DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

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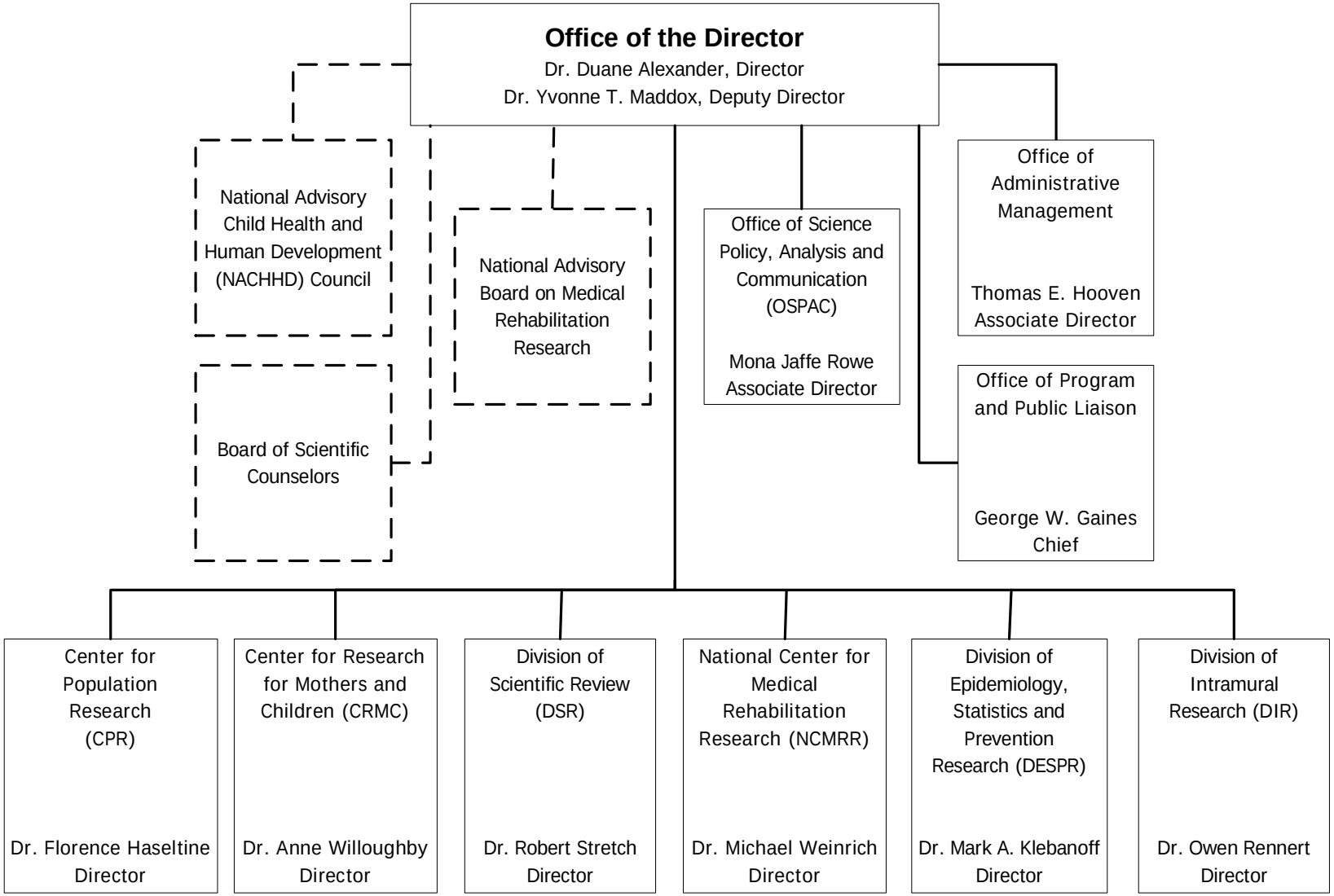


NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

For carrying out Section 301 and title IV of the Public Health Service Act with respect to child health and human development, [$1,250,585,000] *$1,280,915,000*.

[Departments of Labor, Health and Human Services and Related Agencies Appropriations Act, as enacted by the Omnibus Consolidated Appropriations Act for Fiscal Year 2004]

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

Amounts Available for Obligation 1/

Source of Funding	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Appropriation	$1,213,817,000	$1,250,585,000	$1,280,915,000
Enacted Rescissions	(7,890,000)	(8,224,000)	---
Subtotal, Adjusted Appropriation	1,205,927,000	1,242,361,000	1,280,915,000
Comparative transfer from: Fogarty International Center for International Services Branch	115,000	0	0
Comparative transfer to NIBIB for Radiology Program	(102,000)	(101,000)	(0)
Comparative transfer to Buildings and Facilities	(431,000)	(415,000)	(0)
Comparative transfer to Office of the Director for program changes	(1,317,000)	(0)	(0)
Subtotal, adjusted budget authority	1,204,192,000	1,241,845,000	1,280,915,000
Unobligated Balance, start of year	0	0	0
Unobligated Balance, end of year	0	0	0
Subtotal, adjusted budget authority	1,204,192,000	1,241,845,000	1,280,915,000
Unobligated balance lapsing	(19,000)	---	---
Total obligations	1,204,173,000	1,241,845,000	1,280,915,000

1/ Excludes the following amounts for reimbursable activities carried out by this account:
FY 2003 - $24,011,000; FY 2004 - $24,011,000; FY 2005 - $24,011,000
Excludes $248,000 in FY 2003 and $260,000 in FY 2004 for royalties.

Justification
National Institute of Child Health and Human Development

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

Budget Authority:

This document provides justification for the Fiscal Year 2005 activities of the National Institute of Child Health and Human Development (NICHD), including HIV/AIDS activities.

FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Increase or Decrease	
FTEs	BA	FTEs	BA	FTEs	BA	FTEs	BA
611	$1,204,192,000	591	$1,241,845,000	592	$1,280,915,000	1	$39,070,000

Justification of the National Institutes of Health (NIH)-wide FY 2005 AIDS activities can be found in the NIH section entitled "Office of AIDS Research (OAR)."

INTRODUCTION

40 Years of Human Development Research–Advancing Science, Enriching Lives

On October 17, 1962, President Kennedy signed into law the legislation establishing the National Institute of Child Health and Human Development (NICHD). A little more than a year later, members of the National Advisory Child Health and Human Development Council met for the first time. The NICHD was established to investigate broad aspects of human development as a means of understanding not only developmental disabilities and events that occur during pregnancy, but also the many biological, behavioral, and social factors that can influence healthy development over a lifetime.

Forty years later, the progress made toward fulfilling this creative vision is remarkable. The infant mortality rate in the United States reached an all-time low of 6.8 per 1,000 live births in 2001, representing a decrease of more than 70 percent since the Institute's research began.[1] Much of the decline stems from research supported by the NICHD, starting with treatments to prevent respiratory distress syndrome and most recently reflecting the Institute's efforts to reduce infant deaths from Sudden Infant Death Syndrome (SIDS). In fact, the nation's record low infant mortality rate was due in large measure to a dramatic 11 percent decline in the SIDS rate between 2000 and 2001.[2]

Today, the NICHD conducts and supports research on all stages of human development, from preconception through adulthood, to better understand the health of children, adults, families, and

communities. It's important to note, however, that the continued success of the NICHD relies not only on the innovative science conducted by NICHD-supported researchers, but also on the contributions of all of its employees, from those in its intramural labs, to those in the extramural programs and administrative staff. Thus, the NICHD story is not one of solitary accomplishments, but one of continuing advances that represent a range of collaborative efforts, both within and outside the Institute. Highlighted here are some of the NICHD's most recent and significant scientific advances. These advances will eventually improve the health of children, adults, families, and communities worldwide for years to come.

STORY OF DISCOVERY: FROM READING RESEARCH TO PRACTICE

For the first time, educators have the tools to help the majority of children with dyslexia learn to read at average levels or even above. This achievement is the product of a body of research that began with a failed attempt to build a new technology. Shortly after World War II, a team of researchers tried to build a machine that would scan print and read it to the blind. After two decades of research, they learned that human speech was far too complex for the technology of the time to duplicate. At best, the machine could reproduce words at about a tenth the rate of normal speech, impossibly slow for normal reading.

However, along the way, the researchers discovered that the words we speak are made up of individual elements of sound woven together so seamlessly that our technology cannot measure them. The word "bag," for example, consists of three elemental speech units, represented as bbb, aaa, and ggg. An oscilloscope–a device for measuring sound–can detect only a single burst of sound when "bag" is spoken. In all, 40 elemental speech units, known as phonemes, provide the basis of the English language. Unconsciously and automatically, the brain strings phonemes together to produce hundreds of thousands of words.

With NICHD funding, the researchers soon discovered that the ability to identify the phonemes in words was not an automatic process. Rather, this ability, which they called "phonemic awareness," needed to be taught. By the mid-1970s, the researchers had learned that as children progressed through the early grades, their ability to identify the phonemes in words increased. By the early 1980s, other NICHD-funded researchers had confirmed that kindergarten children who lacked phonemic awareness were more likely to have difficulty reading in the later grades. Further studies found that simple tests of children's ability to manipulate phonemes could predict later reading failure. Conversely, still other studies found that simple techniques to show children how to identify the phonemes in words brought about improvements in reading.

Developing children's phonemic awareness skills appeared to prepare them to master the next step necessary in learning to read, phonics. This involves matching phonemes to the letters of the alphabet that represent them. Readers skilled in phonics can make sense of words they haven't seen before, without first having to memorize them.

In the 1990s, NICHD-funded researchers at Yale University used new brain imaging technology to identify the three brain regions that control reading. The technique, known as functional magnetic resonance imaging, allows researchers to track activity in the brain. The researchers found that reading tends to take place in the brain's left half, or hemisphere. Within the hemisphere, reading is controlled by three discrete brain regions working together. In the left front of the brain, one area processes phonemes. Farther back, another brain area "maps" phonemes to the letters that represent them. Still another brain area serves as a kind of long-term storage system. Once the word is learned, this brain region recognizes it automatically, without first having to decipher it phonetically.

Brain scans have shown that as readers become more skilled, this automatic recognition center becomes more active. Poor readers, however, have difficulty accessing the automatic recognition center. Instead, they rely on the phoneme center and the mapping center to process the words they see. In poor readers, these two regions work much harder than normal. For them, recognizing words is not an automatic process. Each time these readers see a word, they must puzzle over it, as if they were seeing it for the first time. Fortunately, however, instruction in phonemic

awareness, phonics, and other reading skills can activate the automatic recognition process. After undergoing such training, brain scans of people who were once poor readers begin to resemble those of good readers.

The researchers also learned that while some reading difficulties seem to result from a disruption in the brain regions controlling reading, most seem to result from environmental factors. In the majority of poor readers, the brain regions controlling reading functioned normally, but had not been activated. The researchers theorized that these readers had not learned the phonemic structure of words when they were younger, but proper instruction could help these individuals learn to read at average or above average levels.

In 1997, NICHD established the National Reading Panel to review the scientific evidence on reading and to identify the most effective ways to teach children to read. The 14-member, independent panel of experts selected evidence from roughly 100,000 reading studies published since 1966 and another 15,000 published before that time. Along with instruction in phonics and phonemic awareness, the panel outlined other effective strategies for teaching children to read. One strategy, guided oral reading, involves having children read aloud while receiving guidance from skilled readers. The other, instruction in reading comprehension strategies, consists of techniques for helping children to understand what they read.

The panel's recommendations were incorporated in a new law seeking to improve the reading ability of American children. In December of 2001, the President signed the No Child Left Behind Act. The legislation requires states to set basic standards for local school systems, and to test students to assure they have met those standards. Under the new law, the Federal government will provide school systems with financial aid, both to improve their reading programs and provide training for teachers on how to teach reading. To qualify for funding, however, school systems must adopt curriculums based on the National Reading Panel's findings that effective reading instruction must include a combination of phonemic awareness, phonics, fluency, comprehension, and vocabulary.

SCIENCE ADVANCES

An Ounce of Prevention. The NICHD devotes a significant portion of its research portfolio to developing new ways to prevent a wide array of diseases and conditions, and finding new ways to keep us healthy. The investment is paying off. In the past year, NICHD-supported scientists made significant advances that have the potential to significantly reduce disease burden and save millions of dollars spent on medical treatment.

New Class of Antimicrobial Agents Found in Human Milk. One of the most common causes of infant mortality worldwide is diarrhea, which is commonly caused by the bacterium *Campylobacter jejuni*.[3,4] To infect a child, the bacterium must go through a series of steps, the first of which is to be ingested and bind to the cell surface. From there the bacterium can invade the cell and produce toxins that cause illness and diarrhea. Through a series of experiments, NICHD-supported researchers not only identified how the bacterium attaches to cells, but also identified a long-chained sugar molecule in breast milk that inhibits the attachment. Furthermore, the investigators showed that these sugar molecules also protect infants from infections from other bacteria and a virus that cause intestinal and respiratory infections. This finding could significantly help to reduce infant mortality worldwide by providing a strong scientific basis to strengthen policies that support breastfeeding, especially in non-hygienic environments. Equally important, this discovery suggests a promising new class of antimicrobial agents that could help prevent and treat bacterial and possibly viral infections. Unlike other antibiotics, these milk sugars work by blocking the bacterium's ability to attach to a cell, rather than by interfering with the bacterium's replication and protein synthesis, the way that many antibiotics work. This suggests that new drugs derived from these natural antibiotics would be

unlikely to induce bacterial resistance, a phenomenon that has reduced the usefulness of a number of antibiotics over time.

Innovative Technology Can be Used to Improve Anthrax Vaccine. Soon after the September 11, 2001 attacks, the U.S. mail was contaminated deliberately with *Bacillus anthracis* (anthrax) spores and 22 people were infected.[5] This spurred national interest in developing a new vaccine to protect against a bioterrorist attack with anthrax. Although safe and effective, the current anthrax vaccine was developed over 50 years ago. When bacteria invade the body, the immune system responds in a number of ways, one of which is by producing antibodies to specific bacterial components, rendering the bacteria harmless. Vaccines work by stimulating production of cells that produce these antibodies. The cells retain the ability to produce the antibodies, should the bacteria return. As a first step in developing a new vaccine, NICHD scientists targeted a surface protein, γ-D-glutamic acid, as a new point of attack, and applied a revolutionary "conjugate" technology they developed. This technology is especially useful when developing vaccines for infants and younger children, as it helps their immature immune systems develop antibodies. By systematically synthesizing, evaluating, and testing γ-D-glutamic acid "conjugates" in mice, the researchers successfully induced a new type of anthrax antibody. In the course of developing the conjugates, the researchers also developed a way to measure and standardize the amount of conjugate antigen needed to produce optimal antibody levels. Overall, these discoveries can help to determine the lowest level of vaccine required, thereby reducing the number of injections needed to reach a desirable and long-lasting immunity level, and minimizing undesirable side effects. This, in turn, increases the potential that more children, families, and communities can be protected against the deadly anthrax infection.

Food Fortification with Folate: Helping the Young and the Elderly. Sometimes measures taken to prevent or treat one disease can have unintended adverse consequences. For example, researchers have long known that high levels of the B-vitamin, folic acid or folate, can mask a deficiency of another essential nutrient, vitamin B12. A vitamin B12 deficiency can result in a type of anemia and irreversible neurological damage. Normally, vitamin B12 deficiency is diagnosed using a blood test for the anemia; however, high levels of folic acid mask the anemia without preventing the neurological damage. Nonetheless, when a decision was made to fortify the nation's supply of bread and cereal products with folic acid to reduce the risk for neural tube defects, without knowing what level of folate intake would mask a B12 deficiency, scientists began to question whether individuals (especially the elderly) with B12 deficiency who consume large amounts of grain products would fail to have the condition diagnosed. After reviewing the medical records of over 1500 veterans, scientists concluded that fortifying cereal grains with folate, which can lead to a two-to-three fold increase in blood folate levels, did not increase the number of undetected cases of vitamin B12 deficiency. These findings reaffirm the value of fortifying the nation's food supply with folic acid to help prevent birth defects in babies and heart disease in adults.

Reducing Infant Deaths. Since the NICHD was established, the nation's infant mortality rate has dropped by 70 percent–in part due to the contributions of Institute-sponsored research.[6] The newest advances of NICHD-funded researchers recently identified an exciting and relatively simple means to prevent preterm birth in some cases and uncovered additional threats to infant life and health, for which preventive steps can be taken.

