

NATIONAL BIRTH DEFECTS PREVENTION STUDY

NBDPS



2006/2007
Newsletter

NEWS

NBDPS News is a periodic newsletter of the 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.



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National Birth Defects Prevention Study (NBDPS) Update

The NBDPS is making great progress. We have talked with more than 25,000 women across the country. Some of these women have had pregnancies affected by a birth defect while others have children without birth defects. We have also collected cheek cell brushes from more than 13,000 families.

As we get more data, we're able to start looking into possible causes of some birth defects.

Researchers are working on more than 200 research projects. New topics are being added regularly. Some of the recent findings from the NBDPS are included in this newsletter.

We're grateful to the families that agreed to be part of this study. What they have shared will bring us closer to knowing the causes of birth defects.

Published Studies from the NBDPS

Orofacial clefts and maternal nutrient intakes

Orofacial clefts are birth defects in which the opening in the lip and palate fail to close during pregnancy. Little is known whether or how nutrition might play a role in causing this defect. We just finished a major study on this topic using NBDPS data. We wanted to see if increasing dietary folate, taking folic acid supplements, or taking certain nutrients would lower the chances of having babies with clefts. The data showed 30% decrease in risk of clefts with increasing intakes of total protein, choline, and methionine.

We also saw a decreased cleft risk with increased intake of cysteine. Intakes of only two micronutrients, iron and riboflavin, were found to reduce the risk in clefts when adjusted for other nutrients. These findings suggest that a woman's diet can affect her chance of having a baby with clefts.

Reference: Shaw GM, Carmichael SL, Laurent C, Rasmussen SA. Maternal nutrient intakes and risk of orofacial clefts. *Epidemiology* 2006; 17:285-291.

Hypospadias and maternal progestin intake

Hypospadias is a birth defect in males where the opening of the tube that carries urine is on the underside of the penis instead of at the tip. We wanted to see if a mother's intake of progestin at the time of conception might affect her chance of having a baby with this defect. Progestins can be given to help women become pregnant. It can also be given during early pregnancy to help prevent pregnancy problems or loss. These drugs are also given with ovulation stimulating drugs and assisted reproductive techniques.

We found that the sons of mothers who took progestins during early pregnancy were more likely to have hypospadias. Knowing this will help doctors and families be better informed when making a decision about progestin use.

Reference: Carmichael SL, Shaw GM, Laurent C, Croughan MS, Olney RS, Lammer EJ. Maternal progestin intake and risk of hypospadias. *Arch Pediatr Adolesc Med* 2005;159:957-62.

Hypospadias and maternal smoking

The purpose of this study was to find out if hypospadias is linked to a mother's smoking 1 month before or during the first 3 months of pregnancy. Earlier studies on hypospadias and smoking did not find a link or found less of a risk.

We're now able to look at this issue using newly collected, detailed data on maternal smoking from the NBDPS. Our data did not show a link between maternal smoking and hypospadias.

Reference: Carmichael SL, Shaw GM, Laurent C, Lammer EJ, Olney RS. Hypospadias and maternal exposures to cigarette smoke. *Paediatr Perinat Epidemiol* 2005;19:406-12.



Medication and Birth Defects

Medicines that can be bought without a prescription are called over-the-counter medications, or OTCs. OTCs are among the most common exposures during pregnancy. Using data from the NBDPS, we found that over 75% of women take at least one OTC during pregnancy. Acetaminophen, found in Tylenol® and many other pain, fever, cough, and cold products, was used by the most women. In fact, two-thirds took it sometime during pregnancy. Ibuprofen, found in popular products like Advil® and Motrin®, was used by one in five women. Pseudoephedrine, found in Sudafed® and other decongestant products, was used by one in seven women.

It is not surprising that medicines taken for headaches, pain, colds and flu are used often during pregnancy because these conditions are common. Yet, we were surprised to find that some OTCs were taken more often during pregnancy than before pregnancy. For example, acetaminophen, pseudoephedrine, diphenhydramine (in Benadryl® and other products) and guaifenesin (in Robitussin® and other products) were taken by more women during pregnancy than during the 3-month period before pregnancy began.

