



NATIONAL BIRTH DEFECTS PREVENTION STUDY NEWSLETTER



NBDPS Update and Research Agenda

The National Birth Defects Prevention Study (NBDPS) continues to collect and analyze data. We have interviewed more than 30,000 women from 9 states. This includes both moms of babies with birth defects and of babies without birth defects. We have also received cheek-cell kits from more than 14,500 families.

As we get more data, we can start to look at some of the rarer birth defects. The researchers are working on more than 220 projects, and new topics are being added often. This newsletter shares some recent findings from the NBDPS.

Many thanks to the families who have taken part in this study. The information you have shared will bring us closer to finding the causes of some birth defects.

Recent Findings from the NBDPS

Few Risks of Birth Defects from Antidepressant Use During Pregnancy

Depression in women is most common during childbearing years. SSRIs, or selective serotonin-reuptake inhibitors, are often used to treat depression in pregnant women. Examples of SSRIs are Prozac, Zoloft, and Paxil. We don't know how safe it is for pregnant women to use SSRIs, so our researchers used NBDPS data to look at the link between these drugs and birth defects.

For most birth defects, including heart defects, SSRI use during pregnancy did not increase risk. SSRIs were linked with a higher risk for three birth defects: anencephaly, craniosynostosis, and omphalocele. But, the increased risks were very small and have not been found before. Overall, the results are reassuring. It is better for both the mother and baby when treatment for depression continues through pregnancy. Women should talk with their doctor about the risks and benefits of taking SSRIs during pregnancy.

Reference: Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM for the National Birth Defects Prevention Study. Use of selective serotonin-reuptake inhibitors in pregnancy and the risk of birth defects. *N Engl J Med* 2007; 356:2684-92.

Small Babies and Heart Defects

NBDPS researchers looked at infants with heart defects to see if they were more likely to be small for their age than babies without a defect. They found that babies with heart defects weighed less at birth than babies without a defect. Also, babies with heart defects were about twice as likely to be small for their age. A baby small for its age with a heart defect is at a higher risk for medical problems. They may need to stay in the hospital longer than a baby with a heart defect alone. Health care providers can use this data to guide them in caring for these babies.

Reference: Malik S, Cleves MA, Zhao W, Correa A, Hobbs CA, and the National Birth Defects Prevention Study. Association between congenital heart defects and small for gestational age. *Pediatrics* 2007; 119:e976-e982.



NBDPS News is a periodic newsletter of the CDC-funded Centers for Birth Defects Research and Prevention.

The purpose of this newsletter is to inform the public of the Centers' activities and current news about birth defects.

IN THIS ISSUE...

Page	Content
1	NBDPS update
1-2	NBDPS Recent Findings
3	Looking at Family History
4-5	A Closer Look at NBDPS
6	A Look Back: Talking with a Past Participant
7	Resources on Birth Defects and Related Topics
8	Directory of the Centers for Birth Defects Research and Prevention



NBDPS Recent Findings continued

Risk Factors for Hypospadias

Hypospadias is a birth defect in boys in which the tube that carries urine opens on the underside of the penis instead of at the tip. About 7 out of 1,000 U.S. boys are born with this defect. We studied data from NBDPS to see what factors about a mother might be linked with this defect. We found that a woman was more likely to have a child with hypospadias if she was older than 35, was overweight, or was giving birth for the first time.

Reference: Carmichael SL, Shaw GM, Laurent C, Olney RS, Lammer EJ, and the National Birth Defects Prevention Study. Maternal reproductive and demographic characteristics as risk factors for hypospadias. *Paediatr Perinat Epidemiol* 2007;21:210-8.



Alcohol Use and Clefts

Cleft lip and cleft palate affect 1 out of 700 births. Animal studies show there could be a link between alcohol and clefts. NBDPS researchers looked at the link between clefts and how much, when, and what type of alcohol mothers used during pregnancy. Children

of moms who drank alcohol while pregnant were more likely to be born with cleft palate. The risk was greatest for women who drank hard liquor and did not take folic acid. We need to do more research with larger numbers of families to confirm these findings.

Reference: Romitti PA, Sun L, Honein MA, Rasmussen SA, Correa A, Reefhuis J, and the National Birth Defects Prevention Study. Maternal periconceptional alcohol consumption and risk of orofacial clefts. *Am J Epidemiol* 2007;166:775-785.

Antifungal Drugs: Low Risk for Birth Defects

During pregnancy, yeast infections are common. Women often treat these infections with antifungal drugs. We used NBDPS data to see if antifungal drugs raise the risk of having a child with a birth defect. These drugs were not linked with the birth defects we looked at, except for hypoplastic left heart syndrome, a rare but serious defect. Pregnant women should treat yeast infections, unless other studies show new information.

