DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

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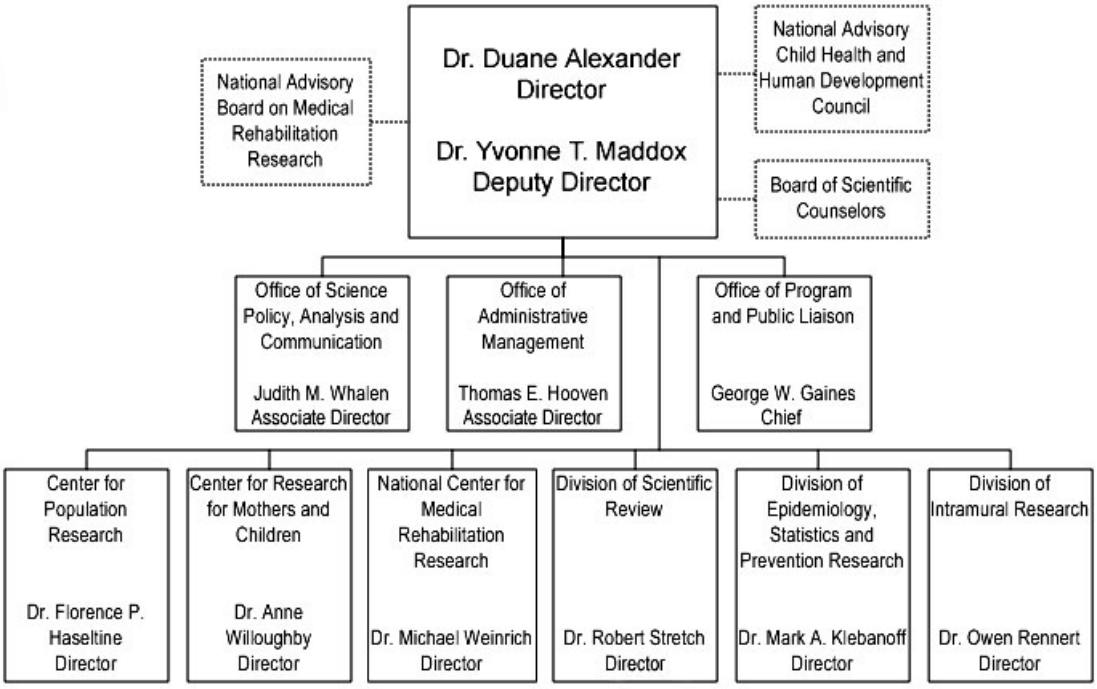

NATIONAL INSTITUTES OF HEALTH

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, $1,245,371,000.

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

Amounts Available for Obligation 1/

Source of Funding	FY 2002 Actual	FY 2003 Amended President's Budget	FY 2004 Estimate
Appropriation	$1,113,605,000	$1,196,093,000	$1,245,371,000
Enacted Rescissions	(1,931,000)	(0)	---
Subtotal, Adjusted Appropriation	1,111,674,000	1,196,093,000	1,245,371,000
Real transfer to:			
Other HHS Agencies through Secretary's one-percent transfer authority	(1,202,000)	(0)	(0)
Comparative transfer from:			
Fogarty International Center for International Services Branch	115,000	115,000	0
Comparative transfer to:			
Office of the Director for program changes	(1,219,000)	(1,317,000)	(0)
National Institute of Biomedical Imaging and Bioengineering	(0)	(0)	(0)
Subtotal, adjusted budget authority	1,109,368,000	1,194,891,000	1,245,371,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,109,368,000	1,194,891,000	1,245,371,000
Unobligated balance lapsing	(13,000)	---	---
Total obligations	1,109,355,000	1,194,891,000	1,245,371,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2002 - $17,020,000 FY 2003 - $17,020,000 FY 2004 - $17,020,000
Excludes $88,000 in FY 2002 and $96,000 in FY 2003 for royalties.

Justification

National Institute of Child Health and Human Development

Authorizing Legislation: Section 301 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
597	$1,109,368,000	600	$1,194,891,000	590	$1,245,371,000	(10)	$50,480,000

This document provides justification for the Fiscal Year 2004 activities of the National Institute of Child Health and Human Development, including HIV/AIDS activities. A more detailed description of NIH-wide Fiscal Year 2004 HIV/AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)".

INTRODUCTION

The NICHD conducts and supports research on the myriad factors that protect and enhance – or impede – the processes of human growth and development. The developmental focus of the NICHD means that its research portfolio is unusually broad. NICHD programs target research on infant mortality; preventing birth defects, including genetic anomalies; cognitive, social, emotional, and physical growth; learning disorders; developmental disabilities such as autism and mental retardation; reproductive biology and health; vaccine development; demographic and behavioral sciences; and enhancing or restoring function in individuals with a physical disability. The unifying goal of NICHD research is to create the scientific knowledge needed to ensure the birth of healthy infants and to maximize the potential of each individual to remain healthy and to learn and grow to achieve his or her full potential in adulthood.

This document reports current NICHD scientific advances that promise major public health and economic benefits, such as helping physicians protect premature infants from a deadly gastrointestinal disease and helping stroke patients better regain lost capacity to perform ordinary daily activities. In one case, research begun decades ago to resolve vaccination problems presented by children's immature immune systems has led to the first vaccine against a major cause of hospital-acquired infection, for adults as well as children. Some advances were achieved in collaboration with other Institutes and Centers, other components of DHHS such as the Centers for Disease Control and Prevention, other federal agencies such as the Department of Education, and the private sector. Faith-based and community organizations are collaborating

with the NICHD in designing and leading campaigns that translate NICHD science into information that families can use, for example to reduce the risk of sudden infant death syndrome (SIDS). The pharmaceutical industry, as well as other Institutes and Centers, use networked NICHD research centers to conduct clinical trials of drugs for children.

This document summarizes NICHD scientific advances under the headings of child health and human development; women's health; reproductive health; health and functional capacity; AIDS; and other advances, primarily in basic science. It also highlights current and future initiatives to help the Institute meet continuing public health and research needs.

SCIENCE ADVANCES

CHILD HEALTH AND DEVELOPMENT

Childhood Diseases and Conditions

Premature Infants and a Deadly Gastrointestinal Disease. The most common gastrointestinal disease in premature infants, affecting 3,000 to 5,000 newborns, is a potentially fatal inflammation of the intestine and colon, known as necrotizing enterocolitis (NEC).[1] Until recently, scientists knew that formula feeding was related to NEC, but they did not know how the disease develops or how to prevent it. This year, scientists reported that a naturally-occurring factor in mother's milk, epidermal growth factor (EGF), prevented NEC in experimental rats, when used as a formula supplement. The finding suggests that the relatively simple intervention of adding EGF supplements to the formulas fed to premature infants could prevent NEC. The research also sheds light on how NEC develops, possibly leading to new ways to treat other gastrointestinal diseases in infants and children.

Very Low Birth Weight and Long-term Outcome. About one percent of infants born in the U.S. are very low birth weight (VLBW), weighing less than 1,500 grams (about three and one-third pounds).[2] VLBW children who would have died in infancy decades ago are now more likely to survive, but often with disabling neurological, respiratory, or other conditions, causing lifetime disabilities. Little was known, until recently, about how these infants fare as adults. This year, scientists reported that at age 20, adults who had been VLBW were significantly more likely than peers to have chronic health problems, especially such conditions as cerebral palsy, blindness and deafness. They also had lower IQs and lower scores on academic achievement tests and were less likely to have earned high school or high school equivalency degrees. Yet the mean of the VLBW adults' achievement test scores was in the normal range and they were almost as successful as other young adults in completing secondary education. Given high rates of serious disabling conditions in the VLBW adults, the relatively narrow differences between them and young adults without these conditions suggests resilience, in them and their families. Further research could identify factors contributing to positive outcomes for these children.

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[1] Dvorak B, Halpern M, Holubec H, Williams, CS, McWilliam DL, Dominguez JA, Stepankova R, Payne CM, McCuskey RS. Epidermal growth factor reduces the development of necrotizing enterocolitis in a neonatal rat model. American Journal of Gastrointestinal Liver Physiology 282: G156-164, 2002.

[2] McCormick, MC. Prematuare infants grow up. The New England Journal of Medicine 346:197-198, 2002.

Story of Discovery: The First Vaccine against Hospital-Acquired Infection

Each year, hospital-acquired infections sicken two million people, killing about 80,000 of them. These infections add nearly $5 billion a year to U.S. health care costs.[3] Moreover, many kinds of bacteria have grown resistant to the antibiotics used to eliminate them.[4] A simple treatment for hospital patients, nursing home residents, and others at risk for hospital acquired infections would yield major benefits. Recently, scientists reported a successful test of a vaccine against one of the most common causes of hospital-acquired infections, *Staphylococcus aureus*, or "staph," bacteria. The method for creating the vaccine also holds promise for vaccines that target other disease-causing organisms, including those that could be used in a terrorist attack.

The new staph vaccine is the latest product of research begun decades ago as scientists sought a vaccine to protect infants and young children against *Haemophilus influenzae* type B (Hib). This often-fatal bacterial infection was the leading cause of meningitis among children under five in the U.S.[5] In 1983, John Robbins, M.D. and Rachel Schneerson, M.D. set up an NICHD laboratory to develop vaccines that were effective against bacteria. The two developed a vaccine to target the simple sugar molecule, or polysaccharide, on the surface of the bacteria that causes Hib. Polysaccharide vaccines were a major improvement on existing vaccines, which consisted of whole bacteria that had been killed or weakened and which could cause severe side effects.

After testing the vaccine, the NICHD scientists found that it was safe and that it stimulated protective levels of antibody in adults and older children. Antibodies are molecules made by the immune system. Like tiny guided missiles, they zero in on a particular substance, tagging if for later destruction by the immune system. Scientists supported by NIAID did further testing and, with the added involvement of industry, three Hib polysaccharide vaccines were produced and licensed in 1985. But infants and very young children – those most at risk of Hib infection – could not be immunized with the first formulations of Hib vaccine because of their immature immune systems. To overcome this problem, Robbins and Schneerson modified the vaccine, creating what is known as a conjugate polysaccharide Hib vaccine. To make the vaccine, the researchers chemically attached, or conjugated, the sugar molecule to a protein molecule. The infants' immune systems easily recognized the protein molecule, and, in the process, learned to recognize the sugar molecule as well. Before this vaccine, Hib infected about 20,000 U.S. children under age five each year, causing about 12,000 cases of meningitis and 1,000 deaths.[6] The Hib vaccine is now routinely used to immunize infants and children in the U.S., Canada, Western Europe, and many other nations. As a result, meningitis caused by Hib has all but disappeared in these countries. In the U.S., universal childhood vaccination with Hib saves a total of $2.9 billion (medical and indirect costs) each year.[7] Robbins and Schneerson shared the prestegious Albert Lasker Award for Clinical Research with their NIAID-funded colleagues.

The trial with the new staph vaccine was conducted in patients with kidney disease receiving dialysis treatment. These patients were chosen because they are at high risk of infection and are among the least likely to respond to immunization. The vaccine protected the patients for a short time against the two strains of *S. aureus* that cause 85 percent of staph infections. Booster shots will be tested to lengthen the period of immunity. More research will be directed to making the vaccine effective against other strains of staph. Similar vaccines against other hospital-acquired infections are now being designed.

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[3] CDC. "Hospital Infections Cost U.S. Billions of Dollars Annually," Press Release, March 6, 2000: Available at http://www.cdc.gov/od/oc/media/pressrel/r2k0306b.htm (cited November, 2002)

[4] For example, see CDC Fact Sheet. "VISA-VRSA-Vancomycin-Intermediate/Resistant *Staphylococcus aureus*. Available at: http://www.cdc.gov/ncidod/hip/aresist/visa.htm. (cited November, 2002)

[5] Zhou F, Bisgard KM, Yusuf HR, Deuson RR, Bath SK, Murphy TV. Impact of Universal *Haemophilus influenzae* Type B Vaccination Starting at 2 Months of Age in the United States: An Economic Analysis. Pediatrics 110:653-661, 2002.