OTC pain medicines, decongestants, and allergy medications were taken most by white, educated, and older women. Women in Iowa were most likely to take OTC pain medicines. Women in California, Iowa, and Georgia used the most decongestants and women in Arkansas used the most OTC allergy medicine. Women in New Jersey used the least amounts of all three types of OTCs.

We do not think that most OTC products pose a risk for birth defects, but it is still important to do these studies to know the safety of the medications. Our studies on OTCs will better guide women and their doctors when they make decisions about how to treat common conditions during pregnancy.

Reference: Werler et al. American Journal of Obstetrics and Gynecology 2005; 193:771-77.



Intake of supplements with folic acid among pregnant women

We wanted to find out how many pregnant women in the NBDPS took vitamin supplements with folic acid, when they began taking them, and what their characteristics were. Of women who took folic acid supplements:

- Fifty-three percent of the women began taking them 3 months before or 1 month after conception.
- Thirty-five percent of the women started taking them 2 to 3 months after conception.
- Eight percent of the women began taking them 4 or more months after conception.

Women who did not take folic acid supplements during the 3 months before or 1 month after conception were more likely to:

- Be non-white
- Speak Spanish
- Have a low level of education
- Be younger than 25 years of age
- Have never had a baby before
- Be smokers
- Have no previous miscarriage nor fertility treatments
- Begin prenatal care and become aware of their pregnancy after the first trimester
- Have not planned the pregnancy
- Eat less breakfast cereal

This study tells us who is more or less likely to take folic acid supplements. Knowing this will help us design our messages to encourage all women of childbearing age to take folic acid before and during early pregnancy.

Reference: Carmichael SL, Shaw GM, Yang W, Laurent C, et al. Correlates of intake of folic acid-containing supplements among pregnant women. Am J Obstet Gynecol 2006;194:203-10.

Spotlight on the Principal Investigators

The NBDPS is conducted in nine states and involves a lot of coordination. Each state has one or two leaders, called principal investigators (PIs), who lead the study site team and direct the scientific projects. They also make sure that things run smoothly at their study sites. In this issue, we asked the PIs what they think is important about the NBDPS. We also asked them about their research interests. And finally, we asked them what they think we can learn from the study.

Why do you think the NBDPS is important?

As a pediatrician, I'm there when babies are born and take care of them during their first moments and days of life. The birth of a baby can be such a joyous event; but, when something isn't right with the mother or the baby, it can be devastating. Over the past 12 years, I've seen the birth of many babies born with major birth defects. The joy that comes with the birth of a healthy baby is replaced by concern and worry while the baby is stabilized and moved into special care. Parents often ask me why their baby was born with a birth defect. Sadly, the causes of most birth defects are unknown, and the families are left with uncertainty and worry that often lasts throughout a baby's childhood and the later pregnancies of the mother.

The NBDPS is a way for parents, doctors, and scientists to work together to learn the causes of birth defects so that more babies can be born healthy. If we know the causes of birth defects perhaps we'll know how to prevent them from happening in the future.

--Dr. Charlotte Hobbs, Arkansas Center

The NBDPS is the largest study of its kind ever conducted in the United States. Its large size allows researchers to study the causes of both common and rare birth defects. It also lets us look at the effects of rare exposures, such as certain medications, on the risk of birth defects. Because the study is ongoing, we can address new concerns that arise. We can also use the data to confirm findings between exposures and birth defects found in other studies. Finally, this study brings leading researchers from several states together, which makes it possible to solve problems that no one researcher could solve alone.

--Dr. Marlene Anderka, Massachusetts Center

The cheek cells that are being collected in this study will let us look at links between birth defects, the environment, and a family's genes.

--Dr. Mark Canfield, Texas Center

This study is carefully designed to gather data from all eligible cases of birth defects within our study area. We also collect data from infants without a birth defect in the same study area. We can compare the groups to find factors related to birth defects. This case-control design is one of the best ways to find risk factors for birth defects. And, we can apply the findings to the entire population.

--Ms. Marcia Feldkamp, Utah Center

What are your research interests?

