

## Achievements in Preventing Morbidity and Mortality by Researchers of the National Institute of Child Health and Human Development

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### SYNOPSIS .....

*In the 20 years since its creation, the National Institute of Child Health and Human Development (NICHD) has become a world leader in promoting research on fertility, high-risk pregnancy, care of newborns, nutrition, learning disorders, mental retardation, development of better contraceptives, and factors that influence family planning. NICHD also supports basic research that sheds light on normal processes in human development.*

*This research has yielded impressive dividends. Improvement in the treatment of premature infants*

*has contributed to a 22 percent decline in infant mortality in the United States between 1976 and 1980. Between 1962 and 1980, the maternal death rate from pregnancy and childbirth dropped 80 percent, owing largely to NICHD-supported research that has led to improved management of a number of conditions that are life-threatening to pregnant women.*

*NICHD-supported research has led to the development of screening tests and treatments for certain metabolic disorders that cause mental retardation. Grantees of the Institute have also discovered a chromosomal disorder known to be a cause of mental retardation in men and have made research advances leading to better home care and a fuller role in community life for persons with Down's syndrome.*

*Other NICHD studies seek to improve family planning methods and to find safer, more effective contraceptives. A promising development in this area is a class of synthetic brain hormones that could provide a new type of birth control pill for women and the first successful chemical contraceptive for men.*

**W**HEN THE NATIONAL INSTITUTE of Child Health and Human Development (NICHD) was established 20 years ago, it became the first noncategorical Institute within the National Institutes of Health, and the first NIH Institute with a mission to study healthy populations as well as those suffering from specific disease.

NICHD's creation in 1962 symbolized an emerging concept: that adult health and well-being are determined in part by episodes early in life, that human development continues throughout life, and that reproductive processes and the management of population problems are of major concern not only to the individual person but to the whole of society. A driving force behind NICHD is the conviction that while the Institute continues to search for solutions to specific disease problems, it must also probe more deeply into all the processes of human development—behavioral and biomedical, normal and abnormal—as a basis for maintaining health and preventing and conquering disease.

The breadth of NICHD's mission has carried it from studies of the regulation of DNA to the forces that shape population growth. In the Institute, the bonding of a steroid hormone to a receptor has been accorded equal importance with the bonding of infant to parent. In essence, the laboratory of NICHD is and has been humankind—from the dissection of molecular events that shape life itself to human interactions.

To carry out its mission, NICHD conducts research at its laboratories in Bethesda, Md., and supports scientific investigations at facilities throughout the country. The Institute has become a world leader in promoting research in such diverse fields as fertility, high-risk pregnancy, newborn care, nutrition, learning disorders, mental retardation, the development of safer and more acceptable contraceptives, and the factors that influence couples' decisions on the number and spacing of their children.

This research has yielded impressive dividends over the past 20 years. More mothers and infants