Progesterone Injections Reduce Preterm Delivery. Preterm delivery (before 37 weeks of gestation) is the most important cause of infant mortality and morbidity in the United States. Furthermore, prematurity contributes substantially to racial/ethnic health disparities in infant mortality. It is also very costly. While preterm births account for 12 percent of births in the United States, new estimates show that hospital charges alone for premature/low-birthweight babies reached $13.6 billion in 2001, accounting for one-half of hospital charges for all newborns.[7,8] In addition, preterm babies are more likely to have long-term health problems. Women whose first baby was preterm are at high risk for subsequent preterm delivery. Until recently, most previously tested strategies to prevent preterm birth in such high-risk women failed to produce effective, reliable results. Early research using progesterone showed promise, but these studies were too small, and the methods and populations were too diverse, to yield conclusive results. Working collaboratively in the NICHD's Maternal-Fetal Medicine Units Network, researchers administered either progesterone (17P) or a placebo to a large group of women who had delivered a previous preterm infant. The 17P-treated women were 30 percent more likely than placebo-treated women to carry their babies to term, and their infants had lower rates of life-threatening complications. African American women benefited as much as white women from the experimental treatment. Furthermore, the researchers found no evidence that 17P caused birth defects or any other problem in the infants of treated mothers. Thus, 17P is a significant breakthrough that holds tremendous promise for reducing preterm birth and life-threatening medical complications in infants of high-risk women. This treatment may also help to reduce the entrenched disparity in birth outcomes for African American infants.

More Babies Survive When Air is Clean. Scientists agree that people who live in areas with polluted air tend to have more health problems. Scientists don't agree, however, as to whether air pollution actually *causes* the health problems and higher mortality. Areas with higher air pollution also tend to have high population densities, low income levels, and high crime rates, all of which could impact health unfavorably. Further, most previous air pollution research focused on adverse health effects in adults, with little attention paid to children due to the complexities of the issues involved. For instance, children may become ill from exposures that would not affect adults, and children may be more vulnerable to some environmental pollutants than are adults due to their size, growth, and behaviors. An economic recession in 1981-82 provided scientists with a kind of natural laboratory to observe the effects of pollution. The economic slowdown reduced air pollution in selected geographic regions. NICHD-supported researchers were able to demonstrate a causal link between total suspended particulate air pollution and changes in infant death rates. The researchers estimated 100 fewer infant deaths per 100,000 live births occurred during this time of lower air pollution. Most of the decline was observed in very young infants between one day and one month of age. These findings strongly suggest that babies who live in clean air areas have a greater chance of living until their first birthday. The findings also have important implications when determining the cost-benefits of policies aimed at reducing certain types of air pollution and in developing federal, state, and local zoning and air pollution standards. Finally, the findings suggest that obstetrical and pediatric health care providers should more closely monitor their patients in high-risk environments.

Modifiable Risk Factors Associated with the High Rate of Sudden Infant Death Syndrome (SIDS) among Northern Plains Indians. The SIDS rate among American Indians (AIs) is the highest of any population group in the United States and overall is slightly more than double that of whites.

The disparity is most acute in the Aberdeen Area of the Indian Health Service (AAIHS), where the SIDS rate is four times greater than that of the U.S. population.[9] The NICHD collaborated with the AAIHS, Centers for Disease Control and Prevention, and the Aberdeen Area Tribal Chairman's Health Board to study infant mortality among AIs and to identify prenatal and postnatal modifiable risk factors that would reduce SIDS risk. The project, which utilized maternal interviews, standardized post mortem procedures, and medical chart reviews, revealed that even one visit by a public health nurse during pregnancy or after birth reduced the infant death rate due to SIDS by one-fifth compared to homes never visited. Furthermore, a mother's binge drinking (five or more drinks at a time) during the first trimester of pregnancy was associated with an eight-fold increased likelihood that her infant would die of SIDS. Finally, infants usually wearing two or more layers of clothing at night, not including the diaper, were six times more likely to die of SIDS. These findings highlight several, key SIDS risk factors that can be targeted in future intervention programs for the AI population.

Encouraging Well-Child Care as a Strategy against Infant Mortality. Despite substantial progress, wide racial disparities in infant mortality remain in the United States. The gap is particularly wide in Washington, D.C., where mortality rates for African American infants in 2000 were 16.1 infant deaths per 1,000 live births–more than double the national rate of 6.9 per 1,000, for all races.[10] A randomized, controlled trial, which was part of the NICHD-funded D.C. Initiative to Reduce Infant Mortality, tested a unique program of educational and supportive services for high-risk mothers and their infants. Nearly all of the mothers in the program were African American, had inadequate or no prenatal care, and had other risk factors including poverty and low educational levels. The program, Pride in Parenting (PIP), provided mothers with information about child health and development and health and social service resources available to them. This information, along with training and social support for the mothers, was provided in home visits, parent-child developmental play groups, and parent support groups. Unlike similar programs that used nurses for home visits, the PIP program achieved better acceptance by recruiting lay visitors from the mothers' own communities, and by training them extensively in child health and development before they began visiting the mothers. Another unique feature was that program staff neither arranged for nor accompanied mothers to health care and social service sites; instead, mothers were given information on available resources and coached in using services, but were solely responsible for ensuring that their children received the well-child care and immunizations. The program deliberately used lay home visitors to lessen the cultural barriers to health care that account, in part, for disparities in infant mortality and morbidity. Compared to mothers who used standard social services, mothers in the PIP program were more likely to 1) begin well-child care earlier, 2) make more frequent well-child care visits, and 3) complete the scheduled immunizations for their infants. If successfully replicated, this model program could enable minority mothers to seek and use health care for themselves and their children more effectively.

Child Health and Development. NICHD research seeks to assure that all children have the opportunity to fulfill their potential for a healthy and productive life, unhampered by disease or disability. During the previous year, research funded by the NICHD found new ways to safeguard the nation's children from abuse, disease, and injury.

School-based Early Education Reduces Child Abuse and Neglect. Each year, approximately three million cases of suspected child abuse and neglect are reported to U.S. child welfare agencies. Estimated federal and state expenditures on child welfare services exceed $11 billion. Approximately 30 percent of confirmed cases of child abuse result in placement of children outside the home, at a yearly cost of $22,000 or more.[11] Researchers recently reported, however, that significant human and financial cost savings could be realized by reducing risks of child maltreatment with a school-based program combining enriched early education for children with extensive support services for their parents. Children in Chicago's poorest neighborhoods who attended such a program had a 52 percent lower rate of being abused and neglected, compared with similar children not in the program. The greatest reduction in risk of child maltreatment occurred among the poorest children in the program and among those that stayed in the program from beginning to end (age three to second or third grade). The risk reduction was also long-lasting and actually strengthened in children age 10 to 17 years, well after they and their parents finished the program. These findings, from a longitudinal study of the Child-Parent Centers (CPCs) of the Chicago School District, contrast with the mixed record of child abuse prevention programs that offer similar services, but typically for shorter periods of time and in non-school settings. Researchers attribute the positive effects of the Chicago schools' program to 1) improving the child's academic and behavioral performance, thereby increasing parents' satisfaction with their child and lessening negative family interactions; and 2) addressing parents' poor parenting practices, low educational levels, social isolation, and other stressors that contribute to the risk of child maltreatment. Cost savings attributable to the CPC program appear to be substantial. The researchers reported that the per-child cost of the enriched early education program is about half of the weighted average annual per-child cost of $9,492 (1998 dollars) of child welfare services generally.

Children Not Harmed by Mothers Leaving Welfare and Going to Work. Major federal welfare reform legislation of 1996 created work requirements for parents on welfare and raised concerns about the effects on children of welfare mothers entering the workplace. With NICHD support, and co-funding from the National Institute of Mental Health (NIMH), five other Department of Health and Human Services (DHHS) agencies, and 14 private organizations, researchers are following a large sample of children in three cities (Boston, Chicago, and San Antonio) whose mothers are moving from welfare to work. The researchers are assessing cognitive achievement, problem behaviors, and psychological well-being in preschool-age children and young adolescents. Findings from the first period of the study (1999-2001) do not show either significantly negative or positive effects in the preschoolers that could be attributed to a parent leaving welfare and entering the workforce.[12] The researchers reported similar results in the older children. In fact, they reported some gains in the adolescents' well-being, which were associated with their mothers' entry into the workforce. These first findings should help to allay concerns about immediate adverse impacts on children of the welfare reform work requirements. Researchers will continue to follow the children to assess longer-term effects.

New Clues to Autism Spectrum Disorders Emerge. Autism spectrum disorders (ASDs) are complex biological disorders of development that impair an individual's capacity to interact and communicate with other people and that may limit the individual's activities and interests. ASDs vary in severity and, depending on diagnosis, affect 10 to 20 of every 10,000 people.[13] New data from clinical centers in the Collaborative Programs of Excellence in Autism add to the growing

body of evidence that may ultimately explain the atypical brain development that occurs at the cellular level in ASD. In one study of three- and four-year-old children with ASD, researchers found that concentrations of five neurochemicals implicated in healthy brain functioning differed significantly in ASD children, compared with concentrations in typically-developing (TDs) three- and four-year-olds. The atypical neurochemical levels occurred throughout various regions of the brain in children with ASD. Because earlier studies indicated that structural anomalies associated with ASD are similarly dispersed, the findings on neurochemical levels add new evidence that atypical development in ASD is not limited to a single region of the brain. Findings from other studies also add to the growing body of evidence on atypical head and brain sizes in individuals with ASD. In one study of three- and four-year-old children with ASD, researchers found that children's brain volumes were significantly larger (9.8 percent) than those of TD children. A second study indicated that the accelerated brain development observed in younger children with ASD stopped by age 12. Researchers concluded that larger head circumferences in adolescents and adults with ASD resulted from early excess brain growth, but their larger, overall head sizes do not accurately reflect brain volumes.[14] Together, these studies can help scientists to better understand the developmental and physiological mechanisms contributing to ASD to identify accurate markers of this complex disorder and, ultimately, to develop new and improved interventions.

Reducing Teens' Motor-Vehicle Accidents by Promoting Parental Limits on Teen Driving. Among adolescents ages 16 through 20, injuries from motor vehicle crashes are the major cause of death.[15] In 2000, nearly 5,000 teenagers died of injuries from motor vehicle crashes, which accounted for 14 percent of all motor vehicle-related deaths, yet teens represented only ten percent of the U.S. population.[16] NICHD researchers addressing this important issue recently reported that a program ("Checkpoints Program") could persuade parents that they could lessen their teenage children's risk of traffic accidents by setting clear, safety-related limits on the teens' driving privileges. The program also teaches parents how to set such limits. In addition to educational materials for parents and teens, the program includes model "driving agreements," to help families negotiate safety limits on teens' driving. Different versions of the program were tested in two states and both versions showed that participation in the program was associated with greater levels of parental controls on teen driving. These studies built on earlier research showing that closer parental involvement with their teenage children could reduce some of their other risk-taking behaviors, and that parents may underestimate their own ability to influence their children's behaviors. Because the explicit parental limits recommended by the program would reduce practices known to contribute to teen traffic accidents, such as driving at night or with multiple teenage passengers, the program could ultimately reduce rates of adolescents' motor vehicle crashes.

HIV and AIDS. Much of NICHD's HIV and AIDS research seeks to prevent HIV transmission from mother to child, and to understand the disease in adolescents. New NICHD studies uncovered affordable ways to help prevent transmission in poor countries unable to provide expensive anti-HIV treatments. Other research findings shed new light on how the course of infection may differ in HIV-infected teens.

Affordable Options for Poor Countries. By the end of 2002, an estimated 42 million people worldwide were infected with HIV.[17] The global epidemic was disproportionately concentrated

in sub-Saharan African and other countries that could least afford programs to prevent and treat HIV infection. Of the estimated 800,000 new cases of HIV resulting from mother-to-child (vertical) transmission, 90 percent occurred in sub-Saharan Africa.[18] The risk of vertical transmission can be reduced if an HIV-infected woman is treated with zidovudine (ZDV) during pregnancy and labor, in addition to treating her newborn. A shortened treatment with ZDV, at the time of birth, can also reduce transmission of the virus. But infected mothers can pass HIV on to their infants during breastfeeding. In the developed world, mothers with HIV are advised not to breastfeed, but to give their infants formula, instead. In developing countries, however, formula feeding may pose a danger of its own. In areas lacking water purification systems, disease organisms in the water used to prepare formula may pose an even greater danger than does HIV. By 1999, researchers conducting a study in Uganda reported that giving single doses of the inexpensive drug nevirapine to HIV-infected women as they were giving birth and to their newborns reduced the chances of vertical HIV transmission by 47 percent when infants were tested for infection at three months of age. However, there still remained the concern about longer-term protection because nearly all of the women in the study breastfed their infants for about 9 months. Researchers continued to follow the infants and recently reported that nevirapine-treated infants were still much less likely to be HIV-infected when the infants were 18 months old.

Pregnancy and Progression of HIV Disease in Women. Although ZDV sharply reduces a pregnant woman's chances of passing HIV on to her child, many are concerned that this benefit would come at the expense of the mother's own health. Specifically, could women in the early stages of HIV infection, who would not take anti-HIV drugs if they were not pregnant, speed the course of their own disease? Could such temporary exposure to ZDV allow the virus to develop resistance to the drug? NICHD-supported scientists recently found that when pregnant women in the earliest stages of HIV infection took ZDV temporarily, they did not experience accelerated HIV disease or excessive ZDV resistance for as long as four years after giving birth. Another study of women who took ZDV during a more advanced stage of HIV disease found a significant but very small increase in levels of the virus 18 months after the women gave birth. Because this small increase occurred both in women who stopped ZDV after delivery and those who continued it, scientists think that the slight elevation in HIV virus levels could stem, at least in part, from such pregnancy-related factors as changes in hormone levels or maternal blood volume following delivery. The findings from the two studies indicate that temporary use of ZDV during pregnancy and delivery neither accelerates HIV disease nor negatively affects a woman's response to later drug therapy. In another study, researchers found that a second pregnancy in an HIV-infected woman who has already had a child does not significantly affect the course of her disease. Together, these studies should help HIV-infected women and their physicians make more informed choices to protect the health of the mother as well as that of her child.

Clue to Adolescent Immune System's Response to HIV Infection. Half of all new HIV infections occur in young people under 25 years of age.[19] Since the time between HIV infection and AIDS diagnosis averages about ten years, scientists believe that many, if not most, adults diagnosed with AIDS in their twenties were infected with the virus as adolescents. However, little is known about the HIV disease process in adolescents and about the best ways to treat the disease in this age group. Because so many developmental changes are occurring, treatments suitable for adults may not apply to adolescents who are infected with HIV. Researchers recently uncovered an

important clue to better understand HIV infection in adolescents. Adolescents with HIV appear to have a higher number of the infection-fighting T-cells than do adults with the virus. These cells are a special target for the HIV virus. Researchers discovered that adolescents in the early stage of HIV infection had an unexpectedly disturbed immune response. The disturbance coincided with the virus reproducing itself rapidly. This altered immune response may indicate that the adolescents' immune systems are already affected even before the infection can be detected by standard monitoring. What appeared to be a clinical state of equilibrium between the immune system and the virus, in reality, may be masking a profound change in immune cell function in HIV-infected youth. This finding opens intriguing questions about the processes of HIV infection and immune-system destruction in adolescents and suggests that this age group may need interventions that go beyond the current approaches to treat HIV in adults.

More Effective Contraception. The NICHD seeks to assure that all children are born healthy and wanted, and that couples can have the families they want when they are ready for them. During the previous year, NICHD-supported scientists gained new insights into the biology of reproduction. These insights may lead to the development of new contraceptive methods.

A Possible New Approach to Contraception. Oocytes, or egg cells, must mature before sperm can fertilize them. This maturation starts with a surging release of luteinizing hormone (LH) from the pituitary gland. In turn, LH activates an enzyme called phosphodiesterase (PDE). This enzyme reduces the high levels of another chemical, cyclic adenosine monophosphate, which keeps oocytes in an immature state. These findings suggest that PDE plays a key role in allowing fertilization to occur. Researchers have known that in rats and mice given a compound that inhibits PDE3 (a form of PDE), the oocytes fail to mature and cannot be fertilized. Until recently, however, they didn't know if the inhibitor would work the same way in non-human primates, thus offering insights into what may happen in the human body. Now, NICHD-supported researchers found that the PDE3 inhibitor also prevents monkey oocytes from maturing. This finding provides the basis for researchers to examine whether interrupting maturation of the egg cell could lead to a new, safe, and effective contraceptive approach for women, which would work well before fertilization occurs.

Improving Pregnancy Outcomes. Much of NICHD's research focuses on ensuring that women can carry their pregnancies successfully to term. Last year, researchers provided new insight into the events that must take place before a pregnancy can be established, which could lead to new treatments for infertility. Other studies provide insights on guidelines concerning the duration of labor.

