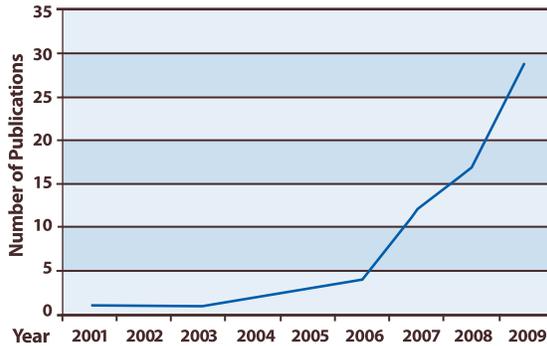


NBDPS Update

The National Birth Defects Prevention Study (NBDPS) is going strong. We have talked to more than 34,000 women from 10 states. This includes women who have had pregnancies affected by birth defects and those who have babies without birth defects. We have also received cheek-cell kits from more than 17,000 families.

We have a good base for studying risk factors for some birth defects. NBDPS researchers have over 200 project ideas. In 2009, 29 papers were published in medical and health journals. The results of some of these papers will be discussed in this newsletter. Thank you to the many families that have taken part in this study. The information you have shared will bring us closer to finding the causes of some birth defects.

Number of Publications Using Data from the National Birth Defects Prevention Study by Year



Recent Findings from the NBDPS



Antibiotics and Birth Defects

During pregnancy, women can get more infections – germs that cause disease – because of all the changes in their bodies. So we were not surprised that the use of antibiotics – drugs that fight infections – goes up during pregnancy. Antibiotics were most often used during the fourth month of pregnancy.

We also looked at the link between antibiotics and birth defects. Antibiotics most used were penicillins, erythromycins, and cephalosporins. Generally, women who used these drugs did not show greater risk for birth defects. But we did see some links between the drugs sulfonamides (such as Bactrim) and nitrofurantoin (such as Macrobid) and birth defects. Women most often use these drugs for urinary tract infections. But we cannot be sure that the drugs caused the birth defects. It is very important to treat infections. Women should talk to their doctors about which antibiotics are safest to use during pregnancy.

Reference: Crider KS, Cleves MA, Reefhuis J, Berry RJ, Hobbs CA, Hu DJ. Antibacterial medication use during pregnancy and risk of birth defects: National Birth Defects Prevention Study. Arch Pediatr Adolesc Med. 2009 Nov;163(11):978-85.

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.

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Neural Tube Defects



Body Mass Index and Heart Defects

Body mass index (BMI) is a measure of body fat based on a person's weight and height. We say someone with a BMI reading of 25 or greater is "overweight" and someone with a BMI of 30 or greater is "obese." In this study we looked at women who had a high BMI before becoming pregnant to see if they were at greater risk of having a baby with heart defects.

We found that women who were overweight or obese before becoming pregnant were at an increased risk for all types of heart defects. This link was strongest among women who also had gestational diabetes. This is type of diabetes that is first diagnosed in a pregnant woman. These findings stress the importance of being at a healthy weight before pregnancy.

Reference: Gilboa SM, Correa A, Botto LD, et al. Association between prepregnancy body mass index and congenital heart defects. *Am J Obstet Gynecol.* 2010;202:51.e1-10.

Birth Defects and Sugar Intake

A mother's nutrition plays a role in the complex causes of neural tube defects (NTDs), (birth defects of the brain and spinal cord). Much of the research has looked at folic acid intake, obesity, and diabetes. But other factors, such as eating a lot of sugar, may affect the risk for NTDs. When someone eats too much sugar, the glucose level, or the sugar in the body's blood, becomes too high. The body makes insulin to take away some of that sugar. This is called "glycemic control." Foods are given a "glycemic index value," which shows how fast a food causes sugar levels in the blood to rise. A candy bar would have a much higher glycemic index value than broccoli.

We wanted to see if women who had diets high in sugar and foods with high glycemic index values were more likely to have babies with NTDs. An earlier study was done in California that showed a greater risk for NTDs in pregnant women who had this type of diet. However, our study using NBDPS data found there was no added risk of NTDs in babies whose mothers

had a similar diet during pregnancy. More research needs to be done to find out why the California study and the NBDPS study did not have the same results.

Reference: Shaw GM, Carmichael SL, Laurent C, Siega-Riz AM. Periconceptional glycaemic load and intake of sugars and their association with neural tube defects in offspring. *Paediatr Perinat Epidemiol.* 2008 Nov;22(6):514-9.