Reference: Carter TC, Druschel CM, Romitti PA, Bell EM, Werler MM, Mitchell AA. Antifungal drugs and the risk of birth defects. *Am J Obstet Gynecol* (Submitted under revision).

Caffeine and Heart Defects

About 89% of women ages 18 to 34 eat or drink caffeine in chocolate, coffee, tea, and soft drinks. We used data from the NBDPS to see if there was a link between heart defects and use of caffeine during pregnancy. We found that use of caffeine during pregnancy does not increase the chance of having a baby with a heart defect.

Reference: Browne ML, Bell EM, Druschel CM, Gensburg LJ, Mitchell AA, Lin AE, Romitti PA, Correa A, and the National Birth Defects Prevention Study. Maternal caffeine consumption and risk of cardiovascular malformations. *Birth Defects Res A Clin Mol Teratol* 2007;79(7):533-43.

Smoking and Orofacial Clefts

Studies have shown that smoking during pregnancy can increase the chances of having a baby with a cleft. We used NBDPS data to look at the number of cigarettes smoked per day and the risk of having a child with a cleft. We found that if the mother smoked more anytime in early pregnancy, the risk of clefts grew. Moms who smoked 25 or more cigarettes a day were more likely to have a child with clefts. This study adds to what we know about smoking during pregnancy.

Reference: Honein M, Rasmussen SA, Reefhuis J, Romitti PA, Sun L, Correa A, Lammer E, Moore C. Effect of maternal smoking and environmental tobacco smoke on the occurrence of orofacial clefts, National Birth Defects Prevention Study, 1997-2001. *Epidemiology* 2007;18(2):226-33.

Obesity and Birth Defects

More than half of women ages 20 to 39 are overweight (body mass index, or BMI, from 25 to <30) or obese (BMI \geq 30). These women are more likely to have trouble getting pregnant, have problems during pregnancy, and have babies with birth defects. We used data from the NBDPS to look at links between a mother's weight before pregnancy and 16 different types of birth defects. We found that obese mothers were more likely to have babies with spina bifida, heart defects, hypospadias, and other defects. They were less likely to have a baby with gastroschisis. Overweight mothers had a greater chance of having a baby with heart defects, hypospadias, and omphalocele. More studies are needed to know why some defects happen more often in babies of obese and overweight mothers.

Reference: Waller DK, Shaw GM, Rasmussen SA, Hobbs CA, Canfield MA, Siega-Riz AM, Gallaway MS, Correa A. Pre-pregnant obesity: a risk factor for structural birth defects. *Arch of Pediatr Adolesc Med* 2007;161:745-50.



Looking at Family History



When someone in the family has a health condition, like a birth defect, we say there is a family history of that condition. Family history can increase a person's risk of getting that condition or having a baby with that condition. For children, we typically learn about family history from their parents. Knowing a child's family history helps doctors and families make choices about care.

We looked at family history responses in NBDPS interviews with moms of children with and without birth defects. We studied how factors such as mother's age, race and ethnicity, and behaviors like smoking affected family history reports. We also looked at the effects of case-control status and type of birth defect. We grouped moms' answers as to how much detail was given for each response about birth defects history. For example, for heart defects, "ventricular septal defect" was rated a high level of detail, "hole in heart" a medium level, and "heart defect" a low level.

We found that reports of birth defects history were linked with case status, non-Hispanic white maternal race and ethnicity, mother's smoking, and fathers who take part in the interview. One or more of these factors might be linked with an actual increase or decrease in the number of affected relatives. But, these factors might have affected the reporting itself. A single tool for measuring family history risk might not fit for all races and ethnicities. And it may not be valid to assume that for all racial and ethnic groups the number of relatives reported reflects the actual number affected. These results point to a need for culturally sensitive tools to collect and analyze family history.

We found that the level of detail in responses varied by defect. This finding can help shape how information on birth defects history is collected. For some defects, such as orofacial clefts, more detail may not be needed. But for others, such as heart defects, more

detail may be important. Doctors might need to look at medical records to clarify the nature of the defect.

To measure risks effectively, health care providers need complete, correct family histories. Studies on birth defects also need this information, because it can give clues about the causes of birth defects. So, it is important for families to know exactly what health issues their children and relatives have. Sharing health histories can help everyone in the family. For children, having both parents take part in gathering family health history is important. The Surgeon General's website My Family Health Portrait (<https://familyhistory.hhs.gov/>) can help families collect their health history to share with their doctors.

