Appropriation | FY 2007 Estimate | Increase or Decrease |
|---|---|---|---|
| **Personnel Compensation:** | | | |
| Full-Time Permanent (11.1) | $29,081,000 | $30,248,000 | $1,167,000 |
| Other Than Full-Time Permanent (11.3) | 19,751,000 | 20,544,000 | 793,000 |
| Other Personnel Compensation (11.5) | 1,563,000 | 1,626,000 | 63,000 |
| Military Personnel (11.7) | 1,720,000 | 1,789,000 | 69,000 |
| Special Personnel Services Payments (11.8) | 16,367,000 | 16,811,000 | 444,000 |
| **Total Personnel Compensation (11.9)** | **68,482,000** | **71,018,000** | **2,536,000** |
| Civilian Personnel Benefits (12.1) | 14,009,000 | 14,572,000 | 563,000 |
| Military Personnel Benefits (12.2) | 1,505,000 | 1,565,000 | |
| Benefits to Former Personnel (13.0) | 0 | 0 | 0 |
| **Subtotal, Pay Costs** | **83,996,000** | **87,155,000** | **3,159,000** |
| Travel (21.0) | 3,760,000 | 3,727,000 | (33,000) |
| Transportation of Things (22.0) | 533,000 | 530,000 | (3,000) |
| Rental Payments to Others (23.2) | 31,000 | 31,000 | 0 |
| Communications, Utilities and Miscellaneous Charges (23.3) | 1,448,000 | 1,437,000 | (11,000) |
| Printing and Reproduction (24.0) | 1,253,000 | 1,242,000 | (11,000) |
| **Other Contractual Services:** | | | |
| Advisory and Assistance Services (25.1) | 1,051,000 | 1,043,000 | (8,000) |
| Other Services (25.2) | 15,499,000 | 15,383,000 | (116,000) |
| Purchases from Govt. Accounts (25.3) | 78,243,000 | 78,721,000 | 478,000 |
| Operation & Maintenance of Facilities (25.4) | 2,364,000 | 2,347,000 | (17,000) |
| Operation & Maintenance of Equipment (25.7) | 2,627,000 | 2,607,000 | (20,000) |
| Subsistence & Support of Persons (25.8) | 0 | 0 | 0 |
| **Subtotal Other Contractual Services** | **99,784,000** | **100,101,000** | **317,000** |
| Supplies and Materials (26.0) | 12,899,000 | 12,802,000 | (97,000) |
| **Subtotal, Non-Pay Costs** | 119,708,000 | 119,870,000 | 162,000 |
| **Total, Administrative Costs** | **203,704,000** | **207,025,000** | **3,321,000** |

## NATIONAL INSTITUTES OF HEALTH

### National Institute of Child Health and Human Development

SIGNIFICANT ITEMS IN THE HOUSE, SENATE AND CONFERENCE APPROPRIATION COMMITTEE REPORTS

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

Item

***Preterm birth-*** Last year, the National Center for Health Statistics reported the first increase in the U.S. infant mortality rate since 1958, and 61% of this increase was due to an increase in the birth of premature and low birth weight babies. The Committee is pleased that NICHD is one of the sponsors of an Institute of Medicine study now underway to define and address the health related and economic consequences of premature birth and encourages NICHD to develop a plan to implement the study's recommendations once they are available. (p. 80)

Action taken or to be taken

The NICHD is committed to reducing the incidence of premature birth and its sequelae, and looks forward to the Institute of Medicine's (IOM) recommendations, which are expected in May, 2006. The Institute co-sponsored the IOM study and participated actively in providing information to the study panel. For example, an August, 2005 presentation to the panel by the NICHD's Pregnancy and Perinatology Branch highlighted its FY 2004 premature birth grant portfolio. The presentation described multiple areas of investigation and provided the number and funding levels of active research grants. Among the activities highlighted in the presentation were the NICHD's long standing Maternal-Fetal Medicine Unit and the Neonatal Research Networks, and its new Genomics and Proteomics Network for Premature Birth Research. The new research network will focus on the expression of the hereditary information encoded in the DNA (genomics) and the expression of the structures and functions of proteins (proteomics), with a goal of enhancing understanding of the underlying processes that lead to preterm birth.

The NICHD has also supported multiple workshops and conferences in the area of preterm birth, both to define research needs and to present and analyze current scientific evidence for clinical practice recommendations. One of the most complex areas in perinatal-neonatal medicine remains the care of the mother delivering a preterm infant at the border of viability, which is referred to as "periviable" gestation. Because of substantial gaps in current scientific knowledge that preclude evidence-based, optimal care for periviable gestation, the Institute organized a March, 2004, *Workshop of the Border of Viability*. Major knowledge gaps and prioritized study suggestions, discussed at the workshop, were summarized and published in *Pediatrics,* in 2005.

"Near-term" birth, which occurs after 35-37 weeks of gestation, presents unique clinical challenges. Although near-term infants have typically been assumed to be normal, they are now known to be at risk for a host of prematurity-related complications, from difficulty feeding to infection, respiratory distress syndrome, and intracranial hemorrhage. These newborns thus require close monitoring, and may need intensive care. The July, 2005 NICHD workshop, *Care of Near-term Fetus and the Near-term Neonate*, reviewed the clinical and epidemiological

aspects related to the care and surveillance of near-term pregnancies and newborn infants. Workshop participants identified knowledge gaps, developed a research agenda to fill the gaps, and also assembled and commented on current evidence, on which clinical care and follow-up guidelines could be based.

Item

***Genomic and proteomic research-*** The Committee is pleased that NICHD has launched a major new research initiative to address the public health problem of premature birth, which affects one in eight babies born in this country and is the leading cause of newborn death. NICHD is encouraged to move forward with this initiative, which focuses on genomic and proteomics, in an effort to accelerate knowledge in the mechanisms responsible for premature birth. The Committee intends to closely monitor this effort because it assigns a high priority to promoting the birth of healthy infants. (p. 81)

Action taken or to be taken

The NICHD's new Genomics and Proteomics Network for Premature Birth Research will focus on the expression of the hereditary information encoded in the DNA and the expression of the structures and functions of proteins (proteomics), with a goal of enhancing understanding of the underlying processes that lead to preterm birth. The network's research will proceed in three phases. The goal of the first phase is to identify DNA abnormalities profiles that increase the risk of, or are predictive of a preterm delivery; the second phase will determine the physiological role or relevance of these identified biomarkers; and the third phase will apply these findings to design effective interventions to help prevent preterm birth. Network researchers will post their results on the Web, allowing free and easy public access to the data and the capability to screen for pattern differences between normal and pathological conditions.

The NICHD is pleased to report an extremely productive first meeting of the Genomics and Proteomics Network for Premature Birth Research (GPN/PBR), on September 26-27, 2005. The agenda included introductions of the network members, who will work collaboratively with each other, presentations of the capabilities of each site, discussions on study design issues and network infrastructure, and the establishment of pertinent subcommittees. Two additional GPN/PBR meetings in the coming year will result in final study priorities and protocols. Research subject recruitment, and collection of clinical data and biological specimens is planned to begin before the end of the coming year. Initial estimates indicate that the network will have access to a population of about 3,000 preterm births (less than 37 weeks of gestation) per year. Of these, approximately 800 preterm infants will have been born after less than 32 weeks of gestation. Because infants of less than 32 weeks gestation have the highest incidence of morbidity and mortality, they will be a major focus of the network. Given estimates of potential subjects, the network research population(s) should offer ample statistical power to perform adequate global genomic and proteomic analyses.

Item

***Stillbirth-*** The Committee applauds NICHD efforts in addressing stillbirth, a major public health issue with morbidity equal to that of all infant deaths. The Committee understands that NICHD has established a cooperative network of clinical centers and a data center to address this issue with a standard protocol. The Committee encourages NICHD to strongly support this effort. (p. 81)

Action taken or to be taken

The NICHD is committed to research efforts in stillbirth, which is a significant public health problem, accounting for a large proportion of perinatal mortality. As the committee is aware, the NICHD established the Stillbirth Collaborative Research Network (SCRN) under a cooperative agreement at the end of FY 2002 to study the extent and causes of stillbirth in the United States. The SCRN network encompasses five clinical sites that cover substantial portions of Rhode Island, Massachusetts, Georgia, Texas and Utah and that reflect urban/rural and racial diversity.

Network members have developed hypotheses in critical areas, including surveillance and epidemiology, fetal and placental pathology, maternal disease mechanisms, immunology and infectious diseases, and genetics. The hypotheses in turn drive the design requirements of the study, including identification and selection of cases, the number and type of controls, and the timing of and approach to data collection and management. The network has developed and piloted a multi-site, population-based case-control study. With completion of the pilot studies, the Network plans to initiate the full study in early 2006. In addition, NICHD staff and SCRN network members work with parents, health professional organizations, and hospitals to advance a research agenda for stillbirth. NICHD staff and members of the SCRN Steering Committee participated in the September, 2005 international meeting, *Together We Will Make a Difference*, sponsored by the International Stillbirth Alliance and First Candle.

