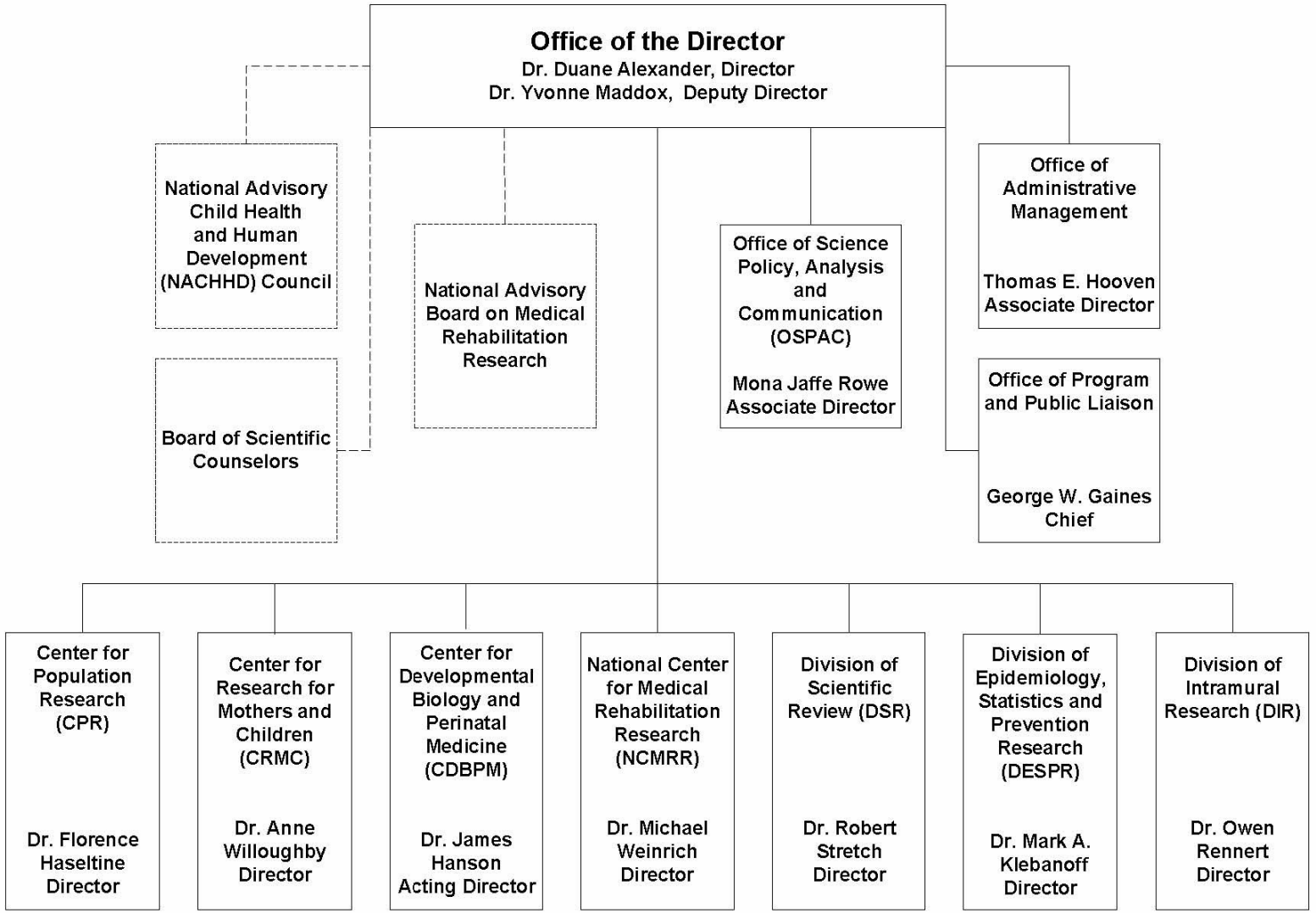
DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

FY 2006 Budget — Page No.

National Institute of Child Health and Human Development



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, [$1,280,915,000] *$1,277,544,000*.

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Consolidated Appropriations Act for Fiscal Year 2005]

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

Amounts Available for Obligation 1/

Source of Funding	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Appropriation	$1,250,585,000	$1,280,915,000	$1,277,544,000
Enacted Rescissions	(8,224,000)	(10,594,000)	0
Subtotal, Adjusted Appropriation	1,242,361,000	1,270,321,000	1,277,544,000
Real transfer under NIH Director's one-percent transfer authority to other ICs	5,616,000	0	0
Comparative transfer to NIBIB for Radiology Program	(101,000)	0	0
Comparative transfer to Buildings and Facilities	(415,000)	0	0
Comparative transfer to/from other NIH ICs for NIH Roadmap	(5,616,000)	0	0
Subtotal, adjusted budget authority	1,241,845,000	1,270,321,000	1,277,544,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,241,845,000	1,270,321,000	1,277,544,000
Unobligated balance lapsing	(37,000)	0	0
Total obligations	1,241,808,000	1,270,321,000	1,277,544,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2004 - $42,521,000 FY 2005 - 42,521,000 FY 2006 - $42,521,000
Excludes $714,000 in FY 2004 and $750,000 in FY 2005 for royalties.

Justification
National Institute of Child Health and Human Development

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

Budget Authority:

FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
547	1,241,845,000	551	1,270,321,000	552	1,277,544,000	1	7,223,000

This document provides justification for the Fiscal Year 2006 activities of the National Institute of Child Health and Human Development (NICHD), including HIV/AIDS activities. A more detailed description of National Institutes of Health (NIH)-wide FY 2006 AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

INTRODUCTION

The research goal of the National Institute of Child Health and Human Development (NICHD) is to conquer the greatest health challenges for women, children, and families, including infertility; preterm birth; birth defects; injuries, problems with learning; risks of adolescence; complications of childbirth; and HIV infection in mothers and children. Breakthrough technologies and rapidly-paced scientific advances against these challenges continue to reinforce the concept that the future health of our nation and, indeed, the world, starts with the health of individual parents, children, and families.

Over the past year, NICHD scientific advances have demonstrated new options for developing nations to protect infants from mother-to-child transmission of HIV. New findings enhanced our understanding of adult stem cells in ways that may enable researchers to expand their use for tissue and organ repair. Investigators increased our knowledge of the disorders that underlie infertility, in ways that may lead to novel therapies. Other NICHD research demonstrated the most effective ways to teach children to read and to learn scientific reasoning skills at an early age. New findings on the powerful effects of television, peers, and parental guidance on behavior suggested relatively simple interventions for families to reduce attention problems in children and risky behaviors in teens. Findings on how to treat the pain of preterm infants on mechanical ventilators could alter clinical practices in our neonatal intensive care nurseries. Systematic information regarding prolonged infant crying after the first three months of life could prompt clinicians to follow these children more closely for signs of developmental delay. Data on factors that encourage people to form may help policy-makers design programs to enhance family stability.

The resounding theme underlying all of these NICHD research advances -- from the most basic at the molecular cellular level, to the most applied aimed at understanding the potential impact of

policies involving children and their families -- is that promise of a healthy future for all of our children and families lies within our reach of understanding.

SCIENCE ADVANCES

Story of Discovery: New Frontiers: Compounds Identified in Mothers' Milk That Provide Protection Against Diarrheal Diseases

Worldwide, about 1.5 million children under age 5 die from diarrheal diseases each year. The incidence is highest in parts of the world where safe drinking water is not available, and young children with severe diarrhea die from the dehydration that diarrhea causes. In the U.S., nearly 200,000 small children are hospitalized for diarrhea each year, and 300 of them die.

Human breast milk is known to protect infants from diarrhea, but the responsible components have not been known. Now, a routine search to understand the purpose of some complex sugar molecules found in human breast milk may lead to a way to prevent these devastating diarrheal diseases from occurring, not just in infants, but in older children and adults as well.

The molecules, called oligosaccharides, are abundant in human milk but do not have any nutritional value. During the last decade, NIH funded researchers have discovered that these molecules stop bacteria and viruses from binding to the cells in the intestinal wall, preventing deadly diarrheal diseases from gaining a foothold.

In one set of studies, the researchers found that some types of oligosaccharides combat E. coli 0157, the deadly bacterium that can infect ground beef and other common foods. Other kinds of oligosaccharides block Campylobacter jejuni, a common cause of bacterial diarrhea in the United States. Still other oligosaccharides block the functioning of the Norwalk virus, which incapacitates thousands of cruise ship voyagers every year. One type of oligosaccharide, called lactadherin, binds to rotavirus, preventing it from reproducing. Worldwide, rotavirus is one of the most common cause of diarrheal diseases in children.

At a minimum, these studies show the importance of breast feeding in safeguarding infant health. Just as importantly, however, these compounds may provide the basis for more effective ways to combat disease.

According to the U.S. Centers for Disease Control and Prevention nearly all significant disease-causing bacteria are becoming resistant to antibiotics. Thus, many types of bacteria now routinely survive the drugs that once were the most effective way to kill them. But unlike traditional antibiotics, which disrupt bacteria's cellular machinery, oligosaccharides function in a fundamentally different way, preventing microorganisms from binding to the intestinal wall. Because of this difference, it appears that bacteria probably cannot become resistant to these sugar molecules.

Researchers now are trying to find ways to synthetically produce these promising compounds. By using the naturally occurring substances or slightly altering the chemical composition of oligosaccharides, researchers may be able to develop a new generation of pharmaceutical agents that protect against diarrhea and are not affected by the problem of antibiotic resistance.

(Morrow AL, Ruiz-Palacios GM, Altaye M, Jiang X, Guerrero ML, Meinzen-Derr JK, et al. Human Milk Oligosaccharides Are Associated with Protection against Diarrhea in Breastfed Infants. J Pediatr 145: 297-303, 2004.)

HIV/AIDS

As increasing numbers of women and children are infected with HIV in the evolving global epidemic, NICHD research continues to test and refine effective interventions to slow HIV

progression in women, reduce mother-to-child transmission, and to treat infants who do not escape the infection. New findings from NICHD research should enable developing countries with differing health policies and resources to achieve, within their financial and logistical capacities, longer, healthier lives for women with HIV and lower rates of HIV transmission from mothers to infants. Other new findings will enable clinicians to better understand the comparative safety and efficacy of different multi-drug treatments for infants with HIV and when to start the treatments.

Multi-vitamins during pregnancy and after birth delay progression of HIV in women. At a time when Tanzania was unable to provide anti-HIV drugs to most of its pregnant women with HIV, researchers were able to use high doses of vitamins B, C, and E, during pregnancy and for five years after birth, to slow significantly the progression of HIV in women without access to drug therapies.[1] These findings are from the first large-scale, placebo-controlled trial of multi-vitamin therapy in pregnant women with HIV for whom standard drug therapies were unavailable. The researchers also found significantly higher levels of infection-fighting cells and lower levels of the HIV virus in women who took the multi-vitamin supplements, compared with those in the study's control group who did not receive the supplements. The findings indicate that the vitamins strengthened the women's immune systems and reduced the rate at which the HIV virus replicated itself. While giving vitamin supplements during or after pregnancy – regardless of HIV status -- is routine in developed countries, this is not generally the case in the developing world. The low cost of the vitamin regimen could enable more countries with limited resources to keep women with HIV healthier, longer, while directing antiretroviral drugs to women in advanced stages of the infection.

Starting anti-HIV drug therapy early in HIV-infected infants is well tolerated and highly effective in reducing viral replication. HIV infection progresses more rapidly in children than in adults, but few studies address the best time to begin anti-HIV drug therapy in HIV-infected infants. Researchers recently reported that starting multi-drug anti-HIV therapies in infants with HIV at age three months or younger significantly suppressed HIV virus replication in the children for up to four years.[2] This effect was less strong in children who were older than three months when they began drug therapy. In a relatively small clinical trial comparing three- and four-drug therapies, the researchers found that the infants tolerated each drug combination well, with relatively few side effects. The four-drug combination of stavudine, lamivudine, nevirapine, and nelfinavir was associated most strongly with long-term viral suppression. Just as importantly, however, the study's data highlighted the best time to start treating infants and demonstrated that combination therapies are safe and effective enough to warrant larger, randomized trials to determine the best drug combination. Researchers caution that ultimately, early antiretroviral treatment must be coupled with a vaccine that would stimulate and maintain immune responses, if long-term treatment of HIV-infected children is to succeed.

[1] Fawzi WW, Msamanga GI, Spiegelman D, Wei R, Kapiga S, et al., A Randomized Trial of Multivitamin Supplements and HIV Disease Progression and Mortality. N Eng J Med 351:23-32, 2004.
[2] Luzuriaga K, McManus M, Mofenson L, Britto P, Graham B, et al. A Trial of Three Antiretroviral Regimens in HIV-1-Infected Children. N Eng J Med 350:2471-2480, 2004.

Genes, Cells, and Health

NICHD research on normal and atypical developmental processes at the molecular and cellular levels continues to move biomedical science toward possible diagnostic and therapeutic breakthroughs for some of the most devastating disorders of children and adults. New findings on adult stem cells, molecular mechanisms of birth defects, and genes associated with type 1 diabetes and with two rare genetic disorders that cause severe disabilities raise the possibility of, ultimately, being able to ameliorate or prevent these conditions.

Adult stem cells that started down a path of becoming a specific cell can be experimentally manipulated to change their mind and return to their original status as a stem cell. Stem cells are unspecialized cells, found in animals and humans. Stem cells have unique capacities to renew themselves and to give rise to specialized cells with specific shapes and functions such as muscle cell contraction or nerve cell signaling. Adult stem cells are found in specialized tissues of adults and yield cell types of the tissue from which they originate. Scientists have long assumed that once a stem cell begins to "differentiate" – that is, to become a tissue-specific cell – it loses its capacity to self-renew. This assumption was turned on its head when scientists used sophisticated genetic techniques to cause germ line stem cells of adult fruit flies to revert back to their original status, capable of self-renewal, after the cells had initiated the process of differentiating into sperm cells.[3] Although fruit flies differ in many ways from higher organisms such as humans, the signaling pathways that cells use to carry out their functions are remarkably similar in all organisms. Understanding the differentiation process of cells in fruit flies could solve a major puzzle for developmental biologists. It also means that stem cells in humans could have the same ability to revert back to their original status after starting to differentiate. This unique ability could one day lead to new therapeutic approaches for multiple disorders.

Different birth defects result from two signaling pathways on a molecule. Cells need to continuously monitor and integrate environmental cues to ensure proper development of the embryo and to maintain homeostasis or stability of tissues in adults. To understand how these monitoring and integrating processes are regulated, scientists need to understand how different cues or signals interact at the molecular level to regulate cell activity. Researchers recently discovered two different signaling pathways on the same molecule, each of which resulted in a different birth defect in an experimental mouse model.[4] This research was the first to show that mutations in different parts of one protein, which plays a critical role in two different signaling pathways, can cause different developmental defects. In addition, new understanding of how a cell can interpret different signals in its environment can assist scientists in directing naïve cells, such as adult stem cells, to develop into a specific type of cell that can repair tissue.

New gene identified in type 1 diabetes. Researchers have identified more than twenty chromosomal regions that are linked to type 1 diabetes, a type of disease in which the body's immune system attacks the body's tissues. Until now, however, researchers had not found an individual gene associated with the disease. NICHD-supported scientists recently discovered a

[3] Brawley C, Matunis E. Regeneration of Male Germline Stem Cells by Spermatogonial Dedifferentiation in Vivo. Science 304:1331-1334, 2004.
[4] Aubin J, Davy A, Soriano P. In Vivo Convergence of BMP and MAPK Signaling Pathways: Impact of Differential Smad1 Phosphorylation on Development and Homeostasis. Genes Dev 18:1482-1494, 2004.

mutated gene in one of the previously-identified chromosomal regions and showed how the gene is causally linked to type 1 diabetes.[5] The gene makes a type of protein that has a critical, indirect role in regulating the immune system. The mutation in the gene interferes with the action of the protein. The scientists found that patients with type 1 diabetes were more likely to have the mutated gene. Moreover, they learned that the gene was expressed at varying levels in the patients' immune tissues, with the highest levels in the lymph nodes and the spleen. The discovery of the previously unknown regulatory pathway in origin and development of type 1 diabetes gives scientists new targets for future genetic and immunological treatments of the disease.

Rett syndrome protein involved in early development. Rett syndrome (RTT) is a genetic disorder that gradually halts the healthy development of infant and toddler girls. Among other problems, girls with RTT lose their ability to talk, to interact with other people and to move independently. Currently, no treatment exists to halt its progression. Researchers have determined that the disorder results from a defect in a particular gene, known as MeCP2, but were unsure of the gene's function. Recently, scientists gained an understanding of the gene's function by studying the underwater frog, *Xenopus*. The researchers determined that a mutant form of the gene affects early embryonic development, resulting in an excess number of the precursor cells that give rise to the brain. Xenopus tadpoles with the mutant gene developed neurological anomalies similar to those seen in RTT.[6] The researcher's findings contribute to an improved understanding of RTT, which may eventually lead to new treatments for the disorder.