Discovering How an Embryo Attaches to the Uterus. A recent NICHD-supported study sheds new light on understanding the first biological steps needed to establish a successful pregnancy. About six days after fertilization, the embryo, or blastocyst, is shaped like a sphere. Its surface is composed of a layer of specialized cells called the trophoblast, which later gives rise to cells that form the fetus' part of the placenta (the placenta is made up of both maternal and fetal tissue). The trophoblast is coated with a protein known as L-selectin, while the wall of the uterus is coated with carbohydrate molecules. Researchers uncovered evidence that as the blastocyst travels along the uterine wall, L-selectin on its surface binds to the carbohydrates on the uterine wall, until the blastocyst gradually slows to a complete stop. The process is similar to a tennis

ball coming to a stop after rolling across a syrup-covered table. Only after the binding takes place, can the fetus implant itself in the uterine wall and a pregnancy begin. This finding may lead to insights into early pregnancy loss and the life-threatening complication of pregnancy known as preeclampsia, both of which may result from failures of the embryo to attach properly to the uterine wall.

Moreover, the finding may lead to a better understanding of some cases of endometriosis-associated infertility. Endometriosis is a disorder in which endometrial tissue–tissue that normally lines the inside of the uterus–begins growing in other parts of the abdomen, such as the outside of the uterus, ovaries, or intestines. Endometriosis affects 10 to 15 percent of women of reproductive age, and is a major cause of infertility in women who have difficulty becoming pregnant.[20] Another NICHD-supported research team found that women with infertility due to endometriosis have very low levels of the enzyme that makes the ligand for L-selectin. The ligand is a rubber-band like molecule that tethers L-selectin to the uterine wall. Researchers believe that without this enzyme, the embryo cannot attach to the uterine wall and a pregnancy cannot begin. The finding may lead to new therapies to treat women with endometriosis-related infertility.

New Standard for Labor and Delivery. More women are giving birth by cesarean section than in previous years, with more than one-fourth of all pregnant women, 26.1 percent, undergoing the procedure in 2002, up from 20.8 percent in 1997.[21] Such factors as a woman's age and general health play a role in doctors' decisions to perform a cesarean section. A recent NICHD study, however, shows that the criteria on which doctors base their decision may no longer apply. Since the mid-1950s, physicians have based labor and delivery practices on the Friedman labor curve, a mathematical model depicting how the stages of labor should progress during normal delivery. However, on average, the characteristics of women giving birth today differ markedly from the population used to devise the Friedman labor curve. Compared to 50 years ago, obesity is far more prevalent, and women give birth later in life. Recently, researchers examined the pattern of labor progression in women in the 1990s giving birth for the first time. The researchers concluded that the Friedman criteria may be too stringent to determine when labor is proceeding much slower than expected. Moreover, the Friedman criteria may not apply to arrest disorders of labor, where the cervix does not dilate for two or more hours. In essence, researchers found that, for today's population of women, labor progressed more slowly than what was once identified as "normal" in the Friedman curve. These findings could have a profound impact on decisions about the need for cesarean delivery.

Compounds Prevent Alcohol from Damaging the Fetus. As many as 12,000 babies are born each year with fetal alcohol syndrome.[22] It is considered the most common non-hereditary form of mental retardation. Currently, however, no medication exists that can prevent alcohol's harmful effects on the developing fetus. This may change now that scientists from the NICHD and the NIMH recently found that NAP and SAL, the active peptides from two brain proteins known to protect nerve cells against a variety of toxins, also protect mouse embryos from ethanol-induced fetal death and growth abnormalities. The researchers also discovered that these peptides interfere with the way ethanol disrupts the chemical ties that hold cells together. NAP protected cells to a greater degree than did SAL, completely preventing ethanol from breaking these chemical ties, even in the presence of ethanol concentrations that kill cells. These discoveries

strengthen the case that ethanol causes birth defects by interfering with cell adhesion. Understanding this process may help researchers design drugs to prevent some of the effects of fetal alcohol syndrome.

Fetal Origins of Adult Disease. Obesity, type 2 diabetes, high blood pressure, and heart disease are becoming increasingly common in the United States. Researchers want to understand whether the environment in the womb plays a role in the development of these disorders during adulthood. Recently, NICHD-supported researchers studied the adult children of mothers who received dietary advice during their pregnancies in 1967-68. The women were told they could prevent high blood pressure by consuming one pound of red meat per day and to cut back on carbohydrate-containing foods like bread and pasta during the second half of their pregnancies. Researchers found that the more meat the women consumed during pregnancy, the higher their adult children's stress hormones were and the higher their blood pressure readings. Stress hormone levels were also higher in the adults whose mothers consumed few green vegetables during their pregnancy, with the highest levels found in those whose mothers consumed the highest amount of meat and the least amount of green vegetables. This research adds to the theory that adult diseases may have their origins in fetal life, and offers new insight into the kinds of diet women need to maintain healthy pregnancies.

NIH ROADMAP

Two major themes of the NIH Roadmap are to develop and disseminate technologically sophisticated resources that capitalize on the sequencing of the human genome, and to reinvigorate the clinical research enterprise.

Building on the success of the human genome project, the quest to understand the causes of disease is moving to ever more in-depth levels. Such efforts require access to new tools that are extremely complex and costly to develop. For this reason, it is important to create large-scale national resources that scientists can use, as needed, rather than having to develop such tools for individual research projects. Examples are databases that contain large amounts of genetic information and the computational infrastructure to analyze it. Also needed are libraries of molecules that researchers can use to understand the molecular events occurring in normal tissue, as well as what goes wrong in disease states. Resources being developed through the Roadmap will enable scientists to probe deeper than ever before into the biology of human systems. Together with these activities, the NICHD plans to develop such resources, customized for research on premature birth and on primary immunodeficiencies (PIDs). The first NICHD initiative will collect, process, analyze, and disseminate information on human genes pertaining to premature birth as well as to the proteins that result from activity of these genes. The resulting national database will offer researchers new tools to search for causes of premature birth at the molecular level. The second initiative will attempt to identify genes and proteins involved in PID in infants to improve treatments for the condition. Both of these efforts should contribute to the success of the newborn screening initiative described in the next section.

Another Roadmap initiative seeks to re-engineer the patient-oriented, or clinical, research enterprise. It takes a holistic vew of clinical research by addressing infrastructure, training, patient access, and the regulatory framework. This approach is intended to identify and

implement needed and systemic improvements in clinical research, particularly in the conduct of clinical trials. The NICHD has been most involved with those initiatives to develop and better train members of multi-disciplinary clinical research teams–physicians, dentists, nurses, pharmacologists, epidemiologists, and other professionals–in unprecedented ways. These new teams will provide the capability to expand clinical research and help to more rapidly translate scientific findings into practices and treatments that directly benefit patients. One initiative will identify barriers to attracting community physicians to participate in clinical research and ways to overcome those barriers. Bringing community physicians into clinical research on a large scale will increase patient access to clinical trials. This, in turn, should speed completion of trials and the availability of new treatments to patients. Another initiative will support the early career development of clinical researchers to build the research teams of the future. These Roadmap efforts will benefit all clinical research, whether it is targeted to children, adolescents, or adults, and enhance the nation's ability to identify successful interventions for preventing and treating a wide range of diseases and debilitating conditions.

NICHD INITIATIVES

Overcome Today's Challenges with Tomorrow's Advances. Over the decade, the NICHD plans to harness and translate rapidly emerging scientific and technological advances to overcome the challenges facing our nation's children, families, and communities.

Innovative Methods of Newborn Screening. Nationwide, newborns are screened routinely for only two disorders: phenylketonuria (PKU) and congenital hypothyroidism. Screening and initiating treatment before symptoms develop prevents severe mental retardation that can result from these disorders. Some states screen for other conditions using techniques such as tandem mass spectrometry that allows about 40 conditions to be detected at birth. Application of new microchip technologies that analyze DNA and proteins hold the potential to identify hundreds more. A panel convened by the DHHS Secretary recommended that the Nation expand and standardize its approach to newborn screening. Given its mission, the NICHD will embark upon a major new initiative to address this research priority. As a first step, the Institute will support development of new microarray chip technologies for newborn screening that can be expanded to screen for many disorders. The goal is to screen newborns for a wide range of genetic diseases that cause mental retardation, immunodeficiency, muscular dystrophy, cystic fibrosis, blood-clotting disorders, and other conditions more inexpensively and effectively, with just one major step, at birth, when chances for treating them successfully are greatest. Large numbers of infants with disorders lacking effective treatments will also be identified so that these children can be enrolled in clinical trials, and eventually effective new therapies can be developed. Thus, this newborn screening initiative will go beyond just providing innovative methods to diagnose disorders, and will become an essential tool for preventing adverse consequences of them as well.

Drug Treatment During Pregnancy and for Mothers Who Breastfeed Their Infants. Over the years, physicians have prescribed drugs to treat millions of pregnant or nursing women with conditions such as asthma, heart disease, and depression. Yet, comparatively little is known about the effects of such drugs in women with genetic differences in how they metabolize drugs. Currently, models exist to simulate how changes in the body of the mother during pregnancy and

lactation influence the disposition of chemical toxins. The information used to devise these models can be used to design new models to help simulate and predict how a broad range of treatment drugs affect pregnant women and nursing mothers. Such models would help researchers better understand how mothers might vary in their response to these drugs, requiring only minimal human studies. This knowledge can then be used to develop improved approaches to optimize treatment outcomes. The NICHD plans to support an effort to devise these models at a number of research centers. Bringing together researchers from a number of different scientific areas will allow the models to be developed more quickly and efficiently. More importantly, the results from this initiative will help physicians prescribe drugs in a way that will be least likely to produce adverse effects.

Research Networks to Improve Treatment for Critically Ill Children. Critical care medicine for children remains a pioneering field, as physicians continue to extrapolate treatment regimens from "adult" care, which have not yet been tested for their effectiveness in a young population. The NICHD will lead the development of a national pediatric critical care research network to accelerate research in the field and to provide subsequent, optimal rehabilitative care to minimize the number of children developing disabling conditions. The initiative will foster collaborations among scientists in many different fields, to compare the effectiveness of new treatments to existing ones. Some expected studies will include 1) developing the best approach to care for children with brain injury, 2) understanding the most effective way to transition a critically ill child from an acute care to a rehabilitation setting, and 3) preparing to care for children who are critically ill in the event of a bioterrorism attack.

Research on How to Best Prepare Young Children for Later School Success. Improving the educational attainment of all children is a national priority, for the American public, the President, and the Congress. The No Child Left Behind Act links federal funding to educational attainment, starting in the preschool years. However, few, if any, research-based criteria exist to measure children's intellectual, social, and emotional development in the early years, particularly on a large scale. A few tests measure limited aspects of intellectual development in English-speaking preschoolers on a large scale. Yet educators have no scientifically proven methods to design tests for millions of non-English speaking, ethnically diverse, educationally-at-risk preschoolers. The NICHD, in collaboration with other federal agencies, plans to develop, refine, validate, and improve the testing required to assess the school readiness of the nation's preschoolers. The results should provide the critical foundation for evaluating national, state, and local interventions that are implemented in relation to the No Child Left Behind Act, and that are of interest to educators and other policymakers.

Trans-NIH Obesity Initiative. The NICHD will lead and participate in several initiatives to address the nation's obesity epidemic, which threatens the long-term health of over 30 percent of adults in the United States, and which often begins in childhood or adolescence.[23] In the last 40 years, the prevalence of overweight children and adolescents has increased by over three-fold.[24] At the same time, an alarming increase exists in the number of children with one or more risk factors for heart disease, most specifically type 2 diabetes. A variety of strategies have been developed to prevent or treat overweight in children and adolescents. However, no single approach has been effective on a scale needed to control this runaway epidemic in the United States. In response, experts now call for researchers to develop a comprehensive approach,

involving the physician's office, the home, schools, pre-school centers, and the community at large.

As a first step, the NICHD will lead a major effort to determine whether primary care physicians can effectively lead comprehensive, community-based weight control programs. Currently, most weight management programs are administered through specialty clinics. Successful programs in primary care settings would be accessible to larger numbers of children and minimize geographic, social, and economic roadblocks to weight control therapy. The Institute will also partner with the National Institute of Diabetes and Digestive and Kidney Diseases to examine ways to help children effectively manage their weight in a variety of different settings–at home, in pre-school, in school, and in other community venues. Finally, the NICHD will collaborate with the National Institute of Environmental Health Sciences to examine if the way a community is physically designed affects overweight and its associated health conditions. The overall goal is to develop innovative and affordable community master plans that promote healthful environments and healthy living.

OTHER AREAS OF INTEREST

NICHD Community Partnerships to Reduce SIDS

African American Outreach Initiative. SIDS rates for African American babies have declined significantly in recent years. Yet, they still remain more than twice those of white infants.[25] To address this health disparity, the NICHD joined with the Alpha Kappa Alpha Sorority, Inc. (AKA), the National Coalition of 100 Black Women, and the Women in the NAACP in a unique, year-long collaboration, "Partnerships for Reducing the Risk of SIDS in African American Communities." The effort produced three regional summit meetings to raise SIDS awareness. The meetings provided the forum to instruct African American men and women, from all walks of life, so they could return to their communities and teach others simple ways to help reduce the risk of infant deaths due to SIDS. Meeting participants received outreach "kits," designed by the NICHD in collaboration with community-based organizations, that stressed the need to place infants on their backs to sleep. The summits also helped build an infrastructure–which includes faith-based, community, and service organizations–that can now be used to disseminate an array of future health messages.

For instance, the AKA extended the Detroit summit with a unique finale, called "SIDS Sunday," which was held as a "kickoff" event at Hartford Memorial Baptist Church in Detroit, the Sunday following the summit. Afterwards, the AKA leadership recruited other churches across the region to hold a "SIDS Sunday," where pastors shared SIDS information from their pulpits, in their church bulletins, and with nurses and caregivers in their childcare centers and nurseries. The successful collaboration of researchers, government officials, and the community will create a strong foundation for launching other interventions to eliminate health disparities.

American Indian/Alaskan Native Outreach Initiative. Like the African American community, SIDS rates in American Indian and Alaskan Native (AI/AN) communities remain more than twice those of white infants, despite the overall progress in reducing SIDS.[26] Building on previous successful efforts, the NICHD is now collaborating with key community members to develop outreach activities and products that encourage parents and families to place babies on

their backs to reduce infant deaths due to SIDS. The Institute launched the collaboration by hosting a meeting with AI/AN community leaders, from regions across the United States that have the highest rates of SIDS. The meeting was held to discuss infant mortality and SIDS, and to gather information about health, cultural, and other challenges for developing a SIDS outreach campaign. The Institute held a follow-up meeting with public health nurses, health educators, community health representatives, tobacco-prevention coordinators, and family members. Working together, the participants agreed to develop a community-driven campaign and strategies to preserve cultural traditions, starting by using existing lines of communication to spread the important health message that babies sleep most safely on their backs.

INNOVATIONS IN MANAGEMENT AND ADMINISTRATION

The NICHD is building on existing databases and taking advantage of the newest computerized technologies to improve the efficiency of decision making and various tasks that support the NIH mission.

Management Dashboard. The design and styling of the automotive dashboard not only enhances aesthetics but captures how the car is performing and alerts the driver to potential problems. Building on this concept, the NICHD created a management "dashboard." This computer-based tool provides access to crucial operational and performance-related data in a way that is easy to understand, allows users to interact with data in new ways, and integrates information from multiple sources in easy-to-view graphs and reports. Specifically, the Dashboard tracks commonly used financial and administrative indicators such as appropriation spending rate, number of employees, and number of grant applications remaining to process prior to award. It can also be used to track the progress of scientific and infrastructure initiatives. The Dashboard is continually being enhanced with measures derived from an expanding array of existing NIH and NICHD data sets. Ultimately, the goal is to provide managers with faster and more accurate access to information critical to enhanced decision making.

Improved Web-based Access to Council Information. The National Advisory Child Health and Human Development (NACHHD) Council is charged with advising, consulting with, and making recommendations to the Director, NICHD, on matters relating to the research and research support activities and functions of the Institute. Over the course of a year, Council members may provide secondary review for over 1100 grant applications, and staff may prepare numerous recommendations and special actions. To ease this workload, the NICHD developed simple computer-based tools to make key information more readily available to Council members, senior managers, and grants administrative and scientific staff. For example, staff can easily use the web-based system to recommend a grant application for funding and prepare a justification for NACHHD Council, or to generate letters to notify investigators about the funding status of their application. The new systems significantly improve the efficiency of the Institute's internal review and approval of staff recommendations, as well as decrease the time required to notify applicants of funding decisions.