[6] *Ibid.*

[7] *Ibid.*

A Precursor to Type 2 Diabetes in Children

Diabetes is a leading cause of death and disability in the U.S., particularly among African Americans, native Americans, and other minorities.[8] "Adult onset," or type 2, diabetes, the most commonly diagnosed form of this condition, was once rare in children. But recent clinical reports suggest that type 2 diabetes is increasing in children, possibly in parallel to epidemic childhood obesity. It is known that lifestyle changes can slow the emergence of diabetes; however, it has been difficult for physicians to identify children at risk of type 2 diabetes for early intervention. Scientists recently reported that they were able to calculate the prevalence of a precursor to type 2 diabetes, impaired glucose tolerance, finding it in twenty-five percent of obese children and youth studied. The ability to identify children with the precursor condition means that they could be targeted for intensive weight loss treatment.

Mental Retardation and Developmental Disability

A Possible Gene for Unexplained Mental Retardation. Mental retardation (MR) occurs in three percent of the population.[9] Scientists have identified some causes of MR but still do not know what causes up to seventy-five percent of MR cases.[10] Recently, however, scientists found a specific gene on the X chromosome that, in an abnormal form, results in MR. The scientists discovered this gene, known as *AGTR2* (Angiotensin II), using an innovative method of studying a single individual with unexplained MR and a known chromosomal translocation. "Translocation" means that, during development, two of an individual's chromosomes break and then the broken pieces switch places. This switches around the genes in the chromosomes which contain the hereditary blueprint of an individual's characteristics. With the new knowledge, the researchers will study more individuals with both MR and the *AGTR2* mutation, to determine if there is a common area on this gene that is altered in some of these individuals or all of them. This work eventually could lead to insights into a variety of innovative therapies and better understanding of the processes involved in normal brain development.

Autism and Secretin. Autistic disorder is a complex developmental disorder that affects one in 500 to one in 1,000 children annually.[11] It impairs the child's ability to communicate and interact with others, and often causes mental retardation and inappropriate behaviors. There is no known treatment for the core communication and social symptoms of autism, other than structured educational and behavioral interventions. Parents, clinicians, and researchers became interested in the potential of a digestive hormone, secretin, after reports of dramatic improvement in three autistic patients who were given a single dose of the hormone (in connection with diagnostic gastrointestinal testing). But, neither the efficacy nor the safety of secretin was established. Recently, scientists tried to reproduce the reported positive effects of a single dose of secretin, as in the original three children. They did not find significant improvements in a group of autistic children ages three to twelve who were given the treatment. The research was conducted in the Collaborative Network on the Neurobiology and Genetics of Autism, supported by the NICHD and NIDCD.

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[8] NIDDK. "National Diabetes Statistics." Available at http://www.niddk.nih.gov/health/diabetes/pubs/dmstats/dmstats.htm. (cited November, 2002)

[9] MEDLINEplus Medical Encyclopedia (National Library of Medicine). "Mental Retardation." Available at http://www.nlm.nih.gov/medlineplus/encyc/article/001523.htm. (cited November, 2002)

[10] *Ibid.*

[11] NICHD. "Autism Facts." Available at www.nichd.nih.gov/autism (Cited November, 2002)

Fragile X Syndrome and Symptoms in Carriers. Fragile X syndrome (FXS) is the most common genetically-inherited form of mental retardation currently known.[12] The syndrome, which accounts for approximately 40 percent of cases with X-linked mental retardation, is caused by a mutation in a specific gene (*FMR1*) on the X chromosome. In its fully-mutated form, the *FMR1* gene interferes with normal development. In a partially mutated (premutation) form, the *FMR1* gene can cause FXS in the children of a carrier (a person who has the premutation gene). Until recently, however, the premutation form was not thought to cause symptoms in carriers. Scientists have now identified a subgroup of premutation *FMR1* carriers with symptoms that appear to be associated with the gene. Symptoms included mild cognitive and emotional problems and, in female carriers, premature menopause. In older male carriers, the premutation gene is associated with a neurological syndrome. Identifying a genetic basis could be a first step toward accurate diagnosis and, possibly, development of new treatments for these symptoms.

Enhancing Performance and Behavior

Head Start and Adult Achievement. Since Head Start began in 1965, there have been questions about whether the preschool program for low-income children has any lasting benefits. Some studies showed that Head Start children had better test scores when they first started school, but other studies suggested that this advantage faded by the time children reached third grade. Reports on other, better-funded, preschool programs showed that children who participated in them were more likely to finish high school and attend college. However, it was unclear whether Head Start, which is less well-funded, could similarly boost children's long-term performance. Recently, economists supported by the National Science Foundation and NICHD reported that Head Start also produced long-lasting positive effects, including completion of high school and college education, in adults as old as thirty. The data also suggest that the positive effects of Head Start may carry over to the brothers and sisters of children who attend Head Start, even if these siblings never participated in the program.

Parental Influence and Teen Driving. Each year, more U.S. teens are killed or injured in motor vehicle crashes than from any other cause.[13] The developmental characteristics of adolescents are known to contribute to higher teen crash rates, along with such other factors as inexperience in driving and driving at night. Research has shown that state "graduated" driver licensing programs reduce teen driving risks by imposing driving restrictions, such as limiting new drivers to daylight driving, for a probationary period. New data suggest that another source of driving restrictions on teens -- parents -- can also reduce risks of adolescent driving accidents. Scientists recently reported that many parents do not set any special rules for their teens' driving, but when parents do set limits such as those in the graduated licensing programs, risky teen driving declines. These scientists are now testing a program to reduce teen driving accidents by educating parents on ways to influence their teens' driving habits, including teen-parent driving contracts. Behavioral contracts of this type are known to succeed in other contexts.

[12] CDC, Human Genome Epidemiology Network. "FMR1 and the Fragile X Syndrome" July, 2001. Available at: http://www.cdc.gov/genomics/hugenet/factsheets/FS_FragileX.htm

[13] Simons-Morton BG. Reducing Young Driver Crash Risk. Injury Prevention 8 (Supplement II): ii1-ii2, 2000.

WOMEN'S HEALTH

Contraceptives and Health Risks

Breast Cancer and Oral Contraceptives. Oral contraceptives are the most widely used method of family planning among women in their twenties.[14] However, scientific research has produced conflicting information on whether taking oral contraceptives increases a woman's risk of breast cancer during her mature years, the period of highest risk. Recently, very large study showed that women who took oral contraceptives at some point in their lives were no more likely to develop breast cancer between the ages of 35 and 64 than other women. The study also showed that oral contraceptives do not pose a higher risk of breast cancer for African American women or for women whose nearest female relatives had breast cancer. The large scale of the study, carried out through the NICHD Women's Contraceptive and Reproductive Experiences Study (Women's CARE), increases confidence in the results.

Osteoporosis and Injectable Contraceptives. Osteoporosis, a disease that thins and weakens bones to the point that they break easily, is a major health risk for 28 million Americans, especially women. More than 1.5 million fractures annually are related to osteoporosis and, in older individuals, fractures may end the ability to live independently or even lead to death.[15] Injectable contraceptives have been implicated in osteoporosis, but evidence has been inconclusive. In the largest and longest study to date of the relationship between injectable contraceptives and bone density, the scientists followed women for four years as they used, and then stopped using, the injectable contraceptive, DMPA. The study showed that women lost bone density while using DMPA, but that a large majority recovered most of their lost bone mass within two years of stopping use of the contraceptive. These findings may reassure women who have used DMPA and may prefer to continue its use, because of its convenience and reliability. But the findings indicate more research is needed with the youngest women (ages 18-21) using DMPA, because their recovery of lost bone mass after stopping DMPA was less clear.

Diseases of Girls and Women

A Genetic Disorder in Girls. Rett Syndrome (RTT) is a severe genetic disorder that gradually halts healthy development in infant and toddler girls. Girls with RTT lose the ability to talk, to interact with other people and to move independently. They may experience seizures and behavior disorders. Scientists do not know how to cure RTT or halt its progression. Recently, NICHD-supported researchers created a genetically modified mouse with RTT-like symptoms that should help scientists understand how RTT develops over time. The experimental mouse may lead to better understanding of molecular events underlying certain stages of RTT and may enable researchers to identify genes involved in regulating motor function, involuntary movements, seizures, and anxiety disorders. The new mouse is superior to earlier experimental mouse models of RTT and it may enable scientists to test medications and other treatments for the disease.

[14] Alan Guttmacher Institute. "Facts in Brief: Contraceptive Use." Available at http://agi-usa.org/pubs/fb_contr_use.html (cited November, 2002)

[15] NIAMS. Health Topics: Osteoporosis: Progress and Promise. Available at http://www.niams.nih.gov/hi/topics/osteoporosis/opbkgr.htm. (cited November, 2002)

Endometriosis and the Immune System. Endometriosis is a complex gynecological disorder associated with pelvic pain and infertility that affects more than 5.5 million women in North America alone.[16] Endometriosis occurs when tissue like that which lines the uterus grows outside of the organ, usually on surfaces in the pelvic and abdominal areas. A single, clear explanation for the cause of this disease has eluded scientists. Recently, scientists reported that women with endometriosis are more likely than others to have autoimmune diseases such as rheumatoid arthritis and multiple sclerosis, in which the body's immune system attacks its own cells, tissues and organs. These diseases affect millions of Americans and some disproportionately affect African Americans, Hispanics or Native Americans.[17] The researchers also found that women with endometriosis were more likely than others to have a variety of other conditions, including chronic fatigue syndrome (strong, lasting fatigue) and fibromyalgia (recurrent muscle, tendon and ligament pain). The findings of multiple conditions that seem to relate to endometriosis and immune system function could yield clues to the causes and better treatment of the associated conditions, as well as endometriosis.

Endometriosis and Immune Response. For many women with endometriosis, treatment with progestins (hormones that prepare the lining of the uterus for implantation of a fertilized egg) can relieve pelvic pain and certain other symptoms. But scientists have questioned the utility of progestin therapy on a long-term basis and some women with endometriosis do not gain pain relief from this treatment. Scientists have long recognized that immune cells and products they secrete, known as cytokines, play an important role in the cellular events that occur as endometriosis develops, particularly as the disease process relates to pain. Recently, scientists reported that the way progestin reduces pelvic pain in endometriosis involves suppression of inflammatory response in the pelvis to endometrial tissue. Understanding the way that the drug works provides insight into both the disease process of endometriosis and the reason that progestin does not always relieve endometriosis-related pain. This knowledge could lead to better therapies for endometriosis.

Uterine Fibroids and Genes. More than a quarter of U.S. women may develop uterine fibroids, the most common non-cancerous tumors in women of childbearing age.[18] The tumors can cause infertility, pain, and uterine bleeding. Treatment options are limited to hormone therapies and surgery, with fibroid tumors accounting for an estimated 200,000 hysterectomies each year.[19] African American women are at greater risk for surgery because they are more likely to develop large or multiple-fibroid tumors. Recently, scientists, using a new technology that permits very rapid analysis of multiple genes, were able to identify genes involved in the development and growth of fibroid tumors. Identifying genes specific to the condition will help scientists better understand how the tumors grow and could lead ultimately to the development of new therapies for this condition. The researchers plan further genetic studies, to identify a "master regulator" of tumor growth and to develop drugs that could shrink fibroids, sparing women from surgery and side effects of other current therapies.

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[16] NICHD. "Fast Facts about Endometriosis." Available at: http://www.nichd.nih.gov/publications/pubs/endometriosis/index.htm. (cited November, 2002).
[17] NIAID. "Understanding Autoimmune Diseases." Available at: http://www.niaid.nih.gov/publications/autoimmune. (cited November, 2002)
[18] NICHD. "Uterine Fibroids: Fast Facts." Available at http://www.nichd.nih.gov/publications/pubs/fibroids/index.htm (cited November, 2002)
[19] *Ibid.*

REPRODUCTIVE HEALTH

Men's Health

Prostate Cancer Risk and Vasectomy. Vasectomy, a simple operation to make a man sterile, is the third-most-used form of family planning among U.S. married couples.[20] But, since 1990, conflicting scientific studies have suggested that having a vasectomy might – or might not – increase a man's risk for developing prostate cancer, the leading form of cancer among U.S. men. Because of possible risk, many urologists began to advise against vasectomy for men with a strong family history of prostate cancer. Recently, however, scientists reported that an exceptionally large study of men with vasectomies showed that they were no more likely than others to develop prostate cancer, even 25 years after the procedure. Even men whose fathers had prostate cancer were at no greater risk if they had vasectomies. The size of the study strengthens the evidence that this method of family planning is safe.