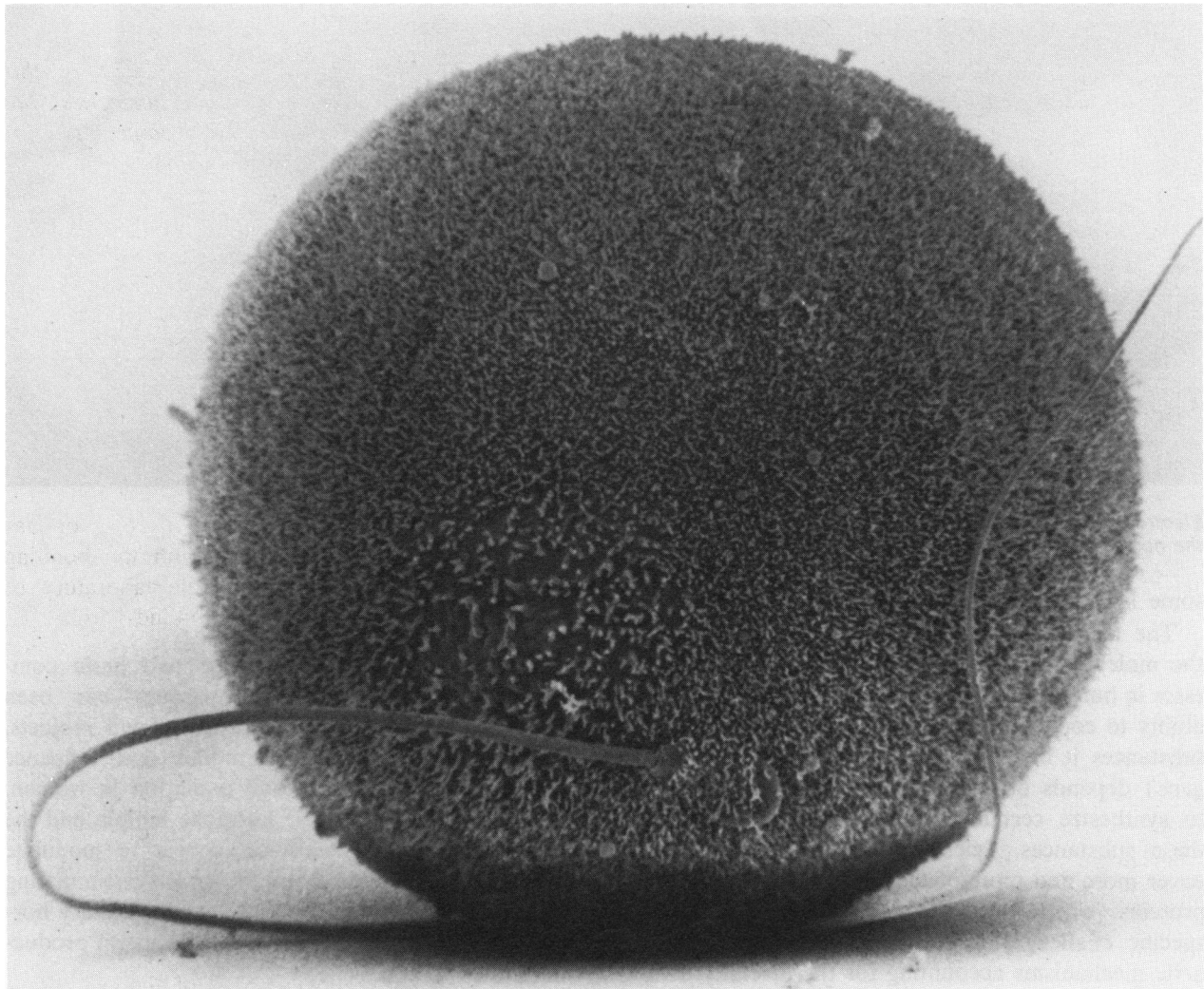
are surviving pregnancy and childbirth today, and children are growing up healthier. Improvements in the treatment of premature infants have contributed to a 22 percent decrease in infant mortality in the United States between 1976 and 1980, a decline that represents the prevention of some 10,000 infant deaths each year. The maternal death rate from pregnancy and childbirth dropped 80 percent between 1962 and 1980, owing in large part to NICHD-supported research advances that led to improved management of toxemia, maternal infections, bleeding, and diabetes—conditions that are life-threatening to pregnant women.

The Institute's research programs have produced many important findings that have overturned old concepts and led to the development of new research strategies and therapies. Following is a sampling of research highlights of the Institute's first 20 years.

## **Molecular Biology**

In 1977, NICHD scientists made a discovery that changed scientific thinking about the organization and function of genes. They found that genes are not arranged in a continuous array of code words as it was originally believed. Instead, segments of genes are separated by intervening sequences of DNA that are not translated into the final product of the gene.

Institute researchers found that DNA segments can be rearranged to form different genes, making it possible for the same piece of DNA to be used in building more than one gene. This finding has helped explain how the body is able to produce almost limitless numbers of antibodies from a limited amount of genetic material. The discovery of intervening sequences also may explain the basis for



*NICHD-supported research on the basic components of fertility—egg and sperm—has greatly enhanced current knowledge of reproductive processes*



*Electronic monitors keep watch as this 3½-pound baby girl sleeps. Research aimed at the number of infants born prematurely has been a priority of NICHD*

some inherited anemias and other genetic disorders.

