The Texas Birth Defects

MONITOR

TEXAS
Department of State Health Services
Birth Defects Epidemiology and Surveillance

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10 Years of Folic Acid Fortification

INSIDE THIS ISSUE:

Background

In September 1992 the U.S. Public Health Service (PHS) recommended that all women of childbearing age consume 400 micrograms (ug) of folic acid daily to reduce their risk of having a pregnancy affected with spina bifida or other neural tube defects. The PHS suggested several approaches by which this level could be reached:

- Improved dietary habits
- Fortification of the U.S. food supply
- Daily use of folic acid supplements by women throughout their childbearing years.

In keeping with the PHS recommendations and those of the U.S. Food and Drug Administration (FDA), a committee was formed to study these issues. As a result of this committee's recommendations, on January 1, 1998 the FDA required that folic acid be added to most enriched breads, flours, corn meals, rice, noodles, macaroni and other grain products. These foods were chosen for fortification with folate because they are staple products for most of the U.S. population, and because they have a long history of being successful vehicles for improving nutrition to reduce the risk of classic nutrient deficiency diseases.

Under the terms of the rule:

- Fortification levels range from 0.43 to 1.4 mg per pound of product.
- Fortification of grain products at these levels would allow the daily intake from all sources to remain below the recommended upper limit of 1 mg per day.
- The amount of folic acid that was expected to be consumed through foods fortified at these levels was considered safe for all population groups.

Manufacturers were allowed to make claims on the labels that the fortified products contain folic acid and that adequate intake of the nutrient may reduce the risk of neural tube defects.

It could be argued that folic acid fortification was an unprecedented public health intervention in that the preventive measure impacts virtually the entire U.S. population while being targeted at only a select portion (women of childbearing age). On the other hand, efforts to address preventable disease in the population through manipulation of the food supply dates back to 1924, when the U.S. first began adding iodine to salt in an ultimately successful effort to prevent mental retardation. The addition of vitamin D to milk to prevent rickets, iron in flour to prevent anemia, and fluoride in water to prevent cavities followed.

Because the studies that precede them can only predict efficacy and safety based on a sample of the population, the outcomes of population-wide interventions such as fortification of the food supply are unknown at the outset. So, what outcomes have we seen after 10 years of folic acid fortification of the U.S. grain supply?

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From the Registry

On the Border

Impact of Different Definitions of the Texas-Mexico Border on Birth Defect Prevalence

Texas shares a 1,255 mile border with Mexico; this is the largest expanse of Mexican border in the United States, and the area has long been a focus of public health and environmental concerns. These concerns include possible higher prevalence of certain birth defects. However, definitions of what actually constitutes “the border” vary and include different areas. Here we examine whether the prevalence of birth defects varies depending on the inclusion criteria for defining a “border county”.

The smallest designation includes the most populous or “Big Seven” counties of Cameron, El Paso, Hidalgo, Maverick, Starr, Val Verde and Webb (Figure 1). These seven counties contain over 90% of the border population.

The next largest definition, typically used by the Texas Birth Defects Epidemiology & Surveillance Branch (BDES), comprises 34,122 square miles in 14 contiguous counties (Figure 2): Brewster, Cameron, El Paso, Hidalgo, Hudspeth, Jeff Davis, Kinney, Maverick, Presidio, Starr, Terrell, Val Verde, Webb, and Zapata.

A third definition is based on a US-Mexico border environmental treaty called the “La Paz Agreement of 1986”. The Texas portion of the La Paz border is defined as the area within 100 kilometers of the Rio Grande river and encompasses the 32 Texas counties as seen in Figure 3. This definition includes some counties that are not touching Mexico: Brooks, Crockett, Culberson, Dimmit, Duval, Edwards, Frio, Jim Hogg, Kenedy, La Salle, McMullen, Pecos, Real, Reeves, Uvalde, Willacy and Zavala counties.

Figure 1: "Big Seven" Counties

Figure 4 depicts our final border county definition which encompasses the 43 counties south of Interstate 10 and west of Interstate 37 including metropolitan San Antonio. The 43-County South Texas Border Region contains 77,519 square miles which is approximately 30% of the state area. Additional counties unique to this definition are: Atascosa, Bandera, Bexar, Jim Wells, Kerr, Kimble, Kleberg, Live Oak, Medina, Nueces, San Patricio and Sutton. (Texas Comptroller, 2003).

We explored various definitions of border residence to determine if any of these definitions affected the prevalence of birth defects on the “border”, first comparing racial/ethnic demographics for each of the areas. Only the largest geographical area (Figure 4) exhibited a different racial/ethnic distribution from the other three definitions of border, with the proportion of White Hispanics relatively smaller and White Non-Hispanics and African Americans accounting for larger proportions of the population (Data not shown.) This is important because some birth defects are associated with different racial/ethnic groups.