Gene discovered for Cornelia de Lange Syndrome. For the first time, scientists have found a mutated gene that is associated with Cornelia de Lange Syndrome, a rare, multi-system disorder characterized by mental retardation, heart defects, and multiple other physical and behavioral anomalies.[7] Researchers studied 12 families in which one or more members have the disorder and identified a gene that had multiple mutations and that was widely expressed in fetal and adult tissues. The gene appears to be involved in the very early stages of embryonic development, and contains information needed to switch on a number of other genes during that period. The gene's discovery is expected to speed development of a prenatal test for the syndrome. A similar test will also be developed to diagnose Cornelia de Lange Syndrome in young children who may have the condition. Discovery of the gene is an important step not only toward understanding and helping to diagnose the disorder, but for possibly developing future interventions to prevent it.

Reproduction and Health

Reproductive health is an issue of critical concern to millions of Americans. It is vital to the formation and continued well-being of the nation's families in general, and to the improvement of women's and men's health in particular. In advances that further our understanding of

[5] Guo D, Li M, Zhang Y, Yang P, Eckenrode S, et al. A Functional Variant of SUM04, a new IκBα Modifier Is Associated with Type 1 Diabetes. Nat Genet 36:837-841, 2004.
[6] Stancheva I, Collins AL, Van den Veyver IB, Zoghbi H, Meehan RR. A Mutant Form of MeCP2 Protein Associated with Human Rett Syndrome Cannot Be Displaced from Methylated DNA by Notch in *Xenopus* Embryos. Mol Cell 12: 425-435, 2003.
[7] Krantz ID, McCallum J, DeScipio C, Kaur M, Gillis LA, et al. Cornelia de Lange Syndrome Is Caused by Mutations in *NIPBL*, the Human Homolog of *Drosophila melanogster Nipped-B*. Nat Genet 36:631-635, 2004.

reproductive processes and increase the promise of new treatment and prevention options, NICHD researchers examined the underlying mechanisms of fertility and infertility, identified early signs of a life-threatening pregnancy complication, and advanced our understanding of the causes of, and possible non-surgical treatments for, non-cancerous uterine tumors known as fibroids.

Study identifies novel puberty gene. The mechanisms that control sexual maturation heralding the onset of adult reproductive function are one of the great mysteries of human biology. Puberty begins when a brain structure known as the hypothalamus begins secreting gonadotropin releasing hormone, the "master" reproductive hormone that regulates fertility. However, NICHD-supported researchers came a step closer to understanding the maturation process when they examined several members of a family who did not experience normal sexual maturation. The researchers found that all of these individuals, along with another, unrelated person, had abnormalities in a gene known as GPR54. The researchers then developed an experimental mouse that did not have the gene in any form.[8] Like their human counterparts with mutations in GPR54, the mice also did not undergo puberty. The researchers found that while GnRH was lacking in its other tissues, the mouse hypothalamus did contain normal amounts of unreleased GnRH. These findings open the door to new ways of treating the ovaries and testes that fail to mature and other conditions of human infertility associated with inadequate release of GnRH.

Changes in key protein levels may cause preeclampsia. Preeclampsia affects about 5 percent of all pregnancies and is a leading cause of maternal and fetal morbidity, disability, and death. A pregnant woman with preeclampsia has dangerously high levels of blood pressure and the condition can progress to seizures and coma (eclampsia). While the high blood pressure and the seizures can be treated, the only cure for preeclampsia is delivery. Surviving infants, often premature, are likely to require intensive neonatal care. In an important step forward, researchers found earlier and more pronounced changes in levels of several proteins in blood samples of pregnant women who developed preeclampsia, compared with those experiencing normal pregnancies.[9] The researchers caution that a larger trial would be needed to determine whether the protein abnormalities would enable clinicians to identify women at risk of preeclampsia and begin treatment before the condition occurs. However, their discovery may ultimately enable clinicians to prevent or cure preeclampsia by administering certain proteins to correct an underlying imbalance of factors that cause it.

Fibroid tumor studies may contribute to developing new non-surgical treatments. NICHD researchers are beginning to unravel the mystery behind the origins of fibroids, the most common benign tumors of the uterus and the leading cause of hysterectomy in the United States.[10] Fibroids, also known as leiomyomas, can cause severe pain and infertility and disproportionately affect African American women. In two recent studies of fibroid tumors, researchers discovered protein abnormalities that could help explain why the tumors grow and

[8] Seminara SB, Seminara MD, Messager S, Chatzidaki EE, Thresher RR, et al. The *GPR54* Gene as a Regulator of Puberty. N Eng J Med 349:1614-1627, 2003.
[9] Levine RJ, Maynard SE, Cong Q, Lim K-H, England LJ, et al. Circulating Angiogenic Factors and the Risk of Preeclampsia. N Eng J Med 350:672-683, 2004.
[10] Leppert PC, Baginski T, Prupas C, Catherino WH, Pletcher S, Segars JH. Comparative Ultrastructure of Collagen Fibrils in Uterine Leiomyomas and Normal Myometrium. Fert Steril 82, Suppl 3:1182-1187, 2004.

how they could be treated medically. In the study of fibroid tissues, the researchers found that the tumors consist largely of abnormally tangled, loosely-packed "threads" (fibrils) of the protein collagen. In the study of fibroid cells, the researchers found abnormally low production of dermatopontin, a protein involved in the manufacture of collagen.[11] The low dermatopontin level may contribute to abnormal collagen formation and ultimately to tumor development. These findings are major steps in understanding how fibroids form and may help in devising effective, non-surgical treatments for the condition.

Learning and Memory

NICHD research encompasses a range of groundbreaking studies of brain function and learning. Basic research may one day enable clinicians to treat Alzheimer's or other memory and learning disorders. Investigations of factors in educational success will enable teachers to use the most effective, science-based methods to teach children, enhancing their chances for success in the workplace and, ultimately, as parents preparing their own children to learn and to succeed. For example, one recent discovery demonstrates the essential role of a protein in long-term memory. Another provides evidence that a specific method of teaching reading produces the type of brain activity observed in children who have mastered this skill. Research findings on how children learn scientific reasoning skills may prompt revisions in current educational programs.

Researchers prove that a protein makes long-term memory possible. From language to literature, from music to mathematics, a single protein appears central to the formation of the long-term memories needed to learn these and all other disciplines, according to recently reported research. The researchers proved that a previously-identified chemical reaction helps the protein to form naturally in the brain, and makes long-term memory possible.[12] The protein (mBDNF) appears to alter nerve cells chemically, boosting their ability to send messages to one another. Scientists had suspected that a precursor form of the protein (BDNF) played a role in memory and previous studies had deciphered chemical reactions leading to the formation of the protein. Scientists did not know, however, whether the same reaction occurs in the brain or whether the protein underlies the formation of long-term memory. The proof emerged from a series of experiments, using mouse brain tissue, that showed conclusively that each compound in the chemical reaction was essential to the formation of the protein, and that the protein is essential to the long-term memory process. These findings set the stage for researchers to investigate whether defects in the BDNF protein system may lead to disorders of learning and memory. It is also possible that the protein may play a role in Alzheimer's disease, as some studies have shown reduced levels of it in the brains of Alzheimer's patients.

Imaging study reveals that brain function of poor readers can improve. NICHD-supported researchers demonstrated that after children with developmental dyslexia received structured intervention and overcame this reading disability, their brains began to function like those of

[11] Catherino WH, Leppert PC, Stenmark MH, Payson M, Potlog-Nahari C et al. Reduced Dermatopontin Expression Is a Molecular Link Between Uterine Leiomyomas and Keloids. Genes Chromosomes Cancer 40:204-217, 2004.

[12] Egan MF, Kojima M, Callicott JH, Goldberg TE, Kolachana BS, Bertolino A, et al. The BDNF val66met Polymorphism Affects Activity-Dependent Secretion of BDNF and Human Memory and Hippocampal Function. Cell 112:257-269, 2003.

good readers.[13] Previous research had shown that a phonetics-based instruction method based on awareness of sounds produced by particular letters can help reading-disabled children become fluent readers. In the latest study, researchers used functional magnetic resonance imaging (fMRI), a brain imaging technology, to compare brain activity in reading-disabled children instructed in this method with brain activity in a control group receiving standard instruction. Those children receiving the specialized instruction outpaced the other children in reading skills and researchers found changes in their brain organization, both at the time of the initial intervention and a year later. These findings show that effective reading instruction not only improves reading ability, but also changes the brain's functioning to better perform reading tasks.

More students learn science by instruction than by discovery. Researchers have shown that a significantly higher proportion of school children learn critical scientific reasoning skills when they are instructed explicitly about experimental procedures rather than when they try, on their own, to develop such procedures to accomplish specific tasks.[14] The new research raises doubts about a widely-accepted conventional belief that children who acquire knowledge by "constructing" it themselves are better able to apply and extend what they have learned when they "discover" phenomena, without instruction. The researchers posed a simple scientific question to the children: figure out what properties of a ramp (steepness, length, smoothness, etc.) affect how far a ball will roll. The researchers assigned third and fourth graders to two instructional conditions. Children in one group were taught explicitly how to use a procedure to design and interpret simple scientific experiments. Children in the other, "discovery" group received only a suggested learning objective, and no other teaching. Children in both groups were then asked to compare several variables, such as steepness, surface, and type of ball, to determine how they affected the distance that a ball traveled after rolling down a ramp. Children in the explicit instruction group were told to change one variable at a time and record the results. The children in the discovery learning group were not given any explanations about the experiment. Seventy-five percent of the explicitly taught children were able to identify the variables that affect the distance a ball will travel compared with only twenty-five percent in the "discovery" group. This study adds to the evidence-base that educators can use to strengthen science curriculum for children.

Behavior and Health

Recent findings in NICHD-supported research illustrate the powerful effects of environmental factors – from television viewing to parental involvement – on children's and adolescents' behaviors and health. Most importantly, however, the findings systematically underscore the critical role that parents can play in making decisions that can preserve and enhance the health and development of their children.

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[13] Shaywitz, BA, Shaywitz, SE, Blachman BA, Pugh, KR, Fulbright RK, et al. Deverlopment of Left Occipotemporal Systems for Skilled Reading in Children After a Phonologically-Based Intervention. Biol Psychiatry 55:926-933, 2004.

[14] Klahr D, Nigam M. The Equivalence of Learning Paths in Early Science Instruction. Psychol Sci 15:661-667, 2004.

Early television exposure linked to attention problems in children. Researchers have had evidence from cross-sectional studies that television viewing at an early age may be associated with decreased attention span in children. However, they had no data from long-term studies to support this observation until NICHD-funded researchers designed an observational study to test a hypothesis: that television exposure at one and three years of age was associated with attentional problems at age seven. The researchers analyzed data on more than 2,600 children who were part of the National Longitudinal Survey of Youth. Using advanced statistical methods, researchers found that the more television very young children watched, the more likely they were at age seven to have attention problems. The researchers cautioned that since they used a special definition of such problems, their findings did not necessarily indicate that early television viewing is associated with clinically-diagnosed attention-deficit/hyperactivity disorder (ADHD) in the older children. Their findings suggest, however, that parents could reduce the risk of such problems by limiting television viewing of children in the early years, when their brains are still rapidly developing.

Watching television with a high level of sexual content is associated with earlier teen sexual behavior. Researchers found that adolescents who watch television with high levels of sexual content are more likely to initiate sexual intercourse at an early age, compared with peers who view relatively little sexual content.[15] The researchers acknowledge that it's nearly impossible to conclusively prove that the sexual content of television shows influences teen sexual behavior. It's conceivable, they wrote, that teens considering engaging in early sex are simply drawn to TV programming with sexual content. However, the researchers believe this latter possibility is highly unlikely. In the study, which followed almost 1800 adolescents between the ages of 12 and 17, the researchers carefully controlled for factors known to influence early sexual activity, such as academic performance and family structure. In two rounds of interviews, a year apart, researchers found that youth in the 90th percentile of watching "television programs with a high level of sexual content" were twice as likely to initiate intercourse as those in the bottom 10 percent.

Parents can influence adolescents' decisions on whether to start smoking. Researchers have found that direct parental involvement with young adolescents, coupled with perceived parental disapproval of smoking, can influence young people *not* to start smoking as more and more of their peers do so.[16] These findings are important because rates of smoking initiation among young adolescents remain high, compared with those of adults, and because starting to smoke as an adolescent increases the likelihood that an individual will be dependent on smoking as an adult. Surveys of children at the beginning and end of sixth grade, and at the end of seventh grade, showed that if children thought that their parents generally "kept tabs" on them and would be upset if they knew that their child smoked, they were less likely to smoke, while children who believed their parents to be less involved with them were more likely to smoke.

[15] Collins RL, Elliott MN, Berry SH, Kanouse DE, Kunkel D, et al. Watching Sex on Television Predicts Adolescent Initiation of Sexual Behavior. Pediatrics 114:e280-e289, 2004.
[16] Simons-Morton, B. The Protective Effect of Parental Expectations Against Early Adolescent Smoking Initiation. Health Ed Res 19:561-569, 2004.

Children and Health

A fundamental goal of NICHD's research is to improve children's health and development. This year, NICHD research provided clinicians and health professionals with several new practical tools to help keep children healthy and well: Doctors have better guidance on the use of pain medication for infants; they have new warning signs for later cognitive problems; and they can identify early markers of future disease among the growing number of overweight children and adolescents.

Using morphine to control pain in premature newborns on mechanical ventilation should be limited. A large clinical trial found that continuous morphine infusions to relieve pain in premature newborns on mechanical ventilation did *not* reduce the frequencies of severe neurological (brain) injuries or deaths in these infants, contrary to results of an earlier pilot study.[17] Rates of the adverse events were even higher in infants who received additional "bolus" doses of morphine to control pain. These results have important implications for clinical practice because routinely starting continuous infusion of morphine for pain associated with mechanical ventilation is a common practice in neonatal intensive care units. The severity of adverse events associated with this practice prompted the researchers to recommend that continuous morphine infusion be used sparingly, to reduce severe or repetitive pain in these infants. The research, however, also highlighted urgent needs to develop both less hazardous pain medications for the infants and better, standardized methods for assessing their pain.

Prolonged crying in infants may signal late cognitive problems. Infants who cry a lot after the first three months of life, without any obvious cause, may later experience cognitive problems, according to new study.[18] The researchers distinguished between colic – extended, unexplained crying that typically stops after the first 12 weeks of life – and the "prolonged" crying of older infants. Prolonged crying is generally considered to be crying more than three hours a day. The research affirmed earlier findings that colic does not affect cognitive development. By contrast, the researchers found that approximately 5 percent of children experiencing prolonged crying as infants had lower IQ scores, poorer fine motor abilities, hyperactivity, and discipline problems at age five. The implications for clinical practice are that children with a history of prolonged, unexplained crying after the age of three months should be followed more intensively to detect emerging developmental problems that might respond to early intervention.

Heavy alcohol drinking during pregnancy causes persistent nerve damage in infants that escape fetal alcohol syndrome. A small, observational study by scientists at the NICHD and the University of Chile found significant damage in the peripheral nervous system of infants whose mothers drank large amounts of alcohol during pregnancy, even though the infants did not show symptoms of fetal alcohol syndrome.[19] This is the first study to find peripheral neuropathy – a condition well-recognized in alcoholic adults – in children exposed to alcohol *in utero*.

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[17] Anand KJS, Hall RW, Desai N, Shephard B, Bergqvist LL, et al. Effects of Morphine Analgesia in Ventilated Preterm Neonates: Primary Outcomes from the NEOPAIN Randomized Trial. Lancet 363: 1673-1682, 2004.
[18] Rao MR, Brenner RA, Schisterman EF, Vik T, Mills JL. Long Term Cognitive Development in Children with Prolonged Crying. Arch Dis Child 89:989-992, 2004.
[19] Avaria MdlA, Mills JL, Kleinsteuber K, Aros S, Conley MR, et al. Peripheral Nerve Conduction Abnormalities in Children Exposed to Alcohol in Utero. J Pediatr 144:338-343, 2004.

Neurological evaluations of these infants at ages six and twelve months showed damage both to the part of the nerve that carries signals to muscles and other tissue and to the part that insulates the nerve. The persistence of the damage at one year suggests that the alcohol exposure interfered with neural development. As the researchers continue to follow the children, they will look for emerging clinical symptoms that could not be measured in infancy. For instance, in adults, alcoholic peripheral neuropathy is associated with muscle weakness, impaired fine motor functioning, and other symptoms.

Overweight, obesity and the metabolic syndrome in children and adolescents. At a time when more U.S. teens are overweight than those in most other industrialized nations,[20] researchers are also reporting high rates of a cluster of metabolic disorders (metabolic syndrome) in obese adolescents as well as in children as young as four years old.[21] Metabolic syndrome -- which includes high blood pressure, high insulin levels, abnormal cholesterol levels, and overweight or obesity -- increases the likelihood of developing diabetes, heart disease, or stroke. The researchers studying the syndrome in children and adolescents found that the prevalence of the syndrome increased with the severity of obesity, reaching 50 percent in severely obese youngsters. They also found that the more obese the children and adolescents were, the more severe were each of the disorders that make up the syndrome. And, in a relatively short period (a year) between the initial testing and follow up, the researchers found a dramatic increase in the development of type 2 diabetes in the research subjects diagnosed with metabolic syndrome. They warned this increase could precede an epidemic of advanced cardiovascular disease as obese adolescents become obese adults.

Families and Health

Understanding that children's health and development are linked to how well families function, NICHD researchers are trying to better understand the mechanisms underlying family formation and the factors that increase the likelihood that parents can form and maintain a stable family unit. NICHD researchers also evaluate public programs designed to influence family functioning positively, to help policy-makers understand whether such programs are effective.