The Institute is involved in many other studies at the molecular level that shed light on normal processes in human development. For example, the body's ability to cope with the countless varieties of foreign substances it ingests (for instance, various carcinogens) depends on its health status and its capacity to synthesize certain proteins that can metabolize these substances. Scientists are continuing to discover more and more of these proteins, called P-450 proteins, which the liver produces in response to specific challenges by foreign substances. The genetic mechanisms accounting for the diversity of the P-450 system proteins may resemble those of the immune system.

## Human Reproduction

A better understanding of the two basic components of fertility—egg and sperm—has been achieved through many NICHD-supported projects. Grantees have identified hormones that influence sperm production in men and ovulation in women. The newly discovered male hormone inhibin and the female hormone folliculostatin appear to modulate secretion of a pituitary hormone (follicle-stimulating hormone) that, together with a second pituitary hormone (luteinizing hormone), controls sperm production and ovulation.

Other findings enhancing current understanding of basic reproductive processes include the discovery, by

a group of NICHD grantees, of a polypeptide that inhibits the maturation of egg cells, and the identification by another group of scientists of enzymes that facilitate the penetration of the egg by the sperm cell. Grantees first established that the pituitary gland secretes gonadotropins in pulses—not continuously. This discovery has vastly improved knowledge of the way reproductive processes are regulated.

Basic research in reproduction often brings a bonus of medical applications. A recent and dramatic example is research on luteinizing hormone-releasing hormone (LHRH), a brain substance whose structure was determined by two NICHD-supported scientists, Dr. Andrew Schally and Dr. Roger Guillemin. The two were awarded a Nobel Prize in 1977 for isolating and determining the chemical composition of LHRH, which indirectly regulates the reproductive systems of both men and women.

Once the hormone's basic structure had been determined, Schally, Guillemin, and others were able to produce modified versions of LHRH, called analogs, that are much more potent than the natural hormone. These analogs can either promote or inhibit fertility, depending on their chemical structure and dosage.

Scientists at NICHD and Institute-funded researchers around the country have put LHRH analogs to work. Researchers recently showed that the analogs may be useful in treating women with endometriosis, a common cause of infertility. Patients with polycystic ovaries and prostatic cancer also have been treated with LHRH analogs.

NICHD-supported researchers cured a rare form of male infertility using an LHRH analog, and scientists elsewhere used an analog to achieve pregnancy in several women who had been unable to ovulate. At the other extreme in fertility studies, some LHRH analogs are now being used in clinical trials as contraceptive drugs for both men and women.

Intramural scientists at NICHD have had remarkable success in treating precocious puberty with an LHRH analog. Until recently, there was no satisfactory treatment for this disorder, which causes children to undergo sexual development and rapid growth years before the normal age of puberty.

## **Obstetrics**

One of the most exciting medical developments in recent decades has been the recognition that many diseases and abnormalities seen at birth or later in life can be traced to events during embryonic development or delivery and can be prevented or treated. With this in mind, scientists have achieved technological breakthroughs that permit early confirmation

of pregnancy, assessment of fetal well-being, detection of many diseases and defects in utero and, in certain situations, corrective measures that can be taken before the baby is born. Three examples of NICHD-supported research in this area are an ultrasensitive pregnancy test, fetal monitoring, and Rho-Gam.

The most sensitive pregnancy test in use today was developed by NICHD scientists in 1977. In a pregnant woman's blood sample, the test can pick up very low levels of human chorionic gonadotropin, a hormone produced by the developing placenta. Pregnancy can be detected as early as 8 days after conception.