Our research team is trying to find lifestyle and genetic causes of congenital heart and neural tube defects. Congenital heart defects are among the most common and serious birth defects. At Arkansas Children's Hospital, heart doctors and surgeons work with our team to identify infants and their parents who can be part of the NBDPS. During the past 6 years, we have found factors in women that seem to increase the risk of having a baby with a heart defect. Now, we are trying to find more lifestyle and genetic factors that might increase the chance of having a baby with a heart defect. If we can spot these factors before pregnancy and create programs to lower these risks perhaps we can prevent some birth defects.

--Dr. Charlotte Hobbs, Arkansas Center

I'm interested in nutrition and birth defects, endocrine disruption, as well as financial, social and mental factors that can affect birth defects. I'm also looking into the link between our genes and the environment, focusing on hypospadias and brain, face, heart, and limb defects.

--Dr. Suzan Carmichael, California Center

My research focuses on neural tube defects, oral clefts, and brain defects. I'm studying links between genes, nutrients, and environment with a focus on folate-related genes. Also, I'm looking at ways biologic testing can be used to record exposures to environmental toxins/metals.

--Dr. Gary Shaw, California Center


I'm looking at how an individual's genes can change the risk of birth defects when a mother smokes or drinks.

--Dr. Paul Romitti, Iowa Center

I am trying to identify risk factors for major birth defects that can quickly lead to prevention efforts. I have done several studies to assess the link between maternal tobacco exposure and certain types of birth defects. I am also very interested in the role of medications used during pregnancy. Many women need medications to treat medical conditions during their pregnancy, but we don't know how safe they are for the fetus. A woman with a chronic condition like asthma needs to know how to treat her condition during pregnancy so no harm will come to the fetus.


--Dr. Jennita Reefhuis, CDC






I am interested in nutrition and medication use in pregnancy and how they might affect a baby. My recent work has focused on treatments for nausea and vomiting during pregnancy and how they might harm the baby. The NBDPS collects data on nausea, vomiting and medication use during pregnancy, so it offers a chance to research questions related to this common condition.

--Dr. Marlene Anderka, Massachusetts Center




I am interested in common exposures, such as caffeine or alcohol, and maternal illness, such as asthma or high blood pressure. I want to know if it's the illness that can be a factor for birth defects or if it's the medications used for these illnesses.

--Dr. Charlotte Druschel, New York Center




I have an interest in pediatric diseases. This includes birth defects, childhood cancer, and related genetic risk factors.

--Dr. Andy Olshan, North Carolina Center



My main interests are hazards in the workplace, home, or in the general environment.

--Dr. Bob Meyer, North Carolina Center




I have studied neural tube defects in Hispanics for many years. I am also interested in other birth defects including those that can be prevented by folic acid. Other areas I am involved in are newborn screening disorders, finding out about the health and lives of children who are born with defects, and surveys that help us find what people are doing to prevent birth defects.

--Dr. Mark Canfield, Texas Center




I am interested in the link between birth defects and substances in the environment and in the workplace.

--Dr. Peter Langlois, Texas Center



I'm interested in looking at underlying genetic risk factors along with exposures that lead to birth defects.

--Ms. Marcia Feldkamp, Utah Center



I want to understand heart defects, their causes, and ways to prevent them from occurring.

--Dr. Lorenzo Botto, Utah Center

What do you think the next big discoveries will be?

Unlike 10 years ago, many of the clues on causes such as exposures and certain genes are becoming available to researchers. We now must piece these clues together into cohesive snapshots that will reveal the complex causal nature of birth defects.

--Dr. Gary Shaw, California Center

We aren't expecting any "magic bullets". Rather, we can expect a more detailed understanding of how certain genes and the environment might act together to cause birth defects.

--Dr. Suzan Carmichael, California Center

The NBDPS will give us important clues to the role of diet, medications, smoking, alcohol and occupation in the causes of birth defects. Knowing this will give us a springboard to develop future prevention programs.

--Dr. Paul Romitti, Iowa Center

We think that most major birth defects are caused by a complex mix of risk factors. The NBDPS will help us understand some of the most important combinations. For example, a mother's smoking might increase the risk of a certain birth defect only if the mother has a specific gene. Or, a medicine might increase the risk of a certain birth defect only among mothers who smoked during pregnancy. I think the NBDPS will help us understand if certain medicines are safe to take during pregnancy.