Earnings, education, and trust help form stable families. New findings in a major study indicate that unmarried parents are more likely to marry each other before their child's first birthday or form a lasting relationship if the father has higher earnings and the mother has graduated from high school. By comparison, couples with less education and income were less likely to stay together to raise their child.[22] The likelihood of forming a stable family is also higher if the mother and father each feel that the other supports the relationship with such behaviors as expressing encouragement and being willing to compromise. Factors that destabilize relationships between new parents include serious health or developmental problems of their child, lower earnings and less education, and a father who has other children with different mothers. These findings can help policy-makers and community programs understand how they

[20] Lissau I, Overpeck MD, Ruan WJ, Due P, Holstein BE, et al. Body Mass Index and Overweight in Adolescents in 13 European Countries, Israel, and the United States. Arch Pediatr Adolesc Med. 158:27-33, 2004.
[21] Weiss R, Dziura J, Burgert TS, Tamborlane WV, Taksali SE, et al. Obesity and the Metabolic Syndrome in Children and Adolescents. N Engl J Med 350:2362-2374, 2004.
[22] Carlson M, McLanahan S, England P. Union Formation in Fragile Families. Demography 41:237-261, 2004.

can better support fragile families so that parents can provide the stability that fosters the health and development of their children.

Physical or sexual abuse interferes with family formation. In a large study of family formation among low- and middle-income women, researchers found that women who were sexually or physically abused or witnessed abuse as children, or who were physically abused as adults, were less likely to be in lasting marriages or stable relationships, compared with women without a history of abuse.[23] Among the women studied, the researchers found very high rates of abuse, with differing effects on relationships, depending on when the abuse occurred. For example, women whose experience of abuse was in childhood typically engaged in multiple, transitory, and often abusive relationships with men, while women with adult experience of abuse tended to avoid any relationships with men. The researchers suggested that the degree to which abuse interferes with family formation in the U.S. may be substantially underestimated and policies to foster stable homes should attempt directly to reduce the prevalence of abuse.

Experimental program in a developing country improves children's health and school attendance by assisting their families. An experimental Mexican government program (PROGRESA) that tied low-income family assistance to health- and education-seeking behaviors resulted in significantly better health, development, and education of children in families receiving the assistance.[24] A NICHD-supported evaluation of PROGRESA provides insights that could be used in designing interventions for other developing countries and also for disadvantaged U.S. families. In the large, randomized PROGRESA trial, researchers compared two groups of families. In one group, families received substantial financial assistance if they regularly brought their children to health and nutrition clinics, had their infants and toddlers immunized, ensured that their children went to school, and used other specific health and nutritional services. The other group of families did not receive any financial assistance. Researchers found statistically significant health improvements and better school attendance in the children of families receiving the assistance. The effects were stronger, the longer the children and families were in the program.

NIH ROADMAP

A highly skilled and versatile clinical research workforce is essential to accelerate the discovery and dissemination of new interventions to prevent and treat illness. Through Roadmap initiatives directed to "Re-engineering the Clinical Research Enterprise," the NIH has improved mechanisms to develop future leaders in clinical research. Seven institutions recently received funding to train post-graduate health professionals in multidisciplinary clinical research, which utilizes teams of specialists from a variety of disciplines. This team approach is critical to solving difficult medical problems that are too complex for scientists working in any single discipline to solve alone. Team members include not only physicians and nurses, but also pharmacologists, statisticians and psychologists, and other disciplines, as required. These

[23] Cherlin AJ, Burton LM, Hurt TR, Purvin DM. The Influence of Physical and Sexual Abuse on Marriage and Cohabitation. American Sociological Review (in press)

[24] Gertler P. Do Conditional Cash Transfers Improve Child Health? Evidence from PROGRESA's Control Randomized Experiment. American Economic Review 94:336-341, 2004.

institutions will each train 15 to 20 Clinical Research Scholars for up to five years, through both classroom instruction and participation in clinical research studies under the guidance of mentors experienced in this arena. To build on the momentum created by these grant awards, a second wave of awards is planned.

A different stage in the development of clinical researchers is being addressed by a proposal to create a National Clinical Research Associates (NCRAs) Program. The NCRAs are envisioned as a nationwide cadre of community primary care and specialty practitioners who will enroll and care for their patients in multiple clinical research studies, especially large-scale clinical trials. The goal is to speed recruitment of clinical research participants, and get clinical breakthroughs into medical practice more quickly and efficiently. A contract has been awarded to design a NCRA Program model, test its feasibility, and identify pilot projects prior to fully implementing the concept.

Both of these new programs will advance not only the NIH mission by providing the skilled clinical researchers needed to implement medical studies, they promise also to aid the NICHD in implementing its many clinical research programs and networks. Just to name a few, NICHD research networks support studies on stillbirth and premature birth, reproductive health, contraception, traumatic brain injury, pelvic floor disorders, HIV/AIDS, and pediatric and obstetrical pharmacology. In addition, the National Children's Study will require hundreds of practitioners to enroll and track their patients in a nationwide longitudinal study of the environmental influences on the health and development of 100,000 children, enrolled before birth and followed until age 21. Without a cadre of diverse health professionals well grounded in clinical research, studies like these cannot be done.

INITIATIVES

The NICHD took giant steps in 2004 to help children live healthier lives today and for generations to come. In collaboration with the Food and Drug Administration (FDA), the NICHD began testing drugs that are widely prescribed for children, although they have only been tested in adults. As a result, physicians will be able to prescribe dosages that are safer and more effective for children. On another front, scientists also began to apply the rigorous standards of randomized, controlled research to determine the best ways to help preschool children succeed in school. In addition, the proposed long-term National Children's Study moved from a plan closer toward reality, as the Institute prepared solicitations for the first proposals, from research institutions around the country, to begin efforts to identify participants into the study. Finally, a new, six-center research network began a new series of studies to understand more about the extent and causes of stillbirth.

Progress in Implementing the Best Pharmceuticals for Children Act. A majority of drugs prescribed for children have never been tested for safety and efficacy in pediatric use. Under the Best Pharmaceuticals for Children Act (BPCA), the NICHD is collaborating with the FDA to identify and test drugs prescribed for children. During 2004, arrangements were made to test several on-patent drugs, including morphine, buproprion, sevelamer, and zonisamide. The NICHD continues to enlarge and improve the process for identifying and prioritizing drugs to undergo pediatric testing, as mandated by the Act. In FY 2004, the NICHD established a

Working Group to oversee the processes for identifying the highest priority drugs that should be tested in children, expanded outreach to professional organizations, extended scientific review from one to two days, assessed available literature, and incorporated into the priority process updated information about the frequency with which specific drugs are used in children. In July, 2004, the NICHD conducted its annual meeting with other NIH Institutes to discuss the status of the FDA's Written Requests and to seek their input concerning which drugs most urgently need to be tested in children.

During this past fiscal year, the NICHD also initiated a series of pediatric clinical studies on its own and through Inter-Agency Agreements with the National Cancer Institute, the Food and Drug Administration, and the National Institute of Environmental Health Sciences. The NICHD awarded contracts to study drugs used to sedate young patients in intensive care, to treat status epilepticus (series of rapidly-repeated seizures), and to reduce blood pressure in children. The NICHD also entered into an interagency agreement with the FDA for primate studies on an anesthetic used in children. In addition, the Institute worked with the National Institute of Mental Health (NIMH) to identify its ongoing pediatric trials and to acquire NIMH-funded data sets for a NICHD study of lithium as used to treat bipolar disorder in children.

Using scientific research to prepare young children for success in school. The NICHD joined with other federal agencies in a major, national initiative to create the base of scientific knowledge needed to understand how preschool programs can best prepare young children for success in school. In the initiative's first year, the Institute and collaborating agencies awarded grants to eight research institutions for projects to evaluate curricula used in preschools, to test internet-based preschool teacher training, and to enhance parents' involvement in readying their children for school. At one site, researchers will compare curricula now used in Head Start classrooms to curricula that are based on scientific findings. These researchers will study more than three hundred children, from 40 randomly selected classrooms, to see if the new curricula improve their language development and social and emotional skills. Another study will allow researchers to assess the effectiveness of a new preschool curriculum that focuses on the social and emotional needs of children from low-income urban areas. A third project will explore ways to improve the training of preschool teachers in math and pre-literacy instruction while a fourth effort will seek to improve school readiness by improving parent-child interactions in the home. The initiative responds to the national priority of improving children's educational attainment, as expressed in the "No Child Left Behind Act." That Act links federal funding to educational achievement, starting in the preschool years.

National Children's Study. Under the lead of the NICHD, the consortium of more than 40 agencies and organizations involved in the development of the proposed National Children's Study (NCS) took steps in the study's extensive planning process and prepared to launch the NCS implementation phase. Planned as the largest study of children ever undertaken in the U.S., the proposed NCS is intended to follow 100,000 children to age 21, examining the actions and outcomes of the many environmental and genetic factors that influence children's health and development. The ultimate goal of the NCS is to pinpoint causes and find prevention and treatment strategies for many of today's childhood diseases and disorders, laying the groundwork for adult health. During FY 2004, the 22 NCS working groups reached consensus on two of the most intellectually challenging aspects of the study: the groups recommended major hypotheses

of the study and they agreed that a national probability sample, i.e., a sample that is representative of all children in the country, would be used in the study design. In November, 2004, the NCS reached another milestone: the first Requests for Proposals for a NCS data coordinating center and for the first study sites were published.

Research network to reduce rates of stillbirth. To better understand the extent and nature of stillbirths that occur without known medical causes, the NICHD established a national, six-center network of specialized research in sites around the country. Stillbirth is defined as the death of a fetus after 20 weeks or more of pregnancy. In some cases, doctors know why the fetus did not survive, but in at least half of all still births, the cause is unknown. While researchers estimate that stillbirth occurs at rates comparable to infant mortality in the U.S., existing data may not capture 10 to 15 percent of stillbirths because reporting of these events is not mandatory and because no standard postmortem protocol exists that would yield uniform information for all stillbirths. Thus, one major goal of the new stillbirth research network is to develop a standard protocol that would specify tests and other procedures to investigate genetic, maternal, and environmental factors associated with stillbirth. A second major goal is to determine the rates at which stillbirths actually occur in the general population and in subgroups in the U.S., and to better understand the causes and potential risk factors for stillbirth. By developing essential baseline knowledge of stillbirths in the U.S., the network will enable researchers to investigate unidentified causes of stillbirth and to develop and improve ways to prevent or ameliorate the effects of these causes.

New Fragile X Syndrome research centers are designed to maximize scientific yield and efficient use of research resources. In response to Congressional priorities, the NICHD has created three new research centers for studies of Fragile X Syndrome, the most common form of inherited mental retardation. To ensure the most productive research collaborations and to maximize efficient use of investigator expertise, study protocols, data collection and analysis, and other scientific resources, the NICHD established the new Fragile X sites as "centers within centers" in the Institute's longstanding Mental Retardation and Developmental Disabilities Centers. Scientists leading the new centers report that this innovative research model is substantially increasing scientific collaborations, attracting new researchers to the field, and resulting in productive expansion of our research efforts in Fragile X.

THE NIH NEUROSCIENCE BLUEPRINT

The Blueprint is a framework to enhance cooperation among fifteen NIH Institutes and Centers that support research on the nervous system. Over the past decade, driven by the science, the NIH neuroscience Institutes and Centers have increasingly joined forces through initiatives and working groups focused on specific disorders. The Blueprint builds on this foundation, making collaboration a day-to-day part of how the NIH does business in neuroscience. By pooling resources and expertise, the Blueprint can take advantage of economies of scale, confront challenges too large for any single Institute, and develop research tools and infrastructure that will serve the entire neuroscience community.

FY2005. For fiscal year 2005, the Blueprint participants are developing an initial set of initiatives focused on tools, resources, and training that can have a quick and substantial impact

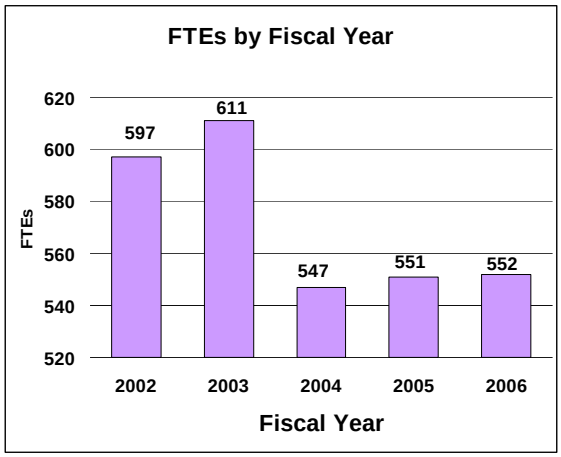
because each builds on existing programs. These initiatives, with the participation of all Blueprint Institutes, include an inventory of neuroscience tools funded by the NIH and other government agencies, enhancement of training in the neurobiology of disease for basic neuroscientists, and expansion of ongoing gene expression database efforts.

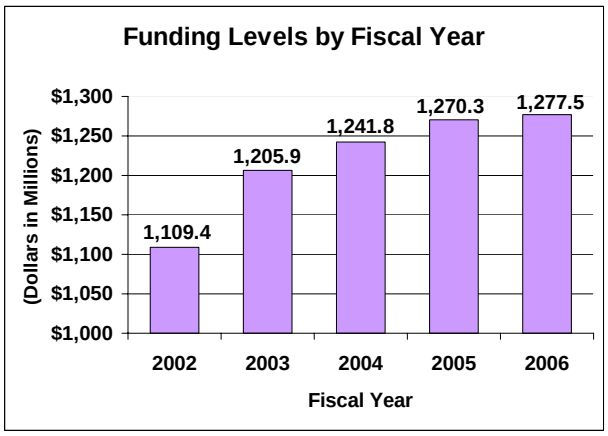
FY2006. Advances in the neurosciences and the emergence of powerful new technologies offer many opportunities for Blueprint activities that will enhance the effectiveness and efficiency of neuroscience research. Blueprint initiatives for fiscal year 2006 will include systematic development of genetically engineered mouse strains of critical importance to research on nervous system and its diseases and training in critical cross cutting areas such as neuroimaging and computational biology.

BUDGET POLICY

The Fiscal Year 2006 budget request for the NICHD is $1,277,544,000, an increase of $7,223,000 and .6 percent over the FY 2005 Appropriation. Also included in the FY 2006 request, is NICHD's support for the trans-NIH Roadmap initiatives, estimated at 0.89% of the FY 2006 budget request. This Roadmap funding is distributed through the mechanisms of support, consistent with the anticipated funding for the Roadmap initiatives. A full description of this trans-NIH program may be found in the NIH Overview.

A five-year history of FTEs and Funding Levels for NICHD are shown in the graphs below.





NIH's highest priority is the funding of medical research through research project grants (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while pursuing new research opportunities. It is estimated that the average cost of competing RPGs will be $325,540 in FY 2006. While no inflationary increases are provided for direct, recurring costs in non-competing RPG's, where the NICHD has committed to a programmatic increase in an award, such increases will be provided.