Craniosynostosis and Smoking

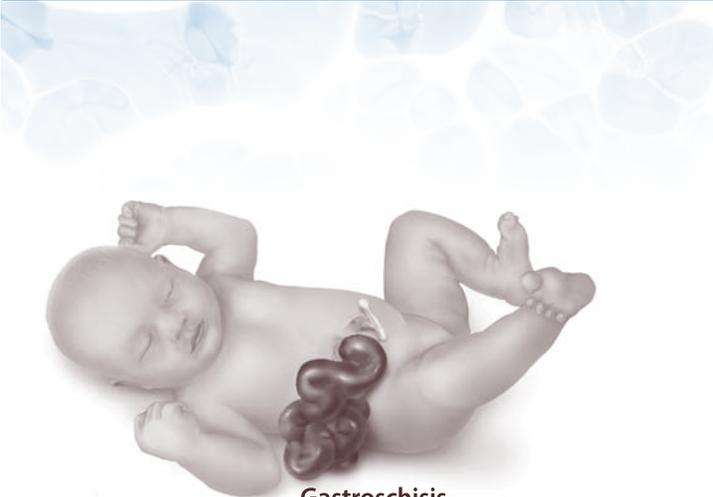
Craniosynostosis is a birth defect where some of the bones in a baby's skull close too early. This changes the growth and shape of the head and face, and sometimes the brain. About 4 out of every 10,000 babies are born with this condition, and they often need surgery. Several studies suggested greater risk for this condition among babies born to women who smoked.

Using NBDPS data, we found that mothers who were heavy smokers during pregnancy (15 or more cigarettes per day) had an increased risk of having a baby with craniosynostosis. This risk is not seen when women quit smoking by early pregnancy. Also, we saw that women who did not smoke but were around cigarette smoke at home had an increased risk. This study adds to what we know about the effects of smoking during pregnancy.

Reference: Carmichael SL, Ma C, Rasmussen SA, Honein MA, Lammer EJ, Shaw GM. Craniosynostosis and Maternal Smoking. *Birth Defects Res A Clin Mol Teratol.* 2008; 82(2):78-85.

Genitourinary Infections and Gastroschisis

Genitourinary (reproductive and urinary organ) infections are common among sexually active women under 25. These include urinary tract and sexually transmitted infections. Chlamydia is a common infection and seems to be rising for these women. We also see a growing trend of babies born with gastroschisis to women 20 and younger.



Gastroschisis



One Child Can Make a Difference:

Watching for Birth Defect Patterns

To study the causes of birth defects, the NBDPS uses a “case-control” study design. This means we look at data from women who have a child with a birth defect and women who have a child without a birth defect. We compare how often women in these 2 groups used a specific drug or food. In the last NBDPS Newsletter, we reported on antidepressant use, antifungal drugs, caffeine, and smoking. Researchers focus on specific types of birth defects, and whether they occur alone or in a pattern. In general, the more enrolled women, more infants, and more data, the better. Although one of the strengths of the NBDPS is its ability to study a large number of cases from several states, sometimes clusters of babies, and even one child, can alert researchers to something important. This does not happen often, but if something unusual is seen in the data, then researchers might try to find out more.

One of the NBDPS study sites became aware of a child whose mother had used a drug during pregnancy known as MMF (mycophenolate mofetil, also known as CellCept®). This drug suppresses the immune system. It may be used by people with an organ transplant or certain autoimmune conditions. NBDPS researchers noted this child had birth defects that were similar to a few other children’s reported in medical journals. They compared the data on the MMF drug use and types of birth defects of this child to the children reported in medical journals. The data showed that this child was probably affected by the same drug. After getting the parents’ consent, information about the case was published in a medical journal article.

When a doctor in an office or a researcher conducting a study sees one child with unusual defects which might represent a new condition, caution is needed. One cannot draw conclusions. In this case, there appears to be support that the drug MMF is a cause of birth defects. Each child is important to the NBDPS. The ongoing research into MMF shows the value of families and researchers working together.

We looked at the data to see if genitourinary infections increase the risk of having babies born with gastroschisis. Women who had these infections just before and during early pregnancy were 4 times more likely to have a baby with gastroschisis. Among the mothers who had babies with birth defects, 43% said chlamydia was the cause of their infection, compared to only 18% among the mothers whose babies did not have birth defects. It is important for women to talk to their doctors and ask for a chlamydia test. (Chlamydia infections often do not show up on pap smears.) If the test result is positive, women should get proper treatment.

Reference: Feldkamp ML, Reefhuis J, Kucik J, Krikov S, Wilson A, Moore CA, et al. Case-control study of self reported genitourinary infections and risk of gastroschisis: findings from the national birth defects prevention study, 1997-2003. *BMJ*. 2008;336(7658):1420-3. Epub 2008 Jun 16.

Diabetes and Birth Defects

Women with diabetes are at increased risk for having a baby born with a birth defect. Women can have pre-existing (type 1 or type 2) diabetes or gestational diabetes (diagnosed during pregnancy).