Male Contraception. For more than 30 years, scientists have worked to develop a safe, effective and reversible hormonal contraceptive for men. In a recent human trial, one dose of acyline, an antagonist of the "master" reproductive hormone, gonadotropin-releasing hormone (GnRH), temporarily halted sperm production by suppressing GnRH and testosterone secretion. Acyline was more effective and less irritating at the site of injection than previously-tested GnRH analogs. Its effectiveness and safety make acyline a strong candidate for inclusion in a male hormonal contraceptive, in combination with hormones to eliminate potentially negative effects on potency. Just as importantly, acyline could eventually help in treating other hormone-dependent conditions including benign prostatic hypertrophy and prostate cancer, infertility, ovarian cancer, and several gynecological conditions. The research was supported through the NICHD Specialized Cooperative Centers Program in Reproduction Research.

Story of Discovery: Finding the Master Reproductive Hormone

Roger Guillemin and Andrew V. Schally, NICHD grantees, opened the way for current treatments for infertility and cancers of the reproductive system. Working independently of each other, the two isolated hormones from the brain region known as the hypothalamus, which regulates blood pressure, body temperature, fluid balance, and other essential body functions. The magnitude of their contribution was recognized when they received the Nobel Prize in Physiology or Medicine in 1977.

Scientists' understanding of the hypothalamus grew out of a series of scientific investigations spanning more than 80 years. The hypothalamus secretes hormones that stimulate the pituitary, a pea-sized gland beneath the brain. The hypothalamus sends its hormonal signals through a network of blood vessels. In the 1920's scientists took a major step in understanding the gland's functioning by cutting these vessels in experimental animals. The animals soon lost their reproductive functioning. Scientists knew that a hormone, called luteinizing hormone (LH), acted on the ovaries and testes, leading to ovulation in women and sperm production in men. Observing that the experimental animals lost the capacity to reproduce, the scientists theorized that a second hormone, which they called luteinizing hormone releasing factor (LHRF), stimulated release of LH from the pituitary, thus controlling reproduction. The search for the "master" reproductive hormone that stimulated this release had begun.

Later two fiercely competitive research teams, one led by Guillemin and the other by Schally, independently discovered the hormone. Lacking precise techniques now available for isolating very small quantities of a substance, the teams needed massive quantities of tissue to work with. Guillemin's team found the hormone by analyzing five million samples from discarded sheep brains. Schally's group found an identical substance in an

[20] NICHD. "Facts about Vasectomy Safety." Available at: http://www.nichd.gov/publications/pubs/vasect.htm (cited November, 2002)

equal quantity of pig brain tissue. The hormone they discovered is now known as gonadotropin releasing hormone (GnRH). GnRH was later found in a number of species, including human beings.

The next step for researchers was to develop GnRH analogs--substances that are similar to GnRH chemically but, due to minor substitutions in their chemical makeup, might work more effectively than GnRH itself. For example, researchers found that injecting experimental animals with a large dose of a GnRH analog first stimulated a surge of reproductive hormones and then led to their complete suppression. Following up on this discovery, a pharmaceutical company developed another GnRH analog, leuprolide, which became a standard treatment for prostate cancer. Leuprolide also became the standard treatment for precocious puberty (a form of abnormally early sexual maturation). This treatment switches off sex hormone production in a child with this condition, until the child reaches an appropriate age. Other GnRH analogs were developed to treat female infertility. In conjunction with other hormones, these analogs "reset" a woman's monthly ovulatory cycle and stimulate ovulation.

Now, other NICHD-funded researchers are testing a GnRH antagonist, a synthetic substance that causes the body to stop producing GnRH immediately. The new agonist holds potential as a component of a male hormonal contraceptive (see above) and may also be useful for treating prostate cancer.

Healthy Pregnancies

Repeated Miscarriage and Genes. Repeated miscarriages (recurrent spontaneous abortion or RSA), without a known cause, affect one to two percent of couples who wish to have a child.[21] Women experiencing multiple miscarriages may undergo exhaustive and expensive diagnostic tests that fail to identify the cause of their miscarriages. Scientists have long assumed that a large percentage of unexplained RSAs is caused by genetic problems, but they have been unable to identify a specific gene as a cause. Recently, scientists reported that fourteen to fifteen percent of women with a history of unexplained RSA have a genetic flaw in one of their two X chromosomes. Also, these women are more likely to miscarry male than female fetuses. The percentage of women with the genetic aberration combined with its selective effect on male fetuses means that the flawed gene may account for up to forty percent of previously unexplained RSAs. Identifying this trait is expected to lead to blood tests to determine the risk of miscarriage in future pregnancies.

Miscarriage and an Anti-Diabetes Drug. Five to ten percent of U.S. women are affected by polycystic ovary syndrome (PCOS),[22] a condition that can make it difficult for a woman to become pregnant or to carry a fetus through the early months of pregnancy. Women with PCOS are three times more likely than other women to miscarry; they also have a condition, insulin resistance, that precedes diabetes. Researchers recently reported that an anti-diabetes drug, metformin, lowered the risk of a miscarriage in the first trimester of pregnancy for women with PCOS. The investigators had already demonstrated that the drug increases blood flow in the uterus and brings about changes in the uterine lining. Further research should confirm the drug's positive effects in a larger clinical trial and also evaluate its safety through the full course of pregnancy.

[21] Lansa, MC, Hogge, WA, Kubik, CJ, Ness, RB, Harger, J, Nagel, T, Prosen, T, Markovic, N, Hoffman, EP. A Novel X Chromosome-linked Genetic Cause of Recurrent Spontaneous Abortion. American Journal of Obstetrics and Gynecology 185:5630568, 2001.

[22] Jakubowicz DJ, Iuornmo MJ, Jakubowicz S, Roberts KA, Nestler JE. Effects of Metformin on Early Pregnancy Loss in the Polycystic Ovary Syndrome. Journal of Clinical Endocrinology & Metabolism 87:524-529, 2002.

Preeclampsia and Insulin Resistance. Preeclampsia, a dangerous condition that complicates three to four percent of pregnancies,[23] strikes without warning and is a leading cause of maternal and fetal death. Delivery is the only known cure for preeclampsia and surviving infants are likely to have suffered a hemorrhage before birth, be small for gestational age, be premature, and have serious disorders requiring neonatal intensive care. Currently, physicians lack a reliable method of identifying women at risk for preeclampsia. Recently, however, scientists reported that women with heightened resistance to the hormone insulin in the early months of pregnancy are at risk of later developing preeclampsia. This finding suggests that physicians will be able to initiate preventive measures early in a pregnancy for women with insulin resistance. The research also implicates insulin resistance as a causative factor in preeclampsia; thus, it may ultimately be possible to prevent the condition by improving insulin sensitivity in at-risk women early in a pregnancy or even before a woman becomes pregnant.

HEALTH AND FUNCTIONAL CAPACITY

Movement and Daily Activities

Activity after Stroke. Muscle weakness and paralysis caused by stroke can rob people permanently of the capacity to perform common daily activities. Rehabilitation for these individuals currently focuses on training limbs less affected or unaffected by the stroke, to help compensate for a weakened or paralyzed limb and to maximize their overall capacity to function. This approach, however, means that the limbs most affected by stroke may deteriorate even more, from lack of use. Scientists recently completed the first controlled clinical trial of a promising new approach to rehabilitation, which focuses on strengthening and retraining the limb most affected by the stroke. Patients receiving this therapy performed routine daily tasks repeatedly with the most affected limb, while having the less affected limb restrained with a simple device. After two weeks of the therapy, stroke patients with weakened or partly paralyzed arms were better able to control motion in their affected limbs. The new approach offers hope for reducing functional impairments and increasing the independence and quality of life for patients with mild to moderate chronic strokes and, possibly, for people with other neurological disorders such as traumatic brain injury.

Pain and Tissue Damage and Artificial Limbs. Each year, injuries, vascular diseases, cancer, diabetes, and other disorders may require patients to have part or all of a leg amputated. These amputees may encounter painful and costly problems as they try to use a prosthesis (artificial limb replacement). Because the residual part of the leg fluctuates naturally in size during the day, the prosthesis socket connection may rub against it, causing blisters and pain. Amputees with poorly fitting sockets commonly try multiple, costly replacements. If unable to solve socket fit problems, individuals with leg amputations tend to reduce activity, adopting a sedentary lifestyle and increasing their risks of weight gain, diabetes, heart disease and other disorders. Recently, a NICHD-supported researcher (who himself has a leg amputation) perfected and completed testing a new type of prosthetic socket that adjusts automatically to changes in size of the residual limb. Amputees using the new socket report more comfort and stability in fit. The invention, now being considered for a patent, promises better mobility and

[23] Wolf M, Sandler L, Munoz K, Hsu, Karen, Ecker, JL, Thadhani, R. First Trimester Insulin Resistance and Subsequent Preeclampsia: A Prospective Study. Journal of Clinical Endocrinology & Metabolism 87:1563-1568, 2002.

quality of life for leg amputees, while saving on costly replacements and care of secondary health conditions.

Infection Risk and Prevention

Urinary Tract Infections and High-risk Patients. Repeated urinary tract infection (UTI) is a potentially serious medical risk for people with internal bladder catheters. These catheters are used when normal voiding of urine is impossible because of spinal cord injury (SCI), stroke, loss of consciousness or critical illness, spina bifida, or other conditions. If not adequately treated, UTIs can lead to kidney damage. Antimicrobial agents are the standard treatment for UTI; however, they can fail and repeated use of these drugs risks creating drug-resistant bacteria. In a recent pilot study, scientists successfully tested a relatively simple, low-cost intervention to prevent UTIs in individuals using bladder catheters. The scientists were able to significantly reduce rates of UTI in SCI patients by inoculating them with a strain of harmless bacteria. A larger clinical trial is expected to confirm that the treatment is effective and safe for patients at high risk of UTI infection. This new approach to preventing UTI could protect thehealth of millions of individuals whose acute, chronic or disabling conditions require them to use internal bladder catheters, while reducing the costs of treating frequently recurring infections and their complications.

AIDS

Drug Safety and Efficacy

Antiretroviral Drugs and Birth Complications. The standard of care for a pregnant woman with HIV, the virus that causes AIDS, includes ongoing treatment with antiretroviral (anti-HIV) drugs. This approach avoids interrupting treatment of the woman while also helping to prevent transmission of the virus to the infant. But doubts about this approach arose when several studies, involving relatively small numbers of women, suggested that treatment during pregnancy with combination antiretroviral therapy increased the risk of premature delivery. Recently scientists reviewed multiple clinical trials and concluded that women who continued antiretroviral therapy (standard combination drug therapies and single-drug therapy) during pregnancy were no more likely to give birth prematurely than those who either stopped combination therapy or took only one antiretroviral drug. These scientists also found that antiretroviral drugs did not generally increase the risk of other complications, including low birth weight, still birth, or impaired condition of a newborn, as indicated by a standard test (Apgar test) at birth. A subgroup of women did appear to have a slightly higher risk of having very low birth weight infants; however, factors other than drugs, such as alcohol or tobacco use, could be responsible. The new findings permit more informed treatment choices by pregnant, HIV-positive women and their physicians.

Pediatric HIV and Drug Treatment. There are limited data on the safety and efficacy of antiretroviral drugs in children and adolescents with HIV, who are treated with drugs that have been more fully studied in adults. Recently, scientists reported that antiretroviral drugs, in various combinations, markedly reduced deaths in infected children and adolescents who were followed over a three-year period. In these children, the drugs reduced the risk of HIV-related death by sixty-seven percent. An important aspect of the study was that scientists were able to assess the effects and safety of the drugs as young patients were treated under ordinary clinical conditions. Scientists also determined that the drugs had similar effects in lowering death rates,

regardless of a child's race, ethnic group, age or sex, educational level of parents or guardians, or stage of HIV infection when the child entered the study.

