

INSIDE THIS ISSUE:



Mortality among Infants with Single Functional Ventricle	2
Linking Birth Defects and Perinatal HIV Exposures	3
Statewide, Registry-Linked NTD Recurrence Prevention	4
Heart Surgery Offers First-Year Survival Benefit	6

IS THE OCCURRENCE OF ORAL CLEFTS HIGHER IN WEST TEXAS?

Since the inception of the Texas Birth Defects Registry in 1993, three of the four cluster investigations conducted specifically for oral clefts have taken place in West Texas (Public Health Service Region 9). Also, the occurrence of cleft lip with/without cleft palate (CLP) is significantly higher in rural areas compared to urban areas, although the same is not true of cleft palate (CP) alone (Messer et al., 2010). Therefore, we used various spatial and cluster analysis methods to determine whether observed regional differences in the occurrence of orofacial clefts were statistically significant.

When we compared regional rates of CLP among deliveries in 1999-2004 with rates for the whole state, the Region 9 rate of 13.0 cases per 10,000 live births was not statistically significantly higher than the State rate of 10.9; however the Region 1 rate of 17.6 was significantly higher (Figure 1). There was a statistically significant different occurrence in CLP between regions ($p < 0.0001$) which remained after adjusting for maternal age, ethnicity, education, and infant sex. Thus variation in regional rates was not explained by the different population distribution of those characteristics in different regions. In general, both crude and adjusted rates of CLP increased when moving north and west from the Gulf coast to the panhandle.

For CP, rates were highest in Region 2, just west of the Dallas/Fort Worth Region; the rate of 8.8 cases per 10,000 live births was significantly higher than the State rate of 5.7 (Figure 2). However, the statistically significant difference between regions ($p < 0.01$) faded when adjusted for the factors above ($p < 0.21$). Thus the variation in rates may reflect difference characteristics of the population of women having babies in the different regions.

Various factors have been associated with higher risk for offspring with oral clefts. These include tobacco smoke, maternal alcohol intake, certain occupational exposures, maternal hyperthermia, and several medications. Periconceptional folic acid intake may reduce the risk of oral clefts. (For more information on risk factors, see www.dshs.state.tx.us/birthdefects/risk/risk-oralclefts.shtm.)

(Continued on page 4)

RESEARCH CENTER

Featured Study: Mortality in First 5 Years among Infants with Single Functional Ventricle

Dr. David Fixler, a Pediatric Cardiologist at the U.T. Southwestern Medical School (Dallas), led a team of researchers who used data from the Texas Birth Defects Registry to describe outcomes among children born with heart defects which result in only a single functional ventricle. These defects include hypoplastic left heart syndrome (HLHS), pulmonary atresia intact ventricular septum, single ventricle, and tricuspid atresia, which can be fatal, especially early in life.

Fixler et al. found that, among infants in the Texas registry who were born with these defects between 1996-2003, 75% with tricuspid atresia survived to their fifth birthday, but only 38% of those with HLHS did. There were also survival differences among ethnic groups, with infants born to black and Hispanic mothers faring less well than children born to white mothers. Children with additional defects other than cardiac were also less likely to survive the first five years of life.

However, there was a hopeful finding for affected families in that five-year survival rates improved by almost 50% between the period 1996-2000 and 2001-2003. This may be attributed to improved surgical techniques for repairing these defects. (See related story on page 6 of this issue, *Newer Heart Surgery Offers First-Year Survival Benefit* .)

For more information on this or other studies of outcomes among children with birth defects, contact Mark Canfield, Ph.D., mark.canfield@dshs.state.tx.us, 512-458-7232 Ext. 6158.

Recent Publications

Bille C, Pedersen DA, Andersen AM, Mansilla MA, Murray JC, Christensen K, Ballard JL, Gorman EB, Cabrera RM, Finnell RH. Autoantibodies to folate receptor α during early pregnancy and risk of oral clefts in Denmark. *Pediatr Res*. 2010 Mar; 67(3):274-9.