The NICHD has also co-funded, with the NIAAA, four cooperative agreements to create the Prenatal Alcohol in SIDS and Stillbirth (PASS) network, now entering its third year of a phase I period. This research network develops community-linked studies of the role of prenatal alcohol exposure in the risk for sudden infant death syndrome (SIDS) and adverse pregnancy outcomes such as stillbirth and fetal alcohol syndrome (FAS), and how the alcohol exposure and adverse outcomes may be inter-related. In its first phase, the PASS network has been planning and piloting multidisciplinary investigations using common protocols, within communities at high risk for prenatal maternal alcohol consumption. In FY 2006, applications will be sought to support a large, phase II longitudinal cohort study, beginning with pregnant women and following mother-baby pairs through infancy. This study could contribute significantly to understanding fetal development, the origins and abnormal processes leading to stillbirth, and developing interventions to reduce adverse pregnancy and infant outcomes.

Item

***Maternal-fetal medicine units networks-*** The Committee recognizes the efforts of NICHD, through its maternal fetal medicine units network (MFMU), to achieve a greater understanding of and pursue development of effective treatments for the prevention of pre-term births, low birth weight infants, and medical complications during pregnancy such as pregnancy related hypertension and diabetes. The Committee is pleased to learn that NICHD is proceeding with a

competitive renewal of the MFMU network in 2006 and encourages a sustained research investment in this program to facilitate resolution of these problems and promote the birth of healthy infants. (p. 81)

Action taken or to be taken

Major scientific advances have resulted from the research of the Maternal Fetal Medicine Units (MFMU) network. The NICHD is fully committed to continuing this network and is reviewing applications for the next funding cycle, which will begin April 1, 2006. Currently, the MFMU Network is conducting multiple clinical trials and studies that are aimed at improving the health of mothers, their children, and children's long-term development. In one MFMU trial, progesterone therapy is being tested as a way to prevent preterm birth in women with multiple gestations, a very high-risk group for preterm birth. This trial builds on the successful MFMU trial that found progesterone supplementation to women at high risk reduced the risk of a subsequent preterm birth. Another current trial adds omega-3 supplementation to progesterone therapy, as an additive strategy to reduce the incidence of prematurity in high-risk women. The network is also finishing its followup of infants in a randomized trial of 2,400 pregnant women on the prevention of cerebral palsy. Network findings of its evaluation of the fetal pulse oximeter – a method of measuring an infant's oxygen level during labor -- will be the lead presentation at the February, 2006 Society for Maternal-Fetal Medicine meeting. Network research also includes studies to evaluate the possibility that vitamins C and E could prevent preeclampsia, and to determine whether detecting and treating mild gestational diabetes with a dietary intervention could reduce neonatal illness and death. The network is preparing to launch a trial of thyroxine, to determine if the treatment of subclinical maternal hypothyroidism affects long-term infant outcome.

Item

***Spina bifida-*** The Committee is pleased that the Institute cosponsored the 2003 spina bifida research conference. However, the Committee has heard concerns that NICHD has not engaged in adequate follow-up on the conference recommendations. The Committee encourages NICHD to enhance research to address issues related to the outcome of the conference and urges NICHD to jumpstart its research efforts in the prevention, and treatment of spina bifida and associated secondary conditions, with a particular focus on improved understanding of urological disorders among children and adults. The Director should be prepared to testify on its efforts to advance these areas of research at the fiscal year 2007 appropriations hearing. (p. 81)

Action taken or to be taken

The NICHD supports a broad portfolio of research in the prevention of spina bifida and related neural tube defects and in the treatment and management of these complex conditions. As a follow-up to the 2003 spina bifida conference, a subsequent NICHD workshop, *Fetal Treatment: Needs Assessment and Future Directions*, led to the development of a research plan. The plan addressed the evaluation and treatment of pregnancies that might benefit from *in utero* therapy as well as the dissemination of the latest scientific information on innovations in maternal-fetal surgery. The NICHD is now funding the multicenter Management of Myelomeningocele study (MOMs), which is a clinical trial comparing the safety and efficacy of fetal surgical repair and traditional postnatal repair of open neural tube defects. The children of trial participants will be followed to age three, to determine treatment effects of both procedures on their neurological and

mental development and on their need for shunting. The NICHD has also provided supplementary funding, specifically for evaluation of urological outcomes in the children.

The NICHD also cooperated recently in organizing and funding the meeting, *Hydrocephalus: Myths, New Findings and Clear Directions,* which resulted in a published white paper that should inform further efforts to advance research in areas explored at the meeting. The meeting highlighted data from a NICHD longitudinal study that followed children from infancy through age nine and a half years. This was the first study to relate early development of children with spina bifida to their later cognitive, behavioral, and motor functioning. Through its many targeted efforts on birth defects, the NICHD is enabling basic scientists, clinicians and genetic epidemiologists to investigate the genetic and environmental factors associated with the susceptibility, health disparities and variability of human malformations associated with neural tube defects. A current project in this program will link nutritional factors, folate status and genetic information from a large number of affected families to define putative risk factors for spina bifida. Information from this study can be used to inform basic studies, using experimentally manipulable model systems, that are essential to clarify the underlying mechanisms of development, and to define gene function and ultimately to open the door to better prevention and treatment options.

Item

***Drug safety for children-*** The Committee recognizes the importance of ensuring that drugs are safe and effective for use by children. The Committee strongly supports continued implementation of the Best Pharmaceuticals for Children Act, which supports the pediatric testing of off-patent drugs, as well as on-patent drugs not being studied through existing mechanisms. The Committee is pleased to note that in 2004 six studies were initiated and five additional studies are planned for 2005. In implementing this provision, NICHD should act as coordinator for all other Institutes within NIH for which pediatric pharmacological drug research may have therapeutic relevance and should consult with the Food and Drug Administration to ensure that the studies conducted are designed to yield improved pediatric labeling. The Committee notes that NICHD has made numerous outreach efforts to other Institutes and Federal agencies to further refine the priority listing process. The Committee requests NICHD to provide an update during its annual appropriations testimony which shall include the role of other Federal agencies in implementing the Best Pharmaceuticals for Children Act; information on the number of studies supported through the Research Fund; the estimated cost of each study undertaken; the nature and type of studies undertaken; the number of label changes resulting from completed studies; the patent status of the drugs studied; the number of drugs remaining on the priority list; and a summary of NICHD's findings on the frequency of pediatric use for medications that may be considered for the priority list. (p. 81)

Action taken or to be taken

The NICHD continues to lead the partnership of NIH Institutes to expedite studies of clinically important drugs for the pediatric population. In addition, NICHD officials meet on a monthly basis with Food and Drug Administration staff, to develop and review Written Requests issued under the Best Pharmaceuticals for Children Act. At the monthly meetings, staff members also refine the list of drugs to be reviewed during the annual listing meeting (November 2005), prior to publication and comment on the list. To date, 46 drugs have been identified as most urgent for

clinical studies in children. A total of 17 Written Requests have been received, and pre-clinical or clinical studies are being conducted on 8 drugs. The NICHD issued contracts or interagency agreements during FY 2005 for the following additional drug studies: 1) Methotrexate (Off-patent; $1,864,169); 2) Daunomycin (Off-patent; $568,191); 3) Lithium (Off-patent; $4,047,577); 4) Hydroxyurea (On-patent; $2,320,000); 5) Methylphenidate (Off-Patent; $1,800,521); and 6) Methylphenidate (Off-patent; $477,500). In addition, the NICHD has also requested contract proposals for the following drugs: 1) oral Baclofen (On-patent); 2) Azithromycin (Off-patent); and 3) Meroprenem (Off-patent).

In FY 2005, NICHD also evaluated medication use among 23 million children (30% of children under 18 in the U.S.) who were enrolled in Medicaid and in commercial insurance plans. The most commonly used medications among these children were: antibiotics, anti-inflammatories, bronchodilators, antihistamines, and antiasthmatics. Industry experience indicates that it takes approximately five years to complete a pediatric drug study and submit data to the FDA for a labeling change; for that reason, no clinical trials have yet been completed that would allow for a labeling change. Finally, the NICHD is currently organizing a meeting of government, industry and academic representatives to discuss how further to stimulate research on pediatric formulations.

Item

***The National Children's Study-*** The Committee remains interested in NICHD efforts to launch the National Children's Study, that is intended to follow 100,000 children to age 21, examining the impacts and influences of many environmental and genetic factors on children's health and development. (p. 82)

Action taken or to be taken

In support of the National Children's Study (NCS) seven contracts to "Vanguard" study centers to pilot the first phase of the study were awarded. A contract for a study coordinating center was also awarded.

No funds are included in the President's Budget Request for FY 2007 for the National Children's Study. The NCS planning activities that are on going under contract in FY 2006 will be brought to a close by the end of the fiscal year. There are no plans for the NIH to continue to pursue the full scale study in FY 2007.