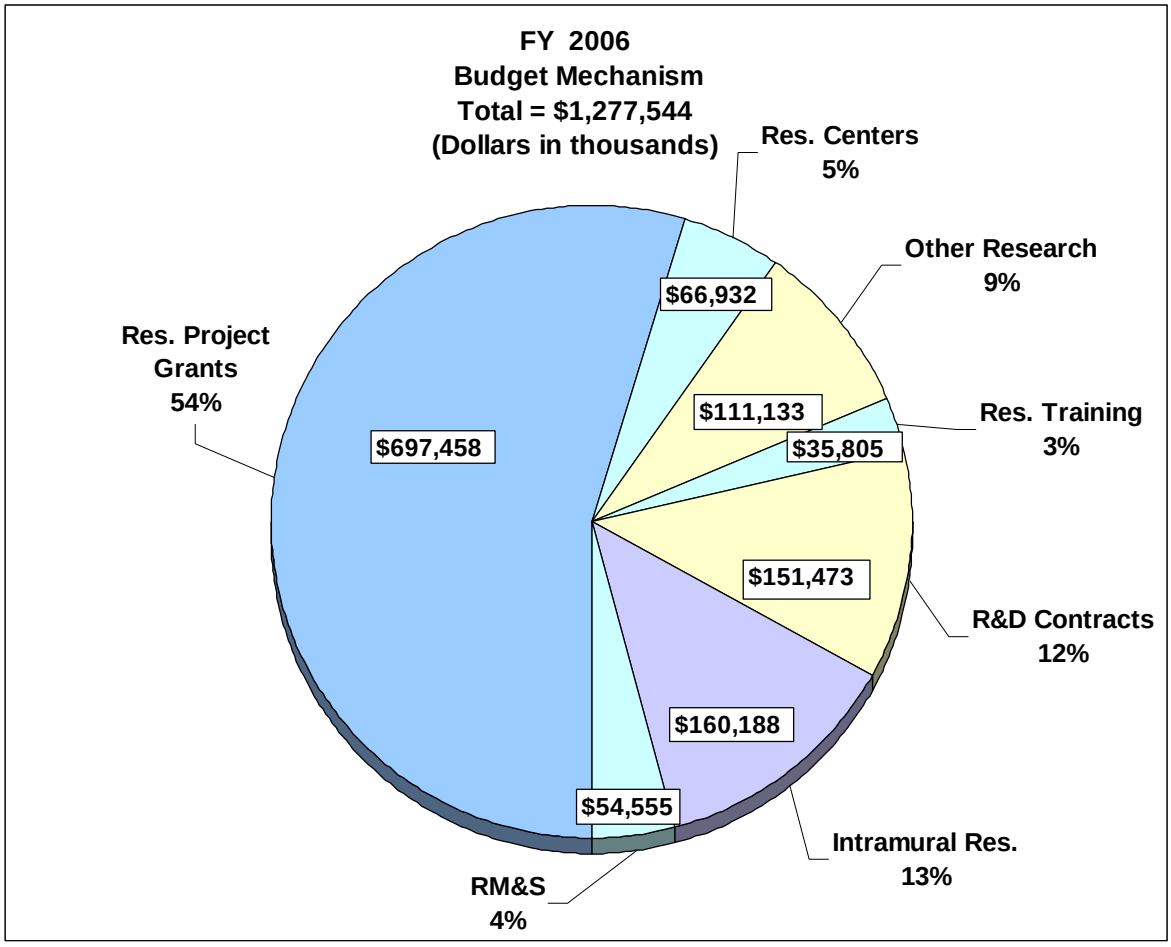
Advancement in medical research is dependent on attracting, training, and retaining the best and the brightest individuals to pursue careers in biomedical and behavioral research. In the FY 2006 request, most stipend levels for individuals supported by the Ruth L. Kirschstein National Research Service Awards are maintained at the FY 2005 levels. To help prevent the potential

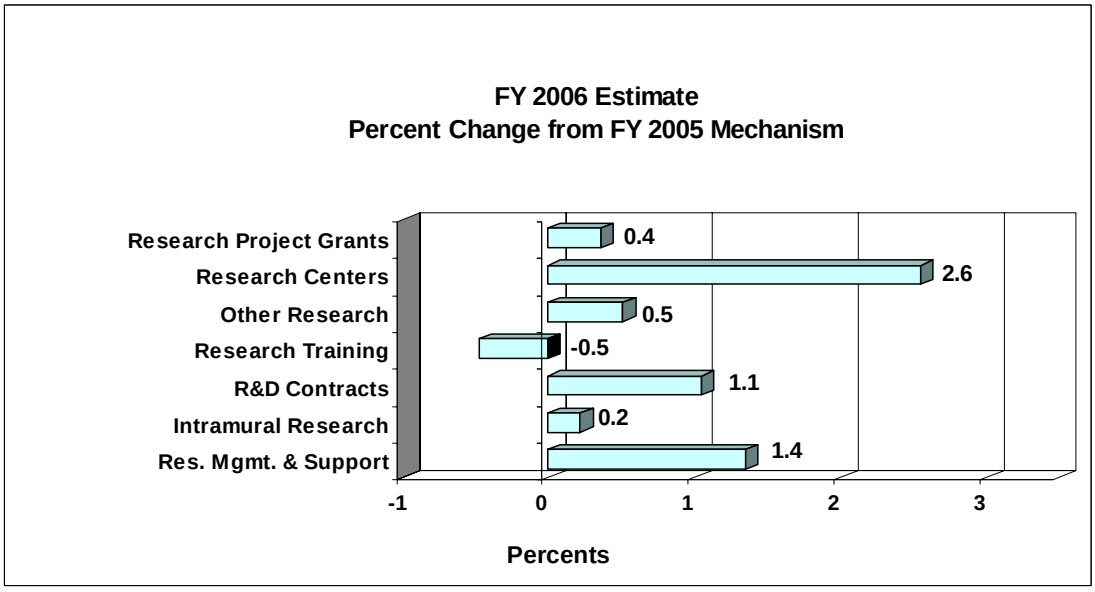
attrition of our next generation of highly trained post-doctoral trainees, stipend levels for post-docs with 1-2 years of experience are increased by 4.0 percent. This will bring these stipends closer to the goal NIH established for post-doc stipends in March 2000. In addition, individual post-doctoral fellows will receive an increase of $500 in their institutional allowance for rising health benefit costs. The need for increased health benefits is particularly acute for these post-doctoral trainees, who, because of their age and stage of life are more likely to have family responsibilities. The increases in stipends and health insurance are financed within the FY 2006 request by reducing the number of full-time training positions. The NIH believes that it is important to properly support and adequately compensate those who are participating in these training programs so that the programs can continue to attract and retain the trainees most likely to pursue careers in biomedical, behavioral and clinical research.

NICHD is participating in the NIH Neuroscience Blueprint. The FY 2006 request includes $900,000 for a variety of Neuroscience Blueprint initiatives, including neuroscience cores, training initiatives, and the Neuromouse project.

The Fiscal Year 2006 request includes funding for 50 research centers, 473 other research grants and 213 R&D contracts. Non road-map related Intramural Research and Research Management and Support activities receive increases of 0.5 percent, the same as the NIH total increase.

The mechanism distribution by dollars and percent change are displayed of the following page.


FY 2006
Budget Mechanism
Total = $1,277,544
(Dollars in thousands)
Res. Centers
5%
Other Research
9%
Res. Training
3%
R&D Contracts
12%
Intramural Res.
13%
RM&S
4%
Res. Project
Grants
54%
$66,932
$111,133
$35,805
$151,473
$160,188
$54,555
$697,458


FY 2006 Estimate
Percent Change from FY 2005 Mechanism
Research Project Grants
Research Centers
Other Research
Research Training
R&D Contracts
Intramural Research
Res. Mgmt. & Support
0.4
2.6
0.5
-0.5
1.1
0.2
1.4
-1
0
1
2
3
Percents

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

Budget Mechanism - Total

MECHANISM	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate	
Research Grants:	**No.**	**Amount**	**No.**	**Amount**	**No.**	**Amount**
Research Projects:						
Noncompeting	1,339	$531,378,000	1,273	$524,696,000	1,218	$491,761,000
Administrative supplements	(63)	7,191,000	(59)	5,681,000	(58)	5,500,000
Competing:						
Renewal	96	48,867,000	98	51,581,000	124	65,025,000
New	305	79,202,000	312	83,601,000	393	105,392,000
Supplements	8	855,000	8	902,000	10	1,137,000
Subtotal, competing	409	128,924,000	418	136,084,000	527	171,554,000
Subtotal, RPGs	1,748	667,493,000	1,691	666,461,000	1,745	668,815,000
SBIR/STTR	112	28,520,000	111	28,500,000	112	28,643,000
Subtotal, RPGs	1,860	696,013,000	1,802	694,961,000	1,857	697,458,000
Research Centers:						
Specialized/comprehensive	44	60,931,000	47	63,956,000	48	65,321,000
Clinical research	0	0	0	0	0	0
Biotechnology	1	1,018,000	1	1,309,000	2	1,611,000
Comparative medicine	0	0	0	0	0	0
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	45	61,949,000	48	65,265,000	50	66,932,000
Other Research:						
Research careers	235	40,198,000	239	41,820,000	242	42,320,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	93	42,742,000	93	45,799,000	93	45,799,000
Biomedical research support	0	23,000	0	30,000	0	34,000
Minority biomedical research support	0	0	0	0	0	0
Other	138	22,629,000	138	22,914,000	138	22,980,000
Subtotal, Other Research	466	105,592,000	470	110,563,000	473	111,133,000
Total Research Grants	2,371	863,554,000	2,320	870,789,000	2,380	875,523,000
Research Training:	**FTTPs**		**FTTPs**		**FTTPs**	
Individual awards	119	5,596,000	115	5,555,000	111	5,555,000
Institutional awards	740	30,362,000	746	30,420,000	732	30,250,000
Total, Training	859	35,958,000	861	35,975,000	843	35,805,000
Research & development contracts	212	136,611,000	212	149,896,000	213	151,473,000
(SBIR/STTR)	(0)	(56,000)	(0)	(56,000)	(0)	(56,000)
	FTEs		**FTEs**		**FTEs**	
Intramural research	375	154,427,000	368	159,833,000	368	160,188,000
Research management and support	172	51,295,000	183	53,828,000	184	54,555,000
Cancer prevention & control	0	0	0	0	0	
Construction		0		0		0
Buildings and Facilities		0		0		0
Total, NICHD	547	1,241,845,000	551	1,270,321,000	552	1,277,544,000
(RoadMap Support)		(4,267,000)		(8,031,000)		(11,424,000)
(Clinical Trials)		(191,405,000)		(195,600,000)		(196,600,000)

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

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2004 Actual		FY 2005 Appropriation		FY 2006 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural research		$1,036,123		$1,056,660		$1,062,801		$6,141
Intramural research	375	154,427	368	159,833	368	160,188	0	355
Research management & support	172	51,295	183	53,828	184	54,555	1	727
Total	547	1,241,845	551	1,270,321	552	1,277,544	1	7,223

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

Summary of Changes

FY 2005 Estimate				$1,270,321,000
FY 2006 Estimated Budget Authority				1,277,544,000
Net change				7,223,000
	FY 2005 Appropriaton		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$60,132,000		$780,000
b. Annualization of January 2005 pay increase		60,132,000		556,000
c. January 2006 pay increase		60,132,000		1,051,000
d. One less day of pay		60,132,000		(240,000)
e. Payment for centrally furnished services		27,566,000		138,000
f. Increased cost of laboratory supplies, materials, and other expenses		72,135,000		1,103,000
Subtotal				3,388,000
2. Research Management and Support:				
a. Within grade increase		23,643,000		367,000
b. Annualization of January 2005 pay increase		23,643,000		219,000
c. January 2006 pay increase		23,643,000		414,000
d. One less day of pay		23,643,000		(94,000)
e. Payment for centrally furnished services		7,386,000		37,000
f. Increased cost of laboratory supplies, materials, and other expenses		22,799,000		349,000
Subtotal				1,292,000
Subtotal, Built-in				4,680,000

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

Summary of Changes--continued

CHANGES	2005 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,273	$530,377,000	(55)	($33,116,000)
b. Competing	418	136,084,000	109	35,470,000
c. SBIR/STTR	111	28,500,000	1	143,000
Total	1,802	694,961,000	55	2,497,000
2. Research centers	48	65,265,000	2	1,667,000
3. Other research	470	110,563,000	3	570,000
4. Research training	861	35,975,000	(18)	(170,000)
5. Research and development contracts	212	149,896,000	1	1,577,000
Subtotal, extramural				6,141,000
	FTEs		FTEs	
6. Intramural research	368	159,833,000	0	(3,033,000)
7. Research management and support	183	53,828,000	1	(565,000)
Subtotal, program	551	1,270,321,000	1	2,543,000
Total changes			1	7,223,000

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

Budget Authority by Object

	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	**551**	**552**	**1**
Full-time equivalent of overtime & holiday hours	**2**	**2**	**0**
Average ES salary	**$149,200**	**$153,100**	**$3,900**
Average GM/GS grade	**11.2**	**11.2**	**0.0**
Average GM/GS salary	**$76,500**	**$78,500**	**$2,000**
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	**$76,200**	**$78,200**	**$2,000**
Average salary of ungraded positions	**114,300**	**117,300**	**3,000**
OBJECT CLASSES	**FY 2005 Appropriation**	**FY 2006 Estimate**	**Increase or Decrease**
Personnel Compensation:			
11.1 Full-Time Permanent	**$29,545,000**	**$30,622,000**	**$1,077,000**
11.3 Other than Full-Time Permanent	**20,284,000**	**21,023,000**	**739,000**
11.5 Other Personnel Compensation	**1,629,000**	**1,688,000**	**59,000**
11.7 Military Personnel	**1,627,000**	**1,686,000**	**59,000**
11.8 Special Personnel Services Payments	**15,659,000**	**15,898,000**	**239,000**
Total, Personnel Compensation	**68,744,000**	**70,917,000**	**2,173,000**
12.0 Personnel Benefits	**13,576,000**	**14,071,000**	**495,000**
12.1 Military Personnel Benefits	**1,430,000**	**1,482,000**	**52,000**
13.0 Benefits for Former Personnel	**25,000**	**26,000**	**1,000**
Subtotal, Pay Costs	**83,775,000**	**86,496,000**	**2,721,000**
21.0 Travel & Transportation of Persons	**3,469,000**	**3,486,000**	**17,000**
22.0 Transportation of Things	**417,000**	**400,000**	**(17,000)**
23.1 Rental Payments to GSA	**22,000**	**22,000**	**0**
23.2 Rental Payments to Others	**572,000**	**575,000**	**3,000**
23.3 Communications, Utilities & Miscellaneous Charges	**1,810,000**	**1,814,000**	**4,000**
24.0 Printing & Reproduction	**1,845,000**	**1,848,000**	**3,000**
25.1 Consulting Services	**1,058,000**	**900,000**	**(158,000)**
25.2 Other Services	**14,970,000**	**14,300,000**	**(670,000)**
25.3 Purchase of Goods & Services from Government Accounts	**128,197,000**	**127,697,000**	**(500,000)**
25.4 Operation & Maintenance of Facilities	**3,750,000**	**3,758,000**	**8,000**
25.5 Research & Development Contracts	**110,646,000**	**112,198,000**	**1,552,000**
25.6 Medical Care	**1,666,000**	**1,660,000**	**(6,000)**
25.7 Operation & Maintenance of Equipment	**2,231,000**	**2,230,000**	**(1,000)**
25.8 Subsistence & Support of Persons	**0**	**0**	**0**
25.0 Subtotal, Other Contractual Services	**262,518,000**	**262,743,000**	**225,000**
26.0 Supplies & Materials	**13,228,000**	**13,200,000**	**(28,000)**
31.0 Equipment	**10,830,000**	**10,800,000**	**(30,000)**
32.0 Land and Structures	**0**	**0**	**0**
33.0 Investments & Loans	**0**	**0**	**0**
41.0 Grants, Subsidies & Contributions	**891,829,000**	**896,154,000**	**4,325,000**
42.0 Insurance Claims & Indemnities	**0**	**0**	**0**
43.0 Interest & Dividends	**6,000**	**6,000**	**0**
44.0 Refunds	**0**	**0**	**0**
Subtotal, Non-Pay Costs	**1,186,546,000**	**1,191,048,000**	**4,502,000**
Total Budget Authority by Object	**1,270,321,000**	**1,277,544,000**	**7,223,000**

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

Salaries and Expenses

OBJECT CLASSES	FY 2005 Appropriation	FY 2006 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$29,545,000	$30,622,000	$1,077,000
Other Than Full-Time Permanent (11.3)	20,284,000	21,023,000	739,000
Other Personnel Compensation (11.5)	1,629,000	1,688,000	59,000
Military Personnel (11.7)	1,627,000	1,686,000	59,000
Special Personnel Services Payments (11.8)	15,659,000	15,898,000	239,000
Total Personnel Compensation (11.9)	**68,744,000**	**70,917,000**	**2,173,000**
Civilian Personnel Benefits (12.1)	13,576,000	14,071,000	495,000
Military Personnel Benefits (12.2)	1,430,000	1,482,000	
Benefits to Former Personnel (13.0)	25,000	26,000	1,000
Subtotal, Pay Costs	**83,775,000**	**86,496,000**	**2,721,000**
Travel (21.0)	3,469,000	3,486,000	17,000
Transportation of Things (22.0)	417,000	400,000	(17,000)
Rental Payments to Others (23.2)	572,000	575,000	3,000
Communications, Utilities and Miscellaneous Charges (23.3)	1,810,000	1,814,000	4,000
Printing and Reproduction (24.0)	1,845,000	1,848,000	3,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,058,000	900,000	(158,000)
Other Services (25.2)	14,970,000	14,300,000	(670,000)
Purchases from Govt. Accounts (25.3)	74,398,000	72,822,000	(1,576,000)
Operation & Maintenance of Facilities (25.4)	3,750,000	3,758,000	8,000
Operation & Maintenance of Equipment (25.7)	2,231,000	2,230,000	(1,000)
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**96,407,000**	**94,010,000**	**(2,397,000)**
Supplies and Materials (26.0)	13,200,000	13,172,000	(28,000)
Subtotal, Non-Pay Costs	117,720,000	115,305,000	(2,415,000)
Total, Administrative Costs	**201,495,000**	**201,801,000**	**306,000**

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

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

FY 2005 House Appropriations Committee Report Language (H.Rpt. 108-636)

Sudden infant death syndrome - The Committee is pleased with NICHD's continued efforts to extend the reach of its `Back to Sleep' campaign to underserved populations and daycare - providers. The Committee encourages NICHD to transition from its SIDS five-year research plan to a more comprehensive plan focusing on SIDS, stillbirth, and miscarriage. The Committee requests that NICHD determine an appropriate means of including research on these causes of infant mortality into one inclusive plan. (p. 84)

Action taken or to be taken

The NICHD recognizes that there are overlapping issues and themes among SIDS, stillbirth, and miscarriage research needs. From a scientific perspective, however, there are unique aspects that the NICHD believes warrant special, and sometimes distinct, consideration. The NICHD will continue to consider the most appropriate methods to ensure that all aspects of infant, perinatal and fetal mortality receive adequate attention and support.

