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ABSTRACT

Providing several examples of current research efforts, this report describes the research on maternal and child health supported by the National Institute of Child Health and Human Development (NICHD). The Institute conducts a coordinated program of research and research training to advance knowledge related to pregnancy and maternal health, fetal growth and maturation, and the well-being of the newborn. Research in the area of high-risk pregnancy includes: the impacts of medications; psychosocial dynamics of pregnancy; and the effects of diabetes, pregnancy-induced hypertension, malnutrition, infections, and hematological problems. In the area of premature labor and birth, research is concerned with the determinants of normal labor, the causes of premature labor, how to stop premature labor, and the causes of fetal growth retardation. Research to reduce disorders of the newborn focusses on neonatal infection, interventricular hemorrhage, respiratory distress syndrome, jaundice, and the care of the low birthweight infant. In the areas of mental retardation and behavioral development, research is directed toward prevention of retardation among the offspring of individuals successfully treated for phenylketonuria (PKU) and toward better understanding the effects of cigarette smoking, eating disorders, and accident proneness. (Author/CB)

Special Report to Congress:

MATERNAL AND CHILD HEALTH

FY 1983

National Institute of Child Health and Human Development

NATIONAL INSTITUTE OF HEALTH

National Institute of Child Health and Human Development

MATERNAL AND CHILD HEALTH

The primary focus for research on maternal and child health at the National Institutes of Health is the National Institute of Child Health and Human Development (NICHD). The Institute supports and conducts a coordinated program of research and research training to advance knowledge related to pregnancy and maternal health, fetal growth and maturation, and the well-being of the newborn. The program emphasizes the interrelationship of specific health and developmental problems occurring in the prenatal, perinatal, and infant periods of life, and the effects of these events upon subsequent child health and development. Major concerns are maternal health problems that affect the fetus and infant, those related to newborn adaptation to extrauterine life, and events in the newborn period that can influence subsequent development.

Maternal and child health research efforts supported by the NICHD are in several general areas: high-risk pregnancy; premature labor and birth; newborn disorders; sudden infant death syndrome; birth defects; mental retardation; and behavioral development. Selection of these priority areas is based partly on the following considerations:

The standardized perinatal mortality rate is lower in the United States than in any other country. This means that if international comparisons of perinatal mortality (late stillbirths plus newborn deaths) are made, controlling for differences in population numbers and birthweight distributions, the chances for fetal and newborn survival are best in this country. However, this statistical comparison tends to conceal several problems.

First, the dramatic improvements in infant and perinatal mortality in this country in recent years are accounted for by sharp drop in newborn mortality. The fetal death rate, which is the other component of perinatal mortality, has shown very little improvement. Therefore, the problems associated with high-risk pregnancy must be a target of future research efforts.

Second, the foregoing statistical calculation of perinatal mortality does not reveal the fact that this country has one of the highest prematurity rates of all developed nations, and that there has been very little improvement in this measure in many years. Prematurity is associated with significantly higher risk of adverse pregnancy outcome, accounting for the United States relatively poor standing among nations when unstandardized comparisons are made of infant mortality. Thus, special priority is assigned to research dealing with premature labor and birth.

Third, despite the impressive improvements in neonatal mortality, the fact remains that three-fourths of all infant mortality occurs in the newborn period, justifying continuing research in this area.

Fourth, the leading cause of mortality in the post-neonatal period (1-12 months) is the sudden infant death syndrome (SIDS). Because of a major emphasis by NICHD in recent years, there is a research momentum in this area which is scientifically productive and clinically relevant to SIDS and to other problems as well. Progress and future research needs concerning SIDS is presented in a separate report.

Fifth, mental retardation remains poorly understood and continues to impair the potential of many children. Research efforts relating to mental retardation comprise a separate report.

Finally, many of the health problems of children must be understood and treated in the context of normal behavioral development. Therefore, a major NICHD research emphasis is the development of human behavior from fetus to adolescence, and into early maturity. The major concern is to determine how biological and socioenvironmental forces interact to produce normal behavioral development.

High Risk Pregnancy

Research under this rubric addresses a variety of conditions complicating normal gestation. Emphasis is placed on examining the roles of the cardiovascular, respiratory, endocrine and genitourinary systems in women during normal pregnancy and their contribution to and/or involvement in abnormal conditions throughout gestation. The problems addressed include diabetes, pregnancy-induced hypertension, malnutrition, infections, and hematologic problems associated with pregnancy. Other research focuses on placental function, maintenance of pregnancy, the impacts of medications, and psychosocial dynamics of pregnancy.

As it has been known for some time that infants of diabetic mothers are at higher risk for congenital abnormalities, four major research programs are seeking to elucidate how the fetal environment may predispose to such events. The unresolved issue of whether infants of diabetic mothers suffer impaired intellectual development is also under investigation by NICHD.