Item

***Neurofibromatosis (NF)-*** Learning disabilities occur with high frequency in children with NF. Enormous advances have been made in the past few years in the successful treatment and curing of learning disabilities in pre-clinical NF animal models. The Committee encourages NICHD to issue requests for applications for NF research and to pursue funding of clinical trials for NF patients in the area of learning disabilities. (p. 82)

Action taken or to be taken

The NICHD has funded multiple projects in recent years to investigate the genetic origins and neurology of neurofibromatosis (NF) and some of the behavioral consequences of this disorder. NICHD-funded learning Disability Research Centers (LRDCs) have spent a decade addressing

learning disabilities (LDs), learning, and behaviors in children with neurofibromatosis and other conditions associated with LDs. Among other things, researchers have determined that the effectiveness of LD interventions does not vary with the many different disorders associated with LD, even though children with NF and LD have a different set of neurocognitive problems than the majority of children with LD. Because scientists have found that intervention effects are the same for LD children, even though the causes of their LDs differ, researchers would not expect clinical trials focused on NF alone to yield new information that would benefit NF children. Researchers do not know, however, whether the LD intervention effectiveness varies if a child has more than one condition associated with LD. For that reason, LRDCs are now investigating the effectiveness of an intervention for reading disabilities in LD students with and without co-existing attention deficit hyperactivity disorder, and with and without other co-occurring learning disabilities (language disability, math LD). Research from previous LDRC work with children with NF suggests that interventions aimed specifically at LD students with co-existing language impairment and visual-spatial deficits will be particularly relevant, given the distinctive nature of LDs associated with neurofibromatosis. The ongoing work of the LDRCs and of other research on the genetics, neurobiology and behavioral aspects of learning disabilities (including reading, language and mathematics, with and without comorbidities) represents an important investment by the NICHD in research that is expected to benefit all children with LD, including those whose LD is caused by NF.

Item

***Fragile X-*** The Committee is pleased that NICHD has funded three Fragile X centers and encourages NICHD to enhance the centers and recruit new researchers to the Fragile X field. The Committee also encourages NICHD to coordinate its Fragile X research efforts and to relate Fragile X research with that in other developmental disorders, such as autism research. (p. 82)

Action taken or to be taken

NICHD's three Fragile X Centers conduct basic and clinical studies and also studies of the prevalence of Fragile X carrier status. A current focus is on Fragile X Ataxia-Tremor syndrome (FXTAS), a condition that was first reported by two NICHD-funded investigators. FXTAS occurs in some grandfathers of children with the full Fragile X gene mutation, and in some young women who are Fragile X carriers and who experience premature ovarian insufficiency. The NICHD continuously monitors these centers to identify additional efforts that could move the research forward. To bring new investigators into the field, the NICHD's extensive portfolio of Fragile X grants includes multiple research training grants, from postdoctoral fellowships to minority student and faculty supplements and to mentored investigator awards. Multiple training opportunities are available to students in research training programs at NICHD's Fragile X "centers within centers," which are targeted research programs that are integrated with the NICHD's Mental Retardation and Developmental Disabilities Centers.

The NICHD also takes full advantage of multiple opportunities for collaborating with other Institutes and public and private partners, to coordinate Fragile X research efforts and to relate Fragile X research with that of other developmental disorders. For example, the NICHD co-sponsors, with the Fogarty International Center, an epidemiologic study to determine the prevalence and incidence of Fragile X, Down syndrome and Williams syndrome in China. In 2005, the NICHD joined with the NIMH, the NINDS, and other public and private-sector

partners to sponsor a major new research initiative, *The Shared Neurobiology of Fragile X and Autism.* Non-NIH partners in this effort include components of the Canadian Institutes of Health Research, the Health Research Board of Ireland, the FRAXA Research Foundation, Cure Autism Now, and Autism Speaks. The NIH solicitation for the initiative, published in May, 2005, seeks studies focusing on topics related to understanding neural pathways, circuits, systems and molecules that play a role in the etiology and pathophysiology of Fragile X and that may be implicated in autism (including autism spectrum disorders and Rett syndrome). The solicitation also specifically encourages studies to identify targets for new drugs to treat these conditions. Scientifically meritorious applications that fall just short of the NIH pay line will be distributed to other partners in the initiative. Additional related research funding opportunities supported by the NICHD include *Research on Autism and Autism Spectrum Disorders, Identifying Autism Susceptibility Genes*.

Item

***Autism-*** The Committee is aware of the important research supported by NICHD into the genetic basis of autism spectrum disorders and of its support for the Baby Sibling study on the incidence of autism among children in the same families. The Committee encourages the Institute to strengthen its support for the Baby SIBS study, and encourages the Institute to expand its work with similar public-private partnerships. (p. 82)

Action taken or to be taken

The High Risk Baby Siblings Research Project (Baby Sibs project) is a multi-site study tracking the early development of siblings of children with autism, who are at elevated risk of this condition. The goal of this project is to identify behavioral and biological markers for autism and eventually enable clinicians to make early, definitive diagnoses. To support this study, the NICHD partners with the National Alliance for Autism Research, a parent-led group. Baby Sibs research that is currently supported by the NICHD includes a study of social orienting in 12- to 18-month-old siblings of children with autism. Social orienting is a social-communicative process that is likely to be impaired in autism. A second study, of siblings and non-siblings at ages 24 and 42 months, is designed to validate an instrument that could be used to screen young children for autism and other pervasive developmental disorders. The NICHD is also providing funds for a study head on circumference, to assess the head growth of high-risk infants (primarily siblings of children with autism) and correlate these data with diagnostic outcomes in the children. The research will test whether children with autism have atypical, accelerated rates of head growth and related symptoms in the first three years of life.

The NICHD continues to support bi-annual meetings of the High-Risk/Baby Sibs Research Consortium. The Consortium supports collaborative research on the early development of autism in high-risk infants through exchange of ideas, combined efforts toward addressing methodological challenges, and through specific projects involving common measures and pooled samples to increase power and efficiency.

The NICHD is pleased to report that investigator-initiated research in autism continues to expand, augmenting the Institute's autism grant portfolio. A planned request for grant applications, "Autism Centers of Excellence" will further integrate and augment these activities and spur research advances by consolidating two NIH autism research networks (Collaborative

Programs of Excellence in Autism (CPEAs) and Studies to Advance Autism Research and Treatment (STAART centers) into Autism Centers of Excellence (ACEs). The CPEAs have focused on possible causes of autism, including genetic, immunological, and environmental factors. The STAART research centers have focused on causes, diagnosis, early detection, prevention and treatment of autism. The research focus of the new ACEs will be on the causes and best treatment of autism, as listed in the 2003 Autism Research Matrix (http://www.nimh.gov/autismiacc/researchmatrix.pdf). The NICHD continues to participate actively in working groups of the InterAgency Autism Coordinating Committee.

Item

***Childhood diseases and the growing skeleton-*** The Committee encourages NICHD to support studies investigating the effects of pharmaceuticals, lifestyle, and chronic childhood diseases on the growing skeleton and fracture risk and bone-formation interventions for children. NICHD is encouraged to support osteogenesis imperfecta research, especially in genetic therapies, animal models, drug treatment and rehabilitation. The Committee encourages NICHD to work with NIAMS to study the rare disorders osteopetrosis and juvenile Paget's disease. (p. 82)

Action taken or to be taken

Failure to achieve genetically determined maximal peak bone mass correlates with the development of osteoporosis and fracture risk in adults. The NICHD's multi-center, longitudinal Bone Mineral Density in Childhood Study (BMDCS), is collecting data that will form a valuable database for clinicians and investigators to use in assessing bone deficits and risk factors for impaired bone health in children. Now in the third of six years, the BMDCS is collecting "reference standard" data on a range of skeletal growth measures, as well as nutrition and exercise in children. This study will answer questions related to the timing and acquisition of optimal peak bone mass. The NICHD recently joined with the American Society of Bone and Mineral Research to bring together leading investigators to review the current state of research on bone growth in children and the effects of various pharmacologic agents on pediatric bone accrual. The current state of pediatric bone growth research and the effects of various pharmacologic agents on children's bone accrual were discussed. Publication of the meeting proceedings, as a supplement to the journal *Pediatrics*, is expected in the spring of 2006.

The NICHD's intramural osteogenesis imperfecta (OI) program recently created a new, transgenic mouse model, to test a potential gene therapy, which would use a specific RNA molecule to suppress the abnormal action of the OI gene mutation. The OI program's ongoing longitudinal pediatric Osteogenesis Imperfecta (OI) study functions as a research "clinic," following OI children as they grow, providing them with medical care, and enabling them to participate in clinical trials of promising interventions. Working with the NIH Clinical Center rehabilitation program, NICHD scientists found that they could not reproduce improvements in children's walking, muscle strength and bone pain that had been reported in uncontrolled trials of a drug, bisphosphonate pamidronate. This osteoporosis drug was being prescribed for children with OI, without adequate safety or efficacy data. When scientists administered the drug to the transgenic mice, they found that it strengthened vertebral bones and the resistance of long bones, such as the femur, to direct force, but the drug also made a critical type of long-bone material more brittle. They concluded that the drug could be used long enough to gain its strengthening effects in children, but stopped before brittle effects occurred.

