

MEDICINE

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Dr. Charlotte Hobbs

Piecing together
the causes of
birth defects



Lifelong inquisitiveness led to a multifaceted educational and career journey for researcher and pediatrician Charlotte Hobbs.

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So many **QUESTIONS** ...

But birth defects researcher Charlotte Hobbs believes that answers to the most baffling congenital disorders can be found.

Charlotte Hobbs, M.D., Ph.D., was a child in Ontario, Canada, in the 1960s when scientists first linked folate deficiency in pregnancy with neural tube defects. It would take 30 years of additional research, however, before folate recommendations were issued for women, foods began to be fortified with folic acid, and massive educational campaigns vastly reduced the incidence of neural tube defects.

“We’ve gained some knowledge from researchers who came before us, but we have not yet identified the causes of most birth defects,” said Hobbs, a professor and chief of the Birth Defects Research Section in the College of Medicine Department of Pediatrics.

Some birth defects are caused by a single gene or chromosomal abnormality, or a specific teratogen, Hobbs explained. However, about 70 percent are due to a complex interaction between environmental exposures, lifestyle choices, and genomic and epigenomic susceptibilities.

“Because it can take such a long time to identify causes, there has to be a strong belief that the causes can be found,” Hobbs said. “Fortunately, recent advances in genomics and epigenomics allow us to look into the black box of causes with new tools.”

And that’s what keeps Hobbs going. “I strongly believe that there are causes that are yet to be found,” she said. “I hope that our work, along with that of other scientists throughout the world, will lead to new discoveries that will reduce the numbers of babies born with defects.”

One in every 33 babies in the United States is born with a defect. In Arkansas, a baby is born with a birth defect every five hours, and every four days, a baby dies because of a birth defect.

Hobbs, who trained as an epidemiologist as well as a physician, is director of the Arkansas Center for Birth Defects Research and Prevention – one of the nation’s leading centers – and scientific director of the Arkansas →

Reproductive Health Monitoring System. Since joining the faculty in 1996, she has been awarded more than \$37 million in competitive research funds and state appropriations for research, comprehensive surveillance of birth defects in Arkansas and prevention activities.

Major New Study Hopes to Shed Light

This year, Hobbs and her colleagues are gearing up for the largest ever investigation of child health in the United States – the congressionally mandated National Children’s Study (NCS). Funded by the National Institutes of Health, the study will track more than 100,000 children at 105 sites across the country from pre-birth to age 21 to learn more about the causes and effects of many childhood diseases and how both genetics and the environment impact children’s health and development. It is hoped that the study will shed significant light on major health issues such as the rising prevalence of autism and prematurity rates.

Benton County in northwestern Arkansas is one of 105 selected sites for the NCS. Hobbs is the principal investigator of a \$14.4 million, five-year grant awarded to the Arkansas Children’s Hospital Research Institute in 2008 to fund Arkansas’ participation in the initial phase of the study. Jim Robbins, Ph.D., a professor of pediatrics in the College of Medicine (and, incidentally, Hobbs’ husband) is serving as the local site investigator.

This summer, in collaboration with Benton County obstetrical care providers, Hobbs and Robbins will lead a team of UAMS investigators in the launch of a pilot study to evaluate a novel recruitment method for potential NCS participants. UAMS will be joined by nine universities, including Yale, in the nine-month pilot project.

One of the earliest cohort studies nationwide will explore the impact of glucose metabolism imbalance on adverse pregnancy outcomes. Hobbs proposed this particular study while serving as the non-federal co-chair of the working group that designed the birth defects-related components of the overall study in 2001 through 2004.

On the Forefront

Hobbs’ achievements as director of Arkansas Center for Birth Defects Research and Prevention demonstrate

why she was selected to co-chair the working group for the new study. The center is highly regarded among the nine programs of its kind funded by the U.S. Centers for Disease Control and Prevention (CDC). The centers participate in the National Birth Defects Prevention Study, an earlier and continuing effort focused on congenital disorders. Hobbs is an active member of the genetic analyses workgroup and holds many other roles. The Arkansas center has the highest rates of participation of mothers in the CDC’s national case-controlled studies and is one of the first sites to engage in genomics research using samples from the national study.

The centers also conduct birth defects surveillance and independent research activities.