Blanton SH, Burt A, Stal S, Mulliken JB, Garcia E, Hecht JT. Family-based study shows heterogeneity of a susceptibility locus on chromosome 8q24 for nonsyndromic cleft lip and palate. *Birth Defects Res A Clin Mol Teratol*. 2010 Apr; 88(4):256-9.

Defant J, Gambello MJ, Monga M, Langlois PH, Noblin SJ, Vidaeff AC. Fetal trisomy 21 and the risk of preeclampsia. *J Matern Fetal Neonatal Med*. 2010 Jan; 23(1):55-9.

Finnell RH, Blom HJ, Shaw GM. Does global hypomethylation contribute to susceptibility to neural tube defects? *Am J Clin Nutr*. 2010 May; 91(5):1153-4.

Fixler DE, Nembhard WN, Salemi JL, Ethen MK, Canfield MA. Mortality in first 5 years in infants with functional single ventricle born in Texas, 1996 to 2003. *Circulation*. 2010 Feb 9; 121(5):644-50.

Langlois PH, Sheu SU, Scheuerle AE. A physician survey regarding diagnostic variability among birth defects. *Am J Med Genet A*. 2010 Jun; 152A(6):1594-8.

Lupo PJ, Symanski E, Chan W, Mitchell LE, Waller DK, Canfield MA, Langlois PH. Differences in exposure assignment between conception and delivery: the impact of maternal mobility. *Paediatr Perinat Epidemiol*. 2010 Mar; 24(2):200-8.

Lupo PJ, Goldmuntz E, Mitchell LE. Gene-gene interactions in the folate metabolic pathway and the risk of conotruncal heart defects. *J Biomed Biotechnol*. 2010; 2010:630940.

Miller EA, Rasmussen SA, Siega-Riz AM, Frías JL, Honein MA; National Birth Defects Prevention Study. Risk factors for non-syndromic holoprosencephaly in the National Birth Defects Prevention Study. *Am J Med Genet C Semin Med Genet*. 2010 Feb 15; 154C(1):62-72.

Mitchell LE, Long J, Garbarini J, Paluru P, Goldmuntz E. Variants of folate metabolism genes and risk of left-sided cardiac defects. *Birth Defects Res A Clin Mol Teratol*. 2010 Jan; 88(1):48-53.

Naufal Z, Zhiwen L, Zhu L, Zhou GD, McDonald T, He LY, Mitchell L, Ren A, Zhu H, Finnell R, Don-

(Continued on page 7)

FROM THE REGISTRY

Pilot Project Links Birth Defects and Perinatal HIV Exposures

Every year hundreds of Texas women of child-bearing age are diagnosed with HIV. When HIV positive women are diagnosed, they are prescribed antiretroviral medications and some women conceive while on these medications. Although current health guidelines recommend that women who are HIV-positive and become pregnant continue their treatment regimen, no association for the use of antiretroviral medications with a higher risk of birth defects has been found in a review of the literature to date. Furthermore, birth defects registries face significant challenges in ascertaining maternal exposure to medications with precision. In order to monitor birth outcomes among women on antiretroviral treatments the TB/HIV/STD Epidemiology and Surveillance Branch-Enhanced Perinatal Surveillance Registry (EPS) was created to collect data on HIV positive women who conceive and deliver a live born infant while using antiretroviral medications. Recently a collaborative linkage project between EPS and the Texas Birth Defects Registry (TBDR) was conducted to verify birth defect outcomes among women in the EPS Registry.

Per CDC requirements the EPS Registry collects data on only live born infants; this means that any potential fetal lethality of antiretroviral treatment will be missed. In addition, about 4% of birth defects that are identified are among fetal death cases. The EPS data used for this linkage project contained live birth deliveries to Texas mothers with HIV-1 from 1999-2003. The TBDR cases contains all pregnancy outcomes but provided infants born during the same time with a definite diagnosis of any monitored birth defect

for which the TBDR conducts surveillance. The two Registry populations exhibited somewhat different demographic profiles. Generally, mothers in the EPS Registry were less likely to have any higher education and were predominately African American. In contrast, Texas mothers who delivered from 1999-2003 were predominately Hispanic and had an even distribution across educational levels.