The NICHD and the NIAMS serve on the Federal Working Group on Bone, whose meetings are attended by a Paget Foundation representative. The NICHD plans to work with the NIAMS in future initiatives on Paget disease and/or osteopetrosis that may be developed by this group.

Item

***Infertility and contraceptive research-*** The Committee notes that infertility is a disease which affects over six million people in the United States and is concerned that the number appears to be growing as age, lifestyle, and environmental factors increasingly impact reproductive health outcomes. The Committee suggests that NICHD conduct additional research to improve reproductive health intervention outcomes. (p. 83)

Action taken or to be taken

The NICHD shares the Committee's concern with the apparent increase in U.S. rates of infertility and is pursuing multiple strategies to determine the etiologies, impacts, and potential interventions for this problem. For example, the NICHD collaborates in supporting the National Survey of Family Growth, which provides national data on the experience of infertility among American men and women, the correlates of infertility risk, and the demographic factors underlying trends in infertility. The Institute also supports studies of access to infertility care, decision-making about care, and the impact of infertility on couples. A 2005 NICHD conference examined health disparities in infertility and infertility treatment.

Among adults at greatest risk for premature reproductive failure are an estimated 800,000 survivors of childhood and young adult cancers. The NICHD began the Fertility Preservation Program to investigate the mechanism that disrupts reproductive function in these young survivors. Program goals include characterizing subgroups of survivors most likely to experience early reproductive failure, and measuring more accurately damage to eggs and the formation of sperm, with the ultimate goal of preventing fertility loss in these survivors.

Contraceptive research is also a priority for the NICHD. The Institute's three Cooperative Contraceptive Research Centers investigate new methods for both male and female contraception. The research includes basic science to identify new targets for contraception as well as research into novel delivery systems for existing drugs, to maintain high efficacy while lowering potential side effects. In addition, a new NICHD-initiated program will explore mechanisms to regulate male fertility by controlling the production or activity of sperm. Two new clinical centers for male contraceptive research in the NICHD's Contraceptive Clinical Trials Network, will enable investigators to test new contraceptives for men. Other projects include studies of whether contraceptive drugs affect HIV transmission and clinical trials of the contraceptive efficacy of microbicides. The goal of the latter projects is new products that could prevent both unintended pregnancy and transmission of sexually transmitted diseases. Finally, the NICHD continues to support a wide range of research to improve outcomes in other disorders that are related to reproductive health. For example, little consensus exists on appropriate surgical procedures to prevent repair of advanced uterine prolapse – a condition associated with childbirth – from causing post-operative urinary "stress" incontinence in women. In response, the NICHD started the Colpopexy and Urinary Reduction Efforts (CARE) clinical trial. When early results showed a 20 percent reduction of stress incontinence in women

receiving the experimental intervention, investigators halted the trial and began dissemination of the results to scholarly journals and to clinicians.

Item

***Demographic research-*** The Committee commends NICHD for its strong support of demographic research. Given the tremendous changes occurring in the U.S. population, demographic research is necessary to analyze trends and determine consequences for the health and well-being of our nation. The Committee encourages the institute to ensure adequate support for demographic training and for critical demographic databases. (p. 83)

Action taken or to be taken

Demographic research provides objective scientific data on factors that impair, or protect, the health and well-being of our nation's people. With NICHD support for demographic research, investigators:

- Evaluate the social, economic, and cultural causes of disparities in health and the pathways linking socioeconomic disadvantage to poor health outcomes;
- Apply rigorous scientific methods to answer questions about the effects, on child development, of teen childbearing, poverty, family instability, and early maternal employment;
- Identify risk factors for too-early sexual involvement among adolescents, as well as the protective effects of religion, close family relationships, and high educational aspirations;
- Document and explain the causes of growing rates of poverty among immigrant children;
- Document the trends, causes and consequences of major transformations in the American family, including nonmarital cohabitation and childbearing, divorce and remarriage; and
- Identify opportunities to strengthen American families, including engaging unmarried fathers at the "magic moment" of their child's birth in interventions to improve fathering skills and strengthen family commitments.

Demographic research requires the integration of scientific methods and expertise across many disciplines in the health, statistical, behavioral, and social sciences. The NICHD is working to maximize the effectiveness of resources for training scientists to conduct this complex research.

Demographic research also requires investment in the collection and dissemination of population data. Prior NICHD investments – in the National Longitudinal Surveys of Youth, the National Longitudinal Study of Adolescent Health (Add Health), the National Survey of Families and Households, the Fragile Families Study, and others – have made possible major innovations in research on the health and development of children and families. For example, Add Health data are being used by over 2,500 scientists nation-wide to answer a broad range of questions about the determinants of health in adolescence and early adulthood. Most recently, these data have revealed a serious deterioration in young people's health as they enter early adulthood, including increases in obesity, asthma, and many health risk behaviors. A fourth wave of this study that will support research on the early development of adult disease will be funded by the NICHD in fiscal year 2006.

Item

***Primary immunodeficiency diseases (PID)-*** The Committee continues to be impressed with NICHD's contributions to the physician education and public awareness program conducted by a voluntary organization to reach earliest diagnosis of this class of about 140 diseases. With regard to research on PI, the Committee is encouraged by the Institute's commitment to develop newborn screening procedures for PI, particularly X-linked SCID, utilizing microarray technologies. (p. 83)

Action taken or to be taken

The NICHD continues to have an active interest in promoting research on Primary Immunodeficiency Diseases (PIDs) while also educating physicians and raising awareness among parents of these disorders. In addition to supporting a portfolio of PID research grants, the NICHD also provides support to the NIAID/NICHD Primary Immunodeficiency Research Consortium (USIDNet Consortium), which is a coalition of the world's most prominent investigators in the field of PIDs. The purpose of this consortium is to help prioritize and coordinate research directions and to develop new resources to study these rare disorders.

The NICHD has also actively supported conferences on a variety of topics related to PIDs in FY 2005, in collaboration with NIAID colleagues. The First Clinical Immunology Society [CIS] Primary Immune Deficiency Consortium Conference capitalized upon a mentoring program to train young investigators in the diagnosis and treatment of PIDs. This training effort, a collaboration between the CIS and the USIDNet Consortium, advances the skills of both seasoned physicians and fellows in the diagnosis, molecular defects, complications, and treatment of these complex diseases. Investigators at the Bi-Annual Meeting of the International Union of Immunological Societies Expert Committee on PID presented cutting-edge basic research in immunology, descriptions of novel gene defects in patients with PIDs, and potential new therapies. The meeting, organized under the auspices of the Jeffrey Modell Foundation, provides an important venue for updating the classification of identified PIDs.

The NICHD plans to continue its efforts to develop newborn screening procedures for a variety of conditions, including PIDs. The field has been moving so rapidly that genes involved with different forms of PID are being identified in increasing numbers. Although the increasing number of such identified genes further complicates the development of newborn screening tests, progress in this area is being made. A current focus of Institute efforts in developing newborn screening for PID is Severe Combined Immunodeficiency (SCID). This disorder, an inherited lack of immunity caused by diverse mutations in several different genes, is lethal if not treated in a timely manner. The recent development of a practical newborn screening test for SCID will allow for infants with this condition to be identified and, ultimately could lead to the development of early, life-saving treatment for them. Consequently, the NICHD will refocus on other PIDs as part of its overall newborn screening efforts. This economy of effort will permit the cost-efficient development of newborn screening biomarkers for PIDs as well as other rare genetic diseases.

Item

***Physical therapy-*** The Committee recognizes the burgeoning growth in rehabilitation services provided to patients, especially the elderly, with musculoskeletal problems and the urgent need to establish a solid scientific basis for clinical practice in this area. The Committee encourages the establishment of a research program in the National Center for Medical Rehabilitation Research (NCMRR) to: (1) evaluate the efficacy and establish optimal schedules and settings for movement-based rehabilitation interventions, such as therapeutic exercise, to improve physical function in individuals with musculoskeletal conditions, including arthritis, back pain, hip fracture and major joint replacements, and (2) further knowledge of the underlying mechanisms of repair, regeneration and recovery of these interventions. The Committee encourages NIA, NIAMS, and NIBIB to collaborate on these initiatives. (p. 83)

Action taken or to be taken

In addition to supporting individual research projects relating to musculoskeletal problems, the NICHD's NCMRR, in collaboration with NIAMS, organized a January, 2006 scientific conference to establish a research agenda on non-operative management of musculoskeletal conditions. Agenda-setting meetings, which identify current scientific knowledge and research needs, are a critical initial step in developing research programs. In other activities, the NICHD funded multiple exploratory grants through the NCMRR, under a special initiative to enable experienced and new investigators to plan clinical trials on the timing, intensity, and duration of rehabilitation services. In part because of investigator achievements in response to that initiative, the NICHD is now receiving applications for large-scale clinical trials that are expected to extend clinicians' understanding of appropriate rehabilitation practices. The NICHD, through the NCMRR, collaborates frequently with other Institutes with shared interests in rehabilitation services. For example, the NICHD is the lead Institute in the current effort to solicit applications for research partnerships, among multi-disciplinary research teams, to conduct basic, applied, and translational research to improve functional outcomes in rehabilitation for people with chronic or acute disease. Participating Institutes include NIA, NIAMS, and NINDS. The Agency for Healthcare Research and Quality also participated in this solicitation. Center also collaborated with the Center for Medicare and Medicaid Services (CMS) to develop a research agenda regarding appropriateness of inpatient rehabilitation for different populations of Medicare beneficiaries. In addition, the NCMRR proposed a collaborative research effort with CMS to develop data on this issue. NCMRR scientific staff are also consulting on the JOINTS study of hip and knee replacement outcomes in patients receiving post-replacement care in skilled nursing facilities and inpatient rehabilitation facilities.