NBDPS researchers wanted to know which types of birth defects were more common among mothers with diabetes. We found that pre-existing diabetes was more common among mothers of babies born with a range of birth defects. These include anencephaly, hydrocephaly, cleft lip with or without cleft palate, absent kidney, limb deficiencies, and over 10 types of heart defects. Mothers with gestational diabetes were often not at increased risk of having a baby born with a birth defect. But if the mother was overweight or obese and had pregnancy diabetes, the risk seemed to go up.

Reference: Correa A, Gilboa SM, Besser LM, Botto LD, Moore CA, Hobbs CA, et al. Diabetes mellitus and birth defects. *Am J Obstet Gynecol*. 2008;199(3):237. e1-9. Epub 2008 Jul 31.



A Legacy of Hope and Love

Bethany Gillham* had never heard of a diaphragmatic hernia until she sat in a doctor's office, about 20 weeks pregnant. This was the appointment when she and her husband, Matt, would find out whether she was carrying a boy or a girl. The couple was nervous, but excited.

The ultrasound test seemed to be taking a long time, Bethany thought. With two young daughters, she'd been through this process before and knew how it was supposed to go. A technician typed letters at the top of the screen. "DIAP, DIAP, DIAP," they read. The letters looked scary above the grainy black and white image of a baby boy. Bethany's doctor explained that the child would come into the world with a serious birth defect, a diaphragmatic hernia. This meant he would have a hole in his diaphragm that would allow his abdominal organs to move into his chest cavity before birth.

"They gave us some handouts with visual diagrams of what a diaphragmatic hernia looks like," Bethany recalled. "It took me a week before I could even remember how to pronounce it. We soon became obsessed with finding out everything we possibly could about this condition."

Over the next few weeks, Bethany and Matt read all they could about diaphragmatic hernias. They learned about possible outcomes. They were scared, but had tremendous support from family, friends, and trusted doctors.

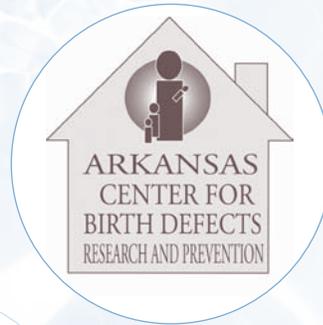
"It's still hard to believe because then, and even now, we have no idea what caused this birth defect," Bethany said. "You know what causes a lot of conditions, but the diaphragmatic hernias just seem unexplained."

Bethany gave birth to Jack Ryan 3 weeks early on July 6. She recalls that his body was limp and gray. His stomach, spleen, colon, large intestine, and some of his small intestine were in his chest, doctors told her.

"He didn't make a face," she said. "He didn't even try to cry."

Six hours after his birth, doctors at Arkansas Children's Hospital placed Jack on a heart-lung bypass pump that helped him breathe. Two days later, surgeons went in to repair the hernia and move his organs into his abdominal cavity. The surgery went quickly. There was just enough room for all of his organs to be placed back where they belonged. Doctors closed the hole with a small GORE-TEX patch.

Jack's fragile body seemed to be handling the heart-lung bypass pump well. After 9 days, the doctors decided to remove him from the machine. But soon after, they discovered clots in the main artery going to his brain, and in his shoulder and neck. Within days, Jack's kidneys began to fail, so he was placed on dialysis, when machines work like kidneys for a person.



After a series of additional complications, little Jack died on August 17.

"He was 6 weeks old to the day," Bethany said. "One of the doctors in the neonatal intensive care unit told us that he was kind of the worst-case scenario. It was just one of those things that couldn't be overcome."

In just 6 weeks, the Gillhams' sweet baby boy inspired a legacy that has gone on to help many Arkansas families. His family started the Jack Ryan Gillham Foundation (<http://jackryangillham.org/>) in his memory to help others who have seriously ill children. They raise money and collect needed items to help families battling congenital birth defects and other serious problems to make it through a very difficult time in their lives.

The Gillhams also support future research that can help them – and others – find out what causes diaphragmatic hernias and how they can be prevented.

"I've come across families since Jack's death who were affected by other birth defects – omphalocele and Trisomy 13, for example – and they don't know what caused this to happen to their children either," Bethany said. "It drives you crazy not to know. I now read everything I can about birth defects and research them."

After their experience with Jack, the Gillhams participated in the NBDPS by completing the interview and providing a DNA sample through a cheek swab. The Arkansas Center for Birth Defects Research and Prevention, based on the Arkansas Children's Hospital campus, sent the Gillhams a packet for taking cheek swab samples and mailing them back.

"It literally took us 5 minutes," Bethany said. "It doesn't require a day or even an hour for your involvement. It's effortless."

The Gillhams, like others who participate, were paid for their involvement. They immediately gave the funds to the Jack Ryan Gillham Foundation.

