

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.

NBDPS Update

The National Birth Defects Prevention Study (NBDPS) continues to search for causes of birth defects. We have talked to more than 37,000 women from 10 states. They include those who have had pregnancies affected by birth defects and those who have babies without birth defects. We also have received cheek cell kits from more than 23,000 families.

Over the years, our work has provided data to study risk factors for birth defects. Currently, NBDPS researchers have about 300 project ideas. In 2010 and 2011, 57 papers were published in medical and health journals using data from the NBDPS. The results of some of these papers will be discussed in this newsletter.

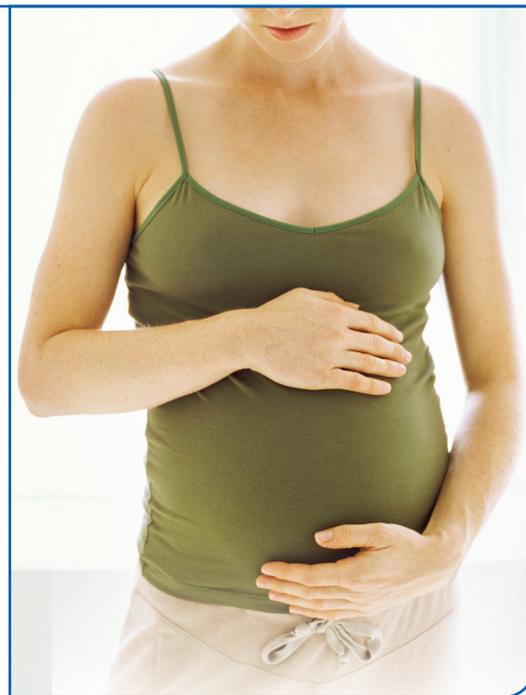
We thank the many families who have taken part in this study. The information they have shared will bring us closer to finding the causes of birth defects.

Recent Findings From the NBDPS

Medication Use During Pregnancy

Using medicine during pregnancy is common. So, it is important to learn how this might affect a mother and her baby. More knowledge will help women and their doctors make better choices about treatments during pregnancy.

Using data from the NBDPS and other sources, researchers have been able to look at medication use over time. They have used these data to see what kinds of medications women were taking during pregnancy. They found that medication use during pregnancy has gone up over the last 30 years. During the first trimester of pregnancy, 70%–80% of women said they took at least one medicine. About 50% of women said they took at least one prescription medicine during that time. This shows the need for continued research on the risks or safety of using these medicines during pregnancy.



In This **i s s u e**

- NBDPS Update* 1
- Recent Findings* 1
- Looking at Physical Activity* 3
- Informing and Helping Families*..... 4
- Genetic Methods in the NBDPS* 5
- Honors and Awards* 6
- Resource Corner*..... 6
- Directory of Study Sites* 7

Mitchell AA, Gilboa SM, Werler MM, Kelley KE, Louik C, Hernandez-Diaz S and the National Birth Defects Prevention Study. Medication use during pregnancy, with particular focus on prescription drugs: 1976–2008. Am J Obstet Gynecol. 2011 Jul;205(1):51.e1-8.

Recent Findings from the NBDPS (continued)



Researchers did not find a link between acetaminophen use and any specific type of birth defect.

Medicine To Ease Morning Sickness and Risk of Birth Defects

Morning sickness, including nausea and vomiting, is common during pregnancy. Certain medicines can be used to treat morning sickness. We wanted to better understand how these medicines might affect a mother and her baby.

Nearly 70% of women in the study reported morning sickness during the first trimester. Of these women, about 15% took a medicine to ease their symptoms. The NBDPS researchers found that most of the medicines did not increase the risk for many of the birth defects that were studied. But for some birth defects, including hypospadias and cleft palate, there might have been some association. More studies are needed to further explore any possible links.

Anderka M, Mitchell AA, Louik C, Werler MM, Hernandez-Diaz S, Rasmussen SA, and the National Birth Defects Prevention Study. Medications used to treat nausea and vomiting of pregnancy and the risk of selected birth defects. *Birth Defects Res A Clin Mol Teratol.* 2012 Jan;94(1):22-30.

