FROM THE DIRECTOR

DIABETES AND OBESITY: EMERGING RISK FACTORS FOR BIRTH DEFECTS

Diabetes and obesity have been described as “among the top public health problems in the United States today” by U.S. Health and Human Services Secretary Tommy Thompson. In recent years evidence has been accumulating that these conditions, often found in tandem, also pose a significant risk for the development of birth defects.

In Texas, the situation is particularly acute. On average, Hispanic/Latino Americans are 1.5 times more likely to have diabetes than non-Hispanic whites of similar age, and the Texas population is about 36% Hispanic. Not surprisingly, Texas ranks 14th among U.S. states having the highest percentage of people with uncontrolled blood sugar. Regarding obesity, 20-25% of the Texas population is obese; and these two conditions often do not function independently. Obesity is known to exacerbate glycemic control problems, and both diabetes and obesity are found in a combination commonly called “metabolic syndrome” or “Syndrome X”.

According to the Behavioral Risk Factor Surveillance System, about 7% of Texas women of childbearing age have been told by a doctor that they have diabetes and 25% are obese. In particular, these conditions have been linked to higher rates of the following defects:

**Diabetes/Hyperinsulinemia**
- Klinefelter syndrome (Moore 2002)
- hypospadias (Aberg 2001)
- hypoplastic left heart syndrome (Abu-Sulaiman 2004)
- esophageal atresia (Aberg 2001)
- atrial septal defect (Ferencz 1997, Loffredo 2001)
- anal atresia or stenosis (Becerra 1990, Stoll 1997, Bianchi 2000, Aberg 2001)
- esophageal/intestinal atresia (Aberg 2001)

**Obesity**
- atrial septal defect (Watkins 2003)

**Combined**

Combating the problems of obesity and diabetes in our population is a multifaceted and complex endeavor. However, at the Texas Birth Defects Epidemiology and Surveillance Branch we are working to further illuminate these links and work toward a reduction of these conditions among women of childbearing age. Activities underway include an examination of folic acid use among diabetic, overweight, and obese women of childbearing age; participation in the Texas Nutrition and Physical Activity Work Group; and leadership of the Texas Center for Birth Defects Research and Prevention on at least four studies examining the link between birth defects and diabetes and obesity.

**Studies about Birth Defects and Diabetes/Obesity**


Abu-Sulaiman RM, Subraih B. Congenital heart disease in infants of diabetic mothers: echocardiographic study. Pediatric Cardiol-
REGISTRY

BIRTH DEFECT TRENDS IN TEXAS HEALTH SERVICE REGION 11, 1996-2003

The Lower Rio Grande Valley (Texas Health Service Region 11) is one of the initial pilot regions for the Texas Birth Defects Registry, and has completed birth defects surveillance through 2003 deliveries. This provides the opportunity to look at birth defect trends over eight years in this region of the state, which had a live birth population of 41,210 in 2003.

For deliveries to residents of Region 11, we examined the prevalence of 49 specific birth defects and any monitored defect from 1996 through 2003, by year. Poisson regression was used to identify statistically significant time trends.

Nine birth defects had statistically significant trends by Poisson regression, meaning they either increased or decreased during 1996-2003 in a pattern that was at least roughly linear. Anencephaly and spina bifida without anencephaly decreased in prevalence. This may relate to folic acid fortification of enriched grain products, which began optionally in mid-1996 and has been mandatory in the U.S. since January 1998, or to other efforts aimed at increasing the intake of folic acid among women of childbearing age along the Texas-Mexico border (see inset).

Seven defects increased in prevalence from 1996 to 2003 in Region 11: encephalocele, microcephaly, ventricular septal defect, pulmonary valve atresia or stenosis, obstructive genitourinary defect, craniosynostosis, and gastroschisis.

For the 9 defects with statistically significant trends by Poisson regression, we also performed a Chi-square test to assess departure from a linear trend. Only obstructive genitourinary defect was significant for departure from linear trend. This means that the data for obstructive genitourinary defect also have a nonlinear pattern that was statistically significant. Examples of nonlinear patterns that are frequently observed with disease prevalence data include seasonal (or cyclical) curves and exponential curves, either upward or downward.