Miscarriage is defined as the loss of pregnancy from natural causes before the 20th week of pregnancy. It is estimated that among women who know they are pregnant, 15% will have a miscarriage. Most miscarriages occur in the first trimester or within 12 weeks of pregnancy. The majority of miscarriages are due to chromosomal abnormalities that are lethal to the developing embryo. In others, particularly repeat miscarriage, the uterine environment does not support the early development of the embryo. Some of the causes of a non-supportive uterine environment are problems with the uterus itself, abnormal levels of hormones needed for a receptive uterine environment, infection or an abnormal immune response to the developing embryo. Miscarriages in the second trimester are often caused by problems with the structure of the uterus or by a weakened cervix that dilates too soon. Given the diverse origins of miscarriage, the NICHD is supporting research on miscarriage in research programs within several branches of the Institute.

Stillbirth, defined as fetal death at 20 weeks or greater gestation, and SIDS have some aspects in common. We know that SIDS is a developmental disorder: it originates during fetal development and occurs within a distinct developmental window. The biological continuum linking fetal and infant health or disease is being carefully explored in the current SIDS strategic plan. The plan considers the possibility that some sudden unexplained stillbirths are part of a continuum of a particular pathology that also can make an infant vulnerable to SIDS. We believe that based on the scientific evidence, this is a valuable approach to understanding and preventing both these tragic events.

However, at least half of stillbirths may have causes unrelated to SIDS. These will be explored in the recently established Stillbirth Collaborative Research Network (SCRN) and future initiatives. In some cases, we know the cause and more research is needed in prevention and therapeutics. In other cases, we have promising leads and need to pursue more research in pathogenesis, prevention, and therapeutics. We are working with parent and health professional organizations to plan a research agenda for stillbirth. In May of 2004, the NICHD staff and members of the SCRN Steering Committee participated in the Stillbirth Research Roundtable sponsored by the International Stillbirth Alliance.

We believe that the best way to plan research agendas for SIDS and stillbirth is to integrate them where appropriate as in the case of unexplained stillbirth and/or the origins of fetal growth restriction. In other cases, the research on each entity needs its own focus, such as stillbirth caused by congenital anomalies, or factors in the postnatal environment that increase SIDS risk. Therefore research planning for SIDS and stillbirth are part of our comprehensive research plan for Pregnancy and Perinatology. The goal of research planning for this area is to improve the health of mothers and children with a focus on maternal health, pregnancy, fetal well-being, labor and delivery, and the developing child. The most recent plan was published in 2003.

Item

Prematurity - The Committee encourages NICHD to support genomic and proteomic research in the area of prematurity to hasten a better understanding of the pathophysiology of premature birth, discover novel diagnostic biomarkers, and ultimately aid in formulating more effective interventional strategies to prevent premature birth. (p. 84)

Action taken or to be taken

The NICHD supports a number of ongoing programs and has just launched a new major initiative involving genomic and proteomic research. In June 2004, the NICHD issued a Request for Applications soliciting proposals for the establishment of a collaborative network for premature birth research. The main objective of the network will be to use wide-scale, high-output genomic and proteomic strategies to accelerate knowledge in the mechanisms responsible for premature birth. It is anticipated that the established network will consist of (1) approximately 1-3 "clinical sites" responsible for subject recruitment and specimen collection, (2) one "analytical site" responsible for genomic and proteomic analyses, and (3) one "data management, statistics, and informatics site" responsible for central data collection, analysis, and management; information technology; and coordination of the administrative activities. The NICHD received an excellent response to this RFA and successful applicants are anticipated to be funded in the first half of 2005 with the first meeting of the network planned for the summer of 2005.

This initiative joins a number of ongoing programs including grants funded under a program announcement that solicited applications in the area of genomics and premature birth. These projects are evaluating how adverse societal, behavioral, and environmental conditions alter gene expression and interact with diverse genetic backgrounds to increase susceptibility for premature birth in high-risk racial and ethnic groups. In addition, the NICHD is in the fourth year of funding a set of six applications through the 2001 RFA on the role of infection and inflammation in preterm delivery. These projects include studies on:

- The Molecular Pathogenesis of Health Disparities in Infants
- Mechanisms for Racial Disparity in Preterm Birth
- Polymorphisms in IL-10 Locus Predispose to Preterm Birth
- Gene Polymorphism, Infection/Inflammation and Preterm Birth
- Gene Polymorphisms, Preterm Birth, And Neonatal Complications
- CD56, Infection and Race in Preterm Delivery

Item

Preterm labor and delivery - The rates of premature birth have increased 29 percent since 1981 to over 480,000 babies in 2002. African-American infants are nearly twice as likely as non-Hispanic white infants to be born prematurely. Premature birth is the leading cause of death in the first month of life. Premature birth can happen to any pregnant woman and the causes of nearly half of all preterm births are unknown. The Committee commends NICHD for its work on preterm birth and encourages enhanced efforts to research the underlying causes of preterm delivery, to identify prevention strategies and improve the treatment and outcomes for infants born preterm. (p. 85)

Action taken or to be taken

The NICHD has a major commitment to understanding and preventing premature birth and invests both in researcher-initiated applications as well as solicitations to focus research into areas where there is a knowledge gap. Researcher-initiated funding, the Maternal Fetal Medicine Units and the Neonatal Research Networks address understanding the underlying causes of preterm delivery, identification of prevention strategies and improving the treatment and outcome for infants born preterm.

Recent studies funded by the NICHD have identified that a protein secreted by the fetal lung can act as a signal for the initiation of labor and serves as a valuable paradigm illustrating the intricate relationship between the maturation of the fetus and the timing of delivery. Thus, the fetus can signal the uterus to indicate that its lungs are sufficiently mature to switch from an aqueous to an air environment (PNAS 101: 4978-4983, 2004). Another NICHD-funded scientist has identified a functional progesterone withdrawal mechanism in nonhuman primates as a possible mechanism for the onset of labor, similar to that seen in other species (J Soc Gynecol Invest 2002; 9:125-36). Another researcher has made significant progress in understanding the biochemical events associated with uterine stretch and its role in the initiation of labor (Am J Physiol Cell Physiol 2002; 283:1530-9).

The NICHD Maternal Fetal Medicine Units Network's recent trial identified progesterone therapy for the prevention of recurrent preterm birth in high risk women (NEJM 2003). This is the first identification of a successful intervention for the prevention of preterm birth. The network is committed to improving research in this area and has an ongoing trial of progesterone for prevention of preterm birth in women with multiple gestations. In addition, the network is initiating a trial of omega-3 supplementation, in addition to progesterone, in high risk women for recurrent preterm birth prevention.

The NICHD Neonatal Research Network (NRN) is committed to improving the treatment of infants born preterm. Strides have been made in the care of small infants. Today, babies born at

birthweights of just over a pound can survive. However, approximately 40-50% of infants born at less than 1000 grams (just over 2 pounds) have long- term neurodevelopmental impairment including cerebral palsy, hearing and vision problems, cognitive delays, and speech and motor problems. In the NICHD Neonatal Research Network, clinical trials conducted in tiny babies perform long term follow up (18-22 months of age) on the smallest survivors of neonatal intensive care. In the past year, the NRN has initiated trials on candidal infection and vaccination with a pneumococcal conjugate vaccine. The NRN is also starting a study to evaluate early continuous positive airway pressure in the delivery room to potentially improve neonatal and long-term outcome for infants born premature. A pilot study to determine the feasibility of this project was recently published (Pediatrics. 2004 Sep;114(3):651-7.

Item

Maternal Fetal Medicine Units Network (MFMU) - The Committee was encouraged about the research results from the NICHD's Maternal Fetal Medicine Units Network on the identification of a therapy, progesterone that prevents recurrent preterm birth in high-risk women. The Committee understands that this is one of the first advances in this area, despite extensive efforts over decades. The Committee encourages NICHD to build on this finding through continued support of the MFMU Network. (p. 85)

Action taken or to be taken

The Institute's MFMU Network is building on the success of the progesterone trial, with an ongoing trial of progesterone therapy in women with multiple gestations, a very high-risk group for preterm birth, in which 600 women with twins and 120 women with triplets will be studied. This trial has already enrolled over 100 twins and 20 triplets since May 2004. The network is also initiating a trial of omega-3 supplementation in addition to progesterone in high-risk women for recurrent preterm birth prevention. Ongoing trials include studies of the prevention of cerebral palsy in a randomized trial of 2400 pregnant women that has finished recruiting, evaluation of the fetal pulse oximeter, a method for measuring oxygen level of the baby during labor with nearly 5,000 of the planned 10,000 patients enrolled; prevention of preeclampsia with vitamins C and E with over 1000 of the planned 10,000 patients enrolled; and treatment of mild gestational diabetes (GDM) to test whether identification and dietary treatment of mild GDM reduces neonatal morbidity and mortality.

Item

Stillbirth - The Committee applauds NICHD efforts in addressing stillbirth, a major public health issue with morbidity equal to that of all infant deaths. The Committee understands that NICHD has established a cooperative network of clinical centers and a data center to address this issue with a standard protocol. The Committee encourages NICHD to strongly support this effort. (p. 85)

Action taken or to be taken

The NICHD is committed to research efforts in stillbirth, which is a significant public health problem, accounting for a large proportion of perinatal mortality. According to annual national vital statistics, the number of stillbirths, defined as fetal deaths at 20 weeks gestation or greater, is similar in magnitude to the total number of infant deaths in the U.S. The causes of about half of all stillbirths are undetermined.

In the end of FY 2002, the NICHD established the Stillbirth Collaborative Research Network (SCRN) under a cooperative agreement to study the extent and causes of stillbirth in the United States. SCRN network encompasses five clinical sites. The network covers substantial portions of 5 states - Rhode Island, Massachusetts, Georgia, Texas and Utah and reflects urban/rural and racial diversity. The network aims include: (1) obtaining a geographic population-based determination of the incidence of stillbirth defined as fetal death at 20 weeks gestation or greater and (2) determining the causes of stillbirth using a standard stillbirth postmortem protocol, to include review of clinical history, protocols for autopsies and pathologic examinations of the fetus and placenta, other postmortem tests to illuminate genetic, maternal, and other environmental influences for stillbirth.

Some of the recent evidence points to the association of repeat fetal deaths with the genetic predisposition for thrombophilias and genetic conditions. Novel neuropathology investigations also suggest a relationship between fetal deaths and central nervous system insults. Other associations include maternal complications (diabetes, hypertension) and umbilical cord accidents. However, there may be a bias in these findings, as only a small portion of stillbirth cases has autopsies or tests performed.

The network in the first year has developed a multi-site, population-based, hypothesis-driven, case-control study, with prospective enrollment of stillbirths as cases and live births as controls. Hypotheses have been developed in the following content areas: surveillance and epidemiology; fetal and placental pathology; maternal disease mechanisms; immunology and infectious diseases; and genetics. With the study design, hypotheses, protocol and research instruments designed, we anticipate starting piloting in the next six months. Over the next 3.5 years we plan to complete the full study protocol.

The NICHD and members of the SCRN network are working with parents, health professional organizations, and hospitals to plan a research agenda for stillbirth. The NICHD staff and members of the SCRN Steering Committee participated in an international meeting, the Stillbirth Research Roundtable, sponsored by the International Stillbirth Alliance in May 2004.

The information derived from this five-year study will benefit families who have experienced a stillbirth, women who are pregnant or who are considering pregnancy, and their physicians. In addition, the knowledge will support future research aimed at improving preventive and therapeutic interventions and understanding the pathological mechanisms that lead to fetal death.

Item

Pediatric liver disease - The Committee urges the Institute to aggressively pursue opportunities to participate with NIDDK and other Institutes in pediatric liver disease research, particularly related to the optimal timing and medical treatment regimens for children infected with the hepatitis C virus. The Committee also encourages NICHD support of biliary atresia research. (p. 85)

Action taken or to be taken

The NICHD shares the Committee's concerns about the rising prevalence of liver disease in pediatric age groups. The World Health Organization estimates that at least 170,000,000

individuals worldwide are infected with the hepatitis C virus (HCV). This epidemic of HCV presages subsequent waves of chronic hepatic cirrhosis and hepatocellular carcinoma in HCV-infected population. The NICHD is funding several major studies on various aspects of HCV infection in adolescents. These studies focus on modes of transmission of HCV among adolescents and on the effect of the host genome on determining chronicity of HCV infection.

In the U.S., the most common liver disease among 10-18 year old children is non-alcoholic steatohepatitis (NASH), also known as fatty liver. This condition is seen almost exclusively in obese children and appears to be increasing in prevalence as a consequence of the obesity epidemic that affects one in every six of the nation's children. Like chronic HCV infection, NASH can lead to chronic cirrhosis and liver failure in afflicted children. The NICHD has joined with the NIDDK in forming a network of investigators who are studying factors associated with the development of NASH. The NASH Network has recently initiated a randomized trial to assess the effects of the antioxidant vitamin E and the effects of metformin, an agent that increases hepatic sensitivity to insulin, on reversing the ravages of NASH in affected children.

The NICHD continues its productive collaboration with the NIDDK on pediatric liver disease. However, according to current NIH referral guidelines, grant applications that focus on biliary atresia are assigned to the NIDDK for funding. Nevertheless, the NICHD retains a strong interest in biliary atresias from a developmental perspective and remain in close contact with NIDDK staff regarding initiatives undertaken by the biliary atresia clinical research consortium. The NICHD also cooperates with the NIDDK and the NCRR in the Rare Diseases Clinical Research Network. Various forms of biliary atresia are being studied within this new network.

Item

Spina bifida - The Committee is pleased that NICHD cosponsored the spina bifida research conference in May 2003 and urges adequate follow-up on the conference findings and recommendations. The Committee encourages NICHD to enhance research related to the outcome of the conference and to significantly expand its research efforts in the prevention and treatment of spina bifida and associated secondary conditions. The Director should be prepared to testify on the Institute's efforts to advance these areas of research at the fiscal year 2006 appropriations hearing. (p. 85)

Action taken or to be taken

The NICHD supports a portfolio of both investigator–initiated grants and special initiatives related to the prevention of spina bifida, and treatment and management of persons with spina bifida and related neural tube defects. To a significant extent, these efforts are informed by the May 2003, conference on spina bifida research cosponsored by the NICHD.

The NICHD is currently funding a multicenter network trial, the Management of Myelomeningocele study (MOMs), evaluating the safety and efficacy of fetal surgical repair and traditional postnatal repair of open neural tube defects. No other U.S. site is offering this procedure outside of the NICHD trial. This study enrolls women who have diagnosed isolated spina bifida who are in the midportion of their pregnancy, into a rigorous and common protocol on the three sites. After consenting, the women are randomized to receive either prenatal surgery

on the mother and fetus or to return at the end of pregnancy to undergo standard closure by the same surgical teams. Follow-up will occur over a 3-year period of all 200 patients enrolled in the study. Study endpoints will include an evaluation of the effect on the mother's health during the index pregnancy and in future pregnancies; fetal outcome; and neonatal and infant need for shunting, treatment for orthopedic and urologic problems common to people with spina bifida; and an evaluation of early childhood neurologic and mental functioning. Information about the trial can be found at the website: www.spinabifidamoms.com

In addition, in follow-up to the May 2003 conference, the NICHD held a workshop in August 2004, entitled "Fetal Treatment: Needs Assessment and Future Directions" to develop a plan for the surgical, maternal-fetal, and neonatal evaluation and treatment of pregnancies which might benefit from in utero therapy and for the dissemination of innovations in maternal-fetal surgery.

In addition to the MOMs study evaluating the safety and efficacy of prenatal surgical interventions to repair spina bifida, the NICHD, through its Birth Defects Initiative, fosters interactions between basic scientists, clinicians and genetic epidemiologists to unravel the genetic and environmental factors associated with genetic susceptibility, ethnic disparities and variability of human malformations as well as to elucidate the developmental processes that go awry leading to the formation of NTDs. As part of this program, a project is underway to link nutritional factors, folate status and genetic information from a large number of affected families to define putative risk factors for spina bifida. An important aspect of this project is to assess the relative contributions of both maternally and embryonically expressed genes to the risk of spina bifida. This study has shown that the maternal genotype for several genes is related to the risk of spina bifida in offspring. In addition, the expression of unrelated genes in the embryo is also significantly related to the risk of this birth defect. The involvement of maternal and embryonic genes as well as the influence of the environment underscores the complexity associated with the occurrence of spinal bifida. Finally, the NICHD supports research dealing with cognitive effects of spina bifida in children and adults.

Item

Primary immunodeficiency diseases - The Committee continues to be impressed with the dedication of resources by NICHD to address the research and awareness issues that surround this class of more than one hundred diseases. The Committee is particularly encouraged by the Institute's research commitment to develop newborn screening procedures for primary immunodeficiency through microarray technologies and encourages NICHD to press ahead with this initiative. (p. 85)

Action taken or to be taken

The NICHD plans to continue its efforts to develop newborn screening procedures for primary immunodeficiency diseases (PIDs). The Request for Applications currently being developed by the NICHD will solicit projects using current and emerging technologies together with bioinformatics to identify new biomarkers for PIDs, especially for Severe Combined Immunodeficiency Disease (SCID). Through this initiative, investigators will identify biomarkers for SCID that can be used for the development of efficient genomic and proteomic screening tests. It is also likely that technologies to improve the rapidity and accuracy of specific genotypic and phenotypic diagnosis of SCID will be generated. This initiative will lead

to the improvement of neonatal screening and diagnosis for SCID and, ultimately, will allow for more rapid initiation of treatment and improve management of patients with this debilitating condition. This initiative will also serve as the basis for developing newborn screening biomarkers of other genetic diseases.