Five percent of babies included in the EPS Registry also appeared in the TBDR which is higher than the 3-4% of birth defects occurrence seen in the general population. Linkage between the 1,775 live born infants found in the EPS and the 67,385 TBDR cases yielded 89 cases with confirmed birth defects which appeared in both registries. Of the 89 cases, 79 (88.8%) were documented in the TBDR as having mothers with HIV/AIDS illness or treatment that was also corroborated by the EPS Registry. The TBDR birth defects data was used to complete the EPS Registry information for all cases identified in both Registries. As there were only 89 cases found for the five delivery years, it was not yet possible to determine if babies delivered to treated HIV infected mothers have an increased risk of birth defects. The two Registries will continue an annual collaborative linkage to increase the sample size and analytic power.

The successful linkage of two state health databases demonstrated that such collaborations can improve the completeness of the data and our knowledge about health hazards and suggests that future linkages can be used to inform treatment choices.

For more information, contact Lisa Marengo, MS at 512-458-7232, Ext 6657 or llisa.marengo@dshs.state.tx.us.

SYMPOSIUM OCTOBER 7, 2010—AUSTIN

The Texas Center for Birth Defects research and Prevention will host the 6th Biennial Birth Defects Research Symposium in Austin. Co-sponsors include the Dell Children's Medical Center and the March of Dimes. Register at www.regonline.com/TX_BD_2010.

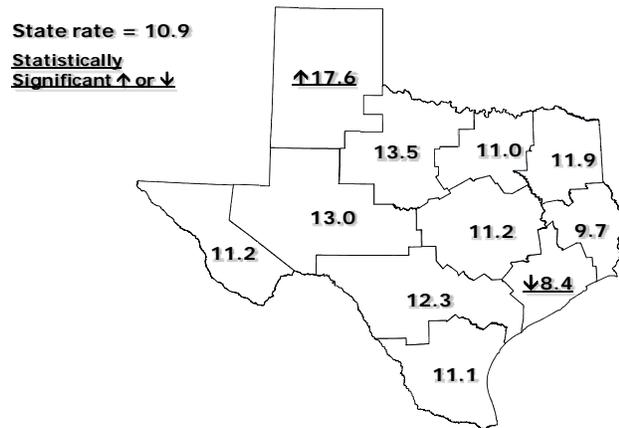
For more information, contact Amy Case at amy.case@dshs.state.tx.us or 512-458-7232 Ext 1-2814.

(Continued from page 1)

Efforts to lower the chance for these birth defects should emphasize preconception care to reduce harmful exposures before women become pregnant.

Identifying and clarifying unusual geographic occurrences of birth defects can help us find populations who could benefit from public health intervention and help identify causes of birth defects by isolating characteristics about the high-rate populations. However, geographic methods of analysis have some limitations. In this analysis, for example, we used Public Health Service Regions, which are very large with somewhat arbitrary

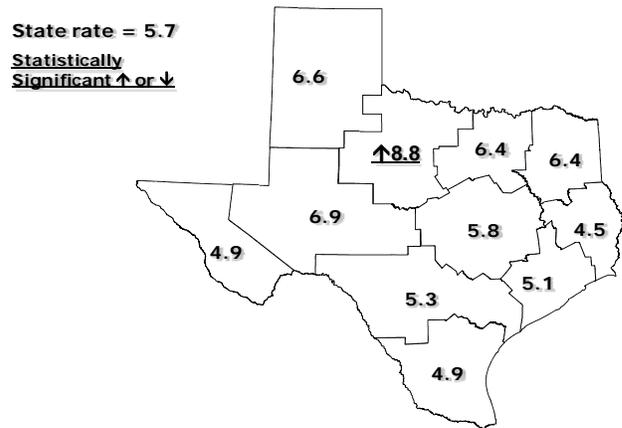
Figure 1: Cleft Lip (with or without Cleft Palate), 1999-2004



boundaries and so they are not very helpful for identifying differences in the populations that underlie higher risk. With this in mind, we are working with the Geography Department at Texas State University - San Marcos to develop useful ways to look at county rates of birth defects that can distinguish nonrandom patterns. We will also explore use of specialized cluster detection software, the Kulldorf scan statistic, to identify potential clusters within counties.