Treatment With Prescription Painkillers (Opioids) and Birth Defects

Doctors often treat severe pain with prescription painkillers called opioids. Small amounts also can be found in

some over-the-counter cough medicines. Unfortunately, we do not have a lot of information about the effects of prescription painkillers on a pregnant woman and her unborn baby. We were able to look at this issue using NBDPS data.

Treatment with these types of painkillers just before or during early pregnancy was reported by 2% to 3% of the women in the NBDPS. Codeine and hydrocodone (sold as Vicodin®) were the most commonly used. Some birth defects, including spina bifida (a birth defect of the baby's spine) and certain heart defects, were linked with use of a prescription painkiller in our study. Previous studies found a similar link between codeine and heart defects. Our study was the first to find painkiller use related to other birth defects. When making treatment choices, women and their doctors should think about the benefits and risks of prescription painkillers.

Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso T, et al. Maternal treatment with opioid analgesics and risk for birth defects. *Am J Obstet Gynecol.* 2011 Apr;204(4):314.e1-11.

Clomiphene Citrate and Birth Defects

Clomiphene citrate, sold as Clomid® or Serophene®, is a drug used to help women who have trouble getting pregnant. It is one of the most common medicines used for infertility. As such, it is important to understand any possible risks connected with using it.

NBDPS researchers found that using this medicine was more common among mothers of babies born with certain birth defects. These include craniosynostosis, some heart defects, and some other birth defects. Some of these links were seen for the first time. That is why more research is needed to learn if the risks came from using clomiphene citrate or from the reason the couple had trouble getting pregnant.

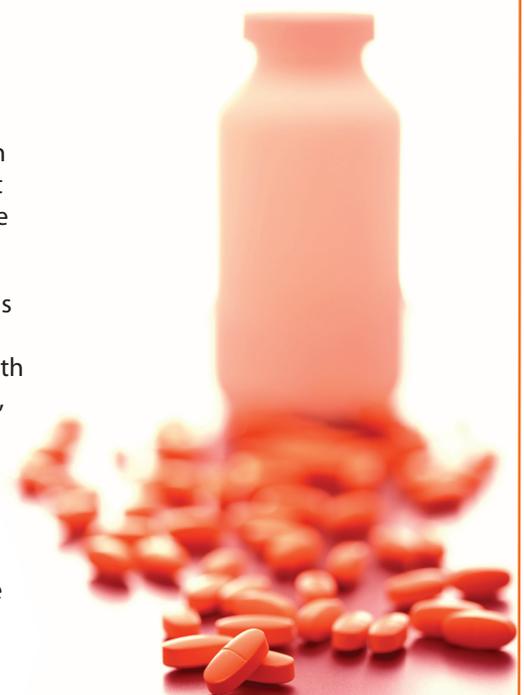
Reefhuis J, Honein MA, Schieve LA, Rasmussen SA and the National Birth Defects Prevention Study. Use of clomiphene citrate and birth defects, National Birth Defects Prevention Study, 1997-2005. *Hum Reprod.* 2011 Feb;26(2):451-7.

Birth Defects and Acetaminophen Use

Acetaminophen, sold as Tylenol®, is an over-the-counter medicine used to treat mild pain or to lower a fever. Often, it is found in cold or flu medications and prescription painkillers. Pregnant women often use it.

This study looked at acetaminophen use during early pregnancy (first 3 months). About 47% of mothers of babies with a birth defect and about 45% of mothers of babies without a birth defect said that they used it during the first trimester. Researchers did not find a link between acetaminophen use and any specific type of birth defect. They did find that acetaminophen used to lower a fever during pregnancy might have lowered the risk for certain birth defects.

Feldkamp ML, Meyer RE, Krikov S, Botto LD. Acetaminophen use in pregnancy and risk of birth defects: findings from the National Birth Defects Prevention Study. *Obstet Gynecol.* 2010 Jan;115(1):109-15.



Recent Findings from the NBDPS (continued)



Smoking and Neural Tube Defects

Smoking cigarettes during pregnancy can lead to harmful effects for the baby. These include being born too small or too early. We looked at the effect of smoking on birth defects of the baby's brain (anencephaly) and spinal cord (spina bifida). We also looked at the effects of secondhand smoke during pregnancy.

When compared to nonsmokers, pregnant women who were around secondhand smoke were more likely to have a baby with a spina bifida or anencephaly.