Examining the data for obstructive genitourinary defect, we see the prevalence was generally stable from 1996 to 1999, then increased slightly in 2000 and 2001, and then increased noticeably in 2002 and again in 2003.

Conclusion: We examined 49 specific types of birth defects and any defect monitored by the registry, and most had neither a statistically significant increasing nor decreasing trend from 1996 to 2003 in Region 11. Anencephaly and spina bifida had significant downward trends, which may be related to folic acid fortification of grains, and/or to regional campaigns to increase the use of folic acid supplements among women of childbearing age. Seven defects exhibited significant upward trends. Possible explanations include changes in clinical practice, referral patterns, surveillance activities, or true changes in the occurrence of these conditions.

NTD Prevention Activities on the Texas-Mexico Border

A six-month folic acid campaign was conducted in the lower Rio Grande valley in early 2002, which included establishment of a network of stakeholders; counseling provided by social workers and discharge nurses at facilities in the 5 border counties at discharge of all postpartum patients; dissemination of information through marriage license packages, at local health fairs and annual rodeos; informative billboards placed throughout the community; broadcast presentations in English and Spanish; and campus campaigns. Several efforts were undertaken cooperatively between Texas communities and their Mexican counterparts. For more information, contact Jorge Trevino, 956-444-3204 or Jorge.Trevino@dshs.state.tx.us.
**FOCUS ON: CLEFT LIP & CLEFT PALATE**

The two main types of oral clefts are cleft lip and cleft palate. Cleft lip is the congenital failure of the upper- and mid-nasal areas to fuse, forming a gap in the lip. Cleft palate is the congenital failure of the palate to fuse properly, forming a grooved depression or fissure in the roof of the mouth. Clefts of the lip and palate can occur individually, together, or in conjunction with other defects. In birth defects studies, cleft lip with cleft palate and cleft lip without cleft palate are often grouped together. Cleft palate without cleft lip is classified as a separate defect.

Oral clefts may occur in combination along with chromosomal abnormalities and syndromes (trisomy 13, amniotic band anomaly, Fryns syndrome, Meckel syndrome, Stickler syndrome, Treacher Collins syndrome, van der Woude syndrome, Velocardiofacial syndrome, etc.).

In Texas, cleft palate alone (CP) affects about 6 pregnancies for every 10,000 live births, and cleft lip with or without cleft palate (CL/CP) occurs in about 11 pregnancies for every 10,000 live births. CL/CP is more common among the offspring of older mothers and male infants (Figure 1), and less common among blacks (Figure 2). Among 1999-2001 Texas deliveries, CL/CP appeared to have significantly higher rates in the Panhandle area; CL/CP also shows some interesting regional variation (Figures 3 and 4). In contrast, CP rates are higher among females compared to males (data not shown), which is consistent with the literature. CP rates are also higher among whites than Hispanics and blacks, and regional variations for these defects are not as pronounced (data not shown).

In addition to genetic and socio-demographic factors, the following maternal exposures have been reported to be associated with higher risk for oral clefts:

- Maternal fever
- Cigarette smoking
- Alcohol
- Illicit drugs such as cocaine and ecstasy
- Amphetamines
- Pseudoephedrine (a decongestant)
- Nonsteroidal anti-inflammatory drugs such as aspirin, ibuprofen, and naproxen
- Isotretinoin (an acne drug)
- Sulfasalazine (Antibiotics)
- Glucocorticoids (immunosuppressant and anti-inflammatory drugs)
- Corticosteroids (anti-inflammatory drugs)
- Anticonvulsant medications

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*Figure 1: Cleft Lip w/ or w/o Cleft Palate, Texas, 1999-2001*

*Figure 2: Cleft Lip w/ or w/o Cleft Palate, Texas, 1999-2001*

*Figure 3: Cleft Lip w/ or w/o Cleft Palate, Texas, 1999-2001*

*Figure 4: Cleft Lip w/ or w/o Cleft Palate, Texas, 1999-2001*
Continued from page 1