OTHER ADVANCES

Genetics

A Genetic Tumor-promoter. In a person with the rare genetic syndrome, Carney complex (CNC), tumors may grow in organs throughout the body, including the heart, skin, breast, nervous system, and endocrine glands (thyroid, pituitary, gonads, adrenal). Depending on their location, these tumors may be benign or malignant. The involvement of tumors in so many organs suggests to scientists that the genetic defects responsible for CNC may be key to the functioning of human cells generally. Recently, scientists identified two chromosomes that harbor the genes responsible for CNC. In one of these, chromosome 17, the scientists found a gene that is mutated in about half of the families with CNC who were studied. The scientists then determined that the gene, known as *PRKAR1A*, is present in almost all human cells as a regulatory subunit of the important protein kinase A. The research indicates that when the regulatory action of *PRKAR1A* is disturbed, tumors form. Finding the CNC genes and understanding their role in tumor formation may eventually lead to new treatments for CNC and for other, non-genetic endocrine tumors.

Tracking Critical Processes inside Cells. Tracking cell growth and other functions as they occur within an individual cell is critical to understanding the processes underlying human health and disease. Scientists recently developed a versatile technique for studying signaling events within a single, living cell. "Signaling" refers to a process that begins when molecules outside a cell attach themselves (bind) to highly specific sites (receptors) on a cell's surface. Binding activates the receptors, which then send messages (signals) into the cell, initiating sequences of chemical changes. For example, when insulin molecules attach to their receptors, they activate pathways that instruct a cell to take in glucose and grow. The research team developed fluorescent "tags" that enable scientists to identify specific molecules that affect steps in the signaling process and to study the function of these molecules in normal and diseased cells. The technique has many potential applications. For example, it can help researchers identify mechanisms at the molecular level that could be targets for drugs to control human disease.

"Jumping Genes" and Therapeutic Possibilities. Genes contain information that tells the body how to make proteins, which perform many basic functions in the body, such as facilitating the synthesis of chemicals. The instructions for making proteins are stored ("encoded") only in certain regions of chromosomes; elsewhere, chromosomes are "silent," without such instructions. However, these silent regions contain transposable elements called transposons – nicknamed "jumping genes" – which can move about and insert themselves into encoding regions of chromosomes. In certain cases, the insertion of a transposon may be linked to a genetic disease. Otherwise, the jump of transposons into the protein-encoding regions has been considered both infrequent and inconsequential. Recently, however, scientists reported that seemingly unimportant transposons were embedded in protein-coding regions, without causing genetic disease, far more frequently than was previously thought. The scientists hypothesize that these transposon insertions may have a positive effect, possibly conferring a survival advantage on organisms that have them. If scientists can insert transposons into genes, they

may be able to produce novel proteins, possibly leading to new therapies for a variety of diseases.

Technology

Uterine Activity Monitors and Preterm Birth. Preterm (premature) birth complicates nearly twelve percent of all births [24] and premature infants are at very high risk of dying within a few days of birth or of surviving with life-long disabilities. Because increased uterine contractions sometimes precede early delivery, women at risk of preterm birth are commonly asked to wear a portable device that monitors uterine contractions. But the usefulness of these devices, known as home uterine monitors (HUMs), has been questioned as previous studies had shown that altered rates of uterine contractions occur in both women who do, and who do not, give birth prematurely. Scientists recently reported that HUMs could not reliably predict which women, with known risk factors, would actually deliver prematurely. This research affirmed earlier, negative findings on HUMs in smaller groups of women. Because the costly devices may be used for several months, discontinuing the use of HUMs should result in considerable savings to third-party payers as well as to individual families, who may pay out-of-pocket for the devices.

NEW INITIATIVES

CHILD AND ADOLESCENT HEALTH

Establishing Links between Childhood Obesity and Metabolic Syndrome

In the past twenty-five years, the prevalence of obesity in boys and girls aged six to eleven tripled.[25] At the same time, the incidence of type 2 diabetes in adolescents increased, but little is known about the molecular, biochemical, and physiologic mechanisms that link the two conditions. To clarify these relationships, the NICHD will encourage scientists to study how obesity leads to insulin resistance and other components of metabolic syndrome (a syndrome that includes such conditions as hypertension and high blood sugar levels, and increases the risk of diabetes). Understanding crucial biochemical and molecular relationships between obesity and insulin resistance should help researchers develop new ways to treat the conditions and possibly to prevent diabetes in children and youth.

Adolescent Literacy

The NICHD will support critically-needed research to better understand the reading process in adolescents and to identify the best way to teach them literacy skills. To date, few researchers have studied issues related to adolescent literacy, despite data indicating a great need in this area. According to the 1998 National Assessment of Educational Progress, twenty-six percent of students in eighth grade fail to read, even at a basic level. By twelfth grade, twenty-three percent of students *still* don't have basic reading skills.[26] Many of these students may drop out of school or be inadequately equipped to perform such basic life skills as writing a letter, explaining an error on a credit card bill, or understanding a bus schedule. These research efforts

[24] NCHS. "Fast Stats: Birthweight and Gestation" (source is National Vital Statistics Reports, Vol. 50, No. 5). Available at http://www.cdc.gov/nchs/fastats/birthwt.htm. (cited November, 2002)

[25] Health, United States, 2002, table 71: Overweight Children and Adolescents 6-19 Years of Age, According to Sex, Age, Race, and Hispanic Origin: United States, Selected Years 1963-65 through 1999-2000.

[26] U.S. Department of Education. Office of Educational Research and Improvement. National Center for Education Statistics. The NAEP 1998 Reading Report Card for the Nation and the States, NCES 1999-500. Washington, DC: 1999.

are key to helping young people, including many who are already disadvantaged, overcome fundamental obstacles to their future success.

Injury Prevention in Children with Attention Disorders

Unintentional injury is a leading cause of death in children, with 20-25 percent of all children, each year, sustaining an injury serious enough to require medical attention.[27] However, non-fatal injuries such as automobile accidents and falls can be even more frequent in children with attention disorders. While research to help prevent injuries in children exists, there is little information on how to prevent injuries in children with such disorders as attention deficit hyperactivity disorder (ADHD); autism spectrum disorder (ASD); and Asperger's Syndrome, a condition that involves a delay in developing fine motor skills. To fill this knowledge gap, the NICHD will encourage researchers to study how problems in neurological functioning, such as those associated with attention deficits, influence behavior and ultimately the risk of injury. In addition, researchers will be asked to develop interventions that can help parents prevent injuries in children with a wide range of these disorders.

WOMEN'S HEALTH

Obstetric-Fetal Pharmacology Research Units

Although pregnant women may need medical care and attention, few research studies provide the information that clinicians need in prescribing therapeutic drugs for women who are pregnant. Physicians may also need to administer drugs to treat certain conditions of the fetus, but such therapies could also directly affect the pregnant woman, and little is known about possible consequences. Thus, the FDA only has scientific information needed to approve a handful of drugs for these uses. Yet to treat conditions in pregnant women, physicians prescribe drugs that may affect these patients differently than others and that may cross the placenta and be potentially toxic to the fetus. To address these issues, the NICHD will support new research on how drugs administered during all phases of pregnancy affect a woman and her fetus. Findings from such studies will allow physicians to treat pregnant women and their unborn children more confidently and increase access to proven drug therapies, while reducing the risk of serious adverse effects.

REPRODUCTIVE HEALTH

Novel Approaches to Male Fertility Regulation

While the search for male contraceptives is not new, few studies have yielded findings that could be used to develop products that are both acceptable to and easily used by men. To fill this long-standing void and increase options for men, the NICHD will support several initiatives that could lead to new male contraceptives, which are also commercially viable. Targeting both the academic and small business community, the NICHD will encourage researchers to develop specific markers that will help clinicians know if a contraceptive agent successfully curtailed sperm production. In a separate initiative, the Institute will encourage researchers to develop new, or to use emerging, technologies to better understand or examine how the neuroendocrine system in men influences their fertility and the reproductive system.

[27] Childhood Injury Fact Sheet. National Center for Injury Prevention and Control, Centers for Disease Control and Prevention. Accessed on November 12, 2002 http://www.cdc.gov/ncipc/factsheets/childh.htm.

HEALTH AND FUNCTIONAL CAPACITY

Biomechanical Modeling of Movement

Interventions to help correct problems in physical movement are not always predictable in outcome and, sometimes, even unsuccessful. This occurs, in part, because scientists do not fully understand what causes abnormal movement patterns, nor do scientists really know how commonly-used rehabilitation methods affect muscle function. As a result, few standard interventions exist for assessing movement problems and for measuring progress during rehabilitation. To address this issue, the NICHD will encourage researchers to develop special models that characterize the biology and dynamics of movement. The models will clarify how joints, muscles, tendons, and ligaments are affected by different movement patterns. In addition, scientists can use the modeling technologies to determine the motor limitations of individuals with an amputation, neurologic impairment, or other condition. Clinicians, in turn, can use these findings to better treat, and/or monitor a patient's progress.

Genetic Basis of Recovery and Rehabilitation

Rehabilitation is intended to improve physical functioning and to minimize disabilities that result from conditions ranging from inherited disorders to spinal cord, brain, or other injuries. However, even in cases where the extent of disability is the same, and patients receive similar care, they may experience different rehabilitation outcomes. While many factors, such as motivation and the initial state of a patient's health, can explain some of these differences, increasing evidence suggests that genetics may play a significant role in accounting for these differences. To address this important issue, the NICHD will encourage researchers to identify genes that not only play key roles in neurological development and functioning, but are also associated with different rehabilitation and recovery outcomes. Findings from these studies could help clinicians improve patient outcomes, allowing specific therapeutic drugs and rehabilitation regimens to be prescribed according to a patient's genetic make-up.

Pediatric Trauma

Many popular medical shows on television dramatize the triumphs of emergency medicine. However, what the public sees are skilled and knowledgeable clinicians saving lives based largely upon standards of care for adult trauma victims. The scientific foundation for developing equivalent standards of care for pediatric trauma victims is weak. To address this problem, the NICHD is supporting a series of initiatives. For instance, the Institute will support research to develop innovative technologies targeting pediatric rehabilitation and critical care. This will address the fact that, while mortality rates in pediatric intensive care units have drastically decreased in the last 15 years, more children survive with disabling outcomes. New technologies to make state-of-the-art care less invasive, more cost-effective, and less disabling are also urgently needed in pediatric critical care units and in rehabilitation settings such as schools and homes. In addition, the Institute will support a new program to train the next generation of pediatric critical care and pediatric rehabilitation scientists.

AIDS

Social and Structural Approaches for HIV Prevention

Scientific findings show that many social and community-related factors influence an individual's risk behaviors. Despite this knowledge, few HIV prevention strategies have been developed that effectively use social and community institutions to help prevent the spread of this infection. To date, these institutions, which include churches, commercial establishments,

schools, social clubs, voluntary associations, local government, and workplaces, among others, have been particularly neglected as a force for prevention. To address this issue, the NICHD will support basic social science research examining how community institutions influence HIV prevention efforts. Projects may include determining how different kinds of community institutions help prevent the spread of HIV by shaping or supporting social norms, by constraining behavior, or by empowering and strengthening families and communities. Findings from these studies will help public health officials and policymakers design more effective, community-based interventions to prevent the spread of HIV.

Improving Ways to Prevent and Treat HIV in Women and Children

The heterosexual transmission of HIV infection is increasing most rapidly among women, especially among young women and women of color.[28] Given these trends, new and effective vaginal microbicides to prevent HIV infection are needed. To address this issue, the NICHD will join the NIAID to expand its research to developing new topical microbicides. Furthermore, with the HIV epidemic affecting an increasing number of children around the globe, the NICHD will evaluate and develop simple and cost-effective means to better prevent and treat infection. For instance, the NICHD plans to support research on how nutrition, including poor nutrition, affects the development, treatment, and prevention of HIV disease in women, infants, and children. Also, in its efforts to encourage the development of innovative behavioral interventions to help prevent HIV/AIDS, the Institute will support training and career development activities to increase the pool of social scientists investigating HIV- and AIDS-related issues.