For more information on geographical analyses of birth defect rates in Texas, contact Peter Langlois at 512-458-7232, Ext. 6183 or peter.langlois@dshs.state.tx.us.

Figure 2: Cleft Palate, 1999-2004



PREVENTION

Developing a Statewide, Registry-Linked NTD Recurrence Intervention

During July and August 2007, the Birth Defects Epidemiology and Surveillance (BDES) branch in collaboration with Spina Bifida Associations in Dallas, Houston, and San Antonio, ran a series of focus groups to pretest print material promoting the use of peri-conceptual folic acid to women at risk for neural tube defect recurrence living in Texas. A brochure was designed using concepts from a behavioral science theory, the Precaution Adoption Process Model (PAPM), and pretested by the target audience. The theory identifies seven stages, beginning with being unaware of the problem and ending with maintaining the behavior change. PAPM is particularly applicable for

targeting behaviors that require deliberate action (Figure 1).

Three focus groups comprising 26 mothers of children with spina bifida pretested the brochure. Each participant received \$50 incentive as well as free off-site child care during the focus group session. One focus group was conducted in Spanish-only and the other two groups were in English with Spanish interpretation if necessary. Prior to the discussion, participants completed a questionnaire on race, marital status, education, and pregnancy planning. They were then given the brochure and asked questions on appearance, comprehension, acceptability, cultural appropriateness, psychological sensitivity and confidentiality. They also picked one role model whose situation best represented their own. Summative content analysis of coded transcripts revealed key

(Continued on page 5)

themes and preferences for health promotion materials.

Results indicated that participants were dissatisfied with the advice they received from their health providers, and some women, particularly the Spanish-only speakers, had low levels of knowledge about their increased risk for a second pregnancy affected by a neural tube defect. Despite this finding, participants largely self-identified with the role model who was knowledgeable about folic acid and deciding what to do. Some participants wanted realistic photographs that visually increased their perceived level of threat. A few participants felt responsible for their pregnancy outcome and reflected on their feelings of guilt and efforts to cope. With respect to style and formatting, participants preferred colorful envelopes, high quality paper, simple words, conversational style sentences, and positive messages.

The findings suggest a brochure is a helpful adjunct to recommendations given by health providers or as part of a multi-component intervention. There may be a need to develop additional educational material for Spanish-only speakers. The findings also highlight the need to create sensitive messages so as not to interfere with coping.

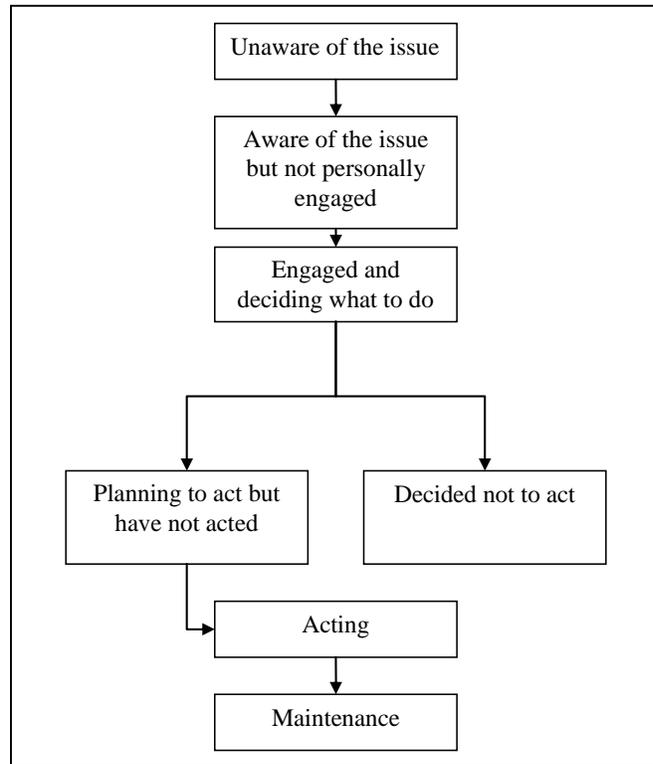
At this time, BDES has mailed over 3,000 brochures to women at risk for neural tube defect recurrence across the state of Texas. A plan for a process and outcome evaluation of the intervention is currently in development.