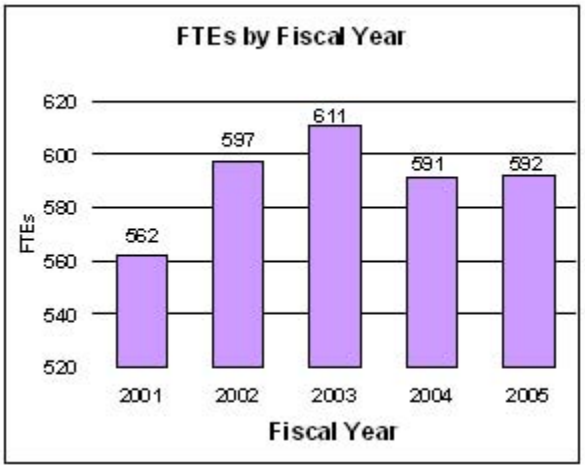
In addition, the NICHD provided Council members with a re-designed web site that allows them to easily access the information they need prior to attending NACHHD Council meetings. It also

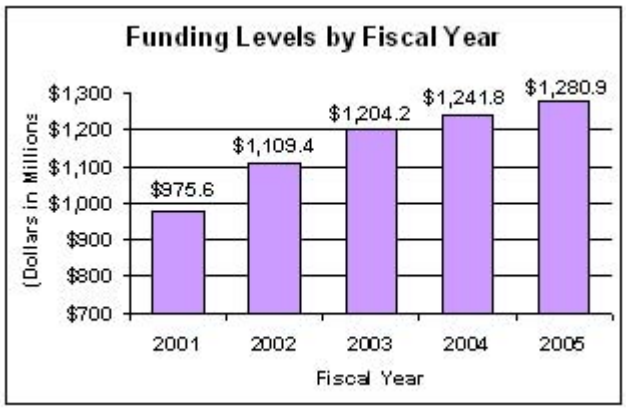
enables members to review approved staff recommendations, vote on whether to expedite grant awards, and view the Institute's portfolio for a given Council meeting. The streamlined business processes, coupled with the availability of a single access point for Council members and Institute staff, allows everyone to prepare for and conduct NACHHD Council meetings more efficiently.

BUDGET POLICY

The Fiscal Year 2005 budget request for the NICHD is $1,280,915,000 an increase of $39,070,000 and 3.1 percent over the FY 2004 final conference level. Also included in the FY 2005 request, is NICHD's support for the trans-NIH Roadmap initiatives, estimated at 0.63% of the FY 2005 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. Note that the Fiscal Year 2001 FTE figure is not comparable to the figures in the succeeding years due to NIH's consolidation of its Human Resources function.





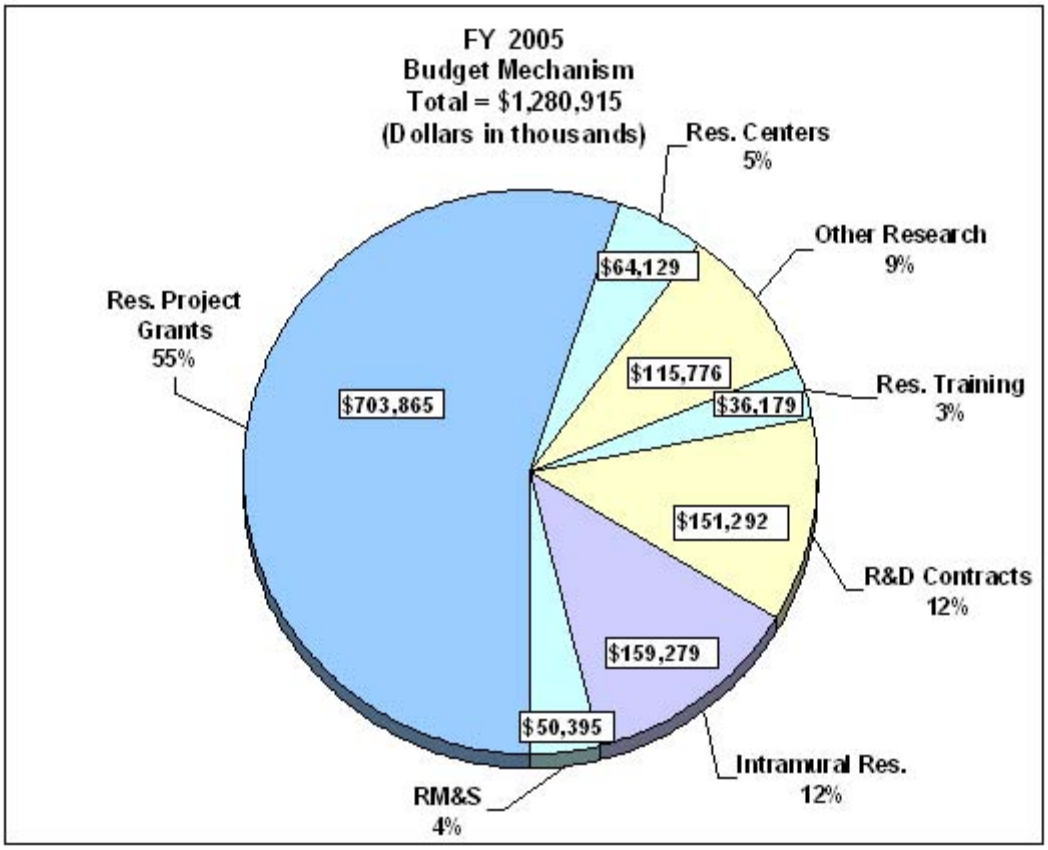
NIH's highest priority is the funding of medical research through research project grant (RPGs). Support for RPGs allows NIH to sustain the scientific momentum of investigator-initiated research while providing new research opportunities. The FY 2005 NIH request provides for an aggregate 1.3 percent increase in average cost for research project grants, consistent with the Gross Domestic Product deflator. The NICHD is providing an average cost increase of 1.9 percent for direct recurring costs in noncompeting continuation awards. Competing RPGs are based on an average cost increase of 1 percent. As a NIH program initiatives, the NICHD request includes an increase of $3,000,000 in the research project grants mechanism for research on childhood obesity.

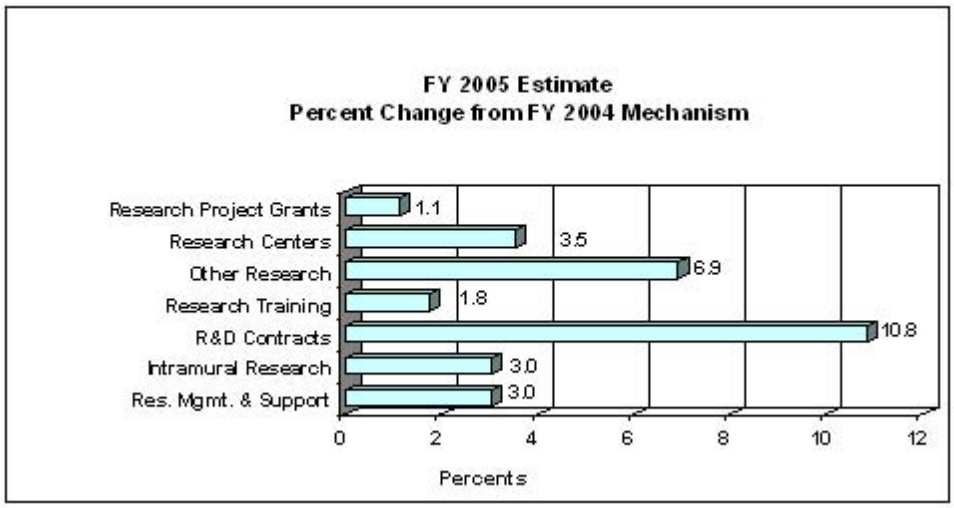
Advancement in medical research is dependent on maintaining the supply of new investigators with new ideas. In the Fiscal Year 2005 request, NICHD will support 852 pre- and postdoctoral trainees in full-time training positions. Stipend levels for pre-doctoral and post-doctoral

recipients supported through the Ruth L. Kirschstein National Research Service Awards will remain at FY 2004 levels.

The Fiscal Year 2005 request includes funding for 43 research centers; 591 other research grants, including 411 career awards; and 207 R&D contracts. Intramural Research and Research Management and Support receive increases to support increased pay and estimated inflationary increases in FY 2005.

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





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NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

Budget Mechanism - Total

MECHANISM	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects:						
Noncompeting	1,297	$515,858,000	1,331	$534,500,000	1,280	$527,240,000
Administrative supplements	(65)	6,691,000	(70)	6,717,000	(71)	7,021,000
Full funded	12	1,690,000	12	2,119,000	12	2,140,000
Single year	496	147,267,000	407	124,853,000	449	138,734,000
Renewal	93	45,955,000	76	38,960,000	83	42,909,000
New	399	100,661,000	328	85,340,000	361	95,221,000
Supplements	4	651,000	3	553,000	5	604,000
Subtotal, competing	508	148,957,000	419	126,972,000	461	140,874,000
Subtotal, RPGs	1,805	671,506,000	1,750	668,189,000	1,741	675,135,000
SBIR/STTR	112	26,334,000	90	27,894,000	91	28,730,000
Subtotal, RPGs	1,917	697,840,000	1,840	696,083,000	1,832	703,865,000
Research Centers:						
Specialized/comprehensive	48	61,670,000	42	60,911,000	42	62,816,000
Clinical research	0	0	0	0	0	0
Biotechnology	0	250,000	1	783,000	1	1,063,000
Comparative medicine	0	250,000	0	250,000	0	250,000
Research Centers in Minority Institutions	0	0	0	0	0	0
Subtotal, Centers	48	62,170,000	43	61,944,000	43	64,129,000
Other Research:						
Research careers	366	36,477,000	406	40,630,000	411	41,852,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	80	38,584,000	92	46,554,000	97	49,485,000
Biomedical research support	0	0	0	24,000	0	30,000
Minority biomedical research support	0	1,144,000	0	0	0	0
Other	102	21,653,000	81	21,073,000	83	24,409,000
Subtotal, Other Research	548	97,858,000	579	108,281,000	591	115,776,000
Total Research Grants	2,513	857,868,000	2,462	866,308,000	2,466	883,770,000
Research Training:	FTTPs		FTTPs		FTTPs	
Individual awards	125	6,037,000	124	6,181,000	124	6,200,000
Institutional awards	715	28,338,000	719	29,373,000	728	29,979,000
Total, Training	840	34,375,000	843	35,554,000	852	36,179,000
Research & development contracts	202	116,572,000	207	136,496,000	207	151,292,000
(SBIR/STTR)	(0)	(0)	(0)	(0)	(0)	(0)
	FTEs		FTEs		FTEs	
Intramural research	393	148,456,000	374	154,579,000	374	159,279,000
Research management and support	218	46,921,000	217	48,908,000	218	50,395,000
Cancer prevention & control	0	0	0	0	0	0
Construction		0		0		0
Total, NICHD	611	1,204,192,000	591	1,241,845,000	592	1,280,915,000
(RoadMap Support)				(4,265,000)		(8,070,000)
(Clinical Trials)		(182,646,000)		(189,400,000)		(196,000,000)

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

Budget Authority by Activity
(dollars in thousands)

ACTIVITY	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate		Change	
	FTEs	Amount	FTEs	Amount	FTEs	Amount	FTEs	Amount
Extramural research		$1,008,815		$1,038,358		$1,071,241		$32,883
Intramural research	393	148,456	374	154,579	374	159,279	0	4,700
Research management & support	218	46,921	217	48,908	218	50,395	1	1,487
Total	611	1,204,192	591	1,241,845	592	1,280,915	1	39,070

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

Summary of Changes

FY 2004 Final Conference				$1,241,845,000
FY 2005 Estimated Budget Authority				1,280,915,000
Net change				39,070,000
	FY 2004 Budget Base		Change from Base	
CHANGES	FTEs	Budget Authority	FTEs	Budget Authority
A. Built-in:				
1. Intramural research:				
a. Within grade increase		$55,100,000		$751,000
b. Annualization of January 2004 pay increase		55,100,000		565,000
c. January 2005 pay increase		55,100,000		628,000
d. One less day of pay		55,100,000		(219,000)
e. Payment for centrally furnished services		26,500,000		795,000
f. Increased cost of laboratory supplies, materials, and other expenses		72,979,000		1,305,000
Subtotal				3,825,000
2. Research Management and Support:				
a. Within grade increase		23,760,000		354,000
b. Annualization of January 2004 pay increase		23,760,000		244,000
c. January 2005 pay increase		23,760,000		271,000
d. One less day of pay		23,760,000		(94,000)
e. Payment for centrally furnished services		4,673,000		140,000
f. Increased cost of laboratory supplies, materials, and other expenses		20,475,000		394,000
Subtotal				1,309,000
Subtotal, Built-in				5,134,000

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

Summary of Changes--continued

CHANGES	FY 2004 Budget Base No.	FY 2004 Budget Base Amount	Change from Base No.	Change from Base Amount
B. Program:				
1. Research project grants:				
a. Noncompeting	1,331	$541,217,000	(51)	($6,956,000)
b. Competing	419	126,972,000	42	13,902,000
c. SBIR/STTR	90	27,894,000	1	836,000
Total	1,840	696,083,000	(8)	7,782,000
2. Research centers	43	61,944,000	0	2,185,000
3. Other research	579	108,281,000	12	7,495,000
4. Research training	843	35,554,000	9	625,000
5. Research and development contracts	207	136,496,000	0	14,796,000
Subtotal, extramural				32,883,000
	FTEs		FTEs	
6. Intramural research	374	154,579,000	0	875,000
7. Research management and support	217	48,908,000	1	178,000
Subtotal, program	591	1,192,937,000	1	33,936,000
Total changes			1	39,070,000

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

Budget Authority by Object

	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Total compensable workyears:			
Full-time employment	591	592	1
Full-time equivalent of overtime & holiday hours	2	2	0
Average ES salary	$150,300	$155,000	$4,700
Average GM/GS grade	11.0	11.0	0.0
Average GM/GS salary	$73,200	$75,500	$2,300
Average salary, grade established by act of July 1, 1944 (42 U.S.C. 207)	$71,200	$73,400	$2,200
Average salary of ungraded positions	107,600	110,900	3,300
OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
11.1 Full-Time Permanent	$28,689,000	$29,798,000	$1,109,000
11.3 Other than Full-Time Permanent	19,049,000	19,768,000	719,000
11.5 Other Personnel Compensation	1,541,000	1,594,000	53,000
11.7 Military Personnel	1,697,000	1,757,000	60,000
11.8 Special Personnel Services Payments	13,600,000	14,400,000	800,000
Total, Personnel Compensation	64,576,000	67,317,000	2,741,000
12.1 Civilian Personnel Benefits	12,779,000	13,239,000	460,000
12.2 Military Personnel Benefits	1,505,000	1,553,000	48,000
13.0 Benefits for Former Personnel	0	0	0
Subtotal, Pay Costs	**78,860,000**	**82,109,000**	**3,249,000**
21.0 Travel & Transportation of Persons	3,160,000	3,207,000	47,000
22.0 Transportation of Things	370,000	376,000	6,000
23.1 Rental Payments to GSA	9,000	9,000	0
23.2 Rental Payments to Others	209,000	212,000	3,000
23.3 Communications, Utilities & Miscellaneous Charges	1,970,000	2,030,000	60,000
24.0 Printing & Reproduction	693,000	705,000	12,000
25.1 Consulting Services	1,300,000	1,320,000	20,000
25.2 Other Services	13,050,000	13,233,000	183,000
25.3 Purchase of Goods & Services from Government Accounts	116,511,000	120,618,000	4,107,000
25.4 Operation & Maintenance of Facilities	873,000	886,000	13,000
25.5 Research & Development Contracts	101,852,000	114,080,000	12,228,000
25.6 Medical Care	2,173,000	2,238,000	65,000
25.7 Operation & Maintenance of Equipment	1,900,000	1,950,000	50,000
25.8 Subsistence & Support of Persons	0	0	0
25.0 Subtotal, Other Contractual Services	**237,659,000**	**254,325,000**	**16,666,000**
26.0 Supplies & Materials	12,800,000	13,400,000	600,000
31.0 Equipment	19,600,000	20,400,000	800,000
32.0 Land and Structures	0	0	0
33.0 Investments & Loans	0	0	0
41.0 Grants, Subsidies & Contributions	886,512,000	904,139,000	17,627,000
42.0 Insurance Claims & Indemnities	0	0	0
43.0 Interest & Dividends	3,000	3,000	0
44.0 Refunds	0	0	0
Subtotal, Non-Pay Costs	**1,162,985,000**	**1,198,806,000**	**35,821,000**
Total Budget Authority by Object	**1,241,845,000**	**1,280,915,000**	**39,070,000**