Non-diabetics have insulin continuously available. New technological advances are near the point of providing comparable insulin availability to diabetics by means of portable computerized insulin pumps. However, before insulin pumps are recommended for use during pregnancy, the potential benefits must be evaluated. Toward this end, a multi-center study has been initiated by NICHD. This study will compare rates of congenital abnormalities in pregnancies with differing degrees of metabolic control. If the results favor "tighter" control of the blood insulin levels, then the insulin pump technology may offer an improved method of therapy.

Pregnancy-induced hypertension (toxemia) remains one of the most common serious complications of pregnancy, accounting for considerable perinatal mobidity and mortality. The baboon model is being developed to investigate the etiology of this disorder by Dr. Dennis Cavanaugh, a grantee at the University of Florida. Early results suggest that a hypertensive syndrome during pregnancy can be produced by uterine artery occlusion, resulting in deficient circulation to the uterus and placenta. Analysis of this syndrome may offer better understanding and control of this disease.

Assessment of fetal status is an area in which significant progress has been made in recent years. Currently, an NICHD-supported investigator--Dr. John Bissonette at the University of Oregon-is evaluating fetal breathing movements as an index of fetal wellbeing. Specifically, the possible relationship between cerebral metabolic status and fetal breathing activity holds potential for assessing prenatally the significance of perinatal insults to the developing brain and nervous system.

Investigation of adverse drug effects has focused on developmental and functional impacts on both embryo and fetus. One concern focuses on possible deleterious effects on fetal development of chemical compounds used prior to pregnancy. Thus, the possibility of adverse pregnancy effects associated with spermacide use has been examined by NICHD staff using data from the Kaiser Permanente Program, Walnut Creek, California. The investigators found no increased teratogenic risk associated with contraceptive use of vaginal spermacides, either before or during early pregnancy.

Maternal health behavior can have important implications for the fetus. Specifically, maternal smoking has been associated with a reduction in average birth weight. It has been suggested that the smoking effect is mediated by reduced maternal appetite and nutrient intake. During FY 1982, NICHD staff analyzed data from the Collaborative Perinatal Study and found that smoking has a negative effect on birth weight that is independent of pre-pregnant weight and gestational weight gain. Grantee Dr. L. Stanley James at Columbia University is carrying out studies of fetal hypoxia in both humans and in a subhuman primate (baboon) model. Evidence suggests that continued smoking can produce chronic fetal hypoxia, which may cause adverse effects such as fetal growth retardation. Other clinical conditions associated with fetal hypoxia, e.g., chronic maternal hypertension, may also be better understood because of the availability of this relevant animal model.

Dr. Gilbert Forbes, an NICHD-support scientist at the University of Rochester, has conducted behavioral studies of pregnant adolescents which show a high frequency of dietary inadequacies, including insufficient protein and excessive calories, coupled with the use of alcohol and tobacco.

Premature Labor and Birth

There is an important research interest in the determinants of the normal onset of labor, why labor sometimes begins prematurely, how premature labor might be stopped without detrimental effects, and the causes and mechanisms of fetal growth retardation.

Understanding the pathophysiology associated with preterm labor will be facilitated by expanding knowledge of the physiologic events leading to normal parturition. Studies being conducted by grantee Dr. Paul McDonald at the University of Texas tends to implicate the fetal membranes as the metabolic focus of steps leading to normal parturition. The membranes may receive biochemical signals from the fetus via amniotic fluid, and convey messages via the metabolically active decidual tissue (placenta) to the contractile myometrium (the muscular wall of the uterus). Scientists working on this project are actively studying prostaglandins--natural substances which cause uterine contractions--in order to characterize the precursor forms and clarify the mechanisms involved in the release of such forms.

Investigators in another project, led by Dr. Robert K. Creasy at the University of California, are using a multifacet approach, to examine endocrine, immunologic, and infectious mechanisms of preterm labor in a prospective manner. The endocrine aspect hypothesizes that preterm labor and birth may result from a failure of hormonal mechanisms that normally inhibit parturition until term. Specifically, a sharp decline in progesterone production precedes parturition in most mammalian species, but this finding has not been documented in humans. These studies suggest, however, that local tissue concentrations of progesterone may be decreased without a reduction in circulating progesterone. Also, a hormonal mechanism has been identified in the fetus which can reduce progesterone production in the placenta. Thus better understanding of the role of progesterone in parturition may offer opportunities to alter its concentration therapeutically with the posssible consequence of inhibiting preterm labor.

These same investigators have developed preliminary data suggesting that an immunosuppressive factor associated with normal pregnancy is deficient in some cases of preterm labor, and that the microorganism chlamydia appears to be relatively prevalent in the genital tracts of women who subsequently go into preterm labor. Thus, a multi-factorial picture of causation of preterm labor is emerging, indicating the importance of individualized diagnosis and therapy.

