



Research Roundtable Summary

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FOURTH**

in a Series of Seminars

on MCHB-funded

Research Projects

Intergenerational Factors in Birth Outcome

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About This Series

The Research Roundtable Series, sponsored by the Maternal and Child Health Bureau (MCHB), disseminates the results of MCHB-funded research to policymakers, researchers, and practitioners in the public and private sectors. The results of these projects influence future service, research, and policy development. The Research Roundtable sessions provide an opportunity for researchers to discuss their findings with policymakers, MCH program directors, service providers, and other health professionals.

The MCHB Research Program is directed by Dr. Gontran Lamberty and administered through the Division of Systems, Education and Analysis, MCHB, Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services. The purpose of the research program is to support applied research relating to maternal and child health services that shows promise of substantial contribution to the advancement of these services.

Introductions

Dr. Wadhvani introduced the speakers for the Research Roundtable. Dr. Irvin Emanuel is a professor at the University of Washington, School of Medicine. He is also associate director of the Maternal and Child Health Program. Dr. Emanuel has published extensively in such journals as the *Journal of the American Medical Association*, *New England Journal of Medicine*, and *Pediatrics*. He has also written several chapters on prenatal health and mental retardation. Dr. Emanuel received his doctorate of medicine from the University of Rochester.

Dr. Mark A. Klebanoff is the acting director of the Division of Epidemiology, Statistics and Prevention Research, National Institute of Child Health and Human Development, National Institutes of Health. Dr. Klebanoff has served as the associate editor for the *American Journal of Epidemiology* and is a member of the Advisory Board of Paediatric and Perinatal Epidemiology. Dr. Klebanoff has also contributed articles to such journals as the *American Journal of Obstetrics and Gynecology*, *Journal of the American Medical Association*, and *New England Journal of Medicine*. Dr. Emanuel received his doctorate of medicine from John Hopkins University.

Presentation of Research and Relevant Findings

Statement of the Problem

Research on factors influencing pregnancy outcome has been mostly restricted to the time of pregnancy and its course. This approach has failed to adequately explain why certain groups of mothers—for example, low-income mothers and African-American mothers—are at excess risk for poor outcomes.¹ There is evidence that maternal stature is inversely related to the risk for suboptimal outcome; thus, a better understanding about how mothers have grown may shed light on pregnancy outcomes. A mother's height is the result of a lifetime of growth, both prenatal and postnatal, which in turn has been influenced by both genetic factors and a wealth of nongenetic environmental factors that are poorly understood.² Low income or low socioeconomic status, however defined, is a very important factor. The factors that influenced the mothers' growth are the same as those influencing the growth of infants and children today; thus, the intergenerational study of growth is a potentially important area of inquiry.

Research Questions

The aim of this study was to investigate how a mother's birthweight and other maternal factors were associated with maternal complications of pregnancy and birth outcomes. In Washington State, it was possible to study four racial/ethnic groups: non-Hispanic whites, African Americans, Native Americans, and Hispanics.

Population Description

Since 1987, all nonfederal hospitals in Washington State have been required to provide the Department of Health with a computerized discharge summary of all admissions. The Department of Health links the summaries of all obstetric and neonatal admissions to all data from the certificates of live births, infant deaths, and fetal deaths, to form the Birth Event Records Database (BERD). We have linked the BERD for 1987–95 to the birth certificates of mothers born in the state since 1949, when birthweight was first recorded on the birth certificates. We took a 10 percent random sample of births to white women and a total sample of births to women in the three minority groups. We had an 88.8 percent successful linkage of the BERD file to mothers' birth certificates. Our final database of 46,000 births to 38,000 mothers in four racial/ethnic groups is rich in biomedical and sociodemographic data.³ We have also successfully linked 76 percent of these births to the driver's license database to obtain mothers' self-reported heights.

Results

The linked series were at slightly lower risk than the unlinked series with respect to sociodemographic characteristics, infant low birthweight (LBW), and preterm birth. All results reported are for singleton live births to singleton mothers. The maternal birthweight distribution of African Americans was skewed downward compared with the distribution of whites, Native Americans, and Hispanics, which were similar.

There were inverse associations between a mother's birthweight and her child's risk for LBW, preterm birth, very low birthweight, very preterm birth (< 34 weeks), and being small for gestational age (SGA). At all maternal birthweight levels, the LBW rates were higher for African Americans than for the other three racial/ethnic groups, which resembled one another. In contrast, at all maternal birthweight levels, the rates of infant preterm birth of the three minority groups were similar and were higher than that of whites. Mean birthweights of mothers of infants with respiratory distress syndrome were significantly lower

than those of mothers of normal infants in three groups: whites, African Americans, and Native Americans.

Mothers who had been SGA were at increased risk for having infants who were SGA. However, in the four groups, fewer than 25 percent of the SGA infants had SGA mothers. Similarly, mothers who had been large for gestational age (LGA) were at increased risk for having LGA infants. Again, fewer than 20 percent of LGA infants had mothers who had been LGA. Among whites and Hispanics, an SGA mother's risk of having an SGA infant was reduced as the mother's or grandmother's height increased. The rate of infant SGA decreased as the mother's prepregnant weight increased in all groups but the African Americans. The rates of infant LGA increased as grandmother's height, mother's height, or mother's prepregnant weight increased in all four groups.