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

Salaries and Expenses

OBJECT CLASSES	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Personnel Compensation:			
Full-Time Permanent (11.1)	$28,689,000	$29,798,000	$1,109,000
Other Than Full-Time Permanent (11.3)	19,049,000	19,768,000	719,000
Other Personnel Compensation (11.5)	1,541,000	1,594,000	53,000
Military Personnel (11.7)	1,697,000	1,757,000	60,000
Special Personnel Services Payments (11.8)	13,600,000	14,400,000	800,000
Total Personnel Compensation (11.9)	**64,576,000**	**67,317,000**	**2,741,000**
Civilian Personnel Benefits (12.1)	12,779,000	13,239,000	460,000
Military Personnel Benefits (12.2)	1,505,000	1,553,000	48,000
Benefits to Former Personnel (13.0)	0	0	0
Subtotal, Pay Costs	**78,860,000**	**82,109,000**	**3,249,000**
Travel (21.0)	3,160,000	3,207,000	47,000
Transportation of Things (22.0)	370,000	376,000	6,000
Rental Payments to Others (23.2)	209,000	212,000	3,000
Communications, Utilities and Miscellaneous Charges (23.3)	1,970,000	2,030,000	60,000
Printing and Reproduction (24.0)	693,000	705,000	12,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	1,199,000	1,217,000	18,000
Other Services (25.2)	13,050,000	13,233,000	183,000
Purchases from Govt. Accounts (25.3)	64,882,000	66,117,000	1,235,000
Operation & Maintenance of Facilities (25.4)	873,000	886,000	13,000
Operation & Maintenance of Equipment (25.7)	1,900,000	1,950,000	50,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**81,904,000**	**83,403,000**	**1,499,000**
Supplies and Materials (26.0)	12,788,000	13,387,000	599,000
Subtotal, Non-Pay Costs	101,094,000	103,320,000	2,226,000
Total, Administrative Costs	**179,954,000**	**185,429,000**	**5,475,000**

NATIONAL INSTITUTES OF HEALTH

National Institute of Child Health and Human Development

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

FY 2004 House Appropriations Committee Report Language (H.Rpt. 108-188)

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. The Committee also commends NICHD's attempts to further its progress in SIDS research by initiating a third SIDS five-year research plan. This third five-year plan will continue the efforts of the past two five-year plans, which have been responsible for many of the research breakthroughs in the effort to reduce SIDS cases in the U.S. The Committee requests that this five year plan be re-examined to determine the appropriateness and scientific validity of including research on stillbirth and miscarriage as components of the five-year plan. (p.73)

Action taken or to be taken

To formulate the third SIDS five-year research plan, the NICHD convened a working group comprising distinguished scientists and health care professionals from around the country. In collaboration with NICHD staff, the working group identified research objectives and strategies designed to achieve these goals. The working group drew on previous and ongoing planning efforts, conferences, workshops, and research findings to develop a strategic plan for a SIDS research and public health agenda that would guide the Institute over the next five years. The draft plan was placed on the web for public comment. The final plan was published on the NICHD website in the summer of 2001. It is available as a pdf file at: http://www.nichd.nih.gov/strategicplan/cells/SIDS_Syndrome.pdf .

The purpose of the strategic plan is to outline a comprehensive research and public health agenda that builds on past successes and forges new paths of discovery. The recommendations go beyond deaths labeled as SIDS by medical examiners and coroners to include all sudden deaths occurring from late fetal life through infancy and early childhood. The plan defines strategies aimed at improving maternal as well as infant health. It encompasses both basic infant care practices and research based on the latest molecular genetic technologies. This framework will provide researchers with the knowledge and resources needed to illuminate the etiology of SIDS and unexplained stillbirth, and, ultimately, to eliminate these needless deaths.

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 will be carefully explored throughout this SIDS strategic plan. Thus 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 based on the

scientific evidence that 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. In some cases we know the cause and more research is needed in prevention and therapeutics. In others cases we have good leads and need to pursue more research in pathogenesis as well as prevention and therapeutics. Therefore we do not believe it would serve either stillbirth or SIDS research well if we include all stillbirths in the SIDS Strategic plan. The same is true for miscarriages, which are very heterogeneous in cause.

Item

Neurofibromatosis (NF) - Learning disabilities occur with high frequency in children with NF. Enormous advances have been made in NF research in just the past year unlocking the mysteries of how the NF gene is related to learning disabilities, which significantly advances the prospects of finding a treatment for learning disabilities not only in children with NF but in the general population as well. The Committee encourages NICHD to enhance this promising NF research. (p.73)

Action taken or to be taken

The NICHD continues to support neurofibromatosis research. At this time, the NICHD is supporting a conference grant for a meeting, and both a developmental research grant and a long standing program project grant that includes a neurofibromatosis project. NICHD continues to encourage research on NF, including the relationship to learning disabilities, and is considering ways to expand NF research including collaborations with other NIH institutes and the Office of Special Education Research and Services in the Department of Education.

Item

Pre-term labor and delivery - Pre-term labor and delivery is the leading cause of neonatal mortality, and many babies born prematurely have serious physical and mental disabilities, such as cerebral palsy, mental retardation, chronic lung disease, and vision and hearing loss. Rates of pre-term birth vary significantly by race and ethnicity. The Committee encourages NICHD to increase its efforts in researching the underlying causes of pre-term delivery, to identify prevention strategies and to improve the treatment and outcomes for infants born pre-term. (p.73)

Action taken or to be taken

According to the National Center for Health Statistics, preterm births (less than 37 weeks) in the United States increased from 8.9 percent in 1980 to 12.0 percent in 2002. The Healthy People 2010 goal for preterm birth is to decrease the rate to 7.6 percent by the year 2010. Preterm birth is the leading cause of infant sickness and death among African American babies and the second leading cause of infant death among all races. Excluding congenital malformations, premature births account for approximately 70 percent of all neonatal deaths and result in nearly 50 percent of long-term neurological problems.

The NICHD has long supported a comprehensive research program to study preterm delivery (PTD) etiology, prevention, and treatment regimens. Research supported by the NICHD has

helped many premature infants to survive. Recently, NICHD scientists in the Maternal Fetal Medicine Units Network made a significant discovery that weekly injections of progesterone, a readily available hormone, can lower premature birth by more than one-third among women who are at high risk of premature delivery because they had a previous PTD. Progesterone is the first successful treatment demonstrated to reduce the risk of recurrent preterm delivery and improve neonatal outcomes in a subset of high-risk women.

NICHD-funded researchers are conducting a multicenter randomized clinical trial of cerclage (a purse-string suture placed around the cervix) to prevent spontaneous preterm birth, which is one of the most controversial issues in obstetrics. Prior studies have demonstrated that the appearance of a short cervix by ultrasound significantly increased the risk of preterm delivery. However, there is no consensus or clear evidence delineating the proper clinical management. Women at significant increased risk for preterm birth and who also have a shortened cervix based on midtrimester ultrasound will be studied to determine if cerclage placement prevents recurrent PTD before 35 weeks.

The NICHD funds a significant number of researcher-initiated applications specifically addressing the area of preterm birth. Recent research indicates that there are many factors involved that may lead to preterm birth. These include intrauterine infection, uterine bleeding, excessive uterine stretch, maternal psychosocial stress, and fetal physiological stress. Hence, premature birth can be precipitated by a variety of factors indicating at this time that different types of interventions may be required depending on the primary cause. Before effective interventions, however, can be formulated to treat premature delivery, it is also essential to understand the mechanisms that are involved in maintaining a normal pregnancy. Significant progress has been made in identifying factors involved in controlling the length of pregnancy; these include the role of placental and fetal-derived hormones and growth factors. Ultimately, future research may indicate that all causes of premature birth converge to a common pathway or that a final common pathway is involved in precipating both normal and premature delivery. If such a pathway(s) can be identified, it is very possible that a single intervention, specifically targeting this pathway, can be effective in preventing premature birth regardless of the cause.

The consistently increased risk of preterm delivery in particular racial groups remains unexplained. The preterm delivery rate is twice as high as African-American women compared to any other racial group of women in the U.S. Infectious diseases and the associated immune response are not only associated with preterm birth and but also with adverse neonatal outcomes in different ethnic populations. NICHD's grants investigating the roles that infections and inflammation play in preterm birth in African American and other ethnic minority populations are expected to identify future targets for prevention of preterm birth. The NICHD initiated and is collaborating with NIEHS and NINR to understand how societal, behavioral, and environmental conditions alter gene expression and interact with environmental conditions to increase a woman's susceptibility for premature birth in high-risk racial and ethnic groups. By using multidisciplinary approaches, the role of genetics in the increased risk of preterm delivery will be elucidated.

The NICHD's Maternal Fetal Medicine Units Network was established in 1986 to improve the treatment and outcomes of pregnancy. This Network has been very successful with over 100

publications and currently has a number of ongoing studies and trials focused on prematurity addressing prevention, etiology and treatment regimens for preterm birth. For additional information of the Maternal Fetal Medicine Network and NICHD research on preterm birth, please refer to page NICHD -41 of this document.

The NICHD's Neonatal Research Network (NRN) was established in 1986 to improve the treatment and outcomes for infants born prematurely or with other problems. Since inception, over 100 peer-reviewed papers have been published and advances have been made to improve the survival of infants. Major medical complications of prematurity continue to occur in the areas of infection, chronic health problems such as bronchopulmonary dysplasia, and neurodevelopmental outcome. Targeting areas such as these are paramount to improving both survival and long-term function for these fragile infants.

Continued support of both Networks with established infrastructure and investigator-initiated research is vital to exploring new modalities of treatment for pregnancies at risk and infants who are victims of preterm birth.

Item

Pediatric liver disease - The Committee urges the Institute to more 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. (p.73)

Action taken or to be taken

The NICHD is collaborating with the NIDDK within the framework of the newly organized Trans-NIH Liver Disease Subcommittee. An important task of this subcommittee is to develop and implement a Liver Disease Research Action Plan. A central aim of this plan is to identify major challenges and research needs in congenital liver disease, treatment of hepatitis C infection in children, pediatric liver transplantation, and other areas of pediatric hepatology. The NICHD agrees with the Committee on the need to optimize medical treatment regimens for children infected with hepatitis C. The NICHD will collaborate with the NIDDK in developing plans to address this key issue. The NICHD is currently collaborating with the NIDDK by co-funding a network of eight centers to treat non- alcoholic steatohepatitis [NASH] in both children and adults. This fatty liver disorder has now become the most common kind of liver disease diagnosed in childhood. The NICHD recognizes the need to develop innovative ways to prevent and treat NASH in childhood and adolescents and has worked with the NIDDK to implement a randomized placebo-controlled trial of vitamin E in children affected with NASH and a parallel trial of metformin to reverse the state of insulin resistance which attends NASH.

The NICHD also recognizes the need to understand the origins of congenital liver disease during fetal life. Therefore the NICHD supports extramural and intramural programs in developmental biology that address problems of organogenesis, including abnormal liver development. The NICHD recognizes the importance of developing innovative and effective therapy for children with biliary atresia and is currently holding discussions with NIDDK staff regarding co-funding of the recently organized Biliary Atresia Network.

Item

Spina bifida - The Committee is pleased that NICHD co-sponsored a spina bifida research conference in May 2003. The Institute is encouraged to pursue research recommendations generated by the conference to address the prevention and treatment of spina bifida and associated secondary conditions. The Institute should be prepared to testify on its efforts to advance these areas of research at the fiscal year 2005 appropriations hearing. (p.73)

Action taken or to be taken

The NICHD has long supported research on the causes and prevention of spina bifida and neural tube defects [NTDs]. These defects represent the most frequent and severe developmental anomalies of the central nervous system, occurring in 1-2/1000 live births and posing a significant burden on the individual and society. The U.S. incidence of NTD's may be beginning to decrease related to food fortification with folate and with preconceptional folate supplementation by women planning pregnancies. However, folate supplementation is not a panacea since many forms of NTDs will still occur even in the presence of folate and not all women at risk of pregnancy supplement preconceptionally with folate.

The Institute has pursued research recommendations generated by the conference including addressing the treatment of spina bifida and associated secondary conditions through the development and funding of a clinical trial on in utero repair of spina bifida. The NICHD has funded a multi-site randomized controlled trial of in utero compared to traditional post-natal repair of spina bifida. No other U.S. site is offering this procedure outside of the NICHD trial. This collaborative, five-year study will compare the safety and efficacy of fetal surgical repair and traditional postnatal repair of open neural tube defects. Study endpoints will include an evaluation of the effect on the mother's health during the index pregnancy and in future pregnancies; fetal outcome; 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.

The NICHD also coordinates a research program assessing the mechanisms of both normal and abnormal development and supports a wide range of basic research initiatives that explore genetic, biochemical, and molecular aspects of developmental biology in a variety of model systems. Neural tube formation is a complicated process involving changes in cell behavior, structure, and molecular determinants. Consequently, the NICHD continues to recognize research into basic mechanisms of normal and abnormal development as a high priority area.

For the past two years, the NICHD, in collaboration with the National Institute of Dental and Craniofacial Research, the National Institute of Environmental Health Sciences, and the Environmental Protection Agency, has also been building upon its birth defects initiative. This initiative is fostering 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 structural birth defects.

While this initiative is looking at structural birth defects in general, several projects do relate to spina bifida. These studies are investigating the genetic deficits and environmental influences on the formation of NTDs by studying both animal models and human populations.

Item

Primary immunodeficiency (PI) diseases - The Committee continues to be impressed with the commitment NICHD has shown to addressing PI. With the availability of cutting-edge microarray technologies, the Committee encourages NICHD to identify specific molecular biomarkers, improve diagnostic methodologies, and develop newborn screening procedures for PI. (p. 74)

Action taken or to be taken

The NICHD is currently planning an Institute research initiative to identify and characterize genomic and proteomic biomarkers for the newborn screening of primary immunodeficiency diseases (PI). This initiative is also responsive to the recommendations of the 2002 NICHD workshop to develop newborn screening technology for severe combined immunodeficiencies (SCID). The proposed initiative will capitalize on the recent extraordinary advances in genomics, proteomics, and biotechnology to develop new approaches, strategies, and paradigms for the newborn screening of PI. It will provide critically needed support for innovative, cutting-edge, and significant basic research studies on genomic and proteomic biomarkers for PI. Findings emanating from these studies will eventually be translated into rapid, large-scale, and cost-effective applications and procedures for the newborn screening of PI. Moreover, these newly developed procedures can be modified and adapted for the newborn screening of other genetic diseases. The ultimate goal of this initiative is to reduce the illness and death of newborns and children with PI by developing effective screening procedures that will identify them early enough for timely and efficacious treatment and management.

Prior to implementing any new genetic newborn screening program, the NICHD plans to organize and conduct workshops and conferences with interested parties and stakeholders to comprehensively address and thoroughly explore the scientific, legal, social and ethical issues associated with newborn screening for genetic diseases.

The NICHD continues to support programs to enhance the awareness of PI. In January 2003, Dr. Duane Alexander, NICHD Director, helped launch the Jeffrey Modell Foundation (JMF) educational program on PID. He sent letters and informational material on PI to all the members of the American Academy of Pediatrics and American Academy of Family Physicians. Later, he participated in two JMF educational symposia on PI and was interviewed for a televised public information announcement on the same subject.

At the end of fiscal year 2003, the NIAID awarded a 5-year contract to the U.S. Immunodeficiency Network for the Primary Immunodeficiency Research Consortium. The NICHD co-sponsored the contract. This comprehensive contract will support basic, clinical, and epidemiologic research, as well as educational and training programs, in PI. In addition, the contract will provide funds for a registry and repository of PI that will provide essential data and specimens for the research.

Item

Juvenile diabetes - The Committee encourages NICHD to work closely with NIDDK on the continued development of Trial Net, which is designed to coordinate and support clinical trials in diabetes with the ultimate goal of preventing juvenile diabetes in high risk individuals. (p.74)

Action taken or to be taken

The NICHD continues to cooperate with the NIDDK in its support of TrialNet and has pledged to provide cofunding for this project for five years. A NICHD staff representative participates on TrialNet's steering committee and votes on the initiation of new protocols and on other key issues. Protocols currently awaiting implementation include use of the immunomodulator mycophenolate mofetil to treat patients with new onset type I diabetes; use of anti-CD3 antibodies to modulate the autoimmune attack on the beta cells of the pancreatic islets; and use of an altered peptide ligand of the B chain of the insulin molecule to prevent or interrupt the autoimmune attack on the beta cells of the pancreatic islets. The NICHD looks forward to a fruitful collaboration with the NIDDK on these and other innovative protocols that aim to prevent the onset of type 1 diabetes in high- risk individuals.