OTHER AREAS OF INTEREST

From Discoveries to Improving the Nation's Health

SIDS Disparities and Community Leadership. When scientific data showed that back sleeping reduced an infant's risk of sudden infant death syndrome (SIDS), the NICHD launched its national "Back to Sleep" campaign, in partnership with public agencies and private organizations. Since the beginning of the campaign, in 1994, the SIDS rate has fallen by more than 50 percent.[29] The good news is that rates of death from SIDS have been going down at about the same rate for African American and white infants. Nonetheless, substantial disparities remain, with a disproportionate number of African American infants still lost to SIDS. To begin closing this gap, the NICHD has enlisted the help of the Alpha Kappa Alpha sorority, The National Coalition of 100 Black Women, and The Women in the NAACP. In discussions with leaders of these organizations, the NICHD has planned and will support a series of "summit" meetings in three U.S. cities with high rates of African American SIDS deaths. These summits will enlist the resources of faith-based and community organizations, public health officials, and service organizations and help establish an infrastructure that will continue to provide information, material, and support for reducing SIDS among African American infants. Each organization will take the lead in organizing one of the summit meetings and will continue to serve as the catalyst for SIDS risk reduction activity in that city and its surrounding region.

[28] CDC, National Center for HIV, STD and TB Prevention. "HIV/AIDS among U.S. Women: Minority and Young Women at Continuing Risk." Available at: http://www.cdc.gov/hiv/pubs/facts/women.htm. (cited November, 2002)
[29] National Center for Health Statistics, CDC. Preliminary Data, 1999.

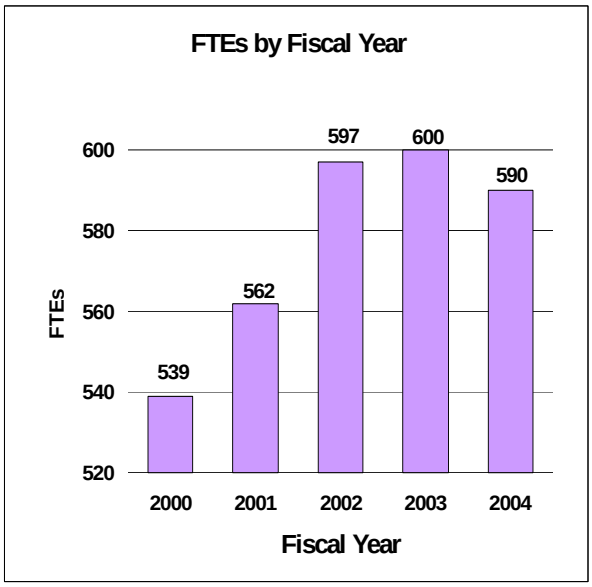
The National Children's Study. The Children's Health Act of 2000 directed the NICHD to plan and conduct a multi-year, comprehensive National Children's Study of environmental effects on children's health and development. Under the NICHD leadership, a broad consortium of federal agencies, including the Environmental Protection Agency, the Centers for Disease Control and
Prevention, and the National Institute of Environmental Health Sciences and other Institutes, have significantly advanced the NCS planning process, integrating the views of community and advocacy groups.

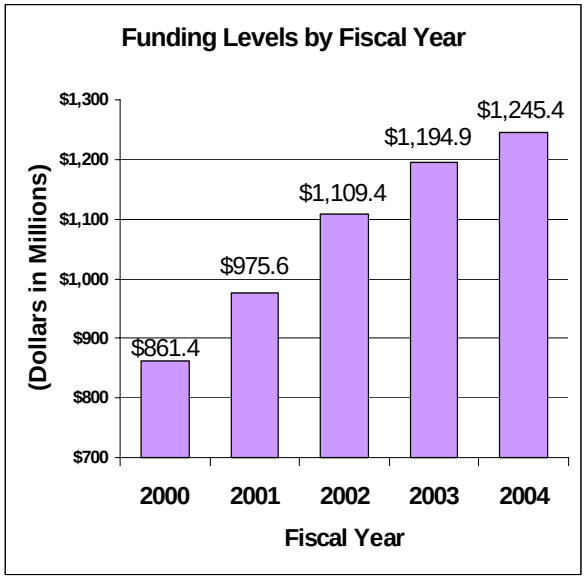
Best Pharmaceuticals for Children. The immature physiology of children means that drugs approved to prevent or treat illness in adults may have different effects in younger patients, requiring children's physicians to prescribe different doses and make other adjustments in drug therapies. However, for approximately seventy-five percent of the pharmaceuticals approved by the Food and Drug Administration (FDA) for adults, there are not enough safety and efficacy data to allow approval for pediatric uses, or to guide physicians in prescribing these drugs for children.[30] The Best Pharmaceuticals for Children Act, signed into law in January, 2002, requires the NIH to issue contracts for testing, in children, prescription drugs already approved for adults. Working with the FDA and other experts, the NICHD is completing a priority list of drugs to be tested through the Institute's Pediatric Pharmacology Research Units (PPRUs) and at other sites. The drug trials will start after publication of the priority drug list early in 2003.

BUDGET POLICY

The Fiscal Year 2004 budget request for the NICHD is $1,245,371,000, including AIDS, an increase of $50,480,000 and 4.2 percent over the FY 2003 amended President's Budget Request.
A five year history of FTEs and funding levels for NICHD are shown in the graphs on the following page. Note that Fiscal Years 2001 and 2000 FTEs are not comparable for the NIH Human Resources functional consolidation.

[30] Wilson, JT. An Update on the Therapeutic Orphan. Pediatrics 104:585-590, 1999.





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 providing new research opportunities. NICHD will provide an aggregate average cost increase of 4.1 percent for these awards.

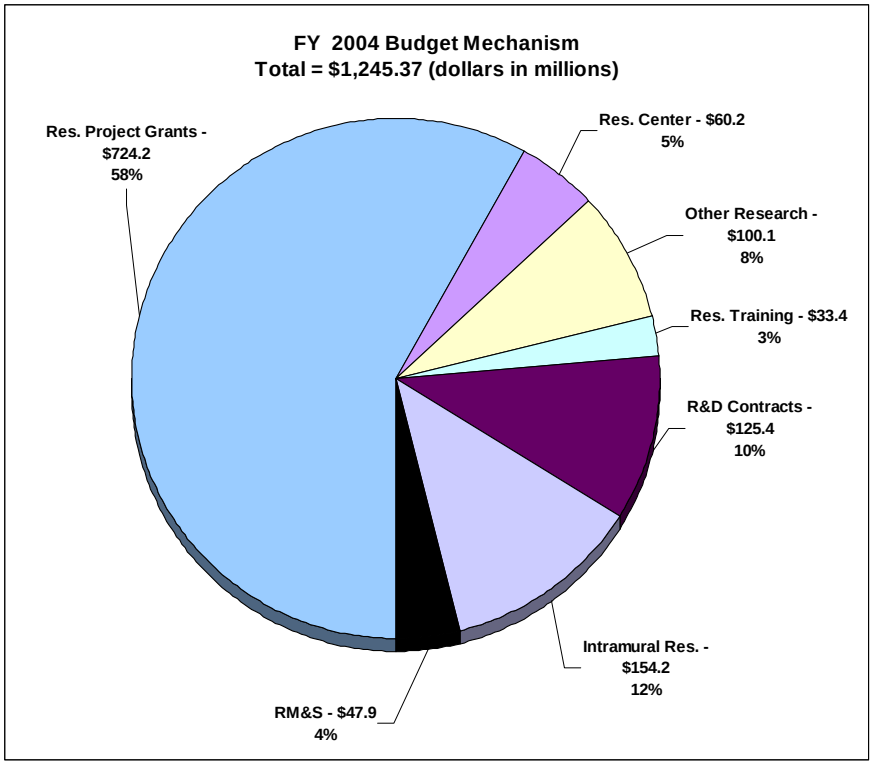
Also in FY 2004, NICHD will fully fund 15 competing grants, that is, provide funding for the total project period, rather than a single year. These grant to receive full funding will be selected based on scientific merit and other budgetary considerations. It is expected that these projects will be a combination Academic Research Enhancement Awards (AREA) which have been fully funded in the past, small grants, and possibility a few of the highest meritorious investigator- initiated projects.

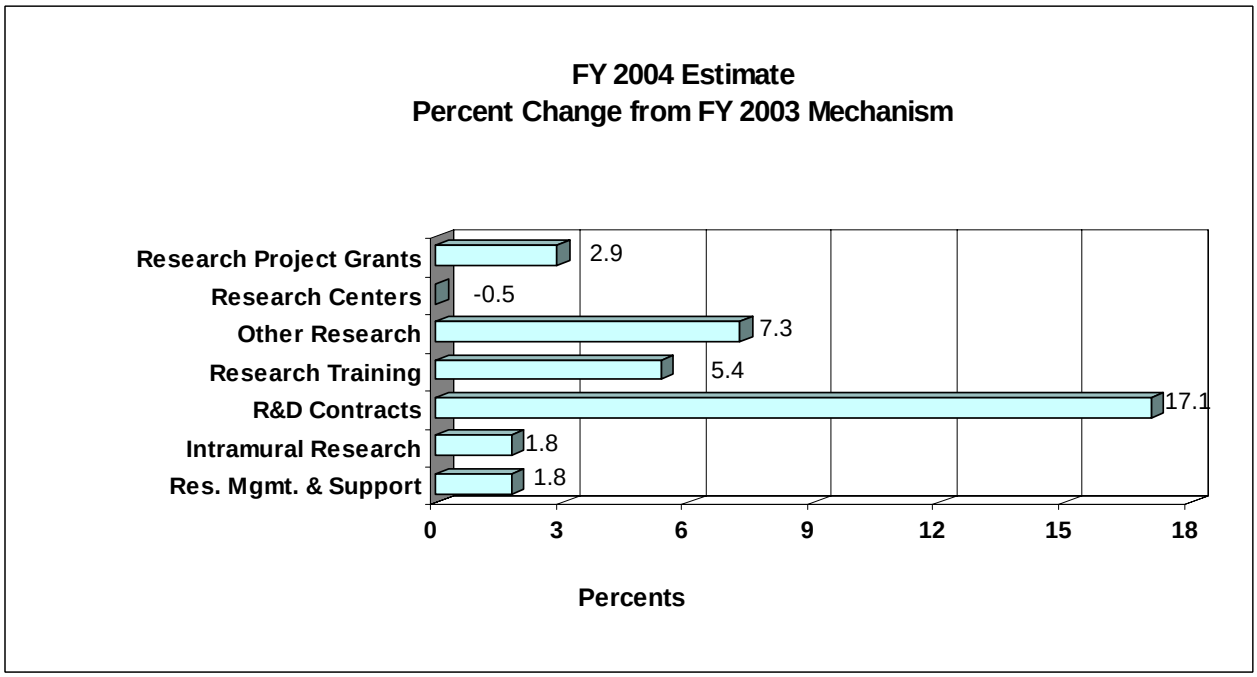
Promises for advancement in medical research are dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2004 request, NICHD will support 830 pre- and postdoctoral trainees in full-time training positions, five more than in FY 2003. Stipend levels for NRSA trainees will increase by 4 percent over Fiscal Year 2003 levels for predoctoral fellows, and from 4-1 percent, based on years of experience, for postdoctoral fellows.

The Fiscal Year 2004 request includes funding for 39 research centers, 508 other research grants, including 344 career awards, and 215 R&D contracts. Intramural Research and Research Management and Support receive increases of 1.8 percent over FY 2003.

As NIH program initiatives, the NICHD request includes an increase of $2,000,000 for research on obesity. In addition, the FY 2004 request provides an increase of $6,748,000 for the initiative to support studies under the Best Pharmaceuticals For Children Act, which will be funded under the R&D contract mechanism.