Item

***Glucose monitoring-*** The Committee recognizes the importance of independent evaluation of blood glucose monitoring technologies. The Committee commends NICHD for its support of the Diabetes Research in Children Network (DirecNet), which aims to improve the management of diabetes in children by understanding how to best apply monitoring technology in this patient population. The Committee notes the unique infrastructure that DirecNet has developed to assess such technologies in children and encourages continued support for this important clinical research program. (p. 83)

Action taken or to be taken

The mission of the Diabetes Research in Children Network (DirecNet) is to investigate the potential use of glucose monitoring technology and its impact on the management of type 1 diabetes (T1DM) in children. The NICHD supports this research network through the special Statutory Funding Program for Type 1 Diabetes Research. Specific goals for the network include assessing the accuracy of continuous monitoring devices, to determine if they help improve glycemic control and prevent hypoglycemia in children with T1DM. A second goal is to determine the best use of continuous glucose monitors in managing pediatric diabetes and the impact, of using the monitors continuously, on the quality of life for a child and family. DirecNet investigators have developed seven protocols and four ancillary studies resulting in 10 peer-reviewed published articles and 4 others in press. Additionally, 20 abstracts from DirecNet investigators have been presented national meetings of the Society for Pediatric Research, American Diabetes Association, the Endocrine Society and other research associations over the past 4 years. DirecNet's well-designed and rigorously controlled randomized clinical trials have determined that capacity of new technologies to improve diabetes control in children. Among other achievements, network investigators were the first to characterize the glycemic profile of nondiabetic children. DirecNet funding, initiated in September 2001, will continue through September 2006. A competitive renewal of the network is planned for this year.

Item

***Pediatric kidney disease-*** The Committee encourages NICHD to study pre- and post-natal exposures that increase the risk of kidney disease, hypertension, and the progression of chronic kidney disease from birth to early adulthood. The Committee encourages NICHD to support research toward understanding the physiologic mechanisms responsible for these risks to further prevent the development of kidney disease and the antecedents of cardiovascular disease. (p. 83)

Action taken or to be taken

The NICHD continues to support important research that will enlarge understanding of prenatal and postnatal exposures that may predispose infants and children to developing chronic kidney disease, hypertension, and cardiovascular disease later in life. In 1990, the Endocrinology, Nutrition, and Growth Branch issued a Request for Applications on the "Fetal Origins of Adult Disease" to help understand the early origins and the earliest appearance in childhood of the precursors of major adult disorders, including hypertension, cardiovascular disease and type 2 diabetes. The funded studies involve the examination and follow-up of thousands of children, to determine the time of onset of elevated blood pressure and abnormal functioning of the kidney, liver, and pancreas. These early malfunctions presage the appearance of chronic renal disease, type 2 diabetes and cardiovascular disease later in life. Initial results of these studies show that hypertension, obesity, and abnormal levels of plasma lipid levels track closely from the first decade of life into early adulthood.

In addition to these major research studies in infants and children, the NICHD maintains a research program in animal models. Investigators are currently studying the effects in rats and microswine (a special breed of swine) of maternal exposure to high levels of glucocorticoids and to diets restricted in protein. These stressful exposures reduce the number of filtration units (glomeruli) in each kidney of the developing offspring in utero. The absence of these units stresses the remaining glomeruli in post-natal life, resulting in disturbances in the regulation of blood pressure. This animal model research will shed light on the role of systemic interactions in prenatal and early-postnatal life in promoting hypertension in adolescence and adulthood.

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

Item
***Autism-*** The Committee is aware of the important research into the genetic basis of autism spectrum disorders and of its support for the Baby SIBS study on the incidence of autism among children in the same families. Accordingly, the Committee encourages the Institute to expand its support and funding for the Baby SIBS study, and encourages the Institute to expand its work with and support for similar public-private partnerships. (p. 122)

Action taken or to be taken
Please refer to page NICHD-37 of this document for the NICHD response to this significant item.

Item
***Behavioral Science-*** The Committee emphasizes its strong support for the broad portfolio of behavioral research at NICHD and supports its efforts to determine the biological, behavioral, and social factors that affect cognitive, social, and personality development of children in a variety of settings. The Committee encourages the institute to maintain its support for research and training in behavioral science as it engages in its priority setting process. (p. 122)

Action taken or to be taken
Strong NICHD support for behavioral science is fundamental to the Institute's ability to achieve its mission "…to ensure that … all children have the chance to achieve their full potential for healthy and productive lives…". Research supported by the NICHD increasingly reaches across disciplinary lines to link psychological and behavioral processes in cognitive, social, and personality development with underlying biological processes, and to understand how social and economic factors affect developmental outcomes.

NICHD has made significant investments in trans-disciplinary science that addresses the biological, behavioral, and social factors that affect children's development. These include studies funded under the following initiative focusing on 1) the effects of poverty on child development; 2) the effectiveness of early childhood programs or interventions in promoting school readiness; 3) tools to measure important early childhood competencies. The NICHD's National Longitudinal Study of Adolescent Health has expanded knowledge of the effects of family, peer, and community factors on adolescent development. Other research has examined the effects on child development of changes to the nation's welfare policies; maternal employment; rural communities, and immigrant status. NICHD has led interagency efforts to

advance research on the antecedents of child abuse and neglect and their impacts on children's health and development.

NICHD has collaborated actively in funding trans-disciplinary research investigating biobehavioral questions in child health. The NIH Pediatric MRI Study of Normal Brain Development is developing a longitudinal database of neuropsychological, cognitive, behavioral, and anatomical brain development in typically developing children, and other projects are supporting the development of new methods for integrating brain development with behavioral measures tapping the development of memory, attention, language, and reading. A new community-based study is planned to examine the social, behavioral and biological processes that produce health disparities in birth outcomes and early child development.

For these priority areas of research to reach their full potential, the NICHD will continue to invest in innovative models of research and training, including training in both the behavioral sciences and interdisciplinary fields.

Item

***Childhood Diseases of the Growing Skeleton-*** NICHD is urged to support studies investigating the effects of pharmaceuticals, lifestyle, and chronic childhood diseases on the growing skeleton and fracture risk and bone-formation interventions for children. The Institute is encouraged to expand the Osteogenesis Imperfecta Clinic and osteogenesis imperfecta research, especially in genetic therapies, animal models, drug treatment and rehabilitation. To the extent feasible, NICHD is encouraged to work with NIAMS to study the rare disorders osteopetrosis and juvenile Paget's disease. (p. 122)

Action taken or to be taken

Please refer to page NICHD-38 of this document for the NICHD response to this significant item.

Item

***Childhood Obesity***- The Committee continues to be concerned about rising rates of childhood obesity and would like to see additional clinical trials that focus on the effectiveness of behavioral interventions. The Committee recognizes the critical importance of prevention efforts in this area and supports continued initiatives to promote healthy behaviors in children and adolescents, and research to prevent health risk behaviors that contribute to this growing public health challenge. (p. 122)

Action taken or to be taken

In response to the rising rates of childhood obesity, the NICHD funded eight behavioral intervention studies under its 2004 solicitation, *Prevention and Treatment of Childhood Obesity in Primary Care*. The studies focus on preventing excessive weight gain in children at-risk of overweight and preventing further weight gain and/or promoting weight loss in obese children. These studies are innovative in both their connection to primary care sites and their use of motivational counseling, family-focused interventions, community resources, and leading-edge technologies. New paradigms for addressing childhood obesity in clinics and other primary care sites could result from this research.

The NICHD also supports several behavioral intervention studies aimed at altering eating patterns and/or increasing physical activity in children and adolescents. Researchers at the University of Buffalo are comparing their standard family-based, behavioral intervention program with a new, innovative program for pediatric obesity based on behavioral economic theory. The decline in physical activity during adolescence, especially for girls, is the impetus for another on-going study which is evaluating the efficacy of a student-centered, after-school program for promoting physical activity among minority girls from low-income families.