The NICHD also continues to actively raise awareness of and promote research concerning PIDs. In addition to a portfolio of grants on these conditions, the NICHD provides both fiscal and intellectual support to the NIAID/NICHD Primary Immunodeficiency Research Consortium, which is a coalition of the world's most prominent investigators in the field of PID. The purpose of this consortium is to help prioritize and coordinate research directions and to develop new resources to study these rare disorders.

The NICHD has been active in supporting conferences devoted to a variety of topics related to PIDs. Recently, the NICHD collaborated with the NHGRI, NHLBI, the NIH Office of Rare Diseases and the Jeffrey Modell Foundation in sponsoring a meeting on Wiskott-Aldrich Syndrome (WAS), a rare, X-linked immunodeficiency. This meeting convened a group of world-renowned leaders to examine the current status of gene therapy for WAS and to develop strategies for applying research findings into safe and efficient gene therapies. Earlier in the year, the NICHD sponsored a Symposium on Screening for Genetic Defects in Immunity. Because of the lack of screening, many individuals affected with more serious forms of PID may die of infection before their underlying defects can be diagnosed. This symposium addressed the issue of early screening for genetically determined immunodeficiency disorders, supporting the NICHD's efforts to develop genomic and proteomic newborn screening technology and procedures for PIDs and other genetic diseases.

Item

Down syndrome - The Committee encourages NICHD to enhance funding for Down syndrome research as it relates to gene expression of chromosome 21, the effects on cell function and cognition, and possible medical treatments to eliminate or reduce the cognitive abnormalities associated with the disorder. The Committee is aware of the shortage of mice used in the research of Down syndrome and encourages NICHD to strengthen its support for greater production of the Ts65Dn mouse model and for the research and development of other mouse models. The Committee also encourages NICHD to work closely with NINDS, NIA, NIH and NHGRI to establish a new, multi-year research initiative to fund Down syndrome biomedical research on cognition, behavior and early dementia. (p. 86)

Action taken or to be taken

The NICHD sponsors an extensive portfolio of both research and training grants on Down syndrome. This fall, a number of new grants have been approved for funding. Several of these grants focus specifically on effects of trisomy 21 on cell function and cognition, and on possible medical treatments to eliminate or reduce cognitive abnormalities associated with Down syndrome.

In response to the needs of the Down syndrome research community for Ts65Dn mice, a supplement was awarded for the Jackson Laboratories to expand, and take into standard production the Ts65Dn stock. It is anticipated that the first year will be used to re-derive the

stocks and to generate sufficient females to first double and then triple. The subcontract will continue in place and will be the source of animals for funded investigators.

The NICHD and NINDS will work together to put on a symposium in spring 2005 on "Down syndrome, Synaptic Function and Cognition," focusing on recent achievements by Down syndrome researchers supported by the NICHD and other Institutes. The symposium is currently in the planning stage.

Item

Limb loss - The Committee is aware of the development of the Amputee Care Center at Walter Reed Army Medical Center to improve the level of care within military medicine for those who are injured and lose limbs. The Committee urges NICHD, working through the National Center for Medical Rehabilitation Research, to work in partnership with Walter Reed to support its efforts to conduct clinical research focused on developing new amputee-care metrics applicable to the rehabilitation of highly active persons with limb loss. Additional clinical research is also needed to better understand the applicability of new technology to various segments of the limb-loss population, ranging from highly functional military personnel who have been injured in Operation Iraqi Freedom to older Americans who might not otherwise ambulate with traditional prosthetic technology. Advances have recently been made by the private sector to develop breakthrough prosthetic limb technologies which have dramatically improved the functionality, stamina and psycho-social well being of patients, in particular, the microprocessor-controlled hydraulic fluid swing and stance phase knee device technology. The Committee encourages NICHD to consider supporting this type of research, using all appropriate mechanisms. (p. 86)

Action taken or to be taken

Recently, the Director and staff from the NICHD National Center for Medical Rehabilitation Research (NCMRR) met with the Director and staff of the Amputee Care Center at Walter Reed Army Medical Center. At that time, Walter Reed staff identified some specific needs and concluded they were not yet ready to embark on controlled clinical trials regarding specific prostheses. The needs perceived by Walter Reed staff include:

- Longitudinal tracking of soldiers receiving prosthetic limbs and qualitative evaluation of the services they received and their perceived quality of life.
- Development of quantitative metrics to evaluate the quality of care and quality of life in soldiers receiving prosthetics.
- Additional expertise on the Walter Reed Human Use Committee (HUC) to allow for the timely review of proposals relating to prosthetics and rehabilitation.

Based upon these discussions, the NCMRR provided Walter Reed with a list of experts in qualitative evaluations and longitudinal studies. Several of these experts are now engaged in working with Walter Reed staff and the VA on amputee issues. In addition, NCMRR provided information on specific funding opportunities for research on prosthetics and sent out an NIH-wide call for volunteers to serve on the Walter Reed HUC to compensate for military medical staff on deployment. The NCMRR Director also now serves on the Walter Reed HUC.

The NCMRR continues to support a wide array of prosthetic research. The Center also sponsored, in March, 2004, a trans-NIH program announcement, "Partnerships to Improve Functional Outcomes," to specifically solicit applications from partnerships between rehabilitation specialists and researchers in other areas to develop innovative solutions to problems such as limb loss.

Item

Spinal muscular atrophy - Spinal muscular atrophy [SMA] is the leading genetic killer of infants and toddlers and is the most prevalent genetic motor neuron disease. Over 25,000 Americans, mostly children, suffer from significant physical disability and impairment as a result of SMA. The Committee encourages NICHD to work closely with NINDS to develop collaborations that will support the SMA Therapeutics Development project, including an expansion of the scope and level of SMA research at NICHD. In addition, NICHD is encouraged to develop formal programs that increase public and professional awareness of SMA. (p. 86)

Action taken or to be taken

The lead NIH Institute for SMA research is NINDS, which supports a large SMA research project. The NICHD monitors the activities of this project, including the SMA Therapeutics Development Program. The NICHD has established a Pediatric Pharmacology Research Network, and participates in the Wellstone Muscular Dystrophy Cooperative Research Centers Program together with NINDS and NIAMS. Both of these programs (and related efforts supported by the Muscular Dystrophy Association) would be potentially useful for clinical trials at such time as treatments are developed by the SMA initiative.

While the NICHD has received few applications for SMA research, the Institute is the lead organization for newborn screening research. Given that genes for SMA have been identified through NINDS and other supported research, and given that early treatment of SMA is a likely key to the success of therapies, ways to screen and diagnose various types of SMA will be considered as a part of the NICHD's current newborn screening initiative, which has the potential to allow screening for hundreds of conditions before the newborn leaves the hospital. Furthermore, the NICHD will plan ways to extend, enhance and coordinate NINDS efforts to increase public and professional awareness of SMA. The NICHD also sponsors pediatrics and basic science training programs that are available for the training of new investigators who have an interest in SMA.

Item

National children's study - The Committee remains interested in the national children's study, which aims to quantify the impacts of a broad range of environmental influences, including physical, chemical, biological and social influences, on child health and development. The Committee encourages NICHD to continue to coordinate closely with the CDC, EPA, other institutes and agencies and non-Federal partners conducting research on children's environmental health and development. (p. 86)

Action taken or to be taken

Since fiscal year 2000, the National Children's Study (Study) has made great progress in completing pilot studies (including exposure, health-related and cross-cutting studies) and

developing a participant sampling plan and a scientific study plan. Strong support from both the four lead federal agencies as well as from private and academic sector partners has fostered the planning process to date. As the legislatively mandated lead agency for the Study, the NICHD heads the consortium of agencies involved in developing the Study (see Children's Health Act of 2000, P.L. 106-310). In this role, the NICHD houses the program office and most of the Study infrastructure. Agencies that have played a central role in this consortium with the NICHD and have contributed significantly to the financial aspects of the planning effort, as well as substantial staff time and in-kind resources include: the National Institute of Environmental Health Sciences, the Centers for Disease Control and Prevention, and the U.S. Environmental Protection Agency. Beyond these, more than 40 agencies and other Federal entities from the majority of the Cabinet Departments have a sufficient interest and stake in this Study that they are actively participating in its planning, making it a truly government-wide effort.

To prepare to move the Study into the field, the collaborating agencies announced several major milestones in November 2004. These milestones represent an important step forward for the Study that could provide data over more than 21 years aimed at pinpointing causes and finding prevention and treatment strategies for many of today's childhood diseases and disorders. A scientific study plan, or protocol, for the study of 100,000 children has been posted for a brief period of public review and comments. Requests for proposals (RFPs) for a coordinating center and several initial study sites have been posted. This fall the NICHD announced an important development in how participant sampling will be drawn and how study sites will be chosen. Based on recommendations from the Advisory Committee, the NICHD and participating agencies are utilizing a probability sampling study design and are undertaking a collaborative strategic planning process between biomedical and behavioral sciences. Other FY 2005 milestones will include increased community outreach**,** the development of the information management system, and further pilot studies.

Item

Fragile X- The Committee believes that the National Center on Birth Defects and Developmental Disabilities' focus on maximizing prevention potential, minimizing impact on families and promoting early intervention through developmental screening should incorporate individuals affected by Fragile X. To support this effort, the Committee recommends that NICHD develop a fragile X public health program to expand surveillance and epidemiological study of fragile X, as well as provide patient and provider outreach on fragile X syndrome and other developmental disabilities. (p. 87)

Action taken or to be taken

The NICHD has for many years supported an extensive portfolio of grants to study Fragile X syndrome. While the Centers for Disease Control and Prevention is the lead agency for surveillance and epidemiologic studies of Fragile X, the NICHD has sponsored some epidemiologic studies relative to Fragile X syndrome. These include studies of the prevalence of the Fragile X carrier status, particularly with respect to Fragile X Ataxia-Tremor syndrome (FXATS), including a newly appreciated condition that occurs in grandfathers of full mutation Fragile X children, men who carry pre-mutation size alleles. This syndrome was co-discovered by two NICHD funded investigators who have now expanded their studies of prevalence and penetrance, as well as neuropathologic sequelae and associated dementing effects, with funding

from NINDS and NIA. Other long-standing Fragile X epidemiology studies focus on the incidence of premature ovarian failure among Fragile X carrier females. A symposium will be held in April 2005 to address Premature Ovarian Failure and Fragile X Pre-mutation Carrier Status, organized in large part by the NICHD intramural and extramural staff. Furthermore, the NICHD supports research related to newborn screening for Fragile X syndrome and related issues.

In addition, it is anticipated that the Fragile X booklet recently prepared and released by the NICHD will be updated as needed to include more recent research findings and to alert families to the newly appreciated effects of the pre-mutation carrier status.

Item

Bone diseases - The Committee encourages the NICHD to support research on the effects of drugs on the growing skeleton and to work to ensure that the impact on the ongoing skeleton is investigated for all therapeutic agents. The Committee also encourages the NICHD to participate in trans-NIH research about other factors - including genetics, diet and exercises - affecting the determination of peak bone mass in children with and without the metabolic bone diseases of osteoporosis and osteogenesis imperfecta. (p. 87)

Action taken or to be taken

Researchers funded by the NICHD have focused on how inherited, environmental and nutritional factors influence bone mineral acquisition. The failure to achieve genetically determined maximal peak bone mass correlates with the development of osteoporosis later in life. The Endocrinology, Nutrition and Growth Branch (ENGB) is funding nine grants in the area of osteoporosis prevention, including six randomized controlled trials designed to test behavioral interventions in children. Two studies are school-based with large study populations of 1800 children each. These trials are centered on interventions that include increased nutritional calcium intake and increased exercise. Investigators concluded that increases in weight-bearing physical activity or calcium intake have positive effects on bone mass in children and adolescents [French SA, Fulkerson JA, Story M. (2000). Increasing weight bearing physical activity and calcium intake for bone mass growth in children and adolescents. *Preventive Medicine*, *31*:722-31].

Furthermore, a school-based intervention designed to increase physical activity among sedentary adolescent females significantly increased physical activity and also served to prevent a decline in cardiovascular fitness in the children participating in the study. These findings are not only pertinent to bone health but also to the obesity epidemic in children [Jamner MS. (2004). A controlled evaluation of a school-based intervention to promote physical activity among sedentary adolescent females: Project FAB. *Journal of Adolescent Health*, *34*: 279-89].

Since 2001, the NICHD has funded a multi-center contract to collect standard reference data for bone mineral density in childhood, taking into consideration skeletal maturation, bone size and volume, and pubertal stage. The Bone Mineral Density in Childhood Study (BMDCS) involves five Clinical Centers, all adhering to a common longitudinal observational protocol of three years' duration. When complete, these data will serve as a gold-standard pediatric bone mineral density database and will be a valuable resource for both clinicians and investigators in this field

who require this information for assessing bone deficits and risk factors for impaired bone health in children.

One of the key benefits of the BMDCS, as a longitudinal study, is to establish whether bone mineral density values obtained in early puberty are predictive of bone mineral density values at sexual maturity. Furthermore, nutrition and exercise questionnaires provide the data needed for understanding the roles of proper nutrition and exercise through childhood and adolescence as bone is still actively increasing. These data will help guide children and young adults, their parents and doctors, on maintaining bone health.

In regard to the effects of pharmacologic agents on skeletal growth, the NICHD routinely includes assessment of linear growth of children as part of the safety evaluation of drugs studied under the provisions of the Best Pharmaceuticals for Children Act (BPCA). The possible effect of topical steroids on bone mineralization was discussed at a pediatric drug prioritization meeting held at the NICHD on October 26, 2004. If studies of topical steroids are initiated under the provisions of the BPCA, controlled studies of bone mineralization will be included as an outcome measurement in such trials.

The NICHD will co-sponsor with the American Society of Bone and Mineral Research a research-planning workshop entitled *Effects Of Pharmacologic Agents On Bone Mineral Density In Childhood* on April 14, 2005. Experts in the field of pediatric bone biology will meet to discuss the effects of bisphosphonates and steroids on bone accrual in children.

Item

Demographic research - The Committee commends NICHD for its support of demographic research. This research has provided critical scientific knowledge on issues such as work-family conflicts, family formation and structure, childcare, adolescent health and wellness, family and household behavior, the role of maternal employment, and parental involvement on child development. The Committee encourages NICHD to continue support for the Population Research Infrastructure program. The diverse research supported by this program has yielded key findings in areas such as fertility, health disparities, immigration and migration trends, and family dynamics. (p. 87)

Action taken or to be taken

The NICHD program in demographic research supports objective investigations on the dynamics and characteristics of our population, research that creates a knowledge base essential to informed social and health policy. Research findings provide insights useful in addressing problems such as rising rates of nonmarital childbearing, increasing racial, ethnic, and linguistic diversity in the population, and persistent health disparities. The program places significant emphasis on the health of the American family, including studies of marriage and divorce, childbearing, parental investment in children, fatherhood, and work/family conflict.

Recent initiatives and accomplishments underscore the Institute's commitment to this area of research. The first nation-wide study of new legal immigrants to the U.S. has now been completed under a grant collaboratively funded by the NICHD, the Department of Homeland Security, and others. Over 2000 scientists nationwide have conducted research using data from

the National Longitudinal Study of Adolescent Health (Add Health); their efforts have yielded important new insights on how families, parents, and schools can influence the health and well-being of young people. Three major studies of poor and middle-class families have been conducted. The Welfare, Children, and Families (Three City) Study, the Los Angeles Family and Neighborhood Study, and the Fragile Families Study have produced critical insights about family strengths and vulnerabilities and disseminated their findings in scientific publications and informational summaries distributed to policy makers. A recently announced initiative will support the development of experimental studies to improve family health by reducing work/family conflict. The NICHD has also re-issued its program announcement on research that examines the mechanisms that link poverty, neighborhood disadvantage, and family economic stress to poor child developmental outcomes.

The continued vitality of this program depends on investments in training and infrastructure at universities across the country. The NICHD currently funds infrastructure programs in fourteen states and training programs in ten. In FY 2000, the NICHD replaced a centers program for demographic research with the new and highly competitive Population Research Infrastructure Program. The new program is successfully stimulating innovation and interdisciplinary research and will begin another five-year cycle in FY 2006.

FY 2005 Senate Appropriations Committee Report Language (S. Rpt. 108-345)

Item

Behavioral Science - The Committee emphasizes its strong support for the broad portfolio of behavioral research at NICHD, and supports NICHD's efforts to determine the biological, behavioral, and social factors that affect cognitive, social, and personality development of children in a variety of settings. The Committee encourages research on effective ways to promote and sustain healthy family formations for low-income families, including families of color. The Committee is particularly concerned about rising rates of childhood obesity and supports continued initiatives to promote healthy behaviors in children and adolescents and research to prevent health risk behaviors. (p. 128)

Action taken or to be taken

Since 2000, the NICHD has increased its support for behavioral research to develop new initiatives to better understand how inherited, neurobiological, environmental, and experiential conditions are integrated in development to mold, moderate, and predict human learning and behavior. Programmatic initiatives in early childhood and school readiness, mathematics development, science learning, child abuse and neglect, cognitive, social, and emotional development, the effects of poverty and family structure on development, health promotion research, pediatric neuroimaging, literacy among English-language learners and adolescent, adult, and family literacy exemplify this focus.