Suarez L, Ramadhani T, Felkner M, Canfield MA, Brender JD, Romitti PA, et al. Maternal smoking, passive tobacco smoke, and neural tube defects. *Birth Defects Res A Clin Mol Teratol.* 2011 Jan;91(1):29-33.

Genital Tract Infections and Birth Defects

Genital tract infections are common during pregnancy. Some studies have shown these infections during pregnancy can lead to adverse outcomes, including babies being born too early. We used NBDPS data to find out if these kinds of infections were linked to birth defects.

We found that genital tract infections were associated with an increased risk for some birth defects, including cleft lip and cleft palate. Some of these increased risks had not been seen before. Therefore, more studies are needed to confirm these findings.

Carter TC, Olney RS, Mitchell AA, Romitti PA, Bell EM, Druschel CM, and the National Birth Defects Prevention Study. Maternal self-reported genital tract infections during pregnancy and the risk of selected birth defects. *Birth Defects Res A Clin Mol Teratol.* 2011 Feb;91(2):108-16.

Caffeine and Selected Birth Defects

Caffeine is found in different foods and drinks, including coffee, tea, chocolate, and soft drinks. Many women consume caffeine during pregnancy (about two of every three women). Often, we are

asked about caffeine use and birth outcomes. To address this issue, we used NBDPS data to find out if using caffeine during pregnancy increased the risks for birth defects. Overall, the findings were reassuring and did not show an increase in risk for the birth defects we studied.

Browne ML, Hoyt AT, Feldkamp ML, Rasmussen SA, Marshall EG, Druschel CM, et al. Maternal caffeine intake and risk of selected birth defects in the National Birth Defects Prevention Study. *Birth Defects Res A Clin Mol Teratol.* 2011 Feb;91(2):93-101.



About 3% of women in the United States have diabetes and over 30% are obese. Obesity and diabetes before pregnancy are risk factors for birth defects.

Looking At Physical Activity

Obesity and diabetes are common among women in the United States. About 3% of women in the United States have diabetes and over 30% are obese. Obesity and diabetes before pregnancy are risk factors for birth defects. Physical activity can have many positive health effects, such as a lower risk of type 2 diabetes and weight loss. But, we do not know much about physical activity and birth defects. Earlier studies have reported mixed results. Some studies have suggested that heavy lifting or a lot of time spent standing might be related to birth defect risk, while others did not find these results. Several studies have suggested that physical activity might lower the risk for some birth defects.

The NBDPS allows us to study this important relationship. The first step in looking at this issue was to decide the types of questions to ask and how to ask them. We wanted to know not only about the level of physical activity, but also the different ways that one can be active. This can include activities done during free time or household work. In October 2010, we added a revised version of the short International Physical Activity Questionnaire to the NBDPS.

Looking At Physical Activity (continued)

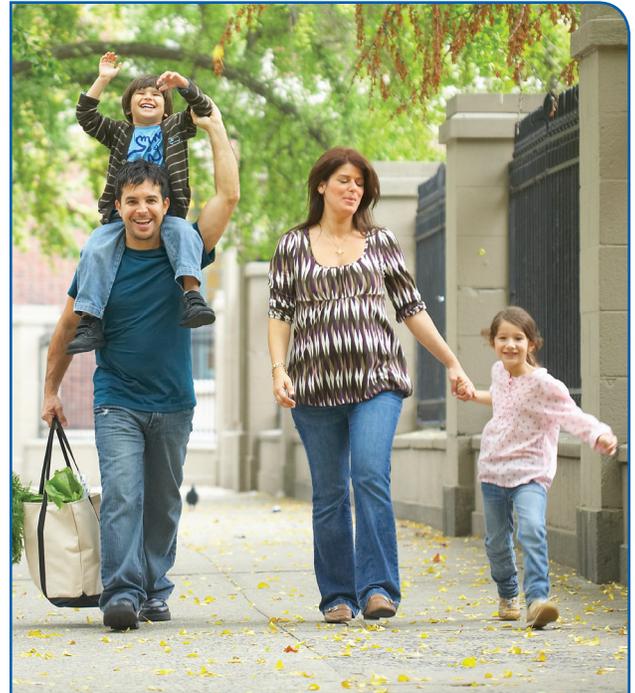


The NBDPS interview now asks women about their physical activity in the 3 months before pregnancy. We look at moderate and vigorous activities. Moderate activities cause breathing to be somewhat harder than normal. They can include gardening, actively playing with children, carrying light loads, or bicycling at a regular pace. Vigorous activities cause breathing much harder than normal. These include heavy lifting or fast bicycling. The questions added to the NBDPS were:

- Number of days per week engaged in moderate and vigorous activities
- Type and duration of activities on those days

Women also are asked about walking, during work, at home, and during travel. Finally, they are asked about the time they spend sitting, such as during visits with friends, reading, working at a desk, or watching television.