Staff of NICHD became aware of published suggestions that bacteria in the maternal genital tract could provide an exogenous source of phospholipase A2, an enzyme capable of initiating a biochemical cascade leading to preterm labor. However, published evidence of the adverse consequences on pregnancy outcome of

asymptomatic genitourinary infection, and of benefits from its therapy was conflicting. A workshop was organized to examine this issue, and to identify research needs. The report of this workshop will hopefully stimulate additional research in this area.

Finally, the problem of preterm labor cannot be separated from the problem of fetal growth retardation. These two problems frequently co-exist in the same infants, but also make separate contributions to the overall problem of low birth weight which is responsible for excessive infant morbidity and mortality. Fetal growth retardation may result in part from a diminished nutrient supply from the placenta. Studies by NICHD grantee Dr. James Lemons at the University of Indiana in a sheep model suggest that fetal/placental adaptability to diminished nutrition exists. However, metabolism may be altered away from growth and toward energy source (glucose) production. Understanding such adaptation will facilitate appropriate nutritional therapy of the growth-retarded fetus, as well as the ability to assess whether the noted "adaptations" are reversible (i.e., returnable to a normal growth pattern).

Research by grantee Dr. Valerie Charlton at the University of California with a sheep model for fetal growth retardation has shown that direct fetal nutritional supplementation can limit the fetal growth retardation usually produced in the model. This line of research ultimately may lead to intrauterine nutritional therapy in humans.

Disorders of the Newborn

Newborn disorders are causes of mortality, and also can produce long-term disability for many affected individuals who survive. Research to reduce the impacts of these problems is directed toward maternal conditions that can affect the fetus, adaptation of the newborn to its environment, and problems in the early weeks of life that influence subsequent development and behavior. Of particular importance are neonatal sepsis (infection), interventricular hemorrhage, respiratory distress syndrome, necrotizing enterocolitis jaundice, and care of the low birthweight infant.

Neonatal infection due to Group B Streptococcus (GBS) can be very serious. The increasing prevalence of this infection has led some clinicians to treat all newborns, and others to treat all maternal carriers of the organism during pregnancy. NICHD researchers led by Dr. Hugh Dillon at the University of Alabama have been studying the epidemiology of the disease in order to determine the best time for possible intervention. Another exciting approach to the same problem is immunologic. Maternal serum antibodies to several specific antigens in an animal model are being measured and correlated with susceptibility to GBS infection by Dr. Neal S. Rote, at the University of Utah. Such studies could lead to clinical methods with which to predict neonatal susceptibility to GBS infection, and to evaluate the efficacy of GBS vaccines now being developed.

The nutritional status of newborns is of great importance, especially in the presence of immaturity and disease. Nutritional status currently must be inferred from gross parameters such as weight, fluid balance, and composition of body fluids. Often, changes in nutritional status are reflected slowly in such measurements. One study by Dr. Jay Perman, a grantee at the University of California, is assessing the adequacy of gastrointestinal absorption in neonates by the analysis of their expired air. Such an approach holds promise for improved clinical care of neonates as well as for providing a better research tool.

Mental Retardation and Behavioral Development

For many years, all newborn infants have been routinely screened for the metabolic disorder, phenylketonuria (PKU), which produces mental retardation. Appropriate dietary therapy has been instituted for those having the disease. Many of the successfully treated children are now entering reproductive age, and research efforts are being directed toward prevention of retardation among the offspring of these individuals. NICHD-supported investigator Dr. Siegfried Pueschel at Brown University has developed an animal model which indicates that fetal levels of the amino acid phenylalanine are higher than maternal levels, suggesting that stricter dietary therapy may be advisable during pregnancy. Currently, comparative placental transfer studies of primate and human placentas are being done to assess the implication of these findings for human pregnancies. Dr. Pueschel is performing chronic phenylalanine feeding experiments during pregnancy in the subhuman primate model, with extensive psychological testing of the offspring. Such experiments should also help identify the strictness of dietary therapy needed during pregnancy in humans with PKU.

Another category of behavioral research includes studies designed to further our understanding of behavoirs which are harmful to health, such as cigarette smoking, eating disorders, and accident-proneness. NICHD investigators have agreed to use biochemical markers as objective measures of smoking activity. Results from an NICHD study by Drs. Maurice Mittelmark and Russell Leupker at the University of Minnesota measured saliva thiocyanate among 7th-12th graders. This test provided an independent assessment of whether or not an individual smoked. The results indicate that the incidence of cigarette smoking among this group may not be declining, as suggested by previous reports.

Maternal and Child Health

	1980	1981	1982	1983 Estimate	1984 Estimate
National Institutes of Health:					
National Institute of Child Health and Human Development	$121,785,000	$128,505,000	$130,267,000	$144,627,000	$148,150,000
TOTAL, NIH	$121,785,000	$128,505,000	$130,267,000	$144,627,000	$148,150,000