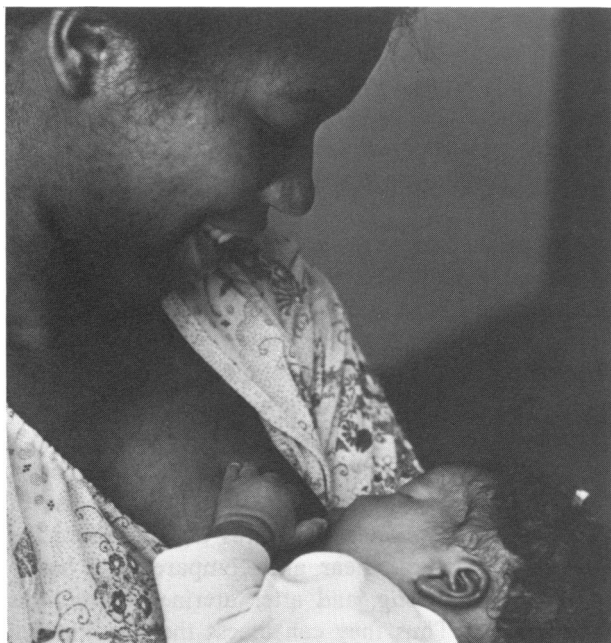
Institute-funded scientists showed that fetal heart rate could be monitored electronically or by use of ultrasound to evaluate fetal status during labor. Today, physicians can hear and compare fetal heartbeats before, during, and after uterine contractions during labor. Thus they can assess the condition of the fetus more precisely and take appropriate steps to ensure its well-being.

In the past, Rh-hemolytic disease (mother-infant blood incompatibility) killed thousands of infants each year. The development of RhoGam, a highly concentrated solution containing immunoglobulins with Rh antibodies, has led to the near elimination of Rh incompatibility by preventing the mother from developing antibodies to Rh-positive fetal blood cells.

## **Neonatal Research**

Each year about 40,000 newborns develop respiratory distress syndrome (RDS). These babies cannot breathe independently because their lungs are immature and lack pulmonary surfactant, a substance that coats the lining of the alveoli in the lung and keeps the lung in the newborn from collapsing or from expanding too much as the newborn begins to breathe. The Institute's finding that lung maturity could be assessed by measuring components of pulmonary surfactant in amniotic fluid opened a new vista of research and treatment. These reports were followed by the finding that glucocorticoids, administered to the pregnant woman, could be an effective therapy to hasten this aspect of maturation of the fetal lung.

A high priority of NICHD has been research aimed at preventing RDS and other ailments of premature infants by learning the causes of premature labor. Recently grantees found that the enzyme released by the amniotic membrane to start labor is also produced by certain bacteria that can infect the female reproductive tract. Investigators are now test-



*NICHD-funded research has virtually confirmed that breast milk is the ideal food for normal, full-term infants, at least for the first 6 months of life*

ing the possibility that the bacterial enzyme may initiate premature labor. If the enzyme is confirmed as a major cause of premature labor, its effects might be readily prevented.

### **Mental Retardation**

NICHD scientists have made important contributions to detailed understanding of the metabolic basis of certain inherited diseases that can lead to mental retardation. The resulting ability to prevent and treat some of these disorders surely ranks among the Institute's significant research achievements.

Technological progress in the past two decades has led to the development of sensitive biochemical tests for newborns that can uncover deviations from normal metabolism, permitting precise diagnoses and prompt treatment. In phenylketonuria (PKU), for example, the body's inability to metabolize an amino acid leads directly to mental deficiency; however, detection of the defect permits treatment.

NICHD-supported scientists recently developed a method of postnatal screening for congenital hypothyroidism, whose incidence (1 affected infant in 4,000 births) exceeds that of PKU. Once identified, this disorder is easily and successfully treated by thyroid replacement. Left untreated, the condition results in severe mental retardation and irreversible damage to the central nervous system. Now, screen-



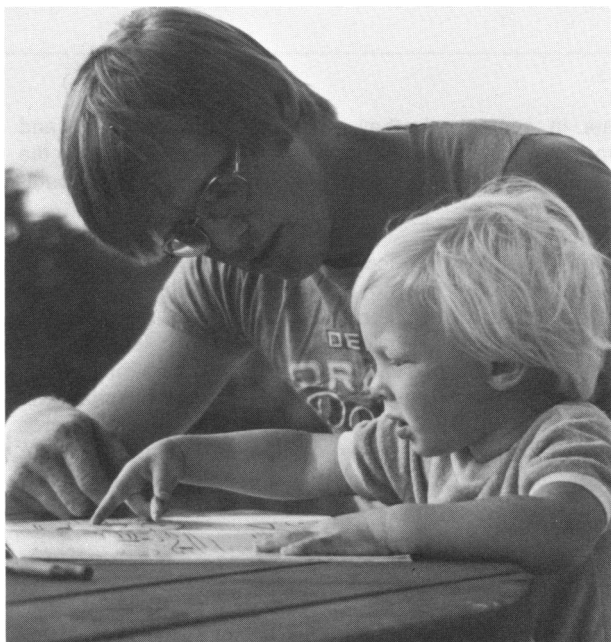
*Routine laboratory screening of the blood sample being taken from this newborn's heel will check for congenital hypothyroidism. The screening method was developed by NICHD-supported scientists*

ing for PKU and congenital hypothyroidism can be done at the same time, using the same drop of infant blood.