"I can't fathom why someone who knows about a birth defect like this wouldn't want to do this to help us find out even more," Bethany said. "It could forever change someone else's life."

***Editor's note:** The Gillham family has allowed us to share their story. The privacy of study participants is important to us. We will not name anyone in the study in any report or publication unless we have been given permission to do so.

Family stories are an important part of the NBDPS newsletter and upcoming website. We hope other families will share their stories with us.



Good Nutrition Helps Babies

Nutrition can help prevent birth defects. We know from studies that women who take vitamins with folic acid can reduce their risk of having a baby with a birth defect. We would like to find other foods or nutrients that might help prevent birth defects.

Why are we interested in knowing what women eat?

We know the food women eat is important to having a healthy pregnancy and a healthy baby. We want to find out what kinds of foods or nutrients (like folic acid) will help keep women and their babies healthy. Collecting information on what women eat will help us find out what women can do to improve their nutrition and help their chances of having a healthy baby.

How did we decide to ask about foods in the way that we do?

Our approach to looking at what foods women ate is called a "food frequency questionnaire." That is, women tell us how often they ate certain foods. Other ways to find out what women ate are to ask them to recall everything they ate in the previous 24 hours or to keep a record of what they ate over the past several days. These do not work for our study because food patterns may change over time. So what women now eat may not be the same as what they ate around the time they became pregnant.



How did we decide which foods to ask about?

First, we ask about foods that are most commonly eaten by most women. Second, we ask about some foods that most women probably don't eat but that are an important source of certain nutrients we want to study. For example, few women eat liver, but for those who do, it's an important source of vitamin A.

How do we go from asking about foods to figuring out how much of a certain nutrient a woman ate?

We have data that tell us the nutrient content of each food. We multiply the number of times a woman ate each food by the amount of nutrient in each food. We total those amounts. That is how we come up with an estimate of a woman's average daily intake of nutrients.

We don't ask about everything everyone ate (there are too many possibilities!), so how good are the data?

We don't expect the data to be perfect, but from past studies we know the questions we ask cover most of the foods women eat. When we put all the data together, we can look at food patterns. We also can tell whether one woman ate more of a certain nutrient than another woman. This type of information allows us to find foods and nutrients that may help women have healthy babies.

What can women do right now to improve their nutrition?

Women can take a multivitamin that contains folic acid. This will improve their own health, and it will help prevent neural tube (brain and spine) defects. Eating healthy foods is also important. More information about healthy diets is available in the resource section.





Resources

The resources are given for educational use only. The National Birth Defects Prevention Study research centers do not endorse the information presented on the sites.

Genetic Alliance

The Genetic Alliance is a network that connects members of parent and family groups, community organizations, disease-specific groups, professional societies, schools, corporations, and government agencies.

www.geneticalliance.org

Health Finder

The U.S. Department of Health and Human Services has resources on a wide range of health topics selected from over 1,600 government and nonprofit groups.

www.healthfinder.gov

Craniosynostosis

The Cleveland Clinic has information about Craniosynostosis and gives a list of support groups.

http://my.clevelandclinic.org/disorders/Craniosynostosis/hic_Craniosynostosis.aspx

Gastroschisis

The University of California, San Francisco Children's Hospital has videos that explain about gastroschisis.

<http://fetus.ucsfmedicalcenter.org/gastroschisis/>

Limb Defects

The University of Kansas Medical Center has a website with support and resources on limb defects.

<http://www.kumc.edu/gec/support/limb.html>

Neural Tube Defects (NTDs)

Medline Plus website has information on neural tube defects. It includes information on prevention and screening, types of NTDs, research, organizations, and much more.

<http://www.nlm.nih.gov/medlineplus/neuraltubedefects.html>

Folic Acid

The Centers for Disease Control and Prevention (CDC) has a website with information about folic acid. Find out what it is, how much women need and when to take it.

<http://www.cdc.gov/ncbddd/features/folic-acid.html>

Medication

The Better Health Channel in Australia has a fact sheet on birth defects and drugs.

http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/Birth_defects_and_drugs?OpenDocument

CDC has fast facts about medication use during pregnancy and breastfeeding.

<http://www.cdc.gov/ncbddd/meds/fast.htm>

Nutrition

The CDC "Nutrition for Everyone" website has basic nutrition information. It also gives resources for food safety and dietary guidelines.

<http://www.cdc.gov/nutrition/everyone/index.html>

This CDC website has a lot of good tips on how to get more fruits and vegetables in a person's diet. It features recipes and budget tips.

<http://www.fruitsandveggiesmatter.gov/>

The U.S. Department of Agriculture has nutrition information for women who are pregnant or breastfeeding. There are interactive tools like a menu planner and a food pyramid tracker.

<http://www.mypyramid.gov/mypyramidmoms/index.html>

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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.

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