First funded in late 1997, the Arkansas center has been renewed for two additional five-year grant periods. Hobbs had just finished her pediatrics residency at UAMS and joined the faculty as an assistant professor when she began working on the initial grant. By then, her lifelong inquisitiveness and interest in health and science already had drawn her into a multi-faceted educational and career journey.

She’s Always Asked “Why?”

“I loved the sciences and math when I was growing up,” Hobbs said. “I loved asking questions. I’ve always been very analytical and wanted to understand why things were a certain way.” She also wondered why some children were born with birth defects while others are not. Her own mother had been treated for an abdominal wall defect at birth and had suffered through a stillborn death in her first pregnancy and two later miscarriages.

Hobbs graduated from Carleton University in Ottawa with distinction in psychology in 1978. After earning a master’s degree in human communication disorders at McGill University in Montreal in 1981, she began working with children who were hearing impaired or had other disabilities that interfered with communication. “But that left me with more questions than answers, in a way,” Hobbs said, explaining her decision to train as an epidemiologist in 1988.

While working toward a doctoral degree at McGill, Hobbs realized how much she also wanted to practice clinically as a physician. After being accepted at 10 medical

schools, she decided to attend McMaster University in Hamilton, Ontario, because it was in the forefront of clinical epidemiology and evidence-based medicine, which are essential building blocks for translational research. Hobbs completed her doctoral dissertation while attending medical school. She received her doctoral degree in epidemiology and biostatistics in 1991 and her medical degree a year later.

Building a Future in Arkansas

Hobbs met Jim Robbins, a Little Rock native and professor of medical sociology and psychiatry, while at McGill, and the couple married the year that she graduated from medical school. Hobbs decided to specialize in pediatrics, and after interviewing for residency in several programs – including Duke and Boston Children’s Hospital – the couple decided that UAMS and Arkansas Children’s Hospital (ACH) were ideal for both of them. Robbins joined the Pediatrics faculty and Hobbs started her residency in 1993.



Their first child, Benjamin, was born in 1995, and twins Samuel and Emma followed in 1997. That also was the year that the Arkansas Center for Birth Defects Research and Prevention received its initial funding, with Hobbs serving as co-director alongside Pat Casey, M.D., a longtime faculty member. In 2001 Hobbs was named chief of the Birth Defects Research Section of the Department of Pediatrics.

In 2002, the center was awarded a second five-year grant, and Hobbs, who had been promoted to associate professor, took the reins as director. In 2004, Hobbs was invested as the Pamela D. Stephens Endowed Chair for Birth Defects Research at ACH. In 2008, she received the UAMS College of Medicine’s Distinguished Faculty Scholar Award.

Hobbs has been a member of the Neonatology Section in the Department of Pediatrics since joining the faculty. “I love caring for newborns and being part of a neonatal team,” she said. “When I attend deliveries of babies who are born with birth defects or other neonatal problems, my passion to continue our research tasks is renewed.”

The Search Goes On

Hobbs’ reputation as a world-class birth defects researcher has grown over the years through her leadership in the National Birth Defects Prevention Study, the National Children’s Study’s birth defects working group, and other activities. Since 2005, she also has served on the National March of Dimes Scientific Advisory Committee on Prematurity.

Meanwhile, Hobbs and other researchers have made progress in unraveling the causes of birth defects. Among many findings, the National Birth Defects Prevention Study confirmed links between maternal obesity and several birth defects, including spina bifida, in which obesity doubles the risk. More also has been learned about the links between smoking and congenital heart defects and craniofacial abnormalities such as cleft lip or palate. Unfortunately, surveillance in Arkansas has shown that 28 percent of mothers smoked during early pregnancy, double the percentage of mothers in center locations such as California, Hobbs said.

Hobbs envisions a day when physicians will have a cadre of tests that can check for biomarkers that reveal the risk for birth defects prior to conception. She and her colleagues are exploring possible links between oxidative stress and congenital heart defects. They have found that women who have had babies with congenital heart defects had higher levels of homocysteine in their blood, and the researchers are continuing to look at metabolites, common genetic variants and possible epigenetic factors, which involve changes in gene expression due to non-genetic factors.

“I think one of our most rewarding, lifelong responsibilities is to use our talents, skills and resources to find new ways to improve the wellbeing of all people,” Hobbs said. “As a clinician-scientist investigating causes of birth defects, I feel privileged to be able to combine my medical skills and knowledge with rigorous epidemiological methods to discover new ways to improve the health of our children and those of future generations.” ■