--Dr. Jennita Reefhuis, CDC

Discovering how genes influence human health.

--Dr. Andy Olshan, North Carolina Center

We want to find out why, if two people are exposed to the same hazard, one develops a condition and the other doesn't. We want to know why some people seem to be more at risk than others for developing a condition.

--Dr. Bob Meyer, North Carolina Center

I hope that we will find dietary information that will help women have a healthy pregnancy and know which exposures might put a pregnancy at risk. Many women need to take medications for their health and some women stop them because they are concerned about their pregnancy. But stopping such a medication can also place the pregnancy and the woman's health at risk. I hope we can find those medications that women need to avoid but also provide information on which medications do not increase risk.

--Dr. Charlotte Druschel, New York Center

It is difficult to tell, and the future will likely surprise us. We can expect to have a better sense of the contribution of genes to birth defects, and of the ways that environmental factors can affect their occurrence. We might also find unexpected causes of birth defects that we had not thought about.

--Dr. Lorenzo Botto, Utah Center



Commonly Asked Questions about the NBDPS

Many women have the same questions about the NBDPS. Here, we've highlighted some of the commonly asked questions again. If you have other questions, please contact your state's center. The contact information for each center is listed on the back of this newsletter.

General Questions About the Study

Why are you studying birth defects?

People are often surprised to learn that birth defects are common, found in 1 in 33 newborns. Most of the time, doctors and scientists do not know what causes them. This study will move us closer to understanding the causes of birth defects and ways to prevent them.

What does the study involve?

The study has two parts: (1) a telephone interview, and (2) a collection of cheek cells from immediate family members.

How does the NBDPS get the names of the participants? How is their information protected?

Part of our on-going work to find causes of birth defects includes studying them when they occur. State law allows us to track cases of birth defects. This is how we find most women in the study. Women whose babies do not have birth defects were selected randomly from women who gave birth in the same year.

The information in this study is confidential. All records are kept under lock and key. The personal answers and results of genetic tests are not seen by anyone outside the study. This means that they are not given to anyone outside the study, including insurance companies or other government agencies, even if requested by a court of law.

What will be done with the study findings?

We publish findings in medical journals and in this newsletter. Because birth defects are of great interest, findings are often covered in the news as well. They can also be used in health education materials. All of our findings pertain to groups of women; no one will be able to identify individual participants from our reports or publications.

About Cheek Cell Collection

Why is information about genes collected?

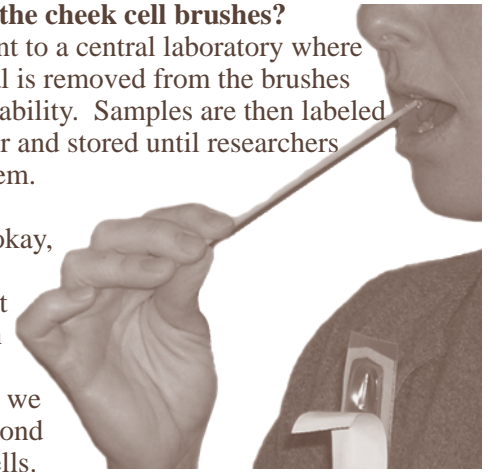
The cheek cell samples provide critical genetic information. The interview provides needed information about factors in the environment that might affect birth defects. This study will help us find out how the two interact.

What happens to the cheek cell brushes?

The brushes are sent to a central laboratory where the genetic material is removed from the brushes and checked for usability. Samples are then labeled with a code number and stored until researchers are ready to use them.

Most samples are okay, but sometimes the laboratory finds out there is not enough material to study.

In these rare cases, we might ask for a second sample of cheek cells.



Will the results from genetic testing be shared with study participants?

No. Participants will not receive individual test results. Instead, families will get a copy of this newsletter. It will inform families of any major findings, especially if the results of a study might be useful for family members who are interested in genetic testing. Families can then talk with a doctor or genetic counselor to help them decide whether the gene test could be helpful to them.

Why are the genetic test results not sent to the participants?