Recognizing that the rapid increase in obesity over recent decades is the product of changes in the nation's physical, technological, and social environment, the NICHD has invested in foundational research on environmental influences on overweight and obese conditions. Current studies include research on the relationships between obesity and household factors that influence parenting and infant feeding patterns, and environmental and other factors that affect activity levels in children. This research may inform future preventive interventions. Research interest has also been stimulated by the 2004 multi-IC solicitation, *Understanding Mechanisms of Health Risk Behavior Change*, seeking studies of biopsychosocial pathways to obesity, substance abuse, and injuries.

To translate research findings into community-based interventions, the NICHD joined with the NHLBI, the NIDDK and the NCI to support the WE CAN (Ways to Enhance Childhood Activity and Nutrition) program, launched by Secretary Leavitt in 2005. WE CAN is a community intervention program to promote healthy child and adolescent behaviors. Its curriculum for parents, an after school curriculum for children, and a guide for promoting community events are based on the Institutes' research. In addition, the NICHD's after school curriculum, Media Smart Youth, focuses on 1) the role of media in shaping snack choices; and 2) the role of physical activity for young people. The Media Smart Youth curriculum has been extremely well received by the communities that have conducted the program.

Item

***Demographic Research-*** The Committee commends NICHD for its strong support of demographic research. Given the tremendous changes occurring in the U.S. population, demographic research is necessary to analyze trends and determine consequences for the health and well-being of our Nation. The Committee strongly encourages the Institute to assure adequate support for demographic training and for critical databases such as National Longitudinal Study of Adolescent Health and Fragile Families. NICHD-supported studies like these yield objective information about population trends and provide unbiased, accurate data to inform policy, programs, and practices to improve the health and productivity of the American people. (p. 123)

Action taken or to be taken

Please refer to page NICHD-40 of this document for the NICHD response to this significant item.

Item

***Drug Safety for Children-*** The Committee recognizes the importance of ensuring that drugs are safe and effective for use by children and are appropriately labeled for pediatric use. The Committee supports continued implementation of the Best Pharmaceuticals for Children Act of 2003, which supports the pediatric testing of off-patent drugs, as well as on-patent drugs not being studied through existing mechanisms. The Committee is pleased to note that in fiscal year 2004, six studies were initiated and five additional studies are planned for fiscal year 2005. The Committee notes that NICHD has made numerous outreach efforts to other Institutes and Federal agencies to further refine the priority listing process. The Committee requests that NIH provide an update during its annual appropriations testimony that shall include the role of other Federal agencies in implementing the Best Pharmaceuticals for Children Act of 2003; information on the number of studies supported through the Research Fund; the estimated cost of each study undertaken; the nature and type of studies undertaken, the number of label changes resulting form completed studies; the patent status of the drug studies; the number of drugs remaining on the priority list and a summary of NICHD's findings on the frequency of pediatric use for medications that many be considered for the priority list. (p. 123)

Action taken or to be taken

Please refer to page NICHD-34 of this document for the NICHD response to this significant item.

Item

***Epilepsy-*** Epilepsy often begins in childhood and can have potentially devastating effects when seizures are not controlled. This disease has a severe impact on cognition and, even in its mildest forms, lifelong effects on employment and other quality of life measures. Recurring seizures are also a heavy burden for children with autism, brain tumors, cerebral palsy, mental retardation, tuberous sclerosis and a variety of genetic syndromes. The Committee urges the Institute to make research in epilepsy a priority, with a particular emphasis on developmental effects, and to coordinate research efforts with the NINDS (p. 123/124)

Action taken or to be taken

Epilepsy is a brain disorder in which clusters of nerve cells (neurons) in the brain signal abnormally, causing seizures. Abnormal brain wiring, imbalance in nerve-signaling chemicals, or a combination of these factors may cause epilepsy to develop. Multiple factors that may cause or contribute to epilepsy have been identified, including genetic anomalies, brain tumors, and head injuries. The NINDS, which receives the vast majority of applications for epilepsy and seizure disorders research, leads the NIH in this area. Current NICHD-supported research that relates to epilepsy includes several projects to help individuals being treated medically for seizures. For example, researchers are developing and testing a child-friendly, electronic “med-minder” that could ensure that children epilepsy receive medications at the time and in the doses that they need to control their conditions. The system’s devices will be packaged for children in small pouches that can carry a child’s medications and the system will enable authorized third parties, such as a child’s physician, to track young patients’ compliance with medication regimes. Clinical trials of the device will be conducted in children with epilepsy, severe asthma, and diabetes. In another study, researchers are determining whether the drug carbamazepine, which is widely used in reproductive-age women for seizures and certain other conditions, may

affect the efficacy of oral contraceptives. Other NICHD-supported research includes a project to map and characterize specific genes that contribute to epilepsy and longitudinal studies of two developmental disorders in which seizures occur, Rett syndrome and autism.

Item

***Family Formation-*** Families constitute the key environment for children's development, and parents are crucial to children's health and academic outcomes. The Committee encourages research on effective ways to promote and sustain healthy family formations, particularly for low-income families and families of color. Additional research is encouraged on the immediate and long-term impact of chronic and acute exposures to violence on child health and development. The institute is encouraged to include research related to family, community and cultural factors that serve as risk or protective factors and promote resilience from exposure to violence in the home, communities, and schools. (p. 124)

Action taken or to be taken

The family is the single most important influence affecting a child's healthy development and future productivity. NICHD research has documented dramatic changes in the American family since the 1960s. Since then, rates of non-marital childbearing, single-parent families, and unstable families have risen. These trends have contributed to high rates of child poverty and have fundamentally changed American childhood. It is critically important to understand what these changes mean for child development, why the changes have occurred, and how families can be strengthened and supported in raising healthy children. The NICHD has a strong commitment to supporting research to answer these questions. For example, by documenting important influences on marriage of cultural values and economic opportunities, NICHD research has provided the scientific basis for efforts to encourage and strengthen marriage among low-income families. NICHD-supported research on fatherhood found that unwed families are most amenable to intervention during the "magic moment" – the time of a new baby's arrival. Building on its long-standing commitment to research on family formation, the NICHD recently funded research on how to improve the stability of marriage.

In recent years, the NICHD has greatly expanded its investment in research on the implications of violence for healthy child development. Ongoing studies have demonstrated that exposure to violence in childhood and adolescence has serious developmental effects, including the ability to form long-lasting family relationships as an adult. The National Longitudinal Study of Adolescent Health has provided a wealth of knowledge concerning risk and protective factors in community, school, peer, and family environments affecting youth involvement with, and exposure to violence. Working collaboratively with partner Institutes and agencies, the NICHD organized the *Children Exposed to Violence* workshop to assess the state of science and research needs related to children exposed to domestic violence, community violence, and war and terrorism. Subsequently, a multi-agency solicitation sought research on the incidence and prevalence of children exposed to domestic or community violence, the impact of such exposures on children's development, and the efficacy of parent skills training interventions for children exposed to violence. To date, the NICHD has funded nine grants under this solicitation and has also held workshops to disseminate existing knowledge in this area. To increase the number of well-trained researchers, the Institute supports career development and research training in the fields of child abuse and neglect.

Item

***Fragile X-*** Title II of the Children's Health Act of 2000 authorized the establishment of at least three Fragile X research centers. The Committee is pleased that the NICHD has funded three Centers, and urges the NICHD to increase the funding for existing centers of excellence by the end of fiscal year 2006, with the goal of enhancing the Centers and recruiting new researchers to the Fragile X field. The Committee also encourages the NICHD to coordinate its Fragile X research efforts internally, by partnering with others, and by relating Fragile X research with that in other developmental disorders, such as autism research. (p. 124)

Action taken or to be taken

Please refer to page NICHD-36 of this document for the NICHD response to this significant item.

Item

***Genomics and Proteomics Research-*** The Committee is pleased that NICHD has launched a major new initiative to address the public health problem of premature birth, which affects one in eight babies born in this country and is the leading cause of newborn death. NICHD is encouraged to move forward with this initiative, which focuses on genomic and proteomics, in an effort to accelerate knowledge in the mechanisms responsible for premature birth. The Committee intends to closely monitor this effort because it assigns a high priority to promoting the birth of healthy infants. (p. 124)

Action taken or to be taken

Please refer to NICHD-31 of this document for the NICHD response to this significant item.

Item

***Infertility and Contraceptive Research-*** The Committee notes that infertility is a disease which affects over 6 million people in the United States and is concerned that the number appears to be growing as age, lifestyle, and environmental factors increasingly impact reproductive health outcomes. The Committee urges that additional research be undertaken to improve reproductive health intervention outcomes, as this research will not only increase the efficacy and effectiveness of reproductive health interventions but will significantly lower costs by reducing the number of interventions necessary to achieve a successful outcome. (p. 124)

Action taken or to be taken

Please refer to page NICHD-39 of this document for the NICHD response to this significant item.