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





NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Budget Mechanism - Total

MECHANISM	FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	1,296	$480,758,000	1,304	$522,095,000	1,289	$541,667,000
Administrative supplements	(117)	7,499,000	(70)	6,353,000	(68)	6,153,000
Full funded	0	0	0	0	15	3,500,000
Single year	474	150,582,000	454	150,000,000	435	145,020,000
Subtotal, competing	474	150,582,000	454	150,000,000	450	148,520,000
Subtotal, RPGs	1,770	638,839,000	1,758	678,448,000	1,739	696,340,000
SBIR/STTR	99	24,429,000	101	25,325,000	110	27,842,000
Subtotal, RPGs	1,869	663,268,000	1,859	703,773,000	1,849	724,182,000
Research Centers:						
Specialized/comprehensive	53	56,763,000	42	59,977,000	39	59,700,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	250,000	0	250,000	0	250,000
Comparative medicine	0	100,000	0	250,000	0	250,000
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	53	57,113,000	42	60,477,000	39	60,200,000
Other Research:						
Research careers	319	29,991,000	341	33,826,000	344	35,002,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	75	36,852,000	79	39,016,000	81	41,706,000
Biomedical research support	0	0	0	0	0	0
Minority biomedical research support	0	1,110,000	0	1,144,000	0	1,167,000
Other	97	20,139,000	80	19,362,000	83	22,250,000
Subtotal, Other Research	491	88,092,000	500	93,348,000	508	100,125,000
Total Research Grants	2,413	808,473,000	2,401	857,598,000	2,396	884,507,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	124	5,684,000	124	5,882,000	124	6,105,000
Institutional awards	701	25,208,000	701	25,851,000	706	27,333,000
Total, Training	825	30,892,000	825	31,733,000	830	33,438,000
Research & development contracts	161	88,393,000	207	107,102,000	215	125,395,000
(SBIR/STTR)	(1)	(63,000)	(1)	(66,000)	(1)	(400,000)
	FTEs		FTEs		FTEs	
Intramural research	378	138,472,000	380	151,435,000	373	154,161,000
Research management and support	219	43,138,000	220	47,023,000	217	47,870,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NICHD	597	1,109,368,000	600	1,194,891,000	590	1,245,371,000
(Clinical Trials)		(174,626,000)		(188,000,000)		(196,700,000)

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

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2002 Actual		FY 2003 Amended President's Budget		FY 2004 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural research		$927,758		$996,433		$1,043,340		$46,907
Intramural research	378	138,472	380	151,435	373	154,161	(7)	2,726
Research management & support	219	43,138	220	47,023	217	47,870	(3)	847
Total	597	1,109,368	600	1,194,891	590	1,245,371	(10)	50,480

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

Summary of Changes

2003 Amended President's Budget				$1,194,891,000
2004 Estimated Budget Authority				1,245,371,000
Net change				50,480,000
	2003 Amended President's Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$52,600,000		$666,000
b. Annualization of January 2003 pay increase		52,600,000		414,000
c. January 2004 pay increase		52,600,000		806,000
d. One extra day of pay		52,600,000		203,000
e. Payment for centrally furnished services		25,757,000		515,000
f. Increased cost of laboratory supplies, materials, and other expenses		73,078,000		1,222,000
Subtotal				3,826,000
2. Research Management and Support:				
a. Within grade increase		23,266,000		313,000
b. Annualization of January 2003 pay increase		23,266,000		182,000
c. January 2004 pay increase		23,266,000		356,000
d. One extra day of pay		23,266,000		89,000
e. Payment for centrally furnished services		5,263,000		105,000
f. Increased cost of laboratory supplies, materials, and other expenses		18,494,000		306,000
Subtotal				1,351,000
Subtotal, Built-in				5,177,000

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

Summary of Changes--continued

CHANGES	2003 Amended President's Budget Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,304	$528,448,000	(15)	$19,372,000
b. Competing	454	150,000,000	(4)	(1,480,000)
c. SBIR/STTR	101	25,325,000	9	2,517,000
Total	1,859	703,773,000	(10)	20,409,000
2. Research centers	42	60,477,000	(3)	(277,000)
3. Other research	500	93,348,000	8	6,777,000
4. Research training	825	31,733,000	5	1,705,000
5. Research and development contracts	207	107,102,000	215	18,293,000
Subtotal, extramural				46,907,000
	FTEs		FTEs	
6. Intramural research	380	151,435,000	(7)	(1,100,000)
7. Research management and support	220	47,023,000	(3)	(504,000)
Subtotal, program	600	1,194,891,000	(10)	45,303,000
Total changes			(10)	50,480,000

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

Budget Authority by Object

	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	600	590	(10)
Full-time equivalent of overtime & holiday hours	1	1	0
Average ES salary	$144,300	$150,800	$6,500
Average GM/GS grade	11.0	11.0	0.0
Average GM/GS salary	$69,000	$72,200	$3,200
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$65,600	$68,600	$3,000
Average salary of ungraded positions	89,500	93,500	4,000
OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$28,335,000	$29,139,000	$804,000
11.3 Other than Full-Time Permanent	17,062,000	17,520,000	458,000
11.5 Other Personnel Compensation	1,428,000	1,468,000	40,000
11.7 Military Personnel	1,633,000	1,686,000	53,000
11.8 Special Personnel Services Payments	14,200,000	14,500,000	300,000
Total, Personnel Compensation	62,658,000	64,313,000	1,655,000
12.1 Civilian Personnel Benefits	12,393,000	12,733,000	340,000
12.2 Military Personnel Benefits	815,000	838,000	23,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	**75,866,000**	**77,884,000**	**2,018,000**
21.0 Travel & Transportation of Persons	2,640,000	2,670,000	30,000
22.0 Transportation of Things	410,000	411,000	1,000
23.1 Rental Payments to GSA	5,000	6,000	1,000
23.2 Rental Payments to Others	56,000	58,000	2,000
23.3 Communications, Utilities & Miscellaneous Charges	1,682,000	1,750,000	68,000
24.0 Printing & Reproduction	1,320,000	1,350,000	30,000
25.1 Consulting Services	1,255,000	1,260,000	5,000
25.2 Other Services	15,039,000	15,309,000	270,000
25.3 Purchase of Goods & Services from Government Accounts	107,152,000	109,080,000	1,928,000
25.4 Operation & Maintenance of Facilities	1,457,000	1,527,000	70,000
25.5 Research & Development Contracts	90,229,000	107,766,000	17,537,000
25.6 Medical Care	2,300,000	2,350,000	50,000
25.7 Operation & Maintenance of Equipment	1,550,000	1,600,000	50,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**218,982,000**	**238,892,000**	**19,910,000**
26.0 Supplies & Materials	11,738,000	12,000,000	262,000
31.0 Equipment	8,156,000	8,400,000	244,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	874,031,000	901,945,000	27,914,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	5,000	5,000	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**1,119,025,000**	**1,167,487,000**	**48,462,000**
Total Budget Authority by Object	**1,194,891,000**	**1,245,371,000**	**50,480,000**

National Institute of Child Health and Human Development

Salaries and Expenses

OBJECT CLASSES	FY 2003 Amended Pres. Budget	FY 2004 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$28,335,000	$29,139,000	$804,000
Other Than Full-Time Permanent (11.3)	17,062,000	17,520,000	458,000
Other Personnel Compensation (11.5)	1,428,000	1,468,000	40,000
Military Personnel (11.7)	1,633,000	1,686,000	53,000
Special Personnel Services Payments (11.8)	14,200,000	14,500,000	300,000
Total Personnel Compensation (11.9)	**62,658,000**	**64,313,000**	**1,655,000**
Civilian Personnel Benefits (12.1)	12,393,000	12,733,000	340,000
Military Personnel Benefits (12.2)	815,000	838,000	23,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**75,866,000**	**77,884,000**	**2,018,000**
Travel (21.0)	2,640,000	2,670,000	30,000
Transportation of Things (22.0)	410,000	411,000	1,000
Rental Payments to Others (23.2)	56,000	58,000	2,000
Communications, Utilities and Miscellaneous Charges (23.3)	1,682,000	1,750,000	68,000
Printing and Reproduction (24.0)	1,320,000	1,350,000	30,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,171,000	1,170,000	(1,000)
Other Services (25.2)	15,039,000	15,309,000	270,000
Purchases from Govt. Accounts (25.3)	77,539,000	78,133,000	594,000
Operation & Maintenance of Facilities (25.4)	1,457,000	1,527,000	70,000
Operation & Maintenance of Equipment (25.7)	1,550,000	1,600,000	50,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**96,756,000**	**97,739,000**	**983,000**
Supplies and Materials (26.0)	11,728,000	11,990,000	262,000
Subtotal, Non-Pay Costs	114,592,000	115,968,000	1,376,000
Total, Administrative Costs	**190,458,000**	**193,852,000**	**3,394,000**

National Institute of Child Health and Human Development

SIGNIFICANT ITEMS IN THE SENATE APPROPRIATION REPORT

The following section represents FY 2003 Congressional requirements for reports and significant items derived from Senate Report 107-216. These actions discussed below are contingent on inclusion of similar language and funding in the final FY 2003 appropriation and related reports. Additional items may be transmitted at a later date as a result of the final Conference report.

Item

Autism - The Committee commends the NICHD for maintaining funding levels for the NIH centers of excellence in autism, and it urges the Institute to continue to do so. In addition, the Committee urges the NICHD to find ways to expand the pool of autism researchers. (p. 120)

Action taken or to be taken

The NICHD continues its history of funding the Network on the Neurobiology and Genetics of Autism Collaborative Programs of Excellence in Autism (CPEA), and in FY 2002 issued a Request for Applications for a Data Coordinating Center to support collaborative studies by this group of grantees. In addition, the Autism Research Centers of Excellence: The Studies to Advance Autism Research and Treatment (STAART) Program was initiated by a Request for Applications issued in FY 2001, and led to the creation of two centers in FY 2002 co-funded by NICHD, NIMH, NINDS, NIDCD, and NIEHS. An additional round of competition under this RFA is planned in FY 2003.

These new centers, in addition to the expanding activities of the CPEA centers and the growing portfolio of investigator-initiated research sponsored by NICHD, are creating exciting new opportunities for an expanded pool of autism researchers. NICHD also supports eight training programs in mental retardation and developmental disabilities research which provide opportunities for research training relevant to autism.

Item

Demographic research - The Committee is pleased with the development of a long-range plan for demographic research supported by the NICHD, and the continued active collaboration with other Federal offices and agencies in carrying out its mission. Contributions of the NICHD program to increasing knowledge of fatherhood, marriage, immigration, and the implications of increasing racial and ethnic diversity are of high importance. The Committee encourages the NICHD to continue focusing attention on family and community factors in examining the health and development of poor children. The Committee further encourages the Institute to continue its attention to data and training needs for policy-relevant demographic research. (p. 120)

Action taken or to be taken

Demographic research undertaken by NICHD has produced important basic and policy-relevant findings during the past year. NICHD-supported research has demonstrated the impact of new welfare policies on the well-being and development of children. The Three Cities Study of Welfare, Children and Families has found that most children are doing well under the new policies, but that children are not faring well in families unable to make a successful transition to work. The Fragile Families study has continued to produce information on the conditions that enable new unmarried parents to sustain commitments to their child beyond the "magic moment" of birth. Other research has demonstrated effects of maternal work on child cognitive development and studied the pathways through which income affects cognitive and behavioral development.

Collaborations between NICHD and other Federal agencies have contributed to these and other research initiatives. An on-going collaboration between NICHD, the National Science Foundation, the Immigration and Naturalization Service, and the DHHS Office of the Assistant Secretary for Planning and Evaluation (ASPE) supports the New Immigrant Survey, a study of the adaptation and integration of legal immigrants to the United States. NICHD also collaborates with the Administration on Children and Families (ACF), the Centers for Disease Control and Prevention (CDC), the Bureau of Labor Statistics (BLS), the National Center for Education Statistics (NCES), and ASPE on the development and funding of major federal studies on topics including the health and development of children and youth, fertility and reproductive health, and marriage and family. NICHD staff have collaborated with ASPE and the Office of Population Affairs on initiatives related to abstinence education and teen pregnancy prevention.

With the Bureau of the Census, NICHD co-led a project that reviewed the availability and adequacy of data on marriage, divorce, and informal cohabitation in federal statistical systems. The "Counting Couples" project, conducted under the auspices of the Federal Interagency Forum on Child and Family Statistics, resulted in a published set of recommendations for improving federal data on these topics. A followup project on measurement is planned under the auspices of the NICHD Family and Child Well-being Research Network and this project will also include agencies such as ACF in planning and implementation.

NICHD's long range plan for demographic research, developed in 2001, has already resulted in several new initiatives. A recently released Request for Applications initiates a new program of research that will study how family decisions regarding investments in children and in the support of other dependent family members influence well-being across generations and how these investments are affected by incentives created through public policy. Another recent initiative will study the impact of the nature, duration, and dynamics of romantic and sexual relationships on the risk of HIV and other STDs. A forthcoming announcement will launch a program of demographic and social science research on race and ethnicity in the United States.