The NICHD and the NIDDK are also collaborating closely on the Diabetes Research in Children Network (DirecNet), a network of five centers and a coordinating center specializing in the care and treatment of juvenile (type 1) diabetes. DirecNet is currently addressing the important issue of hypoglycemia in diabetic children by assessing the accuracy and efficacy of various types of devices designed to measure levels of blood sugar throughout the day and night.

Item

Traumatic brain injury (TBI) - The Committee encourages NICHD to continue and enhance the cooperative multi-center traumatic brain injury clinical trials network in order to identify which intervention variables result in improvements in long-term outcomes for individuals with TBI. (p.74)

Action taken or to be taken

The TBI clinical trials network is designed to evaluate the relationship between acute care practice and rehabilitation strategies to the long-term functional outcome of TBI patients. The primary scientific objective of the network is to identify which intervention variables result in improvements in long-term outcome.

The goals of the TBI Clinical Trials Network include:

- Recruitment of clinical trauma centers and rehabilitation/postrehabilitation programs to participate in cooperative research.

- Establishment of uniform case definitions and standards of care among participating centers that will permit quantitative evaluation of interventions.

- Development of training programs for management of intracranial pressure.

- Development of a database for collection and management of data, including development of web-based support and data sharing among and between Network participants.

- Determine if predictor variables ("proxy measures") can predict long-term outcome.

- Recommend improved treatment methods.

Last year, three additional clinical sites were added to the TBI Clinical Trials Network, bringing the total clinical sites to eight. The TBI Clinical Trials Network is now actively gathering pilot data to test the data systems and determine the demographics of the combined patient population and is evaluating protocols for implementation into clinical trials.

Item
Bone density - The Committee encourages NICHD to conduct research into quantification of bone mass and its biomechanical properties in children, and the relationship of diet and exercise to bone health. The Committee also encourages the expansion of osteogenesis imperfecta research in genetic therapies, drug treatment and rehabilitation. (p.74)

Action taken or to be taken
The NICHD is currently conducting a multicenter study to obtain standard reference bone mineral density measures in 1500 normal children ages 6-18 years. This study takes into consideration skeletal maturation, bone size and volume, body size, and pubertal stage. Additionally, information on nutrition and exercise is being obtained to better understand the relation of these parameters to bone health. These data will serve as an extremely valuable standard pediatric bone mineral density database. It is anticipated that this essential reference will enable pediatricians to study, diagnose and treat children with disorders affecting bone accrual. This NICHD study, entitled the Bone Mineral Density in Childhood Study, is proceeding at five academic clinical centers. The centers adhere to a common three- year longitudinal observational protocol involving a baseline evaluation and three consecutive annual evaluations, including dual x-ray absorptiometry (DXA), bone age x-ray, a physical exam to determine pubertal status, stadiometer height, and weight. Additionally, three sites are performing computerized tomography (CT) or peripheral quantitative CT scans on a subset of children. Information relating to bone health such as diet and exercise is obtained from each child annually.

With regard to NICHD support of research on osteogenesis imperfecta, this information can be found on page NICHD-53 of this document.

Item
Bleeding disorders - The Committee encourages the Institute to work collaboratively with voluntary associations to address issues related to neonatal intracranial hemorrhage and pediatric complications of bleeding disorders, including medical, psychosocial, and quality-of-life issues. (p.74)

Action taken or to be taken
Two major causes have been identified as antecedents for neonatal intracranial hemorrhage, namely prematurity and hypoxia-ischemia (reduced oxygen supply and abnormalities of blood

supply to the brain). For instance, infants born at or below 28 weeks of gestation (3 months premature) have 30-50 times higher incidence of intracranial hemorrhage compared to those born six weeks later (34 weeks and beyond). Similarly, unexpected reduction in maternal blood oxygen levels or fetal conditions can change the intrauterine environment such that the fetus suffers from cardiac arrest and brain injury from bleeding in the brain.

The NICHD continues to focus its efforts to address these critical issues through a number of mechanisms. A number of researcher-initiated studies funded by the Institute have focused their efforts to learn how fetal cerebral blood vessels mature, what factors lead to their breakage and what factors can be altered to improve their integrity. The Institute also sponsored in part an international conference on Perinatal Cerebral Blood Flow and Metabolism and Brain Injury, attended by the world's leading experts in the field. The proceedings of the seminar are likely to help initiate both basic and translational research in the area of preventing brain injury from intracranial hemorrhage and related disorder.

In addition to researcher-initiated studies on this topic, the NICHD's Neonatal Research Network performs clinical trials specifically addressing therapeutic interventions for neonatal IVH. The Neonatal Research Network is composed of 16 university clinical research centers to perform clinical trials in neonatal-perinatal medicine. The network recently completed enrollment for a Whole-Body Cooling Study for Asphyxia to determine if a lower temperature can protect the brain from damage and bleeding. Results of the trial will be available within 2 years. The Neonatal Research Network also is conducting a follow up study to evaluate outcomes of infants born at approximately 2 pounds or less. Infants who suffer from intraventricular hemorrhage (IVH) are followed for outcome at 18-22 months.

The NICHD is interested in identifying and understanding pediatric complications of bleeding disorders, including medical, psychosocial, and quality-of-life issues. For example, sepsis can result in severe bleeding secondary to affecting the liver and impairing the functions of the clotting system. Infants with sepsis can have lifelong handicaps as evidenced by a recent presentation from the Neonatal Research Network by Dr. Stoll at the Pediatric Academic Societies Meeting. Infants with sepsis in the NICU have poorer neurodevelopmental outcomes than infants who do not have sepsis.

The NICHD is working with the American Academy of Pediatrics as the Academy develops a policy statement for patient care and research on several areas related to premature infant care and intracranial hemorrhage. These include proper methods to resuscitate newborn infants; use of vitamin K (a drug that helps in blood clotting) in the delivery room; and improving management of premature infants' lung diseases that may predispose to intracranial bleeding.

Item

Down syndrome - About one in 800 babies born alive in the U.S. has Down syndrome, and approximately 350,000 people in the U.S. live with the disorder. The Committee encourages NICHD to place a high priority on researching the causes and treatment of Down syndrome, particularly in the areas of cognitive enhancement and the early onset of dementia. The Committee encourages NICHD to strengthen its support for the production of the Ts65Dn

mouse, which is used extensively in the research of Down syndrome and Alzheimer's disease. Current production levels of this mouse strain are not adequate for planned research. (p.74)

Action taken or to be taken
The NICHD remains deeply committed to research on Down syndrome. This year the NICHD will co-sponsor a meeting with NIA on the important subject of the "Biology of Chromosome 21 Genes: an Expert Workshop" bringing together two groups of investigators. The first group specifically studies human chromosome 21 and Down syndrome and its mouse models and the second group studies the biology and/or molecular biology of specific genes that map to chromosome 21 or whose pathway components map to chromosome 21.

With respect to cognitive function in Down syndrome, the NICHD currently supports one research project that focuses research on a specific gene that affects cognitive function in development and aging in Down Syndrome, another that deals with genetics, mortality, and dementia in Down syndrome, and two program projects. One of these deals with differences in vulnerability to Alzheimer disease in adults with Down syndrome, maladaptive behaviors in those individuals with Down syndrome who develop Alzheimer disease, criteria for assessing dementia in adults with Down syndrome, and lifespan development and gene expression in individuals with Down syndrome. A second long-standing grant focuses on the development and evaluation of specific mouse models for Down syndrome, creation of specific transgenic mice with only one or three copies of specific genes located on human chromosome 21 and shared with mouse chromosome 16, and specific projects dealing with mechanisms of aneuploidy. In addition, investigators involved with another grant dealing with cellular/molecular pathophysiology of mental retardation, successfully received approval by the FDA Advisory Board for the use of Memantine to treat dementia in Alzheimer disease and Down syndrome patients.

Increasing the availability of Ts65Dn mice to researchers continues to be a high priority for NICHD. Through a contract with the Jackson Laboratories, the NICHD has been active in making these mice available for many investigators. Some individual investigators studying these mice have established their own colonies to meet individual demands. Such efforts are necessary because the mice are hard to breed, the males are sterile, and only a portion of Ts65Dn mice result from a given mating. NICHD continues to work with JAX to find mechanisms to increase the numbers of these mice available to the research community.

Item
Mucopolysaccharidosis (MPS) - The Committee encourages NICHD to enhance efforts to engage in collaborative research support with NINDS and NIDDK with respect to MPS disorders. The Committee also encourages NICHD to examine the issues pertaining to the loss of cognitive function in those affected by MPS disorders and barriers to delivery of effective therapies to the central nervous system. (p.74)

Action taken or to be taken
The NICHD has an active research program related to mucopolysaccharidoses and related disorders associated with lysosomal dysfunction. NICHD's main focus has been on viral vector delivery systems for potential gene therapy. In 2003 NICHD support was provided through a

variety of funding mechanisms including fellowships, mentored scientist awards, and research project grants. In addition, 2 new pilot grants were supported as part of a cooperative RFA with various institutes including NINDS and NIDDK to develop new methods for introduction of corrective factors into specific organ systems with new or modified existing vectors. The NICHD also supported a national meeting on Batten disease, a related storage condition.

Some specific topics of research funded include: the treatment of mucopolysaccharidoses with adeno-associated vectors; studies of AAV gene transfer; the examination of different vector systems in the treatment of specific mucopolysaccharidoses and lysosomal storage diseases; and biochemical mechanisms associated with specific lysosomal disorders.

Item

Maternal-fetal medicine network - The Committee encourages NICHD to strengthen its support of the network so that it can continue to address these important research questions, with an emphasis on issues pertaining to preterm births and low birth weight deliveries. (p.74)

Action taken or to be taken

To ensure that all women can have healthy pregnancies that result in the birth of healthy infants, the NICHD supports basic, clinical, and translational research aimed at preventing and treating those conditions that can adversely influence pregnancy and infant outcomes. One of the Institute's many successful research programs in this area is the Maternal Fetal Medicine Unit (MFMU) Network. Since its inception in 1986, this network has provided the expertise and infrastructure for well-designed clinical trials in obstetrical management. The Network has been very successful as demonstrated by their numerous publications and presentations, including a seminal work published in June in the New England Journal of Medicine that identified a treatment (progesterone, a hormone) to prevent recurrent preterm birth in women at high risk. Prior to this finding, there were no proven therapies that could be offered to women to prevent preterm birth.

The Network has a number of ongoing studies and trials. In keeping with its vision statement, many of these are focused on preterm birth and low birthweight.

The Cesarean Delivery Study is a cohort study to determine the characteristics of women undergoing trial of labor, its efficacy and safety; to determine cesarean delivery rates by payer/provider status; and to describe complications influencing outcome in women undergoing cesarean delivery. The findings from this study on the safety of vaginal birth after cesarean delivery will be presented at the upcoming Society for Maternal Fetal Medicine's national meeting. Subanalyses of this study will further our understanding of optimal delivery management of preterm and low birthweight infants.

The BEARS (Beneficial Effects of Antenatal Repeat Steroids trial), is a double-masked, placebo-controlled trial to test if weekly courses of steroids is safe and effective compared with a single course. This study is focused on optimizing the management of fetuses at risk of delivering preterm. This study was halted after enrollment of 463 of the planned 2400 patients due to safety concerns and the results will be presented at the upcoming Society for Maternal Fetal Medicine's national meeting.

The BEAM trial, Beneficial Effects of Antenatal Magnesium Sulfate in prevention of cerebral palsy, is a double-masked, placebo-controlled trial to determine if antenatal MgS04 can reduce the risk of cerebral palsy in the offspring in women at 24 - 31 weeks gestation. This trial, which is cofunded by the NINDS, includes only women at the highest risk of delivering preterm and the goal is evaluating a therapy to improve their outcome.

The FOX: Fetal Pulse Oximetry Trial is a randomized controlled trial to determine if fetal pulse oximetry affects overall cesarean delivery rate; and cesarean delivery for fetal distress of women.

The Gestational Diabetes Mellitus (GDM) trial is a randomized controlled trial with additional observational cohorts to test whether identification and dietary treatment of mild GDM reduces neonatal morbidity and mortality in women at 24-29 weeks gestation.

The CAPPS (Combined Antioxidant & Preeclampsia Prediction Studies) trial is a double-masked placebo-controlled trial to determine whether antioxidants (Vitamins C and E) reduce the frequency of serious maternal and infant complications associated with pregnancy related hypertension in nulliparous women. Preeclampsia is a major cause of preterm delivery and low birth weight.

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 lost 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, however, to better understand the applicability of new technology to various segments of the limb-loss population, including 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 available mechanisms. (p.75)

Action taken or to be taken

The NICHD National Center for Medical Rehabilitation Research, NCMRR, continues to support an active program in prosthetics and prosthetic research through regular research grants as well as small business innovation research awards. A request for applications to solicit production of training materials on surgical amputation, prosthetic and orthotics was recently published. NCMRR staff have participated in a workshop on amputation and prosthetics held at the Uniformed Services University, and will follow up with staff at Walter Reed to explore opportunities for collaboration. The Center is actively developing a Program Announcement for interdisciplinary research partnerships in improving functional outcomes. This announcement will explicitly encourage collaborations between academia, industry and federal laboratories and clinics to develop and evaluate new and existing approaches to rehabilitation and prosthetics.

Item

Best pharmaceuticals for children - The Committee recognizes the importance of ensuring that drugs are safe and effective for use by children. The Committee strongly supports the research being conducted by NIH to implement the Best Pharmaceuticals for Children Act of 2002. NICHD should coordinate its activities with other Institutes within NIH for which pediatric pharmacological drug research may have therapeutic relevance. The committee requests NIH to provide by March 30, 2004 information on the number of studies supported; the estimated cost of each study 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. (p. 75)

Action taken or to be taken

The NICHD agrees with the Committee that drugs prescribed for use in children should be safe and effective, and that physicians need to know how best to treat children with these drugs. In order to implement the Best Pharmaceuticals for Children Act (BPCA), the NICHD is coordinating its activities closely with other NIH Institutes and Centers.

Upon receipt of delegation of authority for implementing the BPCA, the Director of the NICHD invited Directors of all relevant Institutes and Centers to nominate liaison staff to work with NICHD to implement pediatric drug research with relevance to their Institutes or Centers. These liaisons have been contacted by NICHD staff and were invited to an NIH-FDA briefing on BPCA. Additionally, these Institute liaisons participated actively in compiling the priority list of off-patent drugs, called for in the BPCA, that was published in the Federal Register in January 2003 and a supplemental listing published in the Federal Register in August 2003. They are now working with NICHD staff to compile an updated priority list of off-patent drugs for publication in the Federal Register in January 2004.

The designated Institute liaisons along with NICHD staff also participate in the process of developing Requests for Proposals (RFPs) for pharmacological studies of on-patent drugs that are being used off-label, but not yet studied in pediatric populations. In keeping with the legislation, these RFPs are developed only after the FDA has sent a Written Request to conduct pediatric trials to the pharmaceutical firms involved in manufacturing of the drug, this request has been denied or not responded to within 120 days, and the FDA has referred the drug to the Foundation for the National Institutes of Health to consider for support of the needed studies in children.

The NICHD is currently establishing partnerships with pediatric drug study networks in other NIH Institutes in order to expedite the study of clinically important drugs with special relevance to the research programs of those Institutes, for example, the NCI's Pediatric Oncology Group, and those in NHLBI and NIMH.

The NIH will be pleased to provide by March 30, 2004, information on the number of studies supported; the estimated cost of each study 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.

Item
National children's study - The Committee continues to support implementation of the national children's study, which aims to quantify the impacts 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 so that this study can be completed within its original time frame. (p.75)

Action taken or to be taken
The NICHD is continuing its efforts to coordinate with Federal agencies and non-Federal partners on planning and pilot studies.

FY 2004 Senate Appropriations Committee Report Language (S. Rpt. 108-81)

Item
Behavioral Science - The Committee supports the NICHD's efforts to determine the biological, behavioral, and social factors that affect child development, particularly the important role of family structure and fathers in child development. The Committee is particularly concerned about rising rates of childhood obesity and supports continued initiatives to promote healthy behaviors in children and adolescents and prevent health risk behaviors. (p.129)

Action taken or to be taken
The healthy development of the next generation of citizens, workers, and parents is at the heart of the NICHD mission. Research supported by NICHD has made substantial contributions to understanding the behavioral and social factors that promote healthy child development and reduce risky behaviors.

Results from the National Longitudinal Study of Adolescent Health (ADD Health) demonstrate that children raised by both their parents have better outcomes than those in single-parent and step-parent families because their parents exercise more control over their activities, have closer and warmer relationships with them, and share family meals together more often. These family processes are associated with a lower likelihood of recent substance use, delinquency, and violence, as well as delayed involvement in sexual intercourse. The publically available data from this study continue to be used by researchers across the country.