We are excited to have started asking these questions. It will take some time to gather enough data. Once we do, we plan to study the effects of physical activity on the risk for birth defects. We also plan to study how physical activity might change the relationship between diabetes and obesity and birth defects.



Informing and Helping Families



Every. Life. Inspires.

family's story. Julie wanted the video to include the experiences of other parents raising children with spina bifida. She also wanted to answer the questions she was asked and the questions parents might have been reluctant to ask. The purpose of the video is to give families hope, encouragement, and advice from others who have gone through what they are going through.

As Julie created the video, she met the McGinley family, who would be having twin boys. One boy, Eli, had spina bifida. The family allowed the birth to be videotaped for Julie's project. Eli lived for only 5 days. The video was completed, thanks to donations from family and friends. The video is known as Project ELI (Every Life Inspires). Project ELI is not meant to take the place of medical information, but rather to be a source to help families. Julie has made the video available on DVD for health care providers and their staff members. The Project ELI video is available at <http://www.communityconnectionsar.org/services-programs/project-eli>.

Having a child is a special time in a parent's life. However, when a parent is told that his or her child has a birth defect, that special time can fill with worry. Parents and family members who get a diagnosis of a birth defect can have many questions and concerns.

Julie Mayberry, who works with the Arkansas Folic Acid Coalition, has made a video that addresses some of these concerns. Julie's daughter, Katie, was born with spina bifida. She decided to speak out about her



Genetic Methods in the NBDPS



In the NBDPS, families are asked to collect cheek cell samples. Many wonder how we use these samples to help find the causes of birth defects. Studies have suggested that birth defects are caused by both genetic (inherited) and nongenetic (environmental and lifestyle) factors. To see if that is true, we collect information about each mother's lifestyle, diet, health, and environment before and during her pregnancy. We also collect cheek cell samples to look at each family's genetic material (DNA).

Cheek Cell Collection

Cheek cells contain DNA. NBDPS laboratories remove DNA from the cheek cells and measure the amount of DNA. During this process, we use a coded number to identify the DNA samples to protect each participant's identity. Samples have no names or other personal identifying information directly connected with them. Each study site stores the key to each sample's code in a secure location. Only a limited number of study staff has access to that information. Protecting each participant's identity is very important.

We get information from families who have children with birth defects (case families) and from families who have children with no birth defects (control families). Data from case and control families are compared with each other. For example, we compare information we collect during the interview about a medicine mothers took while they were pregnant. We also compare information from their DNA samples to tell us how quickly or slowly the mothers' bodies are able to break down and remove the medicine. The differences we see between case and control families might tell us that both the medicine and the DNA are involved in causing birth defects.

Improving the NBDPS

We are always looking for ways to make our study better. As a group, birth defects are common and affect 1 of every 33 babies born in the United States. However, individual birth defects are much less common and it takes many years to collect enough DNA samples and environmental information to complete meaningful studies. While we wait for more families to participate, we have

completed focus group discussions with mothers in Georgia who had already participated in the study. During the discussions, we asked mothers why they wanted to be part of the study; whether they wanted to be part of just the interview or wanted to provide DNA; and what challenges they faced when collecting DNA. We also asked them how they felt about the study materials; the best ways to contact them; and about different kinds of DNA collection methods. We are very excited about the ideas the mothers gave us, and the changes we have been able to make based on this information. We have updated the study folders and other materials we send to families. We also have created a website (www.nbdps.org) that has a lot of information to help answer questions about the study, or about birth defects in general. It contains resources in one location for families. It also contains a short video on how to collect cheek cell samples.

And, it is never too late to send in cheek cell samples. DNA does not change over time, so cheek cells can be collected years after birth and still be extremely helpful. Families who have participated in the NBDPS interview, but have not yet provided cheek cell samples are able to do this at any time. They can contact the study staff in their state to request a kit to collect cheek cells.