Another important advance in understanding the causes of mental retardation is the discovery by NICHD-supported scientists of a sex-linked chromosomal disorder called fragile-X syndrome, which is now known to be a frequent cause of mental retardation in men. While much remains to be learned about the relationship between the fragile-X chromosome and mental retardation, it appears that this association is as important as that between Down's syndrome and mental retardation. The discovery of fragile-X syndrome will provide the basis for reliable identification of carriers and for prenatal diagnosis and genetic counseling.

### **Down's Syndrome**

An exciting discovery has been the finding of plasticity of intelligence in the mentally retarded. Because of this observation, it can no longer be claimed that intelligence is fixed and therefore not susceptible to remedial efforts. Behavioral scientists supported by NICHD have found that the functioning level and behavior of children with Down's syndrome can be appreciably improved by use of appropriate educational methods. This type of research has contributed to better home care and a fuller role in community



*Interaction between fathers and their children has been the focus of many NICHD studies. New findings indicate that infants as young as 6 months old are more persistent in problem-solving tasks if their fathers play with them*

life for persons with Down's syndrome as well as to better education of the public about the disorder.

NICHD-supported studies have shown that the father is the source of the genetic defect that leads to Down's syndrome in about 20 to 30 percent of cases. This discovery has led to new approaches in genetic counseling and research design. In addition, NICHD researchers have recently identified a chromosomal abnormality in mice similar to that present in Down's syndrome. The mouse model will allow essential basic experiments to be conducted that are impossible to perform in humans.

Dramatic studies involving both biomedical and behavioral sciences show that in infant monkeys the complexity of the connection between nerve cells of the brain is decreased by isolation, but that this phenomenon is reversed by socialization. This finding supports earlier evidence of changes in central nervous system morphology as a result of socialization.

## **Normal Development**

Child psychologists have shown that newborn and very young infants are not at all oblivious to their environment but can differentiate and respond to a variety of cues. The new techniques that have been developed to measure these responses should enable us to identify those infants whose proper cognitive development is at risk.

NICHD-funded studies have examined the influence of parent-child interactions on child development. Findings that tactile stimulation is important for normal development have encouraged a trend towards more mother-infant and father-infant contact, especially in the period immediately after birth. Studies also show that early contact with the baby improves the mother's confidence in her ability to care for the child.

## **Family Planning**

Other NICHD research is aimed at improving existing family planning methods and developing safer, more effective contraceptives. A number of new developments look promising, including a class of synthetic brain hormones (LHRH analogs) that could be a new type of birth control pill for women and become the first successful chemical contraceptive for men.

Assessing the safety of birth control methods now used by millions of men and women is a major part of NICHD's program in population research. Studies of oral contraceptives have demonstrated the dose-risk relationship and helped define high-risk populations, such as smokers and women over 35. As a result, pill formulas have improved, prescribing practices have changed, and consumers are able to make more informed decisions.

Institute-funded studies recently confirmed some of the pill's other benefits, such as protection from pelvic inflammatory disease and cancer of the ovary and uterine lining. Other major studies have focused on the side effects of the intrauterine device, and several large projects evaluating the safety of vasectomy are in progress.

The increasing popularity of barrier methods of birth control has prompted Institute-funded development and evaluation of new spermicides, diaphragms, and cervical caps, as well as large-scale trials of existing barrier devices.

This brief recounting of the history and accomplishments of NICHD underscores how the Institute's search for understanding has followed the continuum of life itself. But the accomplishments of the past decades are surely only the beginning. The potential offered by new and powerful biological tools and the current revolution in technology undoubtedly will produce great future benefits, not only to the health of Americans but also to that of other people around the world.