Reference: Green RF, Olney RS, Reefhuis J, Botto LD, Romitti PA. Maternal reports of family history from the National Birth Defects Prevention Study, 1997–2001. *Genet Med* 2008;10(1):37–45.

A Closer Look at the NBDPS



How Does It Work? And What Do All Those Words Mean?

Most people don't use words like exposure or research every day. But we use these and many other scientific terms when we talk about the National Birth Defects Prevention Study (NBDPS). Here, we explain how the NBDPS works and define some of the words that might be unfamiliar.

What is the NBDPS studying?

The NBDPS looks at birth defects. Birth defects are conditions present at birth that can cause physical or mental problems. They can also cause a baby to die. By studying things that might cause birth defects, we can figure out how to prevent them or lessen the problems they bring.

What kind of a study is the NBDPS?

The NBDPS is a research study. Research involves collecting information in an organized way to answer specific questions about a certain topic. The information is then analyzed to answer the questions that were asked. Because the study is done in a structured and systematic way, we have some proof that the answers we find are true. More specifically, the NBDPS is an observational, population-based, case-control study. That's a mouthful! Let's take the terms one at a time.

- The study is observational because it simply looks at what is already going on. It does not test medicines or treatments or ask people to do anything differently. In the NBDPS, the researchers interview moms and collect specimens, and they analyze what they find.
- The NBDPS is population-based because it looks at all people with a certain health outcome who live in a certain area. That area could be a state or a number of counties. One of the important things to watch is whether the number of people with a given outcome in the study area changes over time.
- The NBDPS is a case-control study because information is collected from both people who have a health issue (these are called cases) and people who do not have the health issue (these are called controls). The controls might also be called the comparison group. Controls are chosen by random selection. This means they are chosen by chance from the population in the study area. In the NBDPS, controls are chosen by a computer program that picks babies from birth certificates in a given month in the study area.

Who runs the NBDPS?

The person who leads the study team is the principal investigator, or PI. The PI also writes letters to participants. There are many other investigators in a study. They are experts in their field, such as nutrition or laboratory science, who bring their special skills to the study team. Many other people, such as interviewers and study coordinators, collect and manage the study data.

What kind of information does the study collect?

The NBDPS team collects information about things that people do or come in contact with that might be related to birth defects. Each of these things is called an exposure. An exposure can be something a person eats, a drug or medical treatment, something used on the job, or a family trait.





Sometimes, investigators find that an exposure increases the risk of a birth defect occurring. We call that exposure a risk factor. A well-known risk factor for birth defects is cigarette smoking. Sometimes, an exposure seems to prevent a birth defect, such as taking the vitamin folic acid. This is called a protective factor. And sometimes, an exposure seems to have no link at all to birth defects. This is a neutral factor.

How does the team collect information?

The team uses interviews to collect information from moms. A computer guides interviewers in asking the questions, so every mom gets asked the same questions in the same way. Sometimes after an interview, the interviewer will call a mom back to clarify her answers or get more information.

The team also collects cheek cells from moms, dads, and babies, when possible. The cheek cells contain genes. Genes look like beads strung out on long strands of cell material called DNA. Strands of DNA are found inside each of the trillions of cells of the body. Each gene on the DNA



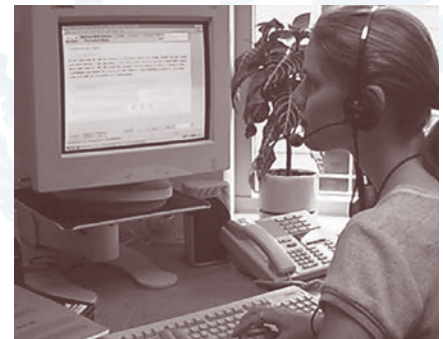
strand has special instructions that tell the cell what to do. For example, one gene might tell the cell how to make the chemicals that help us digest food. Investigators look at the cheek cells in the lab to see if there are differences in specific genes between the cases and controls. Just like an exposure reported in the interview, a gene behavior may be found to be a neutral, protective, or risk factor.

How is the information used?

All of the information collected is saved in a database. Investigators use that information to compare the two groups to see if something happens more or less often in the case group than in the control group. They use a kind of math called statistics to compare the groups. Then, the investigators write papers about what they found. Those papers are reviewed by scientists outside the NBDPS, and the papers are published in medical journals.

When people read about the NBDPS, will they be able to find my information?