An analysis for the four border county definitions was conducted for the 49 selected birth defects commonly reported. Birth prevalence and 95% confidence intervals were compared among each of the border definitions, using the second model (illustrated in Figure 2) as referent.

Figure 2: Fourteen Contiguous Counties

In Texas for delivery years 1999-2004, the most prevalent birth defect categories were heart defects (ventricular septal defect, patent ductus arteriosus, and atrial septal defect) as well as hypospadias. This was found to be true for all border definitions. No significant statistical variation was seen for the selected defects between the 14 county border model and either the “Big 7” nor the “La Paz” border definitions. Only the 43 county border definition displayed some significantly statistically different prevalence values. It is important to note, however, that the defects that do vary significantly between the two models are those that are also known to show statistical significant difference for race/ethnicity, and as noted above, racial/ethnic composition for the 43-county definition is different from the others three definitions.

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Table 1. Comparison of the Ranking of the Top Ten Birth Defect Cases Between Four Border Definitions (Birth Defects in Bold Font are Statistically Significantly Elevated)

Defect	7 County Border Resident				14 County Border Resident			
	Rank	Cases	Prevalence†	95% CI	Rank	Cases	Prevalence†	95% CI
Ventricular septal defect*	1	1974	69.4	66.4 - 72.5	1	1995	69.2	66.2 - 72.3
Patent ductus arteriosus*	2	1731	60.9	58.0 - 63.7	2	1754	60.9	58.0 - 63.7
Atrial septal defect*	3	1294	45.5	43.0 - 48.0	3	1320	45.8	43.3 - 48.3
Obstructive genitourinary defect*	4	705	24.8	23.0 - 26.6	4	714	24.8	23.0 - 26.6
Pyloric stenosis*	5	600	21.1	19.4 - 22.8	5	607	21.1	19.4 - 22.7
Hypospadias or epispadias*	6	516	18.2	16.6 - 19.7	6	527	18.3	16.7 - 19.8
Trisomy 21 (Down syndrome)*	7	424	14.9	13.5 - 16.3	7	430	14.9	13.5 - 16.3
Cleft lip with or without cleft palate*	8	309	10.9	9.7 - 12.1	8	311	10.8	9.6 - 12.0
Pulmonary valve atresia or stenosis	9	246	8.7	7.6 - 9.7	9	252	8.7	7.7 - 9.8
Infants and fetuses with any monitored birth defect*		9651	339.4	332.6 - 346.2		9774	339.1	332.4 - 345.8

Defect	32 County Border Resident				43 County Border Resident			
	Rank	Cases	Prevlence†	95 % CI	Rank	Cases	Prevalence†	95% CI
Ventricular septal defect*	1	2089	68.7	65.7 - 71.6	2	3308	65.2	62.9 - 67.4
Patent ductus arteriosus*	2	1852	60.9	58.1 - 63.7	3	3273	64.5	62.3 - 66.7
Atrial septal defect*	3	1418	46.6	44.2 - 49.1	1	3347	**65.9**	**63.7 - 68.2**
Obstructive genitourinary defect*	4	757	24.9	23.1 - 26.7	4	1336	26.3	24.9 - 27.7
Pyloric stenosis*	5	645	21.2	19.6 - 22.8	6	1116	22.0	20.7 - 23.3
Hypospadias or epispadias*	6	560	18.4	16.9 - 19.9	5	1175	**23.2**	**21.8 - 24.5**
Trisomy 21 (Down syndrome)*	7	452	14.9	13.5 - 16.2	7	742	14.6	13.6 - 15.7
Cleft lip with or without cleft palate*	8	336	11.1	9.9 - 12.2	8	589	11.6	10.7 - 12.5
Pulmonary valve atresia or stenosis	9	272	8.9	7.9 - 10.0	9	457	9.0	8.2 - 9.8
Infants and fetuses with any monitored birth defect*		10413	342.4	335.8 - 348.9		19406	**382.3**	**376.9 - 387.6**

†Prevalence (per 10,000 live births)
**Statistically significant for race-ethnic groups*

Bold indicates statistically significant elevations from the 14 county standard definition utilized by the Registry.

(Border, Continued from page 2)

Table 1 (page 3) shows the ranking among the nine most commonly occurring birth defect categories in Texas in descending order, allowing comparison of birth prevalence estimates among the four border county definitions. Rates for "Infants/ Fetuses with any Monitored Defect" are also shown. Note that the same defects are in the top nine defect categories for all definitions and that the ranking changed only for the larger 43 county border definition.