With regard to research on marriage and family formation, the NICHD has expanded its long-standing program in this area to address the serious challenges facing low-income and minority families. Three major studies – the Fragile Families Study, the Welfare, Children, and Families

(Three City) Study, and the Los Angeles Family and Neighborhood Study – are producing critical new knowledge about the causes of family vulnerability. This knowledge has already been put to use in designing public policies and programs to strengthen families. In addition, the Family Life project, a major study of children in four geographical areas of high child rural poverty, is currently studying a diverse sample of over 1100 children from birth to understand differences within the child, family work and community contexts as these relate to the development of competence and disorder.

In the area of obesity, the NICHD has supported behavioral research to understand how nutritional practices and physical activity in infants, children, adolescents and postpartum women lead to this condition. The NICHD, in FY 2005, will support two new research initiatives. "Understanding Mechanisms of Health Risk Behavior Change in Children and Adolescents" is a trans-NIH effort led by the NICHD, and is aimed at the prevention and treatment of childhood obesity and substance abuse by identifying individual characteristics, interpersonal interactions and contextual factors that influence childhood physical activity and dietary practices and substance abuse. The second initiative involves developing and evaluating site-specific intervention and prevention strategies to reduce or eliminate childhood obesity. This work will be accomplished in partnership with the National Institute of Diabetes and Digestive and Kidney Diseases. The NICHD has also expanded support for research on the economic, social and cultural causes of childhood and adolescent obesity in recent years.

Item

Demographic Research - The Committee commends NICHD for its strong support of demographic research. This research has consistently provided critical scientific knowledge on issues of greatest consequence for American families: work-family conflicts, family formation and structure, childcare, adolescent health and wellness, and family and household behavior. Recent findings have provided invaluable insights into timely issues such as the role of maternal employment and parental involvement on child development. The Committee applauds NICHD for its ongoing support of the Fragile Families, Three Cities Study of Welfare, and National Longitudinal Study of Adolescent Health studies in particular. The Committee encourages the Institute to ensure adequate funding for the large databases such as these that make advances in population research possible. Further, the Committee urges NICHD to maintain stable funding for the Population Research Infrastructure program. The recent retooling of this program has enhanced its ability to support vital interdisciplinary collaboration and innovation in population research at academic and research institutions nationwide. The diverse exceptional research supported by this program has yielded key findings in areas such as fertility, health disparities, immigration and migration trends, and family dynamics. Given the importance of these issues to policymakers and the public, demographic research at the NICHD must continue to thrive. (p. 129)

Action taken or to be taken

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

Item

Down Syndrome- The Committee encourages NICHD to increase funding for Down syndrome research as relates to gene expression of chromosome 21, the effects on cell function and cognition, and possible medical treatments to eliminate or reduce the cognitive abnormalities associated with the disorder. The Committee is aware of a serious shortage of mice used in the research of Down Syndrome and strongly encourages NICHD to increase funding for greater production of the Ts65Dn mouse model and for the research and development of other mouse models. The Committee also urges NICHD to work closely with NINDS, NIA, NIMH and NHGRI to establish a new, multi-year research initiative to fund Down syndrome biomedical research on cognition, behavior and early dementia. (p. 129)

Action taken or to be taken

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

Item

Drug Safety for Children- The Committee recognizes the importance of ensuring that drugs are safe and effective for use by children and are appropriately labeled for pediatric use. The Committee strongly supports continued implementation of the Research Fund within the National Institutes of Health, as established in the Best Pharmaceuticals for Children Act of 2003 (Public Law 107-109) within section 409I of the Public Health Service Act, which supports the pediatric testing of off-patent drugs, as well as on-patent drugs not being studied through existing mechanism. The Committee urges NICHD to act as the coordinating Institute for other Institutes within NIH for which pediatric pharmacological drug research may have therapeutic relevance, and urges consultation with the Food and Drug Administration to ensure that the studies conducted through the Fund are designed to yield improved pediatric labeling. The Committee expects an update prior to the fiscal year 2006 hearings, including information on the number of studies supported through the Research Fund; the estimated cost of each study undertaken; the nature and type of studies undertaken; the number of label changes resulting from completed studies; the patent status of the drugs studied; and the number of drugs remaining on the priority list established through section 409I. (p. 129)

Action taken or to be taken

The NICHD is currently preparing a report as requested above. This report will be forwarded to the House and Senate Appropriations Committees prior to the NICHD 2006 hearings.

Item

Fragile X- Title II of the Children's Health Act of 2000 authorized the establishment of at least three Fragile X research centers. The Committee is pleased that the NICHD has funded three Centers on a first-year basis, and urges the NICHD to issue an RFP with the goal of enhancing the Centers and recruiting new researchers to the Fragile X field. The Committee also encourages the NICHD to coordinate its Fragile X research efforts internally, by partnering with others, and by relating Fragile X research with that in other developmental disorders, and with autism research. (p. 129)

Action taken or to be taken
The NICHD recently established the Fragile X Centers. These centers have conducted studies of the prevalence of the Fragile X carrier status, particularly with respect to Fragile X Ataxia-Tremor syndrome (FXTAS), including a newly appreciated condition that occurs in grandfathers of full mutation Fragile X children, men who carry premutation size alleles. The NICHD is monitoring these centers to determine what additional efforts are needed to move research further ahead in this field. The NICHD believes it may be premature to invest in additional programs to recruit new researchers to the Fragile X field as opposed to other types of enhancements. The NICHD plans to continue to examine these issues to determine what additional specific efforts are warranted.

With respect to coordinating Fragile X research efforts internally, the NICHD recently partnered with the NIMH to support a meeting on Fragile X syndrome and autism, held in June 2005. Increasing interest in prevalence of autism and autistic like behaviors in Fragile X has spurred integration of interests of researchers in both arenas, encouraged by the NICHD staff. The NICHD is planning a High Risk/Baby Sibs Autism Research Meeting for August 2005. By taking advantage of the risk for autistic features among first- degree relatives, a much higher risk group for testing of predictive tests can be utilized. These relationships have led to several successful grant applications in the past two years. The NICHD will continue to search for methods of early detection and treatment for children with Fragile X syndrome and their families.

Item
Infertility and Contraceptive Research - The Committee continues to place high priority on research to combat infertility and speed the development of improved contraceptives. NICHD is urged to continue aggressive activities in this area, including individual research grants and those of the infertility and contraceptive research centers. (p. 129)

Action taken or to be taken
Infertility continues to be a high priority for the NICHD as it is a major health related problem for many Americans, including minorities. A large portfolio of grants is funded in basic and applied aspects of male and female infertility and in reproductive tract diseases that lead to infertility. The NICHD continues to encourage research in the discovery of the basic mechanisms of the formation and growth of uterine fibroids. In regard to polycystic ovary syndrome, a common cause of infertility, the National Cooperative Reproductive Medicine Network is investigating three drug regimens for the treatment of infertility in women with polycystic ovary syndrome. The Specialized Cooperative Centers Program in Reproduction Research (SCCPRR) and the National Cooperative Program in Infertility Research (NCPIR) have made major strides in conducting basic research to understand the genetic basis of infertility. For example, candidate genes for endometriosis have been identified providing possibly new avenues to prevent and to treat infertility due to this disease. The recent discovery of the gene for Idiopathic Hypogonadtoropic Hypogonadism will provide new ways to treat infertility due to lack of sexual maturation. The NICHD is also committed to improving the research capabilities of faculty and students in minority institutions and will continue the Specialized Cooperative Reproductive Science Research Centers at Minority Institutions. The Institute is designing an evaluation of the

Women's Reproductive Health Centers Program to enhance our ability to train physician-scientists in reproductive and infertility research.

Contraceptive research also remains a high priority for the NICHD. Unintended pregnancy is still a major problem in the United States resulting in huge social and financial costs to society. The three Cooperative Contraceptive Research Centers are investigating new methods for both male and female contraception. The research includes basic science to identify new targets for contraception as well as novel delivery systems for existing drugs that will lower potential side effects while maintaining high efficacy. Periodic review of these programs by outside advisors serves to ensure that high quality science is performed and that focus is maintained on product development. The Centers program will undergo re-competition and review in 2006. In addition to the Cooperative Contraceptive Research Centers, the NICHD has initiated a program to support identification of new targets for male contraception. This program explores mechanisms to regulate fertility by control of sperm production and/or function. The NICHD has also expanded the capability to test new products for men by adding two clinical centers for male contraceptive research into the Contraceptive Clinical Trials Network. The Institute is also conducting clinical trials for contraceptive efficacy of microbicides that are expected to yield products with dual action to prevent unintended pregnancy as well as transmission of sexually transmitted diseases.

Item

Learning and School Readiness - The Committee commends NICHD on its commitment to research in reading, learning disabilities, and math and science cognition. NICHD is encouraged to support additional research on developing comprehensive, culturally neutral and developmentally appropriate assessments and instruments to measure cognitive, social and emotional skills for pre-school-aged children that are necessary for school readiness. (p. 130)

Action taken or to be taken

The NICHD research program in learning disabilities and reading disorders is now entering its 39th year. The program has increased from 1 research site to 44. Findings obtained from these sites now serve as the scientific basis for evidence-based reading practices and policies in the United States. In 2002, The NICHD established its mathematics and science learning program to improve understanding of normal and atypical development of mathematical and scientific thinking and learning. In FY 2005, the NICHD, in collaboration with the Administration for Children and Families (U.S. Department of Health and Human Services) and the Office and Special Education and Rehabilitative Services (U.S. Department of Education) will support the development of tools to measure school readiness outcomes for young children. This initiative will support theory-driven development with universal design, to provide appropriate measures for linguistically and culturally diverse populations of young children as well as those with disabilities.

Item

Maternal Fetal Medicine Units Network [MFMU]- The Committee was extremely encouraged by the research results from NICHD's Maternal Fetal Medicine Units Network on the identification of a therapy, progesterone that prevents recurrent preterm birth in high-risk women. The Committee understands that this is one of the first advances in this area, despite

extensive efforts over decades, and urges the NICHD to build on this finding and to fully support the MFMU Network. (p. 130)

Action taken or to be taken
Please refer to page NICHD-32 of this document for the NICHD's response to this significant item.

Item
National Children's Study- The Committee strongly supports full and timely implementation of the National Children's Study. This study aims to quantify the impacts of a broad range of environment influences, including physical, chemical, biological and social influences, on child health and development. The Committee urges the NICHD to coordinate the involvement of the Department, the lead Federal partners - CDC, EPA, and NIEHS - and other interested institutes, agencies, and non-Federal partners conducting research on children's environmental health and development, such that this study is ready for the field no later than 2006. (p. 130)

The Committee is pleased that the National Children's Study Advisory Committee is planning to utilize probability sampling in its design and is undertaking a strategic planning process that emphasizes collaboration between the biomedical and behavioral sciences.

Action taken or to be taken
Please refer to page NICHD-38 of this document for the NICHD's response to this significant item.

Item
Obesity in Children- The Committee strongly urges the NICHD, in collaboration with other relevant Institutes, to support the initiation of a study on the metabolic, psychological, and genetic causes of obesity in children. The Committee requests the Institute be prepared to report on the progress being made in the development of such study during the fiscal year 2006 appropriation hearings. (p. 130)

Action taken or to be taken
The NICHD shares the Committee's interest in understanding the metabolic, psychological and genetic causes of obesity in children. Intramural scientists at the NICHD are in the eighth year of a 15-year longitudinal study of the genetic, metabolic and behavioral origins of obesity in a group of 250 overweight children and children of obese parents. The goals of the study are to delineate the factors, such as resting energy expenditure and insulin sensitivity, that predict obesity in adolescence and young adulthood and to document the onset of co-morbid conditions that accompany obesity. The study will continue through 2011.

The NICHD has supported a group of genetic epidemiologists over the past decade that has been studying the genetic origins of childhood obesity in the population of Muscatine, Iowa. They have discovered several important genetic mutations and polymorphisms in the glucocorticoid receptor gene and the melanocortin 4 receptor gene as well as leptin receptor gene defects. These genetic alterations induce morbid obesity early in childhood.

The NICHD has also supported long-term metabolic studies of obesity and body composition in children within the Fels Longitudinal Study. These studies show remarkable divergence in levels of plasma triglycerides, HDL-cholesterol and levels of plasma insulin in obese versus non-obese children as young as age 12. The metabolic alterations found in these obese children persist into adulthood to coalesce in the metabolic syndrome, a serious condition that leads to premature coronary artery disease and type 2 diabetes. The NICHD has also funded a twenty-year study of the influence of intrauterine exposure to high levels of insulin on degree of obesity during adolescence. This study underscores the importance of metabolic programming early in life in determining long-term obesity.

The NICHD continues to fund investigators at the University of Buffalo to investigate the behavioral underpinnings of childhood obesity. These investigators have shown the importance of parenting styles on children's eating habits. They have also shown children's eating and exercise behavior mimics that of their parents, and that behavioral modification programs in children can only be successful if the parents are involved as well.

The NICHD also plans to study the influence of factors causing childhood obesity in the National Children's Study (NSC).

Item

Pediatric AIDS- The Committee urges the Institute to increase support for AIDS research, especially pediatric HIV/AIDS research. HIV/AIDS affects children differently than it does adults, and it is essential to do specific research for pediatric populations in order to continue making significant strides in treating children with HIV/AIDS. (p. 130)

Action taken or to be taken

The NICHD is deeply committed to research in HIV/AIDS, its complications, and long-term outcomes in infants, children, adolescents, women and families, domestically and internationally. The NICHD supports several clinical trials networks that address treatment and prevention of HIV/AIDS in these populations. The NICHD International Pediatric/Perinatal HIV Clinical Trials Network consists of 21 domestic and 6 international sites in Brazil and the Bahamas. This Network conducts clinical trials in infants, children, adolescents, and pregnant and non-pregnant women, primarily in collaboration with the NIAID-funded Pediatric AIDS Clinical Trials Group (PACTG). The NICHD Network currently supports participation of about 1600 subjects in a variety of clinical trials. Studies conducted by the NICHD Network/PACTG have allowed approval of several new antiretroviral drugs in children at the same time they were approved in adults. The group is currently conducting pediatric trials of several drugs that were approved in adults but not in children, to allow FDA approval for pediatric use.

The NICHD also supports the Adolescent Medicine Trials Network for HIV/AIDS Interventions, a domestic multi-center network that is focused on conducting research, both independently and in collaboration. This study encompasses the full spectrum of research needs for youth: from primary prevention, including HIV preventive vaccine trials, when available, for HIV at-risk youth, to clinical management of HIV-infected youth, including novel regimens, drug adherence, and risk reduction.

During FY 2005, the NICHD is undertaking a new initiative, the Pediatric HIV/AIDS Cohort Study, that will merge two different studies to more cost-effectively address two critical research questions in children: the consequences of fetal exposure to antiretroviral drugs, and the clinical course of perinatally-acquired HIV infection in adolescents. Since 1994, when NIH-funded research demonstrated that antiretroviral therapy of a pregnant mother could reduce HIV transmission to her infant, there has been a dramatic decrease in mother-to-child HIV transmission in the U.S. However, at the same time, there are ever increasing thousands of children who are now uninfected but who have been exposed during pregnancy and as newborns to antiretroviral drugs that their mothers received, with little information on long-term safety of such exposure. Research is needed to address whether there are any adverse long-term consequences of this exposure. Additionally, although the number of newly infected children in the U.S. has decreased, a large number of HIV-infected children remain who acquired HIV infection from their mother who are now entering adolescence. Research is needed to assess the effects of HIV infection and treatments for HIV on growth and development, immunologic status, bone health, sexual maturation, and other aspects of human health in these children. This initiative will conduct research to address these questions in both populations. The Institute is also conducting clinical trials for contraceptive efficacy of microbicides that are expected to yield products with dual action to prevent unintended pregnancy as well as transmission of sexually transmitted diseases.

Item

Pediatric Liver Disease - The Committee urges the Institute to aggressively pursue and fund ancillary studies associated with the recently awarded NIDDK pediatric hepatitis C clinical trial. This clinical trial will provide long term follow up for children treated for hepatitis C, permitting growth and development issues to be more fully explored. The Committee also notes that the Institute has provided only limited support for pediatric liver disease research and urges support to expand ongoing efforts to study biliary atresia and to provide expanded support for the Biliary Atresia Clinical Research Consortium. (p. 130)

Action taken or to be taken

Please refer to page NICHD-33 of this document for the NICHD's response to this significant item.

Item

Prader-Willi Syndrome- Prader-Willi Syndrome is the most common known genetic cause of life threatening obesity in children. The Committee strongly encourages the NICHD to place a high priority on Prader-Willi Syndrome research to study childhood obesity. Furthermore, the NICHD is urged to incorporate Prader-Willi Syndrome into the planning process for The National Children's Study. (p. 131)

Action taken or to be taken

Prader-Willi syndrome (PWS) is a genetic disorder that is characterized by an insatiable appetite for a wide variety of foods, morbid obesity, temper tantrums, and outburst of aggression. The NICHD has had a longstanding research interest in Prader-Willi syndrome and funded research showing that deletion of a long sequence of genetic material from chromosome 15 causes Prader-Willi syndrome. The NICHD support has enabled investigators to demonstrate the importance of

maternally expressed genes on chromosome 15 in the absence of complementary paternal genetic material in causing PWS. This critical observation opened a new field of research on the phenotypic effects of imprinted genes of paternal and maternal origin. The NICHD funded investigators have built on these findings to construct a mouse model of Prader-Willi syndrome. Availability of this model will enable scientists to pinpoint the genes that cause the vexing problems of insatiable appetite and uncontrollable temper tantrums in children with Prader-Willi syndrome. It appears that two or more continguous genes on maternal chromosome 15 are necessary to explain the PWS complex set of behaviors and body composition.