In the future, we plan to use new methods for genetic studies. These new methods will let researchers look at many pieces of each person's DNA or all of their DNA to see if there are changes that might be involved in causing birth defects.

As you can see, there are many exciting opportunities for new studies. We thank the many families who have shared information with us about their lifestyle, diet, health, and environment before and during pregnancy; cheek cell samples; or both. These efforts will help us find answers to what causes birth defects. We hope to help prevent future birth defects by sharing the results of our study with women and their physicians.

If you would like to share ideas for improving cheek cell collection or any other parts of the study, please email us at nbdps@cdc.gov. We are happy to hear about your experiences and to answer any questions or concerns you might have.



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NBDPS Honors and Awards



Drs. Feldkamp, Caton and Holmes Received Awards for Their Work



Marcia Feldkamp, PhD, PA, MSPH

Dr. Feldkamp was awarded the F. Clark Fraser New Investigator Award by the Teratology Society. Dr. Feldkamp is the principal investigator of the Utah Center. She is also Director of the Utah Birth Defect Network. She was honored for her work on gastroschisis, a birth defect where the intestines protrude outside the body through a hole beside the belly button. The award honors those who have built a career in birth defects research within 10 years of graduating. Dr. Feldkamp is committed to the study of birth defects. She works to move research findings into prevention action. Her goal is to increase the number of babies born healthy. Congratulations, Dr. Feldkamp!



Alissa Caton, PhD

Dr. Caton received an award for her article "Antihypertensive Medication Use During Pregnancy and the Risk of Cardiovascular Malformations." Dr. Caton works with the New York State Department of Health. Her article looked at the use of medicine to treat high blood pressure during pregnancy. She found that treatment with medicine or having high blood pressure during pregnancy might increase the risk of having a baby born with certain heart defects. The journal Hypertension selected the article as a top original paper published in 2009 in the population science group. Congratulations, Dr. Caton!



Lewis B. Holmes, MD

Dr. Holmes was awarded the 2012 Godfrey P. Oakley, Jr. Award by the National Birth Defects Prevention Network, Inc. This award is given to an individual who has advanced the field of birth defects. Dr. Holmes is one of the principal investigators with the Massachusetts Center. He has made many major contributions to the field of genetics, teratology, and the epidemiology of birth defects. Congratulations, Dr. Holmes!

Iowa Registry Earns State Leadership Award

The Iowa Birth Defects Registry (IBDR) received a national award for its work in collecting quality data and for its prevention efforts. Dr. Paul Romitti, the principle investigator of the Iowa Center, directs the IBDR. This State Leadership Award is given each year by the National Birth Defects Prevention Network.



Arkansas Center Receives Education & Prevention Award

The Arkansas program was given a national award for its education and prevention work. The award honors the outstanding activities of an agency to promote public awareness of birth defects. It recognizes the Arkansas Center's work on folic acid education, newborn screening for critical heart defects, and birth defects prevention.



Resource Corner

We provide several resources that might be of interest. The Centers are not responsible for the content found on these websites.



Physical Activity

The **March of Dimes** website has recommendations about safe exercises and how women can remain active during pregnancy: http://www.marchofdimes.com/pregnancy/physicalactivity_indepth.html.

The **Office on Women's Health** at the U.S. Department of Health and Human Services runs a website that offers advice to women regarding exercise and how to stay healthy and safe during pregnancy: <http://www.womenshealth.gov/pregnancy/you-are-pregnant/staying-healthy-safe.cfm>.

The **Centers for Disease Control and Prevention (CDC)** provides guidelines for healthy exercise during and after pregnancy: <http://www.cdc.gov/physicalactivity/everyone/guidelines/pregnancy.html>.



Heart Defects

The KidsHealth website from **Nemours Foundation** gives a basic overview of some of the warning signs that a child may have a congenital heart defect and describes some of the more common heart defects: http://kidshealth.org/parent/medical/heart/if_heart_defect.html.

The **National Heart, Lung, and Blood Institute** website contains information for parents and children living with congenital heart defects and provides links to clinical trials that study congenital heart defects: <http://www.nhlbi.nih.gov/health/health-topics/topics/chd/livingwith.html>.