Research Center

Recent Publications


BIRTH DEFECTS IN TEXAS: RESEARCH SYMPOSIUM 2006
Sponsored by the Texas Center for Birth Defects Research and Prevention
Austin, Texas April 19, 2006
CALL FOR ABSTRACTS

Abstracts for oral presentations or posters are invited on epidemiologic or genetic studies that focus on birth defects. Preference will be given to studies where the presenter’s institution is located in Texas or a Texas population is covered by the study. The deadline for submission is January 31, 2006.

Contact Peter Langlois, Ph.D., 512-458-7232, peter.langlois@dshs.state.tx.us
the offspring, researchers used Texas-specific data from the National Birth Defects Prevention Study to evaluate whether gestational diabetes influenced the association of pre-pregnancy maternal obesity and risks for CNS defects. After adjusting for maternal ethnicity, age, education, smoking, alcohol use, and periconceptional vitamin use, obese women were found to have a greater risk of delivering offspring with encephaly (OR 2.3), spina bifida (OR 2.8), or isolated hydrocephaly (OR 2.7), but not holoprosencephaly. Odds ratios were even higher for cases with both maternal obesity and gestational diabetes.

Ramadhani TA, Canfield MA, Waller DK, Case AP. Medical records vs. interview responses: A comparative analysis of selected variables for linked birth defect cases. Birth Def Res Part A 2004;70:592-96. Birth defects data are subject to certain limitations depending on the collection method. In this study, medical records from the Texas Birth Defects Registry and maternal interviews from the National Birth Defects Prevention Network were compared for 1017 deliveries. Prevalence for non-gestational diabetes was 4.3% in the medical records and 3.4% in the maternal interviews, with 98.1% agreement. The prevalence of gestational diabetes was 7.9% in medical records and 9.2% in maternal interviews, with 94.3% agreement. Likewise, high levels of agreement were observed between the two systems for infant/fetus sex, mother’s Hispanic ethnicity, and seizures/epilepsy. Although high concordance was observed for seizure and epilepsy, kappa value was moderate. These results suggest that for some variables such as demographic variables, researchers can use either of the two data sources.

Moorthi RN, Hashmi SS, Langlois P, Canfield M, Waller DK, Hecht JT. Idiopathic talipes equinovarus (ITEV) (clubfoot) in Texas. Am J Med Genet 2005;132A:376-80. Idiopathic talipes equinovarus (ITEV) occurs in about 1 per 1,000 births and is the most common form of clubfoot. Researchers compared 682 cases of nonsyndromic ITEV with all births (n = 923,543) in Texas delivered from 1996 to 1999. The overall prevalence of ITEV was 0.74/1,000 or 1/1,354 live births. While no significant differences were found among rates of ITEV offspring born to whites and blacks, and US and foreign-born Hispanics, college education and higher parity were significantly associated with a lower risk.

This work supported in part by Cooperative Agreement No. U50/CCU613232 from the Centers for Disease Control and Prevention.

Collaborator Wins Recognition

Richard H. Finnell, Ph.D. was named recipient of the prestigious Regents Professor Award. Dr. Finnell is a professor of environmental and genetic medicine and director of the Institute of Biosciences and Technology (IBT) as well as research partner of the Texas Center for Birth Defects Research and Prevention. The award is bestowed annually by the Board of Regents in recognition of awardees’ exemplary contributions to their university or agency and to the people of Texas.

Dr. Finnell was instrumental in developing IBT’s Center for Environmental and Genetic Medicine and holds several National Institutes of Health grants. He received the Pfizer Animal Health Award for Research Excellence in 1995 and the Texas A&M University Distinguished Achievement Award in Research in 1997.

Since publication of “Phenytoin-induced teratogenesis: a mouse model.” (Science. 1981 Jan 30;211(4481):483-4), Dr. Finnell has authored more than 150 manuscripts on the complex interactions of various genes, folate metabolism, and birth defects such as neural tube defects and oral clefts.