The NICHD is also studying the important role of fathers in child development. The Fragile Families Study is monitoring the development of children born to unmarried couples and identifying key factors that keep fathers involved and improve outcomes for these children. Analyses of data from the Panel Study of Income Dynamics Child Supplement reveal that fathers' emotional support and monitoring activities were associated with fewer problem behaviors in children. Paternal activities, such as church attendance, also had positive effects on children's long-term educational attainment, particularly for sons. NICHD's collaboration with the Department of Education's Early Childhood Longitudinal Study-Birth Cohort Study, which supports the collection of information on fathers' involvement, will also expand research on this topic.

Rising rates of childhood obesity are putting the next generation at risk, both in the U.S. and all over the world. The NICHD is supporting research on the economic and social changes responsible for these trends, research that examines the specific ways in which components of social and economic change affect diet, physical activity, and obesity. In addition, NICHD is studying how specific aspects of community environments, such as access to parks and transportation systems, affect physical activity and overweight. These questions are being explored through an expansion of the ADD Health project.

In addition, research supported by the NICHD has underscored the behavioral and environmental contributions to the epidemic of childhood obesity. For example, television watching has been linked to childhood obesity in a dose-response fashion, and decreasing time spent watching television has been shown among the middle-school students who participated in a project titled Planet Health to reverse the prevalence of childhood obesity among the girls. The NICHD has supported pioneering research on using contracts and other behavioral reinforcements between parents and children to decrease television watching time and other sedentary behaviors and, conversely, to increase time spent in active lifestyles. To further increase support of novel research in behavioral and environmental interventions the NICHD will issue a program announcement to encourage school-based behavioral interventions to prevent childhood obesity. The NICHD will also issue an RFA in conjunction with other NIH Institutes and Centers that is designed to encourage health care workers in primary care settings to devise new programs of behavioral and dietary interventions that will prevent obesity in pediatric age groups before it begins as well as to develop behavioral interventions to reverse obesity in the 1 in 5 children already affected by the epidemic of pediatric obesity.

Item

Bleeding Disorders - The Committee expects the Institute to work collaboratively with the National Hemophilia Foundation to address issues related to neonatal intracranial hemorrhage and pediatric complications of bleeding disorders, including medical, psychosocial, and quality-of-life issues. (p.129)

Action taken or to be taken

Please refer to pages NICHD-38, 39 of this document for NICHD's response to this significant item regarding bleeding disorders.

Item

Down Syndrome - Down syndrome is the most common genetic cause of mental retardation. The Committee strongly encourages NICHD to place a high priority on researching the causes and treatment of Down syndrome and to increase funding for research in the areas of cognitive enhancement and the early onset of dementia. The Committee further urges NICHD to increase funding for the production of the Ts65Dn mouse, which is used extensively in the research of Down syndrome and Alzheimer's disease. Current funding for the production of this mouse strain is inadequate to produce the quantity of mice needed for current research. (p.129)

Action taken or to be taken

Please refer to page NICHD-39 of this document for NICHD's response to this significant item regarding Down Syndrome.

Item

Demographic Research - The Committee commends NICHD for its outstanding support of demographic research. This research has consistently provided critical scientific knowledge supporting efforts to strengthen and empower American families through sound public policy. Recent findings related to the effects of maternal employment and paternal involvement on the development of children are particularly noteworthy. The Committee encourages NICHD to continue to invest necessary resources in maintaining the databases that make these studies possible, while strengthening research on the causes of trends in family stability. Continued and adequate support for training and infrastructure funding is necessary to sustain demographic research on these topics and on other critical issues, including the causes of immigration and population movement, the impact of immigration on the American people, adolescent health, and disparities in health among different groups within our population. (p.129)

Action taken or to be taken

Demographic research is an essential component in understanding and improving the nation's health. Low birth rates, family change, and immigration are having profound impacts on the composition and health of our population. Scientific research that examines the policy, economic, social, and behavioral causes of population change and their consequences for health and well-being is an essential component of the larger health mission of the NIH.

The impact of family change on children and adults is a key focus of demographic research at the NICHD. New nationally representative studies of families supported by the Institute are greatly enriching research in this area. Building on a long-standing program of research on the causes of increased out-of-wedlock childbearing in the U.S., the Fragile Families Study is examining the development of children born out-of-wedlock and the factors that improve outcomes for these children. The Three Cities Study of Welfare, Children and Families recently demonstrated that changes in welfare laws that moved impoverished mothers into the labor force have had no short-term adverse effects on their children. In 2003 NICHD and the National Institute on Aging launched a collaborative program to examine how families allocate resources to provide for young and elderly dependents, and how public policy influences these critical family behaviors. Another new initiative is developing research on innovative workplace interventions to improve the well-being of children and adults by easing work-family conflicts for working parents.

Demographic research supported by NICHD contributes to the larger NIH mission by: (1) studying how demographic processes influence health; (2) providing a population perspective on health; and (3) supporting the integration of social science, behavioral, and biomedical approaches to understanding health. Research on immigration is an important example. Recent research on the health of migrants to our shores has provided fresh insights into reasons for the distinctive health patterns found in immigrant populations and clues to the role of culture and socioeconomic disadvantage in health disparities. The New Immigrant Survey, the first nationally representative longitudinal study of immigrant health and adaptation, will greatly expand knowledge about our immigrant families. Other examples include the large body of research on the determinants of adolescent health generated by the NICHD-funded National Longitudinal Study of Adolescent Health and studies that demonstrate the impact of public policies and air pollution on infant health. NICHD funded the largest share of grants resulting from a recent

trans-NIH initiative on education and health, and recently launched the Community Child Health Network, an innovative project that will examine how social environments affect infant health and development in poor minority communities.

Item

Drug Safety for Children- The Committee recognizes the importance of ensuring that drugs are safe and effective for use by children. The Committee urges the Institute to implement the provisions of the Best Pharmaceuticals for Children Act of 2003 (Public Law 107-109) which supports the pediatric testing of off-patent drugs, as well as on-patent drugs not being studied through existing mechanisms. In implementing this provision, the National Institute of Child Health and Human Development should act as coordinator for all other Institutes within NIH for which pediatric pharmacological drug research may have therapeutic relevance and will consult with the Food and Drug Administration. The Committee requests NIH to provide an update during its annual appropriations testimony. This update shall include 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.130)

Action taken or to be taken

Please refer to page NICHD-43 of this document for NICHD's response to this significant item regarding Drug Safety for Children.

Item

Duchenne Muscular Dystrophy- The Committee commends the Institute for initiating the muscular dystrophy cooperative research centers. The Committee expects NICHD to work cooperatively with NIAMS and NINDS to expand the scope and level of research undertaken by the centers program. (p.129)

Action taken or to be taken

The MD-CARE Act mandated that NIH establish centers of excellence for Muscular Dystrophy (MD) research. In September 2002, NIH issued the request for applications (RFA) "Muscular Dystrophy Cooperative Research Centers," to establish research centers, and in October 2003, following peer review of the submitted applications, NIH announced plans to establish three Cooperative Research Centers. NIAMS, NICHD, and NINDS each funded one center.

In the Center at the University of Washington, funded by NICHD, four projects focus on muscular dystrophy. Three of the projects are directed toward eventual clinical trials for gene therapy for Duchenne Muscular Dystrophy. The fourth project explores the molecular pathophysiology of myotonic dystrophy. This project will provide critical information on the molecular pathogenesis of myotonic dystrophy and identify targets for therapeutic intervention, through the study of abnormal gene expression in the cells of individuals with myotonic dystrophy. The interactive environment of this new center will advance knowledge of and treatments for the muscular dystrophies by promoting collaboration, providing shared resources, advancing basic research, stimulating translational research, fostering outreach activities,

developing greater patient awareness of basic and clinical research and enabling their participation in clinical trials, and by facilitating the development of therapy for the MDs.

NICHD will continue to work collaboratively with NINDS and NIAMS on the Centers program. As required in the "Muscular Dystrophy Cooperative Research Centers" RFA, a steering committee to insure overall coordination of the MDCRC program is being formed, and will include the scientific program officers from NIAMS, NINDS, and NICHD. In addition to the Centers Program, NINDS, NIAMS, and NICHD are working together on other ways to further MD research. All three institutes, along with public members, are represented on the Muscular Dystrophy Coordinating Committee (MDCC), which held its first meeting on July 1, 2003 and is in the process of developing a research and education plan for MD. In recent years, the three institutes have worked together to co-sponsor initiatives and workshops on MD and all three institutes also participate in the MD Research Task Force to help guide efforts to intensify research on muscular dystrophy.

Item

Fragile X Research Coordination Conferences - To facilitate effective coordination of research on Fragile X and related disorders, the Committee strongly urges NICHD to regularly convene and conduct a state-of-the-science conference on Fragile X research and further urges the NICHD to continue to hold Fragile X Research Coordination Conferences at least once every 3 years or more frequently if warranted by scientific advancement. Investigators conducting research on Fragile X and related fields who are funded by the NIH, as well as other researchers as appropriate, should be invited to attend and participate in these conferences. The Committee expects the first Fragile X Coordination Conference shall be held in 2004. (p.130)

Action taken or to be taken

Consistent with the intent of the RFA on "Neurobiology and Genetics of Fragile X Syndrome" issued several years ago, the NICHD continues to invite investigators funded in Fragile X research by NICHD and other NIH Institutes to meet annually at a "Fragile X Investigators' Meeting". Fragile X research has enjoyed a steady "expansion" over the past three years with the addition of $2.9 million for Fragile X Research Centers, closely affiliated with existing Mental Retardation and Developmental Disabilities Centers. New investigators not previously affiliated with Fragile X research continue to bring innovative new technologies to bear on the underlying mechanisms of the effects of Fragile X on neurodevelopment and aging.

Current plans are to hold the Third Fragile X Investigators' Meeting, which will also serve as the first Fragile X Coordinating Conference, in Washington, DC in June 2004 in conjunction with the International Fragile X Biennial Meeting. Investigators funded by various NIH institutes, including NICHD, as well as those funded by research advocacy and other organizations will be invited to participate in this important meeting.

The NICHD continues to search for ways to increase involvement and participation of Fragile X organizations in these efforts. Further, efforts by NICHD have expanded to cooperative efforts with NINDS concerning the appearance of a unique neurological condition at age 50 to 70 involving ataxia/tremor in males who carry the premutation. This observation, combined with the observation of premature ovarian failure in approximately 20% of females who carry the

fragile X premutation, has prompted a reevaluation of the "benign" nature of the premutation by program staff, advocacy groups, and extramural and intramural investigators at NICHD.

With respect to premature ovarian failure, a collaboration between extramural and intramural investigators at NICHD has led to the development of a working group involving NIH agencies (NICHD, NIMH, ORWH, ORD, and NIEHS) and outside advocacy groups (FRAXA, National Fragile X Foundation, POF Support Group, Inc.) and professional organizations (American Society for Reproductive Medicine, American Society of Human Genetics, National Society of Genetic Counselors) to organize and convene a conference on "Reproduction and the Fragile X Premutation" tentatively scheduled for fall 2004.

Item
Fragile X Research Coordination Reports - Within 6 months after each Fragile X Research Coordination Conference is held, the Director of the NICHD shall issue a report on the state-of-the-science of research on Fragile X and include summaries of Fragile X and related research being supported by NIH Institutes and Centers, as well as plans for future Fragile X research. (p.130)

Action taken or to be taken
The NICHD will make available within 6 months of each Fragile X Coordinating Conference, a Conference Report outlining the details and findings from each meeting.

Item
Infertility and Contraceptive Research- The Committee continues to place high priority on research to combat infertility and speed the development of improved contraceptives. The NICHD is urged to continue aggressive activities in this area, including grants for individual researchers and for infertility and contraceptive research centers. (p.131)

Action taken or to be taken
Since nearly half of all pregnancies in the U.S. are unintended, the Institute puts a high priority on improvement of existing contraceptive methods and development of new methods. Recompetition of the Contraceptive Development Centers Program focused on basic and clinical contraceptive research including a number of projects devoted specifically to male contraception. The Centers recommended for funding (University of Washington, University of California at Davis and The Population Council, NY) conduct research on several different approaches to male contraception; hormonal suppression of the hypothalamic-pituitary-gonadal axis either in men or in women; development of novel vaginal delivery systems for drugs that inhibit ovulation; and analysis of oocyte development. The Centers share common resources and research information throughout a five year funding period. Emphasis on training opportunities within the Centers is a priority for the Program.

As a part of a strategic goal to develop a contraceptive for males, NICHD issued a request for applications to study novel methods of male fertility regulation. Eight projects will be supported under the cooperative agreement mechanism and the principal investigators will form a Steering Committee to foster communications among the participants. The Committee will review

progress within the individual projects and make recommendations regarding future directions of the program.

A protein, catsper, was discovered that helps to explain the process of sperm mobility. This knowledge provides new insights into fertility and provides a new contraceptive lead. The NICHD has held several workshops to stimulate research in the area of male infertility, fertility and male reproductive diseases. Basic studies funded in the small but growing male reproductive sciences program will provide insights into male infertility and help stimulate the development of contraceptives for men.

The Contraceptive Clinical Trials Network (CCTN) was established in 1996. The centers were selected on the basis of their capability to carry out Phase I, II, and III trials of oral, injectable, implantable, or topical contraceptive drugs and contraceptive devices. Ongoing studies in women include Phase III contraceptive efficacy trials of oral and of vaginal use products. New projects planned include a contraceptive efficacy trial of a potential microbicide with contraceptive activity for use by women and a Phase II efficacy trial of a novel gonadotropin inhibitor for use in men as a contraceptive.

The NICHD continues to fund the Specialized Centers Program in Reproductive Research. These centers include basic and translational scientists working together in concert to seek mechanisms of fertility and infertility. Major progress has been made in regards to endometriosis and polycystic ovarian disease, both significant causes leading to infertility. Scientists from the National Centers Program for Infertility Research have recently reported on a new gene that promotes puberty.

The Reproductive Medicine Network has currently completed the enrollment of approximately 240 subjects into a large randomized double blind trial of metformin vs clomiphene citrate vs combined metformin/ clomiphene in the treatment of the infertility of polycystic ovarian syndrome. This trial is the first to study live births as an outcome in the treatment of polycystic ovarian disease, one of the most common forms of female infertility.

A major breakthrough in understanding how implantation occurs was made this past year with the discovery of how the blastocyst is attracted and then attached to the uterine endometrium by a protein L-selectin. This discovery has great potential to help the infertile couple to achieve a pregnancy.

NICHD also funded grantees to study the basic mechanisms of the formation, growth and development of uterine fibroids, a major cause of hysterectomy in childbearing women, a procedure that leaves them sterile. Even without the need for a hysterectomy, fibroids can lead to decreased fertility. Basic knowledge gained should lead to non-surgical and thus fertility sparing treatments. Research is also being supported that may shed light on why there is such a great health disparity among African American women with regard to uterine fibroids.

Item

Juvenile Diabetes - NICHD is encouraged to work closely with NIDDK on the continued development of Trial Net, which was recommended by the 1999 Congressionally-mandated

Diabetes Research Working Group to coordinate and support clinical trials in diabetes with the ultimate goal of preventing juvenile diabetes in high risk individuals. (p.131)

Action taken or to be taken
Please refer to page NICHD-37 of this document for NICHD's response to this significant item regarding Juvenile Diabetes.

Item
Learning Disabilities- The Committee is pleased that NICHD continues to place high priority on learning disabilities research. The efforts to address the special needs of children affected by a learning disability and improve literacy are showing promising results. The Committee encourages NICHD to continue to focus on reading disability and mathematics development research. Additionally, the Committee urges NICHD to lead an effort to collaborate on research efforts with other Institutes working on related activities. The Committee encourages cooperation in areas where work can be shared across Institutes on behalf of individuals with learning disabilities. (p.131)

Action taken or to be taken
The NICHD has expanded its Learning Disability Research program to support four Learning Disability Research Centers and 40 additional reading research sites to develop scientific knowledge relevant to reading development, reading disabilities, and reading instruction. Moreover, the NICHD has now completed the development and implementation of several related reading research programs that promote the study of literacy development and reading disorders from birth through adulthood as well as studies to better understand how children whose first language is not English learn to listen, speak, read and write in English. Specifically, new programs in early childhood development and school readiness, adolescent literacy, adult and family literacy, and bilingual reading development have been initiated and supported in collaboration with both the Department of Education and HHS. This past year, NICHD, in collaboration with the Department of Education also developed and is now supporting a major research program in mathematics cognition and specific learning disabilities to contribute new knowledge in the following areas: (1) normal development of mathematical proficiency; (2) the role of individual differences; (3) specific learning disabilities in mathematics, including diagnosis, classification, preventive strategies, and early intervention; and (4) the neurocognitive mechanisms that are influential in the expression of mathematical learning abilities and disabilities.