In all but the Hispanics, mothers who were preterm were at increased risk for having preterm infants. However, fewer than 20 percent of the preterm infants had mothers who had been preterm. Preterm mothers were not at increased risk for having SGA infants, and SGA mothers were not at increased risk for having preterm infants.

Predicting infant outcome at the first antenatal visit is a persistent challenge. We developed a multiple linear regression model that included 10 variables usually available at that time, plus the mother's birthweight. Using this model, we found a stronger association with infant birthweight than with pregnancy weight gain, which is known only at the end of pregnancy. In this model, mother's birthweight, height, and prepregnancy weight were the only predictors that were significantly related to infant birthweight in all four groups.

Maternal birthweight was also associated with complications of pregnancy and delivery. Maternal birthweight was related to the risk of gestational diabetes in all four groups. African-American mothers who weighed less than 2,000 g or more than 4,000 g at birth were at increased risk for gestational diabetes; a downward trend related to the mother's birthweight was seen in the other groups. Mother's birthweight and infant birthweight also interacted to produce an increased risk for cesarean section. Women who were (1) small at birth but delivered large infants or (2) large at birth but delivered small infants were at increased risk for cesarean section.

Conclusions

This presentation provides additional evidence to support the concept that the quality of birth outcomes is influenced by the quality of growth of mothers-to-be from one generation to the next. The presence of important risk factors before pregnancy indicates the need for interventions before conception, particularly interventions that might help to optimize prepregnancy weight and to influence child growth and health.

Reactor Response

Dr. Emanuel's work during the past 20 years has amplified and extended observations originally made by Margaret Ounstead and others; thanks to this work, we now recognize that a mother's birthweight is an important predictor of her children's birthweight. In addition, we now have the results of Dr. Emanuel's impressive study of record linkages, in which two generations of birth certificates were linked to hospital summaries and driver's licenses.

These results extend previous observations made by Dr. Emanuel and largely confirmed by others. Women who were SGA at birth were at increased risk of having SGA children, while women who were preterm at birth were at increased risk of giving birth to preterm infants. This was true in women from most of the four racial/ethnic groups studied. Women who were SGA were not at risk of having preterm infants, and women who were preterm were not at risk of having SGA infants. These results confirm those reported previously by Klebanoff et al.⁴

In his last paragraph of results, Dr. Emanuel touches briefly on maternal birthweight as a risk factor for pregnancy complications. These results open the door to an area of research that may ultimately prove to be of far broader importance than the intergenerational association of size at birth: the association between early-life characteristics and the development of chronic diseases during adulthood. Dr. Emanuel notes that both very small and very large women are at risk for developing gestational diabetes, which is a marker for the later development of type 2 diabetes. My colleagues and I have also recently shown that women who were SGA are at increased risk for developing gestational hypertension, which may be a marker for the later development of chronic hypertension.⁵ Rich-Edwards and colleagues have recently reported that low birthweight is a risk factor for type 2 diabetes⁶ and coronary artery disease⁷ in middle-aged women.

Where is this line of research taking us? That size at birth runs in families is now unquestioned. It seems likely, although not yet beyond question, that size at birth is associated with many of the chronic diseases of adulthood. In particular, small size at birth probably puts people at somewhat increased risk of developing hypertension, type 2 diabetes, hyperlipidemia, and coronary artery disease. Large size at birth may perhaps put people at somewhat increased risk of breast and prostate cancer.

The important next step must be to determine the mechanisms by which these phenomena operate. I believe that there are three broad classes of mechanisms. The first one is purely genetic. Might there be genes that influence the size at birth of parents and their children, and might these genes (or other genes closely linked to them) also influence the risk of the chronic diseases noted above?

The second class of mechanisms is purely environmental. Might suboptimal conditions experienced before birth permanently damage individuals and thereby predispose them to give birth to small children 25 years later, develop heart disease 45 years later, and/or succumb to breast or prostate cancer 65 years later?

The final mechanisms represent interactions between our genes and the environment. Might a particular gene make one person more susceptible than another to a particular environmental insult? We have already seen this with folic acid and neural tube defects. Women with a particular variant of methylenetetrahydrofolate reductase (MTHFR) must consume more folic acid than other women to avoid having a child with spina bifida. Recently, genetic polymorphisms have been discovered that make individuals produce especially vigorous inflammation when infected. Since many cases of preterm birth may be due to intrauterine inflammation, might women with this polymorphism be more likely to have a preterm infant should they be infected with, for example, bacterial vaginosis?

It is important to determine which of these three mechanisms is operating. The first one is probably not preventable, but the second and third mechanisms may provide us with avenues to prevent both low birthweight and chronic diseases of adulthood.

Discussion

The discussion focused on the complexity of determining the ways that intergenerational factors influence birth outcomes. Several participants advocated the need for more research that includes the influence of paternal intergenerational factors. The limited existing research suggests that the intergenerational factors of fathers and mothers play a role in birth outcome. More research is needed to explain the exact role these factors play. The audience agreed that future research needs to focus on testing theories of how intergenerational factors of both parents influence birth outcomes.

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