Prevention

Rubella & Congenital Rubella Syndrome

Usually a mild rash illness, rubella (also called German measles) can have devastating effects when a pregnant woman is infected, especially during her first trimester. During the 1962—1965 worldwide rubella epidemic, an estimated 12.5 million cases of rubella occurred in the United States, resulting in 11,250 fetal deaths, 2,100 neonatal deaths, and 20,000 infants born with congenital rubella syndrome (CRS), a constellation of birth defects that often includes blindness, deafness, and congenital heart defects.

Before 1995 most persons with rubella in the U.S. were non-Hispanic; beginning in 1995, most were Hispanic. Beginning in 1998, data on country of origin were collected for rubella patients. These data revealed that during 1998 and 1999, approximately 79% and 65% of patients whose country of origin was known were foreign-born. Of these, 91% in 1998 and

# Congenital Rubella Syndrome Cases in Texas 1998-2002

<table>
<thead>
<tr>
<th># Cases</th>
<th>Year</th>
<th>TX:Mx Border</th>
<th>Race/Ethnicity</th>
<th>Maternal Birthplace</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1998</td>
<td>Yes</td>
<td>Hispanic</td>
<td>TX</td>
</tr>
<tr>
<td>2</td>
<td>1998</td>
<td>Yes</td>
<td>Hispanic</td>
<td>MX</td>
</tr>
<tr>
<td>1</td>
<td>1998</td>
<td>No</td>
<td>Hispanic</td>
<td>MX</td>
</tr>
<tr>
<td>1</td>
<td>2000</td>
<td>No</td>
<td>Non-Hispanic White</td>
<td>TX</td>
</tr>
<tr>
<td>1</td>
<td>2001</td>
<td>No</td>
<td>Hispanic</td>
<td>TX</td>
</tr>
<tr>
<td>1</td>
<td>2002</td>
<td>No</td>
<td>Hispanic</td>
<td>MX</td>
</tr>
</tbody>
</table>

98% in 1999 were born in the Western Hemisphere; 43% in 1998 and 81% in 1999 were born in Mexico.

Using data from the Texas Birth Defects Registry (see table, below) we are able to monitor the number of cases of CRS and compare various characteristics of those cases. Cases of CRS in the Texas Birth Defects Registry reflect a similar pattern, with 85% of cases born to Hispanic mothers, and 57% to mothers who were born in Mexico. Interestingly, since 1998 no cases of CRS have been detected in the Texas counties bordering Mexico—all three of these cases occurred elsewhere in the state.

The CDC Report on the Elimination of Rubella and Congenital Rubella Syndrome, can be found at www.cdc.gov/MMWR/preview/mmwrhtml/mm5411a5.htm.

PUBLIC EDUCATION MATERIALS

Did you know that brochures and posters about birth defects prevention can be obtained for free from a number of organizations? For example:

Physicians for Social Responsibility:


Healthy Fish, Healthy Families http://www.mercuryaction.org/fish/images/Healthy%20Fish.pdf (print-and-copy)

Centers for Disease Control and Prevention:

Dozens of free items for promotion of folic acid: http://www2.cdc.gov/ncbddefaorder/orderform.htm


PREGNANCY REGISTRIES

A pregnancy registry is a surveillance study that enrolls pregnant women who have taken a specific medicine while pregnant. Babies born to women taking a particular medicine are compared with babies of women not taking the medicine. Evaluation of a large number of pregnancies is needed to determine the effect of the medicine on the babies.

Some of the medicines currently being studied through the use of a pregnancy registry include asthma, cancer, and HIV medications, as well as specific drugs such as Lamictal (lamotrigine), Varivax (varicella virus vaccine) and Wellbutrin, Wellbutrin SR, and Zyban (bupropion).