Figure 3: "La Paz" Counties

In summary, three definitions of border county are similar to the 14-county standard in both demographic distribution as well as birth defects prevalence. Only the fourth and geographically largest definition which encompasses 43 counties was found to have statistically significant difference. This border definition varies in its racial/ethnic composition, and the birth defects with significantly different prevalence rates are all known to be associated with racial/ethnic differences. Based on these findings the 14 county border region historically utilized by the Birth Defects Registry is shown to be representative of this important international border region.

Figure 4: Forty-Three Counties

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TEXAS BIRTH DEFECTS REGISTRY REPORT OF BIRTH DEFECTS AMONG 1999-2004 DELIVERIES

Focus on Syndactyly

On September 10, 2007, the Texas Birth Defects Epidemiology and Surveillance Branch released data for birth defects among deliveries occurring to state residents between 1999-2004, representing six complete years of statewide data (www.dshs.state.tx.us/birthdefects/Data/annl99-04.shtm).

Typically, birth defect data reports display rates per 10,000 live births for approximately 48 categories of birth defects, and these are found on our annual report. However, the Texas registry collects data on hundreds of additional specific defects and defect groupings. Data for these defects, while not included in standard reports, are available for use in cluster investigations and by request to researchers. In this and upcoming issues, the Monitor will feature charts which represent the rates for selected defects that we have not included in other reports, along with relevant background information on the defect. In this issue, we begin with two defects, syndactly of the fingers and syndactly of the toes.

Syndactyly is the adjoining of adjacent fingers or toes. For this analysis, syndactly included cases of fused or webbed fingers or toes using birth defects codes 755.100/755.110 (fingers) and 755.120/755.130 (toes), but does not include 756.050/756.055, acrocephalosyndactyly (digits fused at the tips). The condition occurs in the fetal period when apoptosis (a process of programmed cell death) does not proceed normally, leaving the digits fused either at the bones or just the skin.

There were 359 cases of syndactly of the fingers among Texas deliveries in 1999-2004 and the rate was 1.63 cases per 10,000 live births. The rate of syndactly of the toes per 10,000 live births was 2.44, with 538 cases.

Patterns suggested by these crude birth prevalence rates include significantly higher rates of syndactly of the toes among male infants or fetuses. border v. non-border residence (Figure 1) and Region 7 (Austin/Central Texas area) residence at delivery (data not shown). For syndactly of the fingers, male infants or fetuses are much more likely to be affected, but babies delivered to Hispanic mothers are significantly less likely to have the condition than those delivered to white, non-Hispanic mothers (Figure 2). Accordingly, border counties (Figure 2) as well as Region 11, which comprises

Figure 1: Syndactyly of the Foot, Prevalence Patterns among 1999-2004 Texas Deliveries

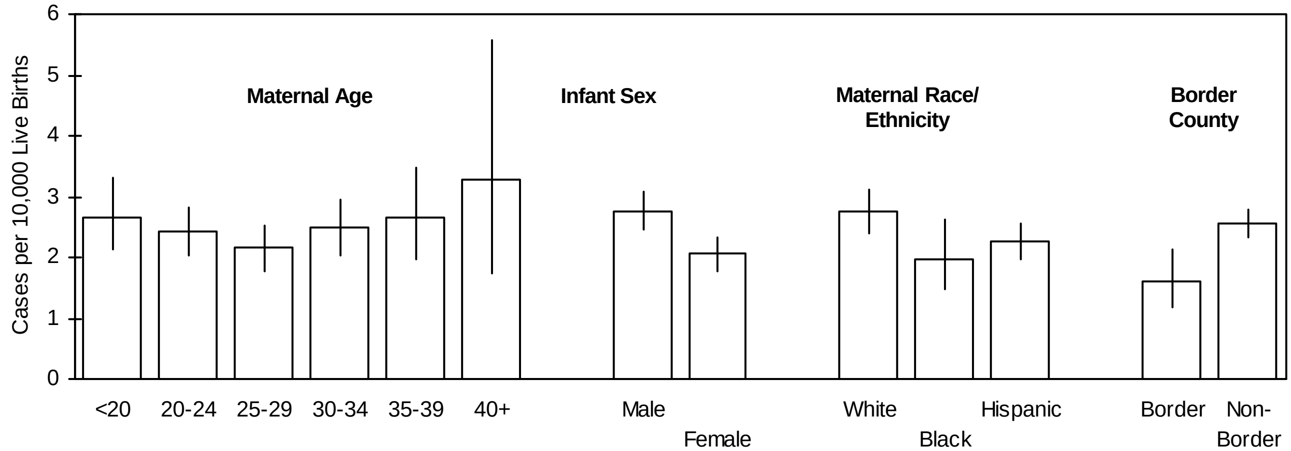