No. The study investigators are not looking at any one person's information, only at the groups. So, study results



will not be reported in a way that lets readers identify any one person. Also, study records that show names or other identifiers are locked up carefully at the study center. Each center signed a Certificate of Confidentiality that said they promised to keep participants' information secret, or confidential. If you would like a copy of the Certificate of Confidentiality, please call Tineka Yowe-Conley at 404-498-4315.

What do you hope will be the outcome of the NBDPS?

We hope to find things that moms and dads can do, or things they can avoid, that will prevent birth defects or lessen the burden for families in the future. The information we collect through NBDPS is vital to finding those answers.



A Look Back: Talking With a Past Spanish-Speaking Participant

A heartfelt note arrived in a 2005 cheek-cell kit. It was from a Spanish-speaking mom in North Carolina. She commended the study staff, saying we are "people who care for the well-being of all human beings, regardless of any particular distinction." We accept this compliment with thanks! She added that she hoped we would keep her informed about the causes of birth defects and offered to talk with us in the future.

We took her up on her offer. In 2007, we caught up with her to find out what she thought of her participation in the study.

We asked if she had a hard time deciding to do the interview, because we know it takes a lot of time. She said that she was happy to share information to help moms like herself. "I was very pleased with your concern and willingness to cover every detail and for the hard work to find answers," she said.

She said her interviewer was professional and "gave her confidence." We asked if any part of the interview was difficult for her. She said she sometimes didn't know the answers to our questions. And at the time, she was under a lot of stress, trying to "adjust to the critical situation we were living through."

She was open and sincere about how her life had changed after giving birth to the baby we interviewed her about. "In the beginning, I felt anguish and desperation because I didn't understand what my baby had or why he had it. Then I felt I matured as a parent and learned to value what I had and to see life from a different perspective." Her advice for other mothers of babies with birth defects: "Be very patient and have a lot of faith. It's best to focus on the available information to understand what has happened and why." It's clear that this mom likes to stay informed about her baby's health issues, and that continued learning gives her strength.

We were glad to reconnect with a past participant. And we were happy to hear that she feels her participation was helpful to others and that she recalls it as a good experience. We hope our newsletters will continue to tell her and all the NBDPS families about our progress in finding the causes of birth defects.

Resources on Birth Defects and Related Topics



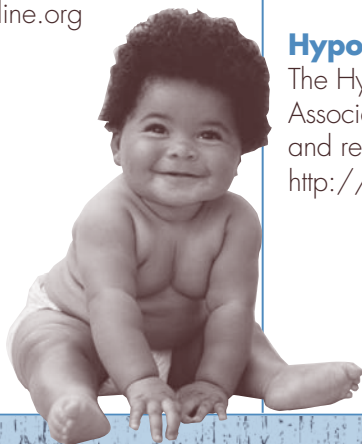
Anencephaly

The Anencephaly Information website shares stories and resources for families who have an affected baby.
<http://www.anencephalie-info.org/e/index.htm>

The Anencephaly Support Foundation website has resources for families who have an affected baby.
<http://www.asfhelp.com/asf/home>

Clefts

The Cleft Palate Foundation website has support and resources for families and health care providers. They have a toll-free telephone number (800-24-CLEFT) and will respond to callers about clefts and other facial conditions.
<http://www.cleftline.org>



Family History

My Family Health Portrait, a tool from the U.S. Surgeon General, helps families collect family history information. Families can print out their family histories to share with their doctors and relatives.
<https://familyhistory.hhs.gov/>

The National Center on Birth Defects and Developmental Disabilities and the National Office of Public Health Genomics at the Centers for Disease Control and Prevention have family history resources and links.
http://www.cdc.gov/ncbddd/bd/family_history.htm
<http://www.cdc.gov/genomics/public/famhist.htm>

Hypospadias and Epispadias

The Hypospadias and Epispadias Association (HEA) website has support and resources for affected families.
http://heainfo.org/shell_resources.htm

Small for Gestational Age

The Medline Plus—Small for Gestational Age (SGA) website defines SGA and offers more information about SGA.
<http://www.nlm.nih.gov/medline-plus/ency/article/002302.htm>

The American Pregnancy Association

has information about intrauterine growth restriction (IUGR), another name for SGA. Types of IUGR, risk factors, and diagnosis for mom are discussed, along with risk factors for infants with IUGR. <http://www.american-pregnancy.org/pregnancycomplications/iugr.htm>

Answers.com— Birth Weight gives an overview of birth weight, SGA, and large for gestational age. Includes risk factors and treatment.
<http://www.answers.com/topic/birth-weight?cat=health>

Directory of the Centers for Birth Defects Research and Prevention

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