Other NICHD investigators are treating children afflicted with PWS with the neurotropic agent topiramate in order to attenuate the self-injurious behavior that is part of the syndrome. Regimens of behavioral therapy that include using food as a reward are also being implemented with some success by other NICHD supported investigators.

The NICHD recently participated in the Prader-Willi Syndrome Association meeting in November 2004 to explore further problem of childhood obesity and obsessive-compulsive disorder with the plan of organizing a strategy of research encouragement in the future.

Item

Prematurity- The Committee encourages NICHD to support a major initiative in the area of prematurity. The rates of premature birth have increased 29 percent since 1981 to over 480,000 babies in 2002. African-American infants are nearly twice as likely as non-Hispanic white infants to be born prematurely. Premature birth is the leading cause of death in the first month of life and most recent data indicate the first rise in infant mortality rates since 1958. Premature birth can occur in any pregnancy; the causes of nearly half of all preterm births are unknown. The Committee commends NICHD for its work on preterm birth and strongly urges the allocation of more funds to reveal the underlying cause of preterm delivery, to identify prevention strategies and improve the treatment of outcomes for infants born preterm.

In addition, the Committee is aware that genomic and proteomic strategies are widely used and have had a major impact on medicine. The Committee believes it is imperative that these techniques also be used to understand prematurity, and strongly encourages NICHD to support an initiative to hasten a better understanding of the pathophsiology of premature birth, discover novel diagnostic biomarkers, and ultimately aid in formulating more effective interventional strategies to prevent premature birth. (p. 131)

Action taken or to be taken

Please refer to page NICHD-30 of this document for the NICHD's response to this significant item.

Item

Primary Immunodeficiency Diseases- The Committee continues to be impressed with the dedication of financial and personnel resources by NICHD to address the research and awareness issues that surround this class of more than 100 diseases. The Committee is particularly encouraged by the institute's research commitment to develop newborn screening procedures for

PI through microarray technologies and urges the NICHD to press ahead aggressively with this initiative. (p. 131)

Action taken or to be taken
Please refer to page NICHD-35 of this document for the NICHD's response to this significant item.

Item
Skeletal Development - The Committee urges NICHD to focus on the effects of a wide variety of drugs on the growing skeleton and how to minimize these effects by working to ensure that the impact on the growing skeleton is investigated for all therapeutic agents in the implementation of the Better Pharmaceuticals for Children Act. The Committee also encourages NICHD to engage in trans-NIH research into other factors - including genetic, diet and exercise - affecting the determination of peak bone mass in children with and without the metabolic bone diseases of osteoporosis and osteogenesis imperfecta. In addition, the Committee urges support for basic research on the pathophysiology, genetics and treatment of osteopetrosis. (p. 131)

Action taken or to be taken
Researchers funded by the NICHD have focused on how inherited, environmental and nutritional factors influence bone mineral acquisition. The failure to achieve genetically determined maximal peak bone mass correlates with the development of osteoporosis later in life. The NICHD is funding nine grants in the area of osteoporosis prevention, including six randomized controlled trials designed to test behavioral interventions in children. Two studies are school-based with large study populations of 1800 children each. These trials are centered on interventions that include increased nutritional calcium intake and increased exercise. Investigators concluded that increases in weight-bearing physical activity or calcium intake have positive effects on bone mass in children and adolescents [French SA, Fulkerson JA, Story M. Increasing weight bearing physical activity and calcium intake for bone mass growth in children and adolescents. *Preventive Medicine*, *31*:722-31, 2000].

Furthermore, a school-based intervention designed to increase physical activity among sedentary adolescent females significantly increased physical activity and also served to prevent a decline in cardiovascular fitness in the children participating in the study. These findings are not only pertinent to bone health but also to the obesity epidemic in children. [Jamner MS. A controlled evaluation of a school-based intervention to promote physical activity among sedentary adolescent females: Project FAB. *Journal of Adolescent Health*, *34*: 279-89,2004].

Since 2001, the NICHD has funded a multi-center contract to collect standard reference data for bone mineral density in childhood, taking into consideration skeletal maturation, bone size and volume, and pubertal stage. The Bone Mineral Density in Childhood Study (BMDCS) involves five Clinical Centers, all adhering to a common longitudinal observational protocol of three years' duration. When complete, these data will serve as a gold-standard pediatric bone mineral density database and will be a valuable resource for both clinicians and investigators in this field who require this information for assessing bone deficits and risk factors for impaired bone health in children.

One of the key benefits of the BMDCS, as a longitudinal study, is to establish whether bone mineral density values obtained in early puberty are predictive of bone mineral density values at sexual maturity. Furthermore, nutrition and exercise questionnaires provide the data needed for understanding the roles of proper nutrition and exercise through childhood and adolescence as bone is still actively increasing. These data will help guide children and young adults, their parents and doctors, on maintaining bone health.

In regard to the effects of pharmacologic agents on skeletal growth, the NICHD routinely includes assessment of linear growth of children as part of the safety evaluation of drugs studied under the provisions of the Best Pharmaceuticals for Children Act (BPCA). The possible effect of topical steroids on bone mineralization was discussed at a pediatric drug prioritization meeting held at the NICHD on October 26, 2004. If studies of topical steroids are initiated under the provisions of the BPCA, controlled studies of bone mineralization will be included as an outcome measurement in such trials.

The NICHD will also co-sponsor with the American Society of Bone and Mineral Research ASBMR, a research-planning workshop entitled *Effects Of Pharmacologic Agents On Bone Mineral Density In Childhood* on April 14, 2005. Experts in the field of pediatric bone biology will meet to discuss the effects of bisphosphonates and steroids on bone accrual in children.

The NICHD will co-sponsor with the American Society of Bone and Mineral Research a research-planning workshop entitled *Effects Of Pharmacologic Agents On Bone Mineral Density In Childhood* on April 14, 2005. Experts in the field of pediatric bone biology will meet to discuss the effects of bisphosphonates and steroids on bone accrual in children.

Item

Spina Bifida- The Committee is pleased that the Institute cosponsored the Spina Bifida Research Conference in May 2003. However the Committee has concerns that without adequate follow-up the conference findings and recommendations will not come to fruition. The Committee strongly encourages NICHD to enhance research to address issues related to the outcome of the conference and urges the Institute to significantly expand its research efforts in the prevention and treatment of Spina Bifida and associated secondary conditions. The Director should be prepared to report on efforts to advance these areas of research at the fiscal year 2006 appropriations hearing. (p. 132)

Action taken or to be taken

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

Item

Spinal Muscular Atrophy [SMA]- SMA is the leading genetic killer of infants and toddlers, and is the most prevalent genetic motor neuron disease. The severity of the disease, its relatively high incidence, and the possibility of imminent treatments have led NINDS to initiate the SMA Project. The Committee believes that the treatment of SMA, and the SMA Project at NINDS, is strategically consistent with the mission the NICHD. The Committee strongly urges the NICHD to work closely with NINDS to develop collaborations and programs which will support and

expand the SMA Project. The Committee strongly urges NICHD to expand the scope and level of SMA research by aggressively soliciting grant applications on an expedited basis. Lastly, the Committee strongly urges the NICHD to develop formal programs that increase public and professional awareness of SMA. The Committee requests that the NICHD report back to the Committee during the fiscal year 2006 appropriations hearings. (p. 132)

Action taken or to be taken
Please refer to page NICHD-38 of this document for the NICHD's response to this significant item.

Item
Stillbirth - The Committee applauds NICHD's efforts in addressing stillbirth, a major public health issue with morbidity equal to that of all infant deaths. The Committee understands that NICHD has established a cooperative network of clinical centers and a data center to address this issue with a standard protocol, and strongly encourages the NICHD to fully fund this effort. (p. 132)

Action taken or to be taken
Please refer to page NICHD- 32 of this document for the NICHD's response to this significant item.

Item
Sudden Infant Death Syndrome- The Committee is pleased with NICHD's continued efforts to extend the reach of its extremely successful `Back to Sleep' campaign to underserved populations and daycare providers. Now that NICHD is focusing more globally on infant mortality, the Committee urges the Institute to transition from its successful SIDS 5-year research plan to a more comprehensive plan focusing on SIDS, stillbirth, and miscarriage. The Committee requests that NICHD determine an appropriate means of including research on these causes of infant mortality into one inclusive plan. (p. 132)

Action taken or to be taken
Please refer to page NICHD-29 of this document for the NICHD's response to this significant item.

Item
Urinary Incontinence- Urinary incontinence is one of the most prevalent chronic diseases in women affecting 30 percent of females; these and other pelvic floor disorders serve as obstructions to healthy living and contribute to depression and obesity. The Committee commends the NICHD for establishing the Pelvic Floor Disorder Network [PFDN] and expects additional resources will enable the network to expand the quality and integrity of clinical and basic scientific research in the field of urogynecology. The Committee is pleased that the NICHD continues to collaborate with the NIDDK in developing research in urinary incontinence. Recent studies have yielded gains in understanding these conditions but the Committee is equally concerned that more needs to be done with basic, clinical and translational research in order to create better foundations for clinical care. The Committee encourages the Institute to provide expanded research for investigator-initiated applications to ensure a self-

sustaining base of ongoing research and encourages a dedicated study section in this area. The Committee also encourages the NICHD to include the effects of pregnancy on a woman's chance for incontinence and pelvic floor disorders in the future National Children's Study. (p. 132)

Action taken or to be taken

The NICHD agrees that there is a strong need for research in urinary incontinence and other pelvic floor disorders, including pelvic organ prolapse and fecal incontinence. In general, the lifetime risk of one or more of these conditions is as high as one of every three women. Furthermore, major surgical procedure(s) for urinary incontinence or prolapse will be performed on an estimated 11% of women in the United States. The demographic aging of population in the United States will correspondingly increase the need for treatment of these disorders. To reduce this morbidity burden, it is essential to conduct studies on the etiology, diagnosis, treatment, and prevention of female pelvic floor disorders. New research findings have the potential for huge public health impact, since pelvic floor disorders are so common and frequently require expensive invasive treatment such as major surgery.

The NICHD has begun a multi-faceted research program on pelvic floor disorders since focusing on this area in 1999. Activities include:

- The Pelvic Floor Disorders Network, which consists of seven clinical sites and a central data coordinating center, and has been actively developing and implementing studies since 2001. The Network has been very successful in its first cycle of funding, providing scientific expertise and infrastructure to support high-quality clinical research in prolapse, urinary incontinence, and fecal incontinence. After just over three years, the Network has initiated 10 studies and completed four.
- Investigators supported under RFAs who are studying molecular mechanisms of pathogenesis in pelvic floor disorders, such as disordered synthesis, modeling and regulation of collagen and other components of the extracellular matrix; altered expression and binding of smooth muscle proteins; and the role of hormonal regulation via estrogen, progesterone, and other key hormones.
- Collaborations between the NICHD and the NIDDK in the Urinary Incontinence Treatment Network (UITN), a multi-center network of nine clinical sites and a central biostatistical coordinating center. The UITN designs and performs studies to improve the management of women with urinary incontinence.

The NICHD is also working with colleagues on developing the National Children's Study. The setting of this study, a long-term longitudinal study of environmental exposures and children's illnesses, provides a unique opportunity to assess the impact of pregnancy on the mothers' health.

In addition, the NICHD is sponsoring a State-of-the-Science Conference on maternal-choice cesarean delivery versus vaginal birth and the risk of pelvic floor disorders. Program staff in maternal-fetal medicine and pelvic floor disorders is collaborating in this important initiative that will produce evidence-based recommendations on this controversial topic for clinicians and patients.

Item

Vulvodynia - Millions of American women suffer from vulvodynia, a painful and often debilitating disorder of the female reproductive system. Despite its prevalence, since fiscal year 1998, the Committee has called on the NICHD to support research on the prevalence, causes and treatment of vulvodynia. While some initial steps have been taken, more must be done. The Committee urges the Institute to fund a collaborative research network to expedite the collection of data on the efficacy of current and future treatments. In addition, the Committee notes that, on average, women with vulvodynia consult five physicians before receiving a correct diagnosis. Therefore, the Committee urges the NICHD to work with the National Vulvodynia Association to implement a national education program for primary care health professionals, patients and the general public to reduce this delay. (p. 133)

Action taken or to be taken

Vulvodynia, along with other painful, but not fully understood, gynecological conditions, continues to be of great interest and concern to the NICHD. A very recent meeting on the current research findings regarding vulvodynia was organized by a NICHD grantee where current research was presented by the NICHD funded investigators and researchers from other countries. As anticipated, incremental progress has been made since a similar meeting held in 2003. The NICHD is pleased that the American College of Obstetricians and Gynecologists (ACOG) has a keen interest in vulvodynia research and has begun to make an effort to educate their membership regarding the research findings, especially the finding that vulvodynia is noted in up to 16% of women, which is more common than previously thought. In addition, the discovery that many women were evaluated by a number of physicians prior to having their condition diagnosed appropriately has been discussed within the ACOG community.

The NICHD will continue to work to educate the clinical community regarding the disease and current research findings as well as work to stimulate new research in this area. Currently, the NICHD supports a scholar under the Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program who is actively conducting vulvodynia research. Finally, the NICHD has issued Program Announcement for Vulvodynia Research to indicate the high priority of this area of research.

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

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2005 Amount Authorized	FY 2005 Appropriation	2006 Amount Authorized	2006 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Institute of Child Health and Human Development	Section 41B	42§285b	Indefinite	$1,234,346,000	Indefinite	$1,241,739,000
National Research Service Awards	Section 487(d)	42§288	a/	35,975,000		35,805,000
Total, Budget Authority				1,270,321,000		1,277,544,000

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

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

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1997	$543,441,000 2/	$631,989,000	$554,251,000 2/	$631,703,000
1998	582,032,000 2/	666,682,000	676,870,000	674,766,000
1999	654,248,000 3/4/	728,817,000	748,482,000	750,982,000
Rescission				(497,000)
2000	694,114,000 2/	817,470,000	848,044,000	862,884,000
Rescission				(4,593,000)
2001	810,501,000 2/	984,300,000	986,069,000	976,455,000
Rescission				(486,000)
2002	1,096,650,000	1,088,208,000	1,123,692,000	1,113,605,000
Rescission				(1,931,000)
2003	1,196,093,000	1,196,093,000	1,213,817,000	1,213,817,000
Rescission				(7,890,000)
2004	1,245,371,000	1,245,371,000	1,251,185,000	1,250,585,000
Rescission				(8,224,000)
2005	1,280,915,000	1,280,515,000	1,288,900,000	1,280,915,000
Rescission				(10,594,000)
2006	1,277,544,000			

1/ Reflects enacted supplementals, rescissions, and reappropriations.
2/ Excludes funds for HIV/AIDS research activities consolidated in the NIH Office of AIDS Research.
3/ Excludes enacted administrative reductions of $557,000.
4/ 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 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Office of the Director	21	21	22
Office of Administrative Management	46	47	47
Office of Science Policy, Analysis and Communication	23	24	24
Center for Developmental Biology and Perinatal Medicine	16	16	16
Center for Population Research	23	23	23
Center for Research for Mothers and Children	25	25	25
National Center for Medical Rehabilitation Research	5	8	8
Division of Scientific Review	14	13	13
Division of Epidemiology, Statistics and Prevention Research	31	31	31
Division on Intramural Research	343	343	343
Total	547	551	552
FTEs supported by funds from Cooperative Research and Development Agreements	(2)	(2)	(2)

FISCAL YEAR	Average GM/GS Grade
2002	11.0
2003	11.0
2004	11.3
2005	11.2
2006	11.2

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

Detail of Positions

GRADE	FY 2004 Actual	FY 2005 Appropriation	FY 2006 Estimate
Total - ES Positions	3	3	3
Total - ES Salary	$432,596	$447,700	$459,400
GM/GS-15	44	44	45
GM/GS-14	73	73	73
GM/GS-13	40	40	40
GS-12	44	45	45
GS-11	31	32	32
GS-10	7	7	7
GS-9	28	29	29
GS-8	18	18	18
GS-7	17	18	18
GS-6	1	1	1
GS-5	0	0	0
GS-4	4	4	4
GS-3	2	2	2
GS-2	2	2	2
GS-1	1	1	1
Subtotal	312	316	317
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General			
Director Grade	13	13	13
Senior Grade	5	5	5
Full Grade	3	3	3
Senior Assistant Grade	1	1	1
Assistant Grade			
Subtotal	22	22	22
Ungraded	198	198	198
Total permanent positions	320	324	325
Total positions, end of year	574	578	579
Total full-time equivalent (FTE) employment,end of year	547	551	552
Average ES salary	$144,199	$149,200	$153,100
Average GM/GS grade	11.3	11.2	11.2
Average GM/GS salary	$74,586	$76,500	$78,500

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

New Positions Requested

	FY 2006		
	Grade	Number	Annual Salary
Office of the Director	15	1	$103,000
Total Requested		1	