There are several reasons why test results are not sent:

- First, the tests done on the samples are for research. This means our study will look for connections between birth defects and genes. Before these connections can be useful, the tests need to be repeated in other laboratories using samples from other families.
- Second, in most cases, birth defects are caused by a combination of genes and other factors, such as exposures to certain medicines or substances in the environment. Because of this, we will learn about the causes of birth defects by examining data from both telephone interviews and gene tests. In most cases, the results from one gene test will not be meaningful without knowing other information.
- Third, while our tests are done carefully, they do not meet the strict standards required for medical tests. Because these standards might not have been met, we will not send individual test results.

Will collecting the cheek cell samples hurt? No, it will cause little to no discomfort.

Will a cold or illness affect the samples? No, being sick won't affect the quality of the cheek samples. A sample can be collected even when a person is sick.

Do the samples have to be mailed right away?

We will get better results if the samples get to us soon after they are collected. If the samples are not mailed within a week, another kit can be sent to collect new samples.

What do you think causes birth defects? Results from a Texas Women's Health Survey

Little is known about the causes of most birth defects. Yet, there are many thoughts about what might cause them. A Texas survey asked women what they think causes birth defects.

Some of these women had children, some did not, and others were pregnant when they took the survey. Most of the reasons they gave involved the use of alcohol, tobacco, and drugs, but many also said heredity was an important cause of birth defects. Many other reasons were suggested by the women answering the survey, such as poor diet, not enough nutrients or vitamins, pollution, stress, mom's age, and physical activities.

Here's what some women said when they were asked, "What do you think causes birth defects?"

- "Stress can affect the baby."
- "No exercise and lack of information."
- "Any harmful or intoxicating substance; you need to keep your body in good condition."
- "It's out of human control."

The NBDPS also asks what women think causes birth defects. These answers will help us know how best to educate future parents as we discover more about the causes of birth defects and how to prevent them.



Resources on Birth Defects and Related Topics

We have come up with a list of resources that might help you. The Centers are not responsible for the content found on these websites.

Selected Birth Defects

The **American Pediatric Surgical Association** webpage has a section on gastroschisis. It shows graphic pictures. Please note that there is a disclaimer over each picture. The reader is unable to see the picture until the computer mouse is clicked over the image.

Website: www.eapsa.org/parents/abdomen.htm

The **Hypospadias and Epispadias Association (HEA)** website has information for affected persons and their families about these conditions. The site has commonly asked questions, personal stories, and resources. Website: www.heainfo.org

The **University of Michigan Medical Center's** website has useful information for families on hypospadias and its treatment. Website: www.med.umich.edu/urology/PatientInfo/PatientInfoPages/Hypospadias.htm

The **Spina Bifida Association (SBA)** website provides the latest information and research on spina bifida. The site also has commonly asked questions, fact sheets, and resources. Website: www.sbaa.org

The **Cleft Palate Foundation (CPF)** web site has a section for patients and families. It has fact sheets and resources. Website: www.cleftline.org

Genetics and Birth Defects

The **Genetic Alliance** website has a disease index database and genetic resources. Website: www.geneticalliance.org

The **Genetic and Rare Conditions** site has information and support group listing for genetic conditions and birth defects. Website: www.kumc.edu/gec/support

The **March of Dimes** website has a page that focuses on birth defects and genetics. Topics include genes and birth defects, genetic counseling, as well as genetics and your pregnancy. Website: www.marchofdimes.com/pnhec/4439.asp

General Birth Defects and Related Topics

The **Compassionate Friends** website offers help to families in dealing with grief following the death of a child of any age. Website: www.compassionatefriends.org

The **National Organization for Rare Disorders (NORD)** has resources on rare diseases, referrals, and other support services for affected families. Website: www.rarediseases.org/

The **Brave Kids** website has an online resource for children with special needs and their families. There are message boards, resources, and games. Website: www.bravekids.org

The **Organization of Teratology Information Specialists (OTIS)** website focuses on medications and other prenatal exposures. They have a toll-free number (866-626-OTIS or 866-626-6847) that families and health care professionals can call to speak to one of the specialists. These calls are free of charge and confidential.

Website: www.otispregnancy.org

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If you no longer wish to receive this newsletter or would like to update your address, please contact your center listed in the directory. Please also let us know if you have topic ideas for future issues.