LIVING WITH BIRTH DEFECTS

PARTICIPATING IN BIRTH DEFECTS RESEARCH

Many families who have been affected by birth defects are interested in participating in research about their specific condition. Although the design of the National Birth Defects Prevention Study requires participants to be identified through birth defects registries, many clinical trial studies allow for patients and even family members to "opt-in" to a study. For example, investigators for two studies are located in Texas and are actively recruiting participants (see below).

A clinical trial is a study that enrolls human subjects to answer specific health questions. Carefully conducted clinical trials find treatments that work in people and ways to improve health. Interventional trials determine whether experimental treatments or new ways of using known therapies are safe and effective under controlled environments. Observational trials address health issues in large groups of people or populations in natural settings.

The clinical trial process depends on the kind of trial being conducted. The clinical trial team checks the health of the participant at the beginning of the trial, gives specific instructions for participating in the trial, monitors the participant carefully during the trial, and stays in touch after the trial is completed. Currently, clinical trials in Texas recruiting participants include one on spina bifida (contact Barbara Weyland, Texas A&M Health Science Center, 866-521-7289), and one on osteogenesis imperfecta, a hereditary disease characterized by abnormally brittle, easily fractured bones (contact Susan Carter, Texas Children's Hospital, Houston, 832-822-1630).


NATIONAL CHILDREN'S STUDY

The National Children’s Study (NCS) will study the complex relationship between health and the environment for approximately 100,000 U.S. children and their families. Enrollment representative of the U.S. population will begin before birth, some even before conception, and follow up will continue for at least 21 years. A thorough history of exposures, biological samples, and health outcomes will be obtained from pregnancy onwards, allowing for comprehensive statistically powerful analyses of the link between a wide range of exposures and genetic factors with child health and development.

Currently, two of the study’s hypotheses proposed to look at birth defects:

- Birth defects from impaired glucose metabolism.
- Increased risk of birth defects and developmental disabilities in children born through assisted reproductive technologies.

NCS staff held conference calls with county executives and health officials
from among the designated study locations in December to discuss the goals of the Study and the role county governments can play in its implementation.

Transcripts of these calls are posted at http://nationalchildrensstudy.gov/events/other_events.

**FAS CORNER**

**SURGEON GENERAL’S ANNOUNCEMENT ON FETAL ALCOHOL SYNDROME**

In February 2005, the U.S. Surgeon General issued an Advisory on Alcohol Use in Pregnancy to raise public awareness about this important health concern. Research demonstrates that prenatal alcohol exposure can result in a spectrum of birth defects that can affect a child’s growth, appearance, cognitive development, and behavior. Fetal alcohol spectrum disorders are preventable if a woman abstains from drinking alcohol while pregnant.


**ANNOUNCEMENTS**

**REVISED RULES FOR BIRTH DEFECTS SURVEILLANCE IN TEXAS**

On July 1, 2005, revisions to the Texas Administrative Code, Title 25, Part 1, Chapter 37 were posted in the Texas Register for public comment. The rules spell out how birth defects surveillance is carried out in Texas. The changes reflect the following:

- Operationalizes HB 1097 (2003) birth defects law, which reads, “In addition to providing for the active collection of birth defects information under Subsection (c)(7), the board and the department may design the program to also provide for the passive collection of that information.”
- Responds to a stakeholder request to allow for the reporting of FAS cases of any age, because of a project that involves the screening and diagnosis of FAS. This also involves passive reporting of FAS cases.
- Updates program and agency names brought about by recent consolidation and agency changes.

The revised rules can be viewed at www.sos.state.tx.us/texreg/archive/July12005/PROPOSED/25.HEALTH%20SERVICES.html#132, or a copy may be requested at 512-458-7232.

**79TH TEXAS LEGISLATURE**

The Regular Session 79th Texas Legislature convened on January 11, 2005, and adjourned on May 30. Although the funding of public education took center stage this session, lawmakers addressed a number of issues pertinent to birth defects surveillance and prevention, as well as maternal and child health:

**Insurance**

**SB53:** Relating to the use of genetic testing information by insurers.

**Child Health**

**HB 984:** Requires school personnel to be trained on diabetes and its management to include hyperglycemia and hypoglycemia. It requires elementary and secondary students with diabetes seeking care at school to have a diabetes management and treatment plan furnished by the parent or guardian and signed by the student’s medical care provider.