March of Dimes Promotes Folic Acid with "Vitamin B RV"

March of Dimes volunteers in San Antonio used a 24-foot recreational vehicle (RV) as an educational tool during the annual March for BabiesSM on May 8 at SeaWorld San Antonio. Walkers were not sure what to make of "Vitamin B RV" at first sight. "Some walkers thought we were selling tickets for a drawing", said Tracy Holmes-Brazil, Program Services Committee Chair. "But we were happy to tell them what we were really up to."

Participants were invited to take a 10-question quiz testing their knowledge of the B vitamin folic acid and its benefits for women. Program Services volunteers reviewed the quizzes with par-

Figure 1. Precaution Adoption Process Model (PAPM) Weinstein, N.D. 1988 The precaution adoption process. Health Psychol. 7: 355-386



Participants who then entered the RV equipped with a television and DVD player where they viewed a 3-minute video that reinforced the knowledge gained through the quiz. "We borrowed the idea from the Indiana Chapter," said Holmes-Brazil. "The RV was utilitarian and attention-getting. In just 4 hours we spoke with 200 people."

Vitamin B RV was just part of the annual Folic Acid Awareness outreach in San Antonio. March of Dimes partnered with Spina Bifida San Antonio and San Antonio Metropolitan Health District WIC on a variety of activities, including interior transit bus panels and newspaper PSAs, television spots featuring folic acid rich foods, and educational activities in community health clinics.

The March of Dimes is the leading nonprofit organization for pregnancy and baby health. With chapters nationwide, the March of Dimes works to improve the health of babies by preventing birth defects, premature birth and infant mortality. For more information about folic acid, visit marchofdimes.com or nacersano.org.

LIVING WITH BIRTH DEFECTS

Newer Heart Surgery Offers First-Year Survival Benefit

Infants born with a severely underdeveloped heart who undergo a newer surgical procedure are more likely to survive their first year, according to a report by researchers supported by the National Heart, Lung, and Blood Institute (NHLBI), which is part of the National Institutes of Health. They are also less likely to require a heart transplant than those who have a more traditional surgical procedure. The study of 549 newborns, however, suggests that after the first year, the two surgical procedures for the relatively rare condition yield similar results.

The Single Ventricle Reconstruction (SVR) Trial is the largest clinical trial to compare treatments for congenital heart disease, and the first North American, multi-center, randomized trial of surgical therapy for congenital heart disease patients.

The normal heart has two pumping chambers called ventricles. The right ventricle pumps blood to the lungs, and the left ventricle pumps blood to the body. This trial studied babies born with a severe form of congenital heart disease in which babies are born with a functioning right ventricle and a small, underdeveloped, nonfunctioning left ventricle. The condition is sometimes referred to as hypoplastic left heart syndrome. Without treatment, these babies usually die shortly after birth.

The SVR Trial compared two surgical procedures that are commonly used to treat babies born with only the functioning right ventricle to determine whether one procedure improves outcomes more than the other. The SVR Trial was conducted at 15 sites that are part of the NHLBI's Pediatric Heart Network, a multi-center clinical research consortium supported by the NHLBI since 2001 to study congenital and acquired heart diseases that occur in childhood.

In general, three surgeries are needed to treat a single right ventricle. The first procedure, is usually performed within the first two weeks of life and is one of the highest risk procedures in congenital heart surgery. A shunt, or small tube, is implanted to provide a connection for blood to flow

from the heart to the blood vessels in the lungs, or pulmonary arteries, so that blood can pick up oxygen and release carbon dioxide. Follow-up procedures are done at 4-6 months and 18-36 months.