The NICHD has also taken steps to enhance mechanisms for much-needed interdisciplinary training in population research. Two new initiatives have been launched: a career-development program for junior investigators, and a mechanism supporting educational workshops focused on interdisciplinary training, dissemination of research data, and innovative methodologies.

Finally, following the recommendation of the "Counting Couples" project noted above, NICHD is launching a planning effort to design optimal strategies for future integrative studies of families and family change in the United States.

Item

Environmental effects on child health and development.- The Committee applauds the NICHD on its efforts to work collaboratively with the Environmental Protection Agency and the Centers for Disease Control and Prevention on developing the Longitudinal Cohort Study on Environmental Effects on Child Health and Development, which is now called the National Children's Study. This study aims to quantify the effects of environmental exposures plus the biological and social factors on child health and development. The Committee is pleased that the NICHD is undertaking a strategic planning process that strongly emphasizes a collaborative process between the biomedical and behavioral sciences and reaffirms its commitment to this entire effort. (p. 121)

Action taken or to be taken

The National Children's Study is a longitudinal cohort study designed to explore a broad range of environmental factors that influence the health and well-being of children, with environment broadly defined to include chemical, physical, social and behavioral influences. This study will make it possible to identify subtle but important effects of low-level exposures that may affect health and development. By combining measures of multiple exposures and multiple outcomes, the National Children's Study can examine multiple causes and effects.

Input on study design, measurement, and recruitment is being gathered from a wide array of sources to determine the best scientific framework for the study, and also to engage a large number and variety of enthusiastic partners into the process. Pilot and method development studies are underway. To date, the four lead agencies in this effort (NICHD, NIEHS, CDC, and EPA) have contributed funds from existing budgets to pay for planning and early pilot work.

Item

Fragile X - The Committee notes that the Children's Health Act of 2000 calls for the establishment of at least three Fragile X research centers. The Committee is pleased that the NICHD has issued a Request for Applications to implement this in fiscal year 2003. The Committee strongly urges the NICHD to allocate sufficient funds for expediting, expanding, and enhancing the work of these centers. (p. 121)

Action taken or to be taken

In continuing its history of strong support for research related to Fragile X, the NICHD issued a Request for Applications to establish at least three Fragile X research centers. These centers will be supported using a novel mechanism which builds on the administrative infrastructure of NICHD's successful Mental Retardation and Developmental Disabilities Research Centers

program. Five high quality applications have been received and reviewed. Final selection of the successful applicants is expected in January 2003, with awards soon thereafter. An investigators meeting is planned for the grantees and program staff in the spring of 2003 to facilitate the implementation of this program and to report on the latest Fragile X research progress and important new directions.

Program staff have participated in two workshops on Fragile X research issues co-sponsored by NICHD, as well as in numerous public meetings sponsored by advocacy organizations during FY 2002 and early FY 2003. The NICHD continues to support an active and growing portfolio of investigator-initiated research on Fragile X, including newborn screening pilot proposals.

Item

Infertility and contraceptive research - The Committee continues to place a high priority on research to combat infertility and speed the development of improved contraceptives. The NICHD is urged to continue aggressive activities in this area, including individual research grants and those of the infertility and contraceptive research centers. (p. 121)

Action taken or to be taken

NICHD continues to support the highly successful collaborative Specialized Cooperative Centers Program in Reproduction Research (SCCPRR). The centers are located at 14 universities throughout the country and have a unique approach to research in infertility and the fundamental reproductive processes. The knowledge gained assists the scientific community in the understanding and alleviation of conditions leading to infertility and provides leads for new contraceptives. SCCPRR investigators at all 14 centers have access to up-to-date technologies that promote scientific discoveries. One example of important research using these facilities is a study elucidating underlying cellular gene expression in pelvic tissues of women with endometriosis, a disease leading to infertility and chronic pelvic pain. The finding of this study opens the door for new treatment modalities for this disorder. NICHD encourages innovative reproductive science among SCCPRR investigators by a competition for renewal of two sites annually.

The National Cooperative Program for Infertility Research (NCPIR) was renewed in FY 2002. One exciting study will focus on the search for genetic inheritance among families with several members affected with polycystic ovarian syndrome (PCOS), a disease that can cause female infertility, and also obesity and adult onset diabetes. PCOS affects six-seven percent of reproductive age women and is responsible for 40% of infertility in women. In response to new evidence that insulin-sensitivity drugs may be utilized to treat infertility in PCOS, NICHD, through its Reproductive Medicine Network, has initiated a double blind, randomized clinical trial of metformin vs. clomiphene citrate vs. combined metformin/clomiphene citrate. This study will have great public health impact as it is designed to answer the question of which drug regimen is most successful in promoting live birth. It is planned to recruit a total of 678 women subjects.

Another condition affecting fertility is uterine fibroids, the number one cause of hysterectomy in childbearing women. NICHD has made this a priority research area and has issued an RFA to encourage scientists to discover the basic mechanism of fibroid growth.

NICHD is concerned as well with male factor infertility and has launched an initiative in this area encompassing basic science, translational, and clinical studies. As a first step, NICHD funded studies in phenotyping strains of mice with loss of genes involved in reproduction. These mouse strains will serve as models of biological mechanisms that can be applied to infertility in humans.

NICHD continues to emphasize research on the development and evaluation of new and existing contraceptive modalities. In FY 2002 the Contraceptive Development Center grants were successfully recompeted. Major emphasis in these centers is on the research development of new and improved methods for control of fertility in both males and females. Considerable focus is on the development of both hormonal and non-hormonal methods of male fertility regulation. One of the new contraceptive centers is conducting preliminary male contraceptive studies employing a potent GnRH inhibitor called Acyline. This hormonal approach to male contraception blocks sperm production as well as the production of male sex hormone. Recognizing the need for replacement of the endogenous male sex hormone, testosterone, the Institute has aggressively pursued the development of a potent synthetic substitute that is active when given by injection or orally. Toxicological studies will be undertaken prior to clinical evaluation. The Institute is also actively engaged in the evaluation of non-hormonal compounds that have been shown to be contraceptive in animal models. The non-hormonal approaches being evaluated will not affect male libido.

In its pursuit of developing improved contraceptives, the NICHD funds the Contraceptive Clinical Trials Network. Currently, the Network consists of nine sites and has participated in the evaluation of safety of new spermicides/microbicides as well as in more advanced clinical evaluation of the efficacy of new contraceptive modalities. While the initial focus of the Network has been on the evaluation of female methods, the future recompetition plan calls for additional sites that can conduct male contraceptive studies.

In its pursuit of new contraceptive technologies the NICHD employs a wide range of funding mechanisms that allow for productive interactions not only with academic institutions, but also with for-profit institutions. These arrangements result in more expeditious translational research and speed up the process of moving products to marketing.

In the evaluation of existing contraceptives, NICHD supported researchers have completed a major study on the impact of lifetime use of existing oral contraceptives on breast cancer. The long-term safety of existing products has been reaffirmed. NICHD is also active in providing support for the training of new investigators for research in both infertility and fertility regulation.

Item

Maternal-fetal medicine - The Committee is pleased with the progress of the Maternal Fetal Medicine Units (MFMU) Network. The Committee urges the NICHD to continue and expand its support of the Network to enable researchers to continue to collect data and more efficiently study complicated pregnancies with a focus on pre-term birth and maternal complications. In addition, the Committee urges the NICHD to increase research in the area of pregnancy-related complications, with a special emphasis on issues related to minority health disparities. (p. 122)

Action taken or to be taken

The NICHD Maternal Fetal Medicine Unit Network (MFMU) includes 14 academic institutions and one data center, in collaboration with the NICHD. These sites encompass over 120,000 deliveries per year and are recompeted on a 5-year cycle to optimize their productivity and competitiveness. Typically the Network has four to six studies and/or trials ongoing at any given time, which provides optimal efficiency and cost-effective research. Over the last year, two trials studying progesterone for the prevention of preterm birth in high-risk women, and Factor V Leiden mutation have been completed. The Network has five ongoing studies and trials:

- The Beneficial Effects of Magnesium Sulfate for the Prevention of Cerebral,
- Repeat Courses of Antenatal Steroids, Cesarean Section Registry to Evaluate the Safety of Vaginal Birth after Cesarean Section,
- Fetal Oximetry Trial,
- and Mild Gestational Diabetes.

In addition, in January 2003 the MFMU will begin a combined study and trial on prevention and prediction of preeclampsia.

The NICHD has been able to expand support of the MFMU through the partnership with other Institutes and Agencies. Currently two Institutes, NHLBI and NINDS, co-fund trials in the MFMU. The NINDS co-funds the Beneficial Effects of Magnesium Sulfate for the Prevention of Cerebral Palsy Trial and the NHLBI co-funds the Combined Antioxidant Trial for Prevention of Preeclampsia and the Preeclampsia Prediction Study. The Office of Research on Women's Health supported the Factor V Leiden Study and the Obstetrical-Fetal Pharmacology studies in the Network. In addition, the Food and Drug Administration (FDA) supported the development of the programming and software for the Fetal Oximetry Trial.

NICHD sponsored a planning workshop on the role of genetics in preterm delivery in the spring of 2001, *Genetics of prematurity and low birth weight babies, targeting racial/ethnic populations*. This led to a Program Announcement on *The Role of Gene-Environmental Interactions Underlying the Health Disparity of Premature Birth*. In addition, the NICHD has six awarded grants in response to the RFA on *Health Disparity in Preterm Birth: The Role of Infectious and Inflammatory Processes*.

The NICHD also supports basic and clinical research directed toward improving the outcome of pregnancy, reducing infant mortality, and minimizing maternal and infant morbidities. A significant amount of basic research is currently being supported to understand the physiological and biochemical mechanisms of pregnancy, preterm labor, and maternal complications of

pregnancy. Pregnancy is a complex process involving maternal and fetal components that interact with one another. Thus, understanding the basic mechanisms underlying these processes is essential for the rational design of effective interventions to prevent pregnancy related conditions and complications

Item

Pediatric kidney disease - Kidney disease remains a persistent and little-understood problem among infants, children, and adolescents. The NICHD is strongly urged to undertake research to identify factors responsible for poor linear growth, abnormal bone formation and cognitive deficits in children; epidemiological studies designed to quantify the magnitude of the problem and identify which kidney diseases present the highest risk; and initiatives aimed at maximizing the academic potential of children with kidney disease. (p. 122)

Action taken or to be taken

The NICHD agrees that pediatric kidney disease remains a persistent and serious public health problem, about which much more needs to be learned. The NICHD, by supporting twenty Child Health Research Centers, is devoted to training the next generation of clinical scientists with an interest in solving the problems posed by chronic renal disease in children, at both the basic and clinical levels.

Among the serious clinical issues that attend end-stage renal disease in children are the vexing problems of calcium balance, abnormal bone formation in soft tissues of the body, and loss of bone mineral density with consequent skeletal weakness. The NICHD's Pediatric Pharmacology Research Unit Network has just initiated a multi-center placebo-controlled trial of doxercalciferol, a novel analogue of vitamin D that is designed to prevent renal osteodystrophy by maintaining normal levels of serum calcium.

The NICHD also supports intramural studies designed to prevent the onset of nephrocalcinosis and kidney failure in children with hypoparathyroidism by treating them with parathyroid hormone (PTH 1-34) instead of with calcium and vitamin D_3. Results of these studies are promising. It appears as if the children treated with PTH 1-34 are better able to maintain normal levels of serum calcium and renal function than those treated conventionally with calcium and vitamin D_3.

In FY 2003 the NICHD plans to join the NIDDK and the NINDS in supporting a 5-year prospective study of the progression of mild-to-moderate renal disease in 600 affected children. The major goals of this important initiative are to ascertain significant risk factors for declines in renal function; the incidence of impaired cognitive development in children with chronic kidney disease; risk factors for the development of impaired cognitive function; and the long-term effects of growth retardation that attends renal disease in children. A related aim will be to document the effects of treatment of this kind of growth retardation on subsequent morbidity and mortality. This carefully designed study of the epidemiology of chronic pediatric kidney disease promises to be informative and important for the development of new and more effective modes of preventive interventions.