Item

***Learning Disabilities-*** The Committee is pleased that NICHD continues to place a high priority on learning disabilities research. The efforts to address the special needs of children affected by a learning disability and improve literacy are showing promising results. The Committee encourages NICHD to continue to focus on reading disability and mathematics development research. Additionally, the Committee urges NICHD to lead a cooperative effort to collaborate on research efforts with other Institutes working on related activities. The Committee encourages

cooperation in areas where work can be shared across Institutes on behalf of individuals with learning disabilities. (p. 125)

Action taken or to be taken
The NICHD has had a longstanding interest in the study of normal language and reading development, learning disabilities, and disorders that adversely affect the development of listening, speaking, reading, writing, and mathematics abilities. Research at the Institute's network of multidisciplinary Learning Disability Research Centers (LDRCs) focuses on the definition, classification, origins and treatment of learning disabilities (LDs) and related disorders. This network has yielded a number of discoveries and advances, including the identification of critical cognitive and linguistic factors in the normal acquisition of basic reading abilities and reading failure and their neurobiological and genetic correlates. Network researchers have produced converging evidence on the importance, in learning to read, of strategies to enhance phonemic awareness, reading fluency and comprehension, vocabulary and other skills.

Comprehensive models of specific ways to enhance fluency, vocabulary, and comprehension must still be articulated, however. Following the 2005 LRDC recompetition, those centers that are funded will continue to integrate anatomical and functional neuroimaging protocols with descriptive and treatment studies. The goal of this research is to better understand the specific neural systems that relate to the multiple skills needed for reading, and the degree to which interventions may alter the systems. NICHD program staff are communicating with NIMH program staff about potential funding for a LRDC Center that would examine attention deficit hyperactivity disorder as a co-existing condition with reading disability, with in-depth genetic studies of the two disorders.

With the U.S. Department of Education, the NICHD has funded a network of five innovative research projects on specific learning disabilities in mathematics. Network projects include studies of the neurobiological bases of mathematical LDs, investigations of math LD subtypes, and teaching interventions. Having recently expanded to include four additional projects, this research network should enhance the convergence of methods, measures, and subsequent findings to improve educational practice.

Item
***Learning and School Readiness***- The Committee continues to support NICHD's commitment to research in reading, learning disabilities and math and science cognition. The Committee is encouraged that NICHD has made progress on developing comprehensive, culturally neutral and developmentally appropriate assessments and instruments to measure cognitive, social and emotional skills for pre-school aged children that are necessary for school readiness. (p. 125)

Action taken or to be taken
Building on years of high quality research, developmental scientists must now refine and use this knowledge to create ways to assess accurately the developmental capacities of young children, in areas that are important in understanding early child development and readiness for school. The need for this knowledge is particularly great for specific developmental outcomes and for children from diverse populations. To stimulate research in this area, the NICHD issued the

solicitation, *Developing Outcome Measures for Young Children*. The goal of this solicitation is to develop measures that can be translated from the laboratory into real world applications. In FY 2005, the NICHD, in collaboration with the Administration on Children and Families and the Institute for Education Sciences in the Department of Education, awarded grants under this solicitation to develop culturally and linguistically appropriate measures for preschool children. These projects will construct measures of early social competencies, executive functioning, early mathematical competence, and phonological processing in young children who speak one language and are learning a second. During the grant period, the investigators will work together to establish rigorous standards for the measures, before they are adapted to real word applications. Once developed, the measures will be usable in diverse early childhood settings, to monitor children's progress in acquiring key school readiness skills, to provide feedback on program performance and, in some cases, directly to inform instructional strategies for young children.

Item

***Maternal-Fetal Medicine Units Network-*** The Committee recognizes the efforts of NICHD, through its Maternal Fetal Medicine Units Network [MFMU], to achieve a greater understanding and pursue development of effective treatments for the prevention of pre-term births, low birth weight infants, and medical complications during pregnancy such as pregnancy-related hypertension and diabetes. The Committee is pleased to learn that the NICHD is proceeding with a competing renewal of the MFMU's in 2006 and encourages a sustained research investment in this program to facilitate resolution of these problems and promote the birth of healthy infants. (p. 125)

Action taken or to be taken

Please refer to page NICHD-32 of this document for the NICHD response to this significant item.

Item

***National Children's Study-*** The Committee is pleased with NICHD efforts to launch the National Children's Study, which would be the largest study of children ever undertaken in the United States and is intended to follow 100,000 children to age 21, examining the impacts and influences of many environmental and genetic factors on children's health and development. The Committee urges that the National Children's Study include an adequate sample of children to enable examination of the health and development outcomes of children conceived with the assistance of reproductive health technologies.

The Committee further urges the NICHD to coordinate the involvement of the Department, the lead Federal partners--CDC, EPA and NIEHS--and other interested institutes, agencies and non-Federal partners conducting research on children's environmental health and development, such that this study is ready for the field by no later than 2007 (p. 125)

Action taken or to be taken

In support of the National Children's Study (NCS) seven contracts to "Vanguard" study centers to pilot the first phase of the study were awarded. A contract for a study coordinating center was also awarded.

No funds are included in the President's Budget Request for FY 2007 for the National Children's Study. The NCS planning activities that are on going under contract in FY 2006 will be brought to a close by the end of the fiscal year. There are no plans for the NIH to continue to pursue the full scale study in FY 2007.

Item

***National Cooperative Program for Infertility Research-*** The Committee understands that the NICHD is planning to merge its National Cooperative Program for Infertility Research with its Specialized Cooperative Centers Program in Reproduction Research to form the Specialized Cooperative Centers Program in Reproduction and Infertility Research. The Committee understands that this merger will allow a greater focus on human infertility research and a more efficient translation of knowledge from non-human animal models to humans to ensure rapid development of novel approaches for the diagnosis, treatment and amelioration of such reproductive diseases and disorders as polycystic ovarian syndrome, endometriosis, hypogonadotropic, hypogoandism, and idiopathic male infertility. The Committee looks forward to hearing more about the progress towards this merger. (p. 125-126)

Action taken or to be taken

We are pleased that the Committee has recognized the merger of two outstanding NICHD research programs, to create the new Specialized Cooperative Centers Program in Reproduction and Infertility Research (SCCPRIR). The consolidated program will be poised to make major advances in the diagnosis, treatment and amelioration of reproductive diseases and disorders that impair human fertility. In particular, the merger of the programs will facilitate and expand research collaborations of basic and clinical investigators in the area of Polycystic Ovary Syndrome (PCOS). PCOS is special focus of one component of the new program, the National Cooperative Program for Infertility Research (NCPIR). The merger will also enhance efforts to translate scientific findings in animal models into new approaches to diagnosing, treating, and ameliorating other reproductive diseases and disorders, including endometriosis and male infertility. The Institute will publish the solicitation for the new, consolidated research program in the fall of 2005, with an anticipated program start date of April, 2007. The NICHD will be pleased to update the committee on the progress of this merger.

Item

***Neurofibromatosis-*** Learning disabilities occur with high frequency (30-65 percent) in children with NF and in approximately 5 percent of the entire world's population. Enormous advances have been made in the past few years in the successful treatment and curing of learning disabilities in pre-clinical NF animal models. Therefore the Committee encourages NICHD to issue RFAs for NF research and aggressively pursue and expand funding of clinical trials for NF patients in the area of learning disabilities. The Committee is mindful that finding a treatment and cure for learning disabilities will not only benefit children, but also reduce costs of special education. (p. 126)

Action taken or to be taken

Please refer to page NICHD-35 of this document for the NICHD response to this significant item.

Item

***Pediatric Kidney Disease-*** The National Children's Study provides a unique opportunity to identify pre- and post-natal exposures that increase the risk of kidney disease, hypertension, and the progression of chronic kidney disease from birth to early adulthood. The Committee urges NICHD to support research toward understanding the physiologic mechanisms responsible for these risks to further prevent the development of kidney diseases and the antecedents of cardiovascular disease. (p. 126)

Action taken or to be taken

Please refer to page NICHD-43 of this document for the NICHD response to this significant item.

Item

***Prader-Willi Syndrome-*** Prader-Willi Syndrome is the most common known genetic cause of life threatening obesity in children. The Committee strongly encourages the NICHD to place a high priority on Prader-Willi Syndrome research to study childhood obesity. Furthermore, the NICHD is urged to incorporate Prader-Willi Syndrome into the planning process for The National Children's Study. (p. 126)

Action taken or to be taken

Prader-Willi syndrome (PWS) is a genetic disorder that is characterized by an insatiable appetite for a wide variety of foods, morbid obesity, temper tantrums, and outburst of aggression. The NICHD has had a longstanding research interest in Prader-Willi syndrome and funded research showing that deletion of a long sequence of genetic material from chromosome 15 causes Prader-Willi syndrome. The NICHD support has enabled investigators to demonstrate the importance of maternally expressed genes on chromosome 15 in the absence of complementary paternal genetic material in causing PWS. This critical observation opened a new field of research on the phenotypic effects of imprinted genes of paternal and maternal origin.