In the SVR trial, participants were randomly assigned shortly after birth to receive one of two types of shunts for their initial surgery, as part of the Norwood procedure. About half of the newborn participants received a modified Blalock-Taussig (MBT) shunt, the traditional approach, which places the shunt from a branch off of the aorta, the major blood vessel that takes blood from the heart to the rest of the body, to the pulmonary artery. The other participants received a newer type of shunt, called an RVPA shunt, which is placed between the right ventricle and the pulmonary arteries.

Each type has advantages and disadvantages, but small studies of the RVPA shunt have suggested that it provides better survival and other outcomes than the MBT shunt. However, randomized clinical trials have not been conducted to demonstrate whether one procedure is better than the other.

Researchers followed study patients for at least 14 months and evaluated the number of deaths and heart transplantations in each group at one year, as well as the number of complications linked to each type of shunt.

The researchers report that after 12 months, 74 percent of infants with the RVPA shunt survived and didn't need a heart transplant, compared to 64 percent of infants with the MBT shunt. The newborns with the RVPA shunt, however, had significantly more complications requiring additional interventions, for example, insertions of stents or balloons to keep the shunt open. Other outcomes, such as the size and pumping ability of the right ventricle at 14 months, were similar in the two groups of participants.

Other analyses to study the effects of the procedures in older children are underway.

The Pediatric Heart Network (PHN) is the clinical cornerstone of the NHLBI's Bench to Bassinet program in translational pediatric cardiovascular research.

--Source: *The National Institutes of Health, National Heart Lung, and Blood Institute (NHLBI).*

ANNOUNCEMENTS

Genetic Services Report

The Texas Interagency Council for Genetic Services Resource Allocation Plan for 2010-2012 has been published and is available online at www.dshs.state.tx.us/genetics/pdf/rap2010-2011.pdf. This biennial report details recommendations for allocating funds for genetic services. It also describes the current situation and challenges and opportunities presenting Texas state agencies in allocating these resources.

EIS Officer Joins Environmental Epidemiology and Disease Registries (EEDR) Section

The Texas Department of State Health Services is pleased to welcome Dr. Noha Farag to the EEDRS

Section as our Epidemiology Intelligence Service Officer beginning August 1, 2010. She received her Ph.D. in epidemiology from the University of Oklahoma in 2009, and is currently a postdoctoral fellow at the University of Oklahoma Prevention Research Center. Her research expertise and publication history include the study of risk factors for cardiovascular disease. She will be working on a number of projects with birth defects researchers.

The Epidemic Intelligence Service (EIS) is a unique 2-year post-graduate training program of service and on-the-job learning for health professionals interested in the practice of applied epidemiology.

For more information on the role of this EIS Officer at DSHS, contact Mark Canfield, Ph.D., mark.canfield@dshs.state.tx.us, 512-458-7232 Ext. 6158.

SYMPOSIUM OCTOBER 7, 2010—AUSTIN

The Texas Center for Birth Defects Research and Prevention will host the 6th Biennial Birth Defects Research Symposium in Austin. Co-sponsors include the Dell Children's Medical Center and the March of Dimes. Register at www.regonline.com/TX_BD_2010.

For more information, contact Amy Case at amy.case@dshs.state.tx.us or 512-458-7232 Ext 1-2814.

(Continued from page 2)

nelly KC. Biomarkers of exposure to combustion by-products in a human population in Shanxi, China. *J Expo Sci Environ Epidemiol*. 2010 Jun; 20(4):310-9.

Nembhard WN, Salemi JL, Wang T, Loscalzo ML, Hauser KW. Is the prevalence of specific types of congenital heart defects different for non-Hispanic white, non-Hispanic black and Hispanic infants? *Matern Child Health J*. 2010 Mar; 14(2):184-93.

Nembhard WN, Wang T, Loscalzo ML, Salemi JL. Variation in the prevalence of congenital heart defects by maternal race/ethnicity and infant sex. *J Pediatr*. 2010 Feb; 156(2):259-64. Epub 2009 Oct 9.