Item

Pediatric liver disease - The Committee urges the Institute to pursue opportunities to participate with the NIDDK and other Institutes on pediatric liver disease research, particularly in the areas of biliary atresia and non-alcoholic steatohepatitis. (p. 122)

Action taken or to be taken

The NICHD agrees with the Committee about the importance of non-alcoholic steatohepatitis. This disorder is being seen with increasing frequency in obese children and adolescents. In FY 2002 the NICHD joined the NIDDK to support a clinical research network in the area of non-alcoholic steatohepatitis. This network of eight major clinical centers is in the process of developing common pediatric protocols to evaluate promising new approaches to preventing and treating non-alcoholic steatohepatitis in children and adolescents.

The Institute agrees that biliary atresia is an important congenital defect. The condition appears in about one in every 15,000 live births in the United States and is the most common reason for liver transplantation in childhood. In view of the serious nature of this hepatic disorder, the NICHD will pursue opportunities to support research on this topic within the recently assembled consortium of 10 clinical centers devoted to research on biliary atresia. This consortium was initiated in FY 2002 and is supported by the NIDDK.

The NICHD also supports both basic and clinical research programs on developmental gastroenterology, much of which focuses on the functional development of the liver during infancy. Clinical jaundice is the most common medical condition in newborn babies. More than one-half of them display significant hyperbilirubinemia (jaundice) during the first week of life. The NICHD supports studies aimed at increasing our understanding of why newborn babies develop cholestatic liver disease (jaundice) including research on the induction of bile acid synthesis and the biologic controls that determine the rate of bile acid transport out of the liver and into the intestine. The NICHD also funds research designed to ascertain how phototherapy works to reverse this neonatal disorder and how to improve the efficacy of phototherapy in the newborn nursery. The NICHD also funds research on the causes and cures of inborn errors of metabolism that involve aberrant liver enzymes, such as phenylketonuria and hyperammonemia.

As part of the Institute's research program on pediatric pharmacology, the NICHD supports research on how hepatic drug metabolizing enzymes work to activate some drugs and to prepare toxic metabolites of other drugs for excretion into the bile duct.

Item

Skeletal growth - The committee encourages the NICHD to support research in abnormal and normal skeletal growth and development, including rickets and chronic under-nutrition, use of oral contraceptives and anabolic steroids, lactation, and pregnancy. (p. 122)

Action taken or to be taken

The NICHD shares the Committee's interest in furthering our understanding of normal and abnormal skeletal growth and development. The NICHD is currently supporting several large studies of children's skeletal growth in conditions of both normal nutrient intake and chronic under-nutrition. Investigators are examining gene-environmental interactions in skeletal development among nearly 1,300 children and adolescents in the Fels Longitudinal Study. These results will be compared to results of a similar study of bone maturation in 900 children growing up in rural Nepal. The NICHD is also supporting the longitudinal Bone Mineral Density in Childhood Study in order to obtain reference data for bone mineral density in 1,500 American girls and boys between the ages of six and 16. This study is designed to ascertain the effects of nutrient intake, exercise and stages of puberty on bone mineral density.

It is important to measure bone mineral density in children because it appears that osteoporosis has its roots in childhood. Many children enter adulthood with compromised skeletal systems that stem from poor nutrition and exercise habits. In order to ascertain the scope of this problem and to develop new ways of increasing bone mineral density, the NICHD is funding 13 prospective studies of osteoporosis prevention in several thousand children. Preliminary findings from these studies indicate that interventions consisting of supplemental calcium and exercise increase bone mass in pre-adolescent girls. The NICHD also administers the Milk Matters campaign, an important educational program that is designed to encourage children to increase their calcium intake. The National Institute of Dental and Craniofacial Research (NIDCR) and the American Academy of Pediatrics are working with the NICHD to achieve this important goal.

The NICHD is also concerned about the reappearance of rickets, especially among African American infants who are being breast-fed. In FY 2003 the NICHD will initiate a study of vitamin D supplementation in 540 pregnant women, divided equally among African American, Hispanic and Caucasian women. In partnership with the NIH Office of Dietary Supplements and the Centers for Disease Control and Prevention (CDC), the NICHD will convene a workshop in March, 2003, that will focus on the current state of knowledge of vitamin D levels in women, infants and children in the United States. The participants will address the unique needs for vitamin D of pregnant and lactating women and their infants, with attention to the special needs of minority populations. The goal of the meeting will be to develop a coordinated research agenda to address crucial gaps in our knowledge of this problem. The NICHD also is working in partnership with the National Center for Health Statistics of the CDC to collect data on bone mineral parameters in the population-based National Health and Nutrition Examination Survey 2003-2004. Of special interest in this new survey will be measurements of bone density and calcium intake in children ages eight to 19.

The NICHD shares the Committee's concerns about the effects of contraceptive steroids, such as Depo-Provera (medroxyprogesterone acetate) on bone growth during adolescence. The NICHD is currently funding four prospective studies on this topic. Preliminary results indicate that use of Depo-Provera over a 2-year period causes a 3% decrease in bone mineral density in adolescent girls. This agent also slows bone maturation. It appears that these effects are reversible, and that bone growth resumes once ovarian function is reestablished, within 6 months of the last dose of Depo-Provera. The negative effects of this contraceptive steroid are caused by

a state of relative estrogen deficiency. By adding estradiol to the contraceptive progestin, bone mineral density can be maintained at the expected level.

The NICHD also supports studies of calcium balance during pregnancy. Findings from these studies indicate that the state of pregnancy induces increased calcium loss and increased calcium absorption, and that both of these parameters return to normal within one month of delivery. Studies of calcium balance in lactating adolescents show a non-significant difference in bone mineral density compared with non-lactating adolescents, although there is a trend towards lower bone mineral density among the lactating adolescents.

Item

Urogynecology program - The Committee is encouraged by the NICHD's accomplishments to date in establishing a research portfolio on pelvic floor disorders and urinary incontinence. The Committee encourages the Institute to fund grant applications for tissue structure, epidemiological studies, urinary incontinence, and clinical trials intervention programs. The Committee also encourages the NICHD to include the effects of pregnancy on a woman's chance for later urogynecologic problems in the future ``National Children's Study." (p. 123)

Action taken or to be taken

The NICHD agrees that there is a strong need for further research in urogynecology disorders. In FY 1999, the NICHD, in collaboration with NIDDK, issued an RFA for the formation of a Urinary Incontinence Treatment Network. In response, four clinical sites and one biostatistical coordinating center were selected. The RFA was reissued in FY 2001 to select additional clinical sites and as a result was expanded to eventually consist of nine clinical sites and one biostatistical coordinating center.

In FY 2000, NICHD issued a RFA on Epidemiologic Research on Female Pelvic Floor Disorders which resulted in a total of 35 applications. From those, ten awards were made. The grants ranged across a wide gamut of topics in female pelvic floor disorders, including: reproductive risk factors and the natural history of pelvic organ prolapse; the epidemiology of fecal incontinence after childbirth and later in life; genetic and racial determinants of pelvic floor disorders; and risk factors for urinary incontinence including the analysis of familial (genetic) and acquired (childbirth) issues.

In July 2001, the NICHD established the Pelvic Floor Disorders Network (PFDN), which consists of seven clinical sites and one data coordinating center. One of the major protocols is the Colpopexy and Urinary Reduction Efforts (CARE) Study with the primary aim of determining whether women with advanced prolapse, but without stress incontinence symptoms, should receive a surgical procedure to prevent stress incontinence (Burch colposuspension) at the same time that abdominal sacral colpopexy is performed. In addition to the CARE study, there are four supplementary studies and 15 ancillary analyses planned.

A second protocol of the PFDN is the Childbirth and Pelvic Symptoms (CAPS) Study, which was initiated in the seven clinical sites in September 2002. The primary aim of the CAPS study

is to determine the prevalence and incidence of fecal incontinence, and other symptoms including urinary incontinence and sexual dysfunction, in women after childbirth. Three groups of women will be involved with the study: women after vaginal delivery with anal sphincter laceration, women after vaginal delivery without anal sphincter laceration, and women after cesarean delivery without labor. Data from this study will be used to develop sample size estimates for a trial of pelvic muscle physiotherapy to prevent or treat fecal incontinence and other symptoms in women after childbirth. Currently, there are three supplementary studies and nine ancillary analyses planned in association with the CAPS study.

In addition to the current research endeavors, the NICHD also sponsored a 1-day workshop in NIH Grants Fundamentals in conjunction with the annual scientific meeting of the American Urogynecologic Society in October 2002. The program was so well received that the Executive Director and newly elected President of the American Urogynecologic Society have requested that a similar workshop be held in conjunction with next year's annual scientific meeting of the American Urogynecologic Society scheduled for September 2003.

In November 2002, the NICHD sponsored a 2-day meeting on Basic Science and Translational Research in Female Pelvic Floor Disorders. The objective of the meeting was to bring together investigators performing basic science and translational research in female pelvic floor disorders to present their ongoing research, to discuss state-of-the-art research in the field, to identify important knowledge gaps in understanding the pathophysiology of pelvic floor disorders, and to identify educational and training issues impeding the progress of research in the field. The proceedings of this meeting will be prepared for publication in a peer-reviewed format and will be used by NIH staff in developing a research agenda for basic science and translational research in pelvic floor disorders.

NICHD is considering ways to study urogynecologic problems in the “National Children’s Study.” Investigators representing urogynecologic problems are actively participating in the planning process and the urogynecology community has been made aware of this study and encouraged to participate in its design.

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

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2003 Amount Authorized	2003 Amended President's Budget	2004 Amount Authorized	2004 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Institute of Child Health and Human Development	Section 41B	42§285	Indefinite	$1,163,158,000	Indefinite	$1,211,933,000
National Research Service Awards	Section 487(d)	42§288	a/	31,733,000	b/	33,438,000
Total, Budget Authority				1,194,891,000		1,245,371,000

a/ Amounts authorized by Section 301 and Title IV of the Public Health Act.
b/ Reauthorizing legislation will be submitted.

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/
1995 3/	516,736,000	513,159,000	513,159,000	512,852,000 4/
Rescission				(0)
1996	526,177,000 3/	595,162,000	518,585,000 3/	595,162,000
Rescission				(615,000)
1997	543,441,000 3/	631,989,000	554,251,000 3/	631,703,000
1998	582,032,000 3/	666,682,000	676,870,000	674,766,000
1999	654,248,000 4/5/	728,817,000	748,482,000	750,982,000
Rescission				(497,000)
2000	694,114,000 3/	817,470,000	848,044,000	862,884,000
Rescission				(4,593,000)
2001	810,501,000 3/	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			
2004	1,245,371,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes enacted administrative reductions of $6,305,000.
3/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
4/ Excludes enacted administrative reductions of $557,000.
5/ 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 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 Estimate
Office of the Director	19	19	19
Office of Administrative Management	69	69	68
Office of Science Policy, Analysis and Communication	25	25	25
Center for Population Research	33	33	32
Center for Research for Mothers and Children	42	43	42
National Center for Medical Rehabilitation Research	8	8	8
Division of Scientific Review	23	23	23
Division of Epidemiology, Statistics and Prevention Research	28	28	27
Division on Intramural Research	350	352	346
Total	597	600	590
FTEs supported by funds from Cooperative Research and Development Agreements	(2)	(2)	(2)

FISCAL YEAR	Average GM/GS Grade
2000	11.1
2001	10.9
2002	11.0
2003	11.0
2004	11.0

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

Detail of Positions

GRADE	FY 2002 Actual	FY 2003 Amended Pres. Budget	FY 2004 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	$414,301	$432,900	$452,400
GM/GS-15	44	44	42
GM/GS-14	74	74	73
GM/GS-13	38	38	38
GS-12	56	56	55
GS-11	33	33	33
GS-10	6	6	6
GS-9	33	34	34
GS-8	30	30	30
GS-7	45	45	44
GS-6	18	18	17
GS-5	9	10	10
GS-4	5	5	5
GS-3	1	1	1
GS-2			
GS-1			
Subtotal	392	394	388
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	11	11	11
Senior Grade	7	7	7
Full Grade	6	6	6
Senior Assistant Grade	2	2	2
Assistant Grade	0	0	0
Subtotal	26	26	26
Ungraded	205	206	202
Total permanent positions	423	425	419
Total positions, end of year	626	628	619
Total full-time equivalent (FTE) employment,end of year	597	600	590
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$138,100	$144,300	$150,800
Average GM/GS grade	11.0	11.0	11.0
Average GM/GS salary	$66,090	$69,000	$72,200