The NICHD-funded investigators have built on these findings to construct a mouse model of Prader-Willi syndrome. Availability of the animal model enables scientists to pinpoint the genes that cause the insatiable appetites and uncontrollable temper tantrums of children with Prader-Willi syndrome. Two or more contiguous genes on maternal chromosome 15 now appear necessary to explain the PWS complex set of behaviors and body composition. Other NICHD investigators are treating children with PWS with the neurotropic agent topiramate, to lessen the self-injurious behavior that is part of the syndrome. NICHD supported investigators also implement, with some success, regimens of behavioral therapy that include using food as a reward. Building on a joint meeting with the Prader-Willi Syndrome Association in November 2004, the NICHD plans to encourage future research into the problem of PWS-associated obesity and obsessive-compulsive disorder in children. One strategy currently under discussion with the Prader-Willi Syndrome Association is convening a meeting on this topic to assess the current state-of-the-science.

Item

***Primary Immunodeficiency Diseases-*** The Committee continues to be impressed with the dedication of financial and personnel resources by NICHD to the physician education and public awareness program conducted by the Jeffrey Modell Foundation to reach earliest diagnosis of this class of about 140 diseases. With regard to research on PI, the Committee is strongly encouraged by the Institute's commitment to develop newborn screening procedures for PI, particularly X-linked SCID, utilizing microarray technologies. The Committee believes that NICHD should move ahead aggressively with this initiative, in partnership with the Foundation and private industry. (p. 126)

Action taken or to be taken

Please refer to page NICHD-41 of this document for the NICHD response to this significant item.

Item

***Vulvodynia-*** The Committee commends NICHD for its commitment to chronic pain conditions including vulvodynia. This condition has profound impacts on the health and quality of life for millions of women. As a result of efforts funded by NICHD, the number of high-quality researchers interested in research on vulvodynia has increased. NICHD is strongly encouraged to reissue its request for applications in this area and to fund high-quality applications, with a particular emphasis on etiology and multi-center therapeutic trials. (p. 127)

Action taken or to be taken

The NICHD continues to work proactively with the Office of Women's Health Research (ORWH) and other components of the NIH to stimulate research in the cause and potential treatment of vulvodynia and to enhance public and clinician awareness of this painful condition. Since 1997, periodic NIH-sponsored conferences have brought together investigators to share their most current findings. The investigators, the public and clinicians can now access the proceedings of the 2003 research conference, *Vulvodynia: Toward Understanding a Pain Syndrome* and other information about vulvodynia on the NICHD, ORWH, and Office of Rare Diseases Web sites. Information about vulvodynia can also be accessed through the NIH "Health Information" home page. (http://health.nih.gov/index.asp).

The NICHD and the ORWH will issue the third NIH vulvodynia research solicitation of the last decade, inviting applications for support of studies of the etiology and pathophysiology of this disorder, the pain mechanism associated with it, and its treatment. Investigator-initiated applications for NICHD funding to study aspects of vulvodynia are reviewed by a standing Institute committee with expertise in gynecology and reproductive health (also androgoly). To review applications relating to vulvodynia that are submitted in response to Requests for Applications, the NICHD convenes a Special Emphasis Panel, the members of which are all urogynecologists.

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**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 | 11,302,000 | Indefinite | 15,179,000 |
| National Institute of Child Health and Human Development | Section 41B | 42§285b | Indefinite | $1,217,989,000 | Indefinite | $1,206,925,000 |
| National Research Service Awards | Section 487(d) | 42§288 | a/ | 35,478,000 | | 35,314,000 |
| Total, Budget Authority | | | | 1,264,769,000 | | 1,257,418,000 |

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

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Appropriations History**

| Fiscal Year | Budget Estimate to Congress | House Allowance | Senate Allowance | Appropriation 1/ |
|---|---|---|---|---|
| 1998 | 582,032,000 2/ | 666,682,000 | 676,870,000 | 674,766,000 |
| 1999 | 654,248,000 2/ 3/ | 728,817,000 | 748,482,000 | 750,982,000 |
| Rescission | 0 | 0 | 0 | (497,000) |
| 2000 | 694,114,000 2/ | 817,470,000 | 848,044,000 | 862,884,000 |
| Rescission | | | | (4,593,000) |
| 2001 | 810,501,000 2/ | 984,300,000 | 986,069,000 | 976,455,000 |
| Rescission | | | | (486,000) |
| 2002 | 1,096,650,000 | 1,088,208,000 | 1,123,692,000 | 1,113,605,000 |
| Rescission | | | | (1,931,000) |
| 2003 | 1,196,093,000 | 1,196,093,000 | 1,213,817,000 | 1,213,817,000 |
| Rescission | | | | (7,890,000) |
| 2004 | 1,245,371,000 | 1,245,371,000 | 1,251,185,000 | 1,250,585,000 |
| Rescission | | | | (8,224,000) |
| 2005 | 1,280,915,000 | 1,280,515,000 | 1,288,900,000 | 1,280,915,000 |
| Rescission | | | | (10,594,000) |
| 2006 | 1,277,544,000 | 1,277,544,000 | 1,310,989,000 | 1,277,544,000 |
| Rescission | | | | (12,775,000) |
| 2007 | 1,257,418,000 | | | |

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research
3/ Reflects a decrease of $468,000 for the budget amendment for Bioterrorism

**NATIONAL INSTITUTES OF HEALTH**

**National Institute of Child Health and Human Development**

**Detail of Full-Time Equivalent Employment (FTEs)**

| OFFICE/DIVISION | FY 2005 Actual | FY 2006 Appropriation | FY 2007 Estimate |
|---|---|---|---|
| Office of the Director | 24 | 23 | 23 |
| Office of Administrative Management | 57 | 39 | 40 |
| Office of Science Policy, Analysis and Communication | 22 | 21 | 21 |
| Center for Developmental Biology and Perinatal Medicine | 18 | 18 | 18 |
| Center for Population Research | 26 | 24 | 24 |
| Center for Research for Mothers and Children | 27 | 25 | 25 |
| National Center for Medical Rehabilitation Research | 7 | 7 | 7 |
| Division of Scientific Review | 12 | 12 | 12 |
| Division of Epidemiology, Statistics and Prevention Research | 31 | 31 | 31 |
| Division of Intramural Research | 324 | 323 | 325 |
| Total | 548 | 523 | 526 |
| Includes FTEs which are reimbursed from the NIH Roadmap for Medical Research | | | |
| FTEs supported by funds from Cooperative Research and Development Agreements | (2) | (2) | (2) |

| FISCAL YEAR | Average GM/GS Grade |
|---|---|
| 2003 | 11.0 |
| 2004 | 11.3 |
| 2005 | 11.8 |
| 2006 | 11.7 |
| 2007 | 11.6 |

**NATIONAL INSTITUTES OF HEALTH**
**National Institute of Child Health and Human Development**

**Detail of Positions**

| GRADE | FY 2005 Actual | FY 2006 Appropriation | FY 2007 Estimate |
|---|---|---|---|
| ES-6 | 0 | 0 | 0 |
| ES-5 | 0 | 0 | 0 |
| ES-4 | 2 | 2 | 2 |
| ES-3 | 1 | 1 | 1 |
| ES-2 | 0 | 0 | 0 |
| ES-1 | 0 | 0 | 0 |
| Subtotal | 3 | 3 | 3 |
| Total - ES Salary | $152,210 | $156,320 | $162,104 |
| GM/GS-15 | 44 | 41 | 41 |
| GM/GS-14 | 72 | 67 | 67 |
| GM/GS-13 | 43 | 35 | 35 |
| GS-12 | 52 | 49 | 50 |
| GS-11 | 28 | 28 | 28 |
| GS-10 | 8 | 8 | 8 |
| GS-9 | 31 | 29 | 29 |
| GS-8 | 22 | 21 | 21 |
| GS-7 | 18 | 16 | 16 |
| GS-6 | 2 | 2 | 2 |
| GS-5 | 5 | 5 | 5 |
| GS-4 | 2 | 2 | 2 |
| GS-3 | 0 | 0 | 0 |
| GS-2 | 0 | 0 | 0 |
| GS-1 | 0 | 0 | 0 |
| Subtotal | 327 | 303 | 304 |
| Grades established by Act of July 1, 1944 (42 U.S.C. 207): | | | |
| Assistant Surgeon General | | | |
| Director Grade | 10 | 10 | 10 |
| Senior Grade | 6 | 6 | 6 |
| Full Grade | 5 | 5 | 5 |
| Senior Assistant Grade | 3 | 3 | 3 |
| Assistant Grade | | | |
| Subtotal | 24 | 24 | 24 |
| Ungraded | 209 | 207 | 197 |
| Total permanent positions | 413 | 392 | 385 |
| Total positions, end of year | 563 | 537 | 528 |
| Total full-time equivalent (FTE) employment,end of year | 548 | 523 | 526 |
| Average ES level | ES-4 | ES-4 | ES-4 |
| Average ES salary | $152,210 | $156,320 | $162,104 |
| Average GM/GS grade | 11.8 | 11.7 | 11.6 |
| Average GM/GS salary | $81,693 | $83,735 | $86,833 |

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