Item
Maternal-Fetal Medicine Network [MFMU] - The Committee recognizes the outstanding contributions of the Maternal-Fetal Medicine Network [MFMU] in addressing clinical questions related to the care and treatment of high risk and complicated pregnancies. By studying large numbers of patients, the Network has demonstrated that it offers the most effective and cost-efficient way to study high-risk conditions. However, the Committee is concerned that additional funds are needed in order for the Network to continue to make progress in these issues of concern to the health of women and their babies. Therefore, the Committee urges the NICHD to expand its support of the Network and to provide increased funds to continue to address these

important research questions, with an emphasis on issues pertaining to pre-term births and low birth weight deliveries. (p.131)

Action taken or to be taken
Please refer to page NICHD-41 of this document for NICHD's response to this significant item regarding the maternal fetal medicine network.

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 environmental influences, including physical, chemical, biological and social influences, on child health and development. The Committee urges the Director of the NICHD to continue to closely coordinate with the CDC, EPA, other Institutes and agencies and non-Federal partners conducting research on children's environmental health and development, such that this study is ready for the field by no later than 2005. To that end, in fiscal year 2004, the Committee expects the Director of NICHD to increase support for study planning, administration, and initial pilots that will provide the information necessary to develop and implement the full national study. (p.131)

Action taken or to be taken
Please refer to page NICHD-44 of this document for NICHD's response to this significant item regarding the National Children's Study.

Item
National Center for Medical Rehabilitation Research - The National Center for Medical Rehabilitation Research supports research grants, training, centers and clinical trials in medical rehabilitation to improve the function of persons with physical disability and is the focal point within NIH for this field of science. Recent initiatives have involved efforts to expand the use of assistive technology by persons with disabilities and clinical research to determine improved outcomes of care for persons with Traumatic Brain Injury, stroke, hip fracture and limb loss. The Committee encourages the Institute and NCMRR to continue its focus on assistive technology, clinical trials and other research on improved outcomes. The Committee would also encourage the Institute and NCMRR to review needs and plan to expand medical rehabilitation research to improve outcomes for trauma victims. (p.132)

Action taken or to be taken
In addition to the investigator initiated applications on assistive technology and clinical trials funded through the regular grant application process, NCMRR has published a set of special initiatives to solicit applications in these areas. These include: RFA HD-03-023 Innovations in Powered Mobility Devices; RFA HD-03-019 Training Materials on Surgical Amputation, Prosthetics and Orthotics; HD-03-014 Innovative Technologies for Pediatric Critical Care and Rehabilitation; and HD-03-011 Biomechanical Modeling of Movement. NCMRR staff have actively participated in inter-agency assessments and meetings regarding trauma and trauma resuscitation and continue to collaborate with other institutes and agencies in this area.

Item

Neurofibromatosis -The Committee urges the Institute to consider the progress being made in NF research, expand the NF research portfolio and to identify possible areas for collaboration. (p.132)

Action taken or to be taken

Please refer to page NICHD-32 of this document for NICHD's response to this significant item regarding Neurofibromatosis.

Item

Osteogenesis Imperfecta - The Committee understands that research is urgently needed into quantification of bone mass and its biomechanical properties in children, and the relationship of diet and exercise and co-morbid conditions to bone health. A greater understanding of the genetic and other determinants of peak bone mass will help children with Osteogenesis Imperfecta [OI], osteopetrosis, etc. The Committee encourages NICHD to expand OI research in genetic therapies, animal models, drug treatment and rehabilitation. (p.132)

Action taken or to be taken

The NICHD has placed additional emphasis on disorders of bone matrix, such as osteogenesis imperfecta, by creating a new Branch in the Intramural Program, the Bone and Extracellular Matrix Branch, to focus clinical and laboratory research on these disorders. Both clinical and laboratory work on osteogenesis imperfecta have been expanded. The clinical program has been conducting the first controlled trial of the bisphosphonate drug, pamidronate, as a possible therapy for OI. This is a study that is possible only in the longitudinal pediatric OI study population of the NICHD, because off-label use has become popular with parents of children with OI. The study has shown that bisphosphonates increase vertebral bone density and area in OI children. Growth of bones is unaffected. The changes in pain perception and functional mobility reported in previous small uncontrolled trials were shown to be a placebo effect. In addition, the head of this program was invited to write a cautionary commentary for the New England Journal of Medicine on the side effects of long term use of these drugs in growing children. The response of parents and the OI Foundation has been substantive and a fact sheet has been issued proposing end points of treatment.

The clinical trial has been complemented by a treatment trial of bisphosphonate in the mouse model for this disorder, the Brtl mouse, generated at the NIH by this program. This murine trial has focused on the femurs of the mice and the effect of drug on their mechanical properties. Bisphosphonate treatment was shown to increase the stiffness of the bones but to exacerbate their brittleness, making them more liable to abruptly snap. This information would not be possible to obtain without the unique knock-in mouse model for OI made in the NICHD Intramural Research Program.

Other laboratory studies on mosaic carriers have provided crucial information for the level of transplanted cells that will be necessary for mesenchymal cell transplant to affect bone strength and quality. Genetic studies are continuing to be provided for affected families. The NICHD investigators are also leading an international effort to assemble all known mutations and perform genotype-phenotype modeling.

Item

Pediatric Liver Disease - The Committee notes the Institute's limited involvement in issues relating to pediatric liver disease and urges the Institute to initiate research in this area and collaborate with NIDDK on these efforts. For example, the Committee notes the lack of involvement of NICHD to support the collaborative network of centers established to gather data and study specific hypothesis of the cause and treatment of Biliary Atresia. The Committee would also encourage NICHD to cooperate with NIDDK on research questions relating to optimal timing and medical treatment regimens for children infected with the hepatitis C and the need to support a database and registry to track the outcome of children who receive liver transplants. (p.132)

Action taken or to be taken

Please refer to page NICHD-34 of this document for NICHD's response to this significant item regarding Pediatric Liver Disease.

Item

Pre-term Labor and Delivery -The Committee strongly urges NICHD to allocate more funds to reveal the underlying causes of pre-term delivery and most importantly to identify prevention strategies. p.133)

Action taken or to be taken

Please refer to page NICHD-32 of this document for NICHD's response to this significant item regarding pre-term labor and delivery.

Item

Primary Immunodeficiency Diseases - The Committee strongly encourages the NICHD to identify specific molecular biomarkers, improve diagnostic methodologies, and develop newborn screening procedures for PI. Rapid, cost-effective, and accurate molecular screening procedures and strategies for PI that are incorporated into a universal newborn screening program will significantly enhance the early identification, treatment, and management of PI patients. This will help reduce the morbidity and mortality of affected children, improving their health and well-being. The Committee strongly encourages NICHD to bring together the stakeholders in newborn screening to assess comprehensively the scientific, legal, social and ethical issues associated with such screening. (p.133)

Action taken or to be taken

Please refer to page NICHD-36 of this document for NICHD's response to this significant item regarding Primary Immunodeficiency diseases.

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. NICHD is encouraged to enhance research to address issues related to the outcome of the conference and urged to significantly expand its research efforts in the prevention and treatment of Spina Bifida and associated secondary conditions. (p.133)

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

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. The Committee also commends NICHD's attempts to further its progress in SIDS research by initiating a third SIDS 5-year research plan. This third 5-year plan will continue the efforts of the past two 5-year plans, which have been responsible for many of the research breakthroughs in the effort to reduce SIDS cases in the United States. The Committee requests that this 5-year plan be re-examined to determine the appropriateness and scientific validity of including research on stillbirth and miscarriage as components of the plan. (p.134)

Action taken or to be taken
Please refer to page NICHD-31 of this document for NICHD's response to this significant item regarding SIDS.

Item
Urogynecology Program - Urinary incontinence and other pelvic floor disorders serve as barriers to healthy living. The Committee commends the NICHD for developing the Pelvic Floor Disorder Network [PFDNO] and expects additional resources will enable the network to excel in 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 on 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 and translational research in order to create better foundations for clinical care. The Committee encourages the Institute to provide more research to investigator-initiated applications to ensure a self-sustaining core of ongoing research and encourages a dedicated study section in this area. (p.134)

Action taken or to be taken
The NICHD agrees that there is a strong need for further research in urogynecologic disorders. In general, the lifetime risk of one or more of these conditions is believed to be as high as one out of every three women. Furthermore, major surgical procedure(s) for urinary incontinence or pelvic organ 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 surgery.

NICHD has developed a comprehensive research program on these disorders since focusing on this area in 2000. Activities include:

- The NICHD program in Reproductive Gynecology and Medicine established in 1998 studies the basic science of pelvic floor disorders. NICHD investigators have extensively studied the pelvic nerves of the female and have discovered a new nerve which is called the levator ani nerve. This nerve can be traced to the pelvic floor muscles and passes very close to a part of the pelvic bone at one point, thus it is susceptible to damage during surgery or by the pressure of the fetus during childbirth. This new knowledge will provide clinicians with important information that will lead to new preventive approaches to pelvic floor disorders and eventually to their treatment. Another researcher is studying the role of estrogen on the nerves of the vagina. He found that estrogen appears to suppress nerve density in the reproductive tract of rodents. Other researchers have studied the molecular mechanisms that are responsible for the underlying cause in pelvic floor prolapse. Using gene chip technology, smooth muscle proteins, actin and myosin were found to be over-expressed in women with this condition. However, myosin binding protein and other proteins are under-expressed. These studies suggest that the weakness of the pelvic floor might be due to decreased amounts of actin or myosin and also may have to do with regulatory proteins. The role of progesterone and estrogen in the causation of pelvic floor prolapse is currently under study.

- Basic Science and Translational Research in Female Pelvic Floor Disorders Workshop was held November 2002 to discuss of state-of-the-art research and knowledge gaps. The focus of this workshop was to stimulate basic and clinical scientists to work together and foster the development of collaborative relationships involving laboratory and clinical research in urogynecology.

- The Pelvic Floor Disorders (Clinical Trial) Network (PFDN) is currently implementing four clinical protocols and preparing to implement four others. The first study is a randomized trial to determine which surgical procedures yield the best results in preventing future urinary incontinence for women with advanced prolapse but no incontinence. Another study will determine the occurrence of fecal incontinence, urinary incontinence, and sexual dysfunction in three groups of women after childbirth: women with anal sphincter disruption and repair after vaginal delivery; women without apparent anal sphincter damage after vaginal delivery; and women after cesarean delivery without labor. Magnetic resonance imaging (MRI) and anal ultrasound will be performed in a subset of women to examine the correlation of symptoms with physical dysfunction, to guide evaluation and management in women after anal sphincter disruption and repair at delivery. Additional protocols include the anatomic and functional outcomes after surgery in elderly women with advanced prolapse; a comparison of different catheters used in urodynamic testing; the description of voiding function with and without prolapse and urinary incontinence; and the development of an instrument that measures adaptation in women with pelvic floor disorders. The PFDN currently consists of 7 clinical sites.

- NICHD is funding institutional training in epidemiology and clinical trials for obstetricians and gynecologists. It is also providing mid-career training funding to build the cadre of qualified researchers.

- With NIDDK, NICHD co-funds a randomized trial of the outcomes of different incontinence surgical procedures through the Urinary Incontinence Treatment Network This network will also support a randomized comparison of pharmacologic and behavioral therapies for overactive bladder symptoms (urgency, frequency, and urge incontinence).

- In collaboration with the National Capital Consortium (NICHD, Walter Reed Army Medical Center, and Washington Hospital Center) and the Fellowship in Female Pelvic Medicine and Reconstructive Surgery, NICHD allows Fellows in this 3-year program to spend one year in laboratory research working with NICHD intramural scientists. The first project will study joint hypermobility as a potential marker for different clinical and tissue characteristics in women during and after pregnancy.

- NICHD is considering ways to study urogynecologic problems in the National Children's Study, which offers a unique opportunity to follow a large number of women during and after pregnancy in a longitudinal cohort to observe changes that occur in pelvic anatomy and function with time.

Item

Vulvodynia - Preliminary new research indicates that millions of American women suffer from vulvodynia, a painful and often debilitating disorder of the female reproductive system. Despite its prevalence, inadequate attention has been paid to the disorder by health professionals or researchers. 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. Therefore, the Committee expects the Institute to provide a significant increase in funding for vulvodynia. (p. 134)

Action taken or to be taken

The NICHD continues to fund ongoing research in this area. An epidemiological study funded by NICHD has demonstrated that vulvodynia occurs in almost 16% of women. NICHD is providing support for a clinical trial of low oxalate diet therapy for vulvodynia and through the BIRCWH program, a young faculty member in an obstetrics and gynecology department has been funded this year to conduct a randomized clinical trial of a topical local anesthetic for the treatment of the pain of vulvodynia. Another NICHD funded investigator has organized a large regional conference in New Jersey to acquaint obstetrician/ gynecologists with the latest information regarding this pain syndrome.

The NICHD co-sponsored a Workshop on Vulvodynia in April 2003 where new data were presented which emphasized that vulvodynia is a chronic pain syndrome with some overlap with other syndromes such as interstitial cystitis and irritable bowel syndrome. Newer approaches to basic mechanisms of pain and pain treatment were also explored and the implications of the new basic discovery of the levator ani nerve in the female and its innervation for vulvodynia was presented. Information from this workshop is being widely disseminated to the clinical community. The NICHD is currently working with a Johns Hopkins scientist who plans to submit a conference grant for an international workshop on vulvodynia to be held in two years.

NICHD staff continues to work to encourage new, innovative research into the basic mechanisms and epidemiology of vulvodynia that will provide the basis for a rational approach to treatment and management. The Institute is also participating in a trans-NIH effort to address chronic pain issues.

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

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2004 Amount Authorized	2004 Final Conference	2005 Amount Authorized	2005 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite		Indefinite	
National Institute of Child Health and Human Development	Section 448	42§285g	Indefinite	$1,206,291,000	Indefinite	$1,244,736,000
National Research Service Awards	Section 487(d)	42§288	a/	35,554,000	b/	36,179,000
Total, Budget Authority				1,241,845,000		1,280,915,000

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

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

Appropriations History

Fiscal Year	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation 1/
1996	526,177,000 2/	595,162,000	518,585,000 2/	595,162,000
Rescission				(615,000)
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/ 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 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
Office of the Director	19	19	20
Office of Administrative Management	61	61	61
Office of Science Policy, Analysis and Communication	25	24	24
Center for Population Research	33	33	33
Center for Research for Mothers and Children	48	48	48
National Center for Medical Rehabilitation Research	9	9	9
Division of Scientific Review	23	23	23
Division of Epidemiology, Statistics and Prevention Research	30	30	30
Division on Intramural Research	363	344	344
Total	611	591	592
FTEs supported by funds from Cooperative Research and Development Agreements	(2)	(2)	(2)

FISCAL YEAR	Average GM/GS Grade
2001	10.9
2002	11.0
2003	11.0
2004	11.0
2005	11.0

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

Detail of Positions

GRADE	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
ES-6			
ES-5			
ES-4	2	2	2
ES-3	1	1	1
ES-2			
ES-1			
Subtotal	3	3	3
Total - ES Salary	$427,500	$451,000	$465,000
GM/GS-15	42	42	43
GM/GS-14	74	72	72
GM/GS-13	33	32	32
GS-12	54	53	53
GS-11	34	33	33
GS-10	7	7	7
GS-9	32	32	32
GS-8	32	31	31
GS-7	45	43	43
GS-6	8	8	8
GS-5	9	8	8
GS-4	5	5	5
GS-3	1	2	2
GS-2	2	0	0
GS-1			
Subtotal	378	368	369
Grades established by Act of July 1, 1944 (42 U.S.C. 207):			
Assistant Surgeon General	0	0	0
Director Grade	12	12	12
Senior Grade	6	6	6
Full Grade	5	5	5
Senior Assistant Grade	1	1	1
Assistant Grade			
Subtotal	24	24	24
Ungraded	217	206	206
Total permanent positions	405	395	396
Total positions, end of year	622	601	602
Total full-time equivalent (FTE) employment,end of year	611	591	592
Average ES level	ES-4	ES-4	ES-4
Average ES salary	$142,500	$150,300	$155,000
Average GM/GS grade	11.0	11.0	11.0
Average GM/GS salary	$69,345	$73,200	$75,500

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

New Positions Requested

	FY 2005		
	Grade	Number	Annual Salary
Health Scientistist Administrator	GS-15	1	120,000
Total Requested		1	