**Newborn Screening**

**House Bill 790:** Provides legislative direction to the Department of State Health Services (DSHS) to expand the number of required newborn screening tests by November 1, 2006, to the extent funding is available. Also requires that DSHS conduct a study by March 1, 2006, to determine the most cost-effective method of conducting newborn screening to maximize the number of newborn screenings that may be conducted. Study to exclude newborn hearing screening and include consideration of outsourcing newborn screening to a qualified laboratory, and allows DSHS to adjust amounts charged for newborn screening fees, including fees assessed for follow-up services, tracking confirmatory testing, and diagnosis.

**Vital Statistics**

**SB 271:** Creates an optional certificate of birth resulting in stillbirth from Vital Statistics, upon request of a bereaved parent providing recognition that a child was born.

**Women’s Health**

**SB 747:** Requires the Health and Human Services Commission to create a Medicaid waiver program expanding eligibility to women living at or below 185 percent of the federal poverty level for preventative health and family planning services, increasing access to these services and allowing the state to draw down additional federal Medicaid funding.

**PREDCTORAL TRAINING PROGRAM**

The NICHD Institutional Predoctoral Training Program in Reproductive, Perinatal and Pediatric Epidemiology supports broad and fundamental, early stage graduate research training in reproductive, perinatal, and pediatric epidemiology via institutional training grants.

Trainees appointed to the program must have the opportunity to carry out supervised research in reproductive, perinatal or pediatric epidemiology, with the primary objective of developing their research skills and knowledge in preparation for a career in reproductive, perinatal or pediatric epidemiology.

CALENDAR

2005

October 24-27: Newborn Screening and Genetic Testing Symposium, Portland, OR Contact: Terry Reamer 202-822-5227 x 220, treamer@aphl.org


2006


April 19: Texas Center for Birth Defects Research and Prevention Symposium, Austin. Contact: Amy Case, 512-458-7232, amy.case@dshs.state.tx.us.


June 20-22: TxHIMA Galveston www.txhima.org

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TEXAS BIRTH DEFECTS MONITOR READER SURVEY

1. Where do you work? (circle one)
   a. State health department
   b. Local/county/city health department
   c. Federal government
   d. University
   e. Hospital
   f. Private healthcare practice
   g. Private industry
   h. Not-for-profit/advocacy organization
   i. Other

2. Are you the parent of a child with a birth defect or disability?
   • Yes
   • No

3. What is your primary professional role: (circle one)
   a. Birth defects surveillance
   b. Birth defects research
   c. Disability services
   d. Direct care
   e. Health promotion
   f. Administration
   g. Other disease surveillance or research
   h. Other

4. What content in the Monitor do you generally find most useful (select up to 3):
   a. Defect-specific data tables and highlights
   b. Other registry data tables and highlights
   c. Special studies from registry data
   d. Research updates
   e. Program updates
   f. “Living with birth defects”
   g. Birth defects prevention information
   h. Fetal alcohol syndrome-focused information
   i. Announcements
   j. Calendar
   k. Other

5. Which best describes how you use the Monitor (select up to 3)?
   a. Read it online only
   b. Review it then ‘recycle’
   c. Read it thoroughly
   d. Send to library
   e. Pass it along to colleagues
   f. Keep nearby as a reference
   g. Keep copies of particular articles
   h. Rarely or never read it

6. What is your impression of the graphics, style, and layout?

7. Have you requested data from Texas BDES in the past two years?
   • Yes
   • No

8. Do you prefer to receive the Monitor:
   a. PDF attachment to email
   b. Notice of electronic copy when available on the web site
   c. Hard copy
   d. None of these e. Other: ___________________________

9. If you receive a hard copy and would prefer to get the Monitor electronically, please give your name, mailing address and email:

10. Other comments?

Please fax to Amy Case at 512-458-7330 or email to amy.case@dshs.state.tx.us.