Shahrukh Hashmi S, Gallaway MS, Waller DK, Langlois PH, Hecht JT; National Birth Defects Prevention Study. Maternal fever during early pregnancy and the risk of oral clefts. *Birth Defects Res A Clin Mol Teratol*. 2010 Mar; 88(3):186-94.

Shimshoni JA, Yagen B, Wlodarczyk B, Finnell RH, Schurig V, Bialer M. Evaluation of stereoselective anticonvulsant, teratogenic, and pharmacokinetic profile of valnoctylurea (capuride): a chiral stereoisomer of valproic acid urea derivative. *Epilepsia*. 2010 Mar; 51(3):323-32.

Vendola C, Canfield M, Daiger SP, Gambello M, Hashmi SS, King T, Noblin SJ, Waller DK, Hecht JT. Survival of Texas infants born with trisomies 21, 18, and 13. *Am J Med Genet A*. 2010 Feb; 152A(2):360-6.

Waller DK, Gallaway MS, Taylor LG, Ramadhani TA, Canfield MA, Scheuerle A, Hernández-Díaz S, Louik C, Correa A; National Birth Defects Prevention Study. Use of oral contraceptives in pregnancy and major structural birth defects in offspring. *Epidemiology*. 2010 Mar; 21(2):232-9.

Wen S, Zhu H, Lu W, Mitchell LE, Shaw GM, Lammer EJ, Finnell RH. Planar cell polarity pathway genes and risk for spina bifida. *Am J Med Genet A*. 2010 Feb; 152A(2):299-304.



The Monitor is published twice a year by the Birth Defects Epidemiology and Surveillance Branch, Texas Department of State Health Services:

Glenda Rubin Kane, Chair, Texas Department of State Health Services Council

David L. Lakey, M.D., Commissioner, Texas Department of State Health Services

Adolfo Valadez, M.D., M.P.H., Assistant Commissioner for Prevention and Preparedness Services

Lucina Suarez, Ph.D., Acting Director, Environmental Epidemiology and Disease Registries Section

Mark A. Canfield, Ph.D., Manager, Birth Defects Epidemiology and Surveillance Branch

EDITOR: Amy Case, M.A.H.S., Program Specialist, Birth Defects Epidemiology and Surveillance Branch. Contributors: Peter Langlois, Ph.D. and Lisa Marengo, MS, Texas Birth Defects Epidemiology & Surveillance Branch; Elvia Ledezma, MPH, DSHS HIV/STD/TB Epidemiology and Surveillance Branch; Tasneem Husain, DrPH, ICF Macro.

Please visit the BDES website for updated information: www.dshs.state.tx.us/birthdefects.

CALENDAR

2010

September: Infant Mortality Awareness Month

October 7: Texas Birth Defects Research Symposium, Dell Children's Hospital, Austin. Contact: Amy Case, 512-458-7232 Ext 2814, amy.case@dshs.state.tx.us.

October 19-22: Texas Environmental Health Association, Austin. Contact: <http://myteha.org/AnnualConference.htm>.

December 3-10: American Epilepsy Society Meeting, San Antonio. Contact: info@aesnet.org. www.aesnet.org/go/meetings-and-events/annual-meeting.

November 4-7: Texas Pediatric

Society Meeting, San Antonio. Contact: crystal.zamarron@txpeds.org or 512-370-1517. www.txpeds.org/annual_meeting/

December 15-17: Sixteenth Annual Maternal and Child Health Epidemiology Conference., San Antonio. Contact: mchepireg@unmc.edu or 402-561-7500. (Pre-Conference Trainings: December 13-14)

2011

April 8-10: Association of Women's Health, Obstetric, and Neonatal Nurses, Texas Section Conference, Austin. <http://www.awhonn.org/awhonn/section.by.state.do?state=Texas&name=Texas-Section-Conference>.

This publication was funded in part by the Office of Title V & Family Health, Texas Department of State Health Services, using Title V Maternal and Child Health Block Grant Funds.