The **American Heart Association** has information about congenital heart defects, such as risks, care, treatment, tools and resources: http://www.heart.org/HEARTORG/Conditions/CongenitalHeartDefects/Congenital-Heart-Defects_UCM_001090_SubHomePage.jsp.

The **Cincinnati Children's Hospital** has a wealth of information available in the Heart Institute Encyclopedia, including information on health topics such as cardiac anomalies and congenital heart defects: <http://www.cincinnatichildrens.org/patients/child/encyclopedia/default/>.

The **Royal Children's Hospital (RCH) of Melbourne** has detailed information on heart defects. On the home page, select "Departments & Services," then "Cardiology." On the cardiology department page, a list of common heart defects is given. You can click on each one for more in-depth information for a specific heart defect: <http://www.rch.org.au>.

Genetics

The **Dolan DNA Learning Center** website provides numerous resources on fragile X syndrome, phenylketonuria (PKU), Tay-Sachs disease, and other genetic disorders, including video clips of parents and children describing what it is like to have such diseases: <http://www.ygyh.org/index.htm>.

The **March of Dimes** website contains information on the causes and diagnosis of chromosomal abnormalities and offers links to support groups for families of affected babies: http://www.marchofdimes.com/baby/birthdefects_chromosomal.html.

Directory of the Centers for Birth Defects Research and Prevention National Birth Defects Prevention Study Sites

ARKANSAS

Charlotte Hobbs
University of Arkansas for Medical Sciences
Arkansas Children's Hospital
Telephone: (501) 364-5001; (877) 662-4567 (toll-free)
E-mail: hobbscharlotte@uams.edu
Internet: <http://arbirthdefectsresearch.uams.edu>

CALIFORNIA

Gary Shaw, DrPH
Stanford University
Telephone: (650) 721-5746
E-mail: gmslaw@stanford.edu
Internet: <http://www.cdph.ca.gov/programs/cbdmp/Pages/default.aspx>

Directory of the Centers for Birth Defects Research and Prevention National Birth Defects Prevention Study Sites (continued)

GEORGIA/CDC

Jennita Reefhuis, PhD
Sarah Tinker, PhD
Centers for Disease Control and Prevention
Telephone: (404) 498-4315
E-mail: nbdps@cdc.gov
Internet: <http://www.cdc.gov/ncbddd>

IOWA

Paul Romitti, PhD
University of Iowa
Telephone: (888) 850-8534 (toll-free)
E-mail: NBDPS@uiowa.edu
Internet: <http://www.public-health.uiowa.edu/ircid>

MASSACHUSETTS

Marlene Anderka, ScD, MPH
Massachusetts Department of Public Health
Telephone: (888) 302-2101 (toll-free)
E-mail: marlene.anderka@state.ma.us
Internet: <http://www.mass.gov/birthdefectscenter>

NEW YORK

Charlotte Druschel, MD, MPH
New York State Department of Health
Telephone: (518) 402-7990; (888) 296-8192 (toll-free)
E-mail: cmd05@health.state.ny.us
Internet: <http://www.health.state.ny.us/nysdoh/cmr/cmrhome.htm>

NORTH CAROLINA

Andrew Olshan, PhD
University of North Carolina, Chapel Hill
Robert Meyer, PhD
North Carolina Dept. of Health & Human Services
Telephone: (877) 204-5994 (toll-free)
E-mail: alison_woomert@unc.edu
Internet: <http://www.schs.state.nc.us/SCHS/bdmp>

TEXAS

Mark Canfield, PhD
Peter Langlois, PhD
Texas Department of State Health Services
Telephone: (512) 458-7232; (888) 844-4633 (toll-free)
E-mail: mark.canfield@dshs.state.tx.us
Internet: <http://www.dshs.state.tx.us/birthdefects>

UTAH

Marcia Feldkamp, PhD, PA
Lorenzo Botto, MD
Utah Department of Health
Telephone: (866) 818-7096 (toll-free)
E-mail: ubdn@utah.gov
Internet: <http://www.health.utah.gov/birthdefect>

share your stories

If you want to share your experience about the NBDPS, please contact your Center listed in the directory.

Newsletter Ideas and Mailing:

Please contact your Center listed in the directory if you:

- No longer wish to receive this newsletter,
- Need to update your mailing address, or
- Would like to receive this newsletter via e-mail.

Also, please let us know if you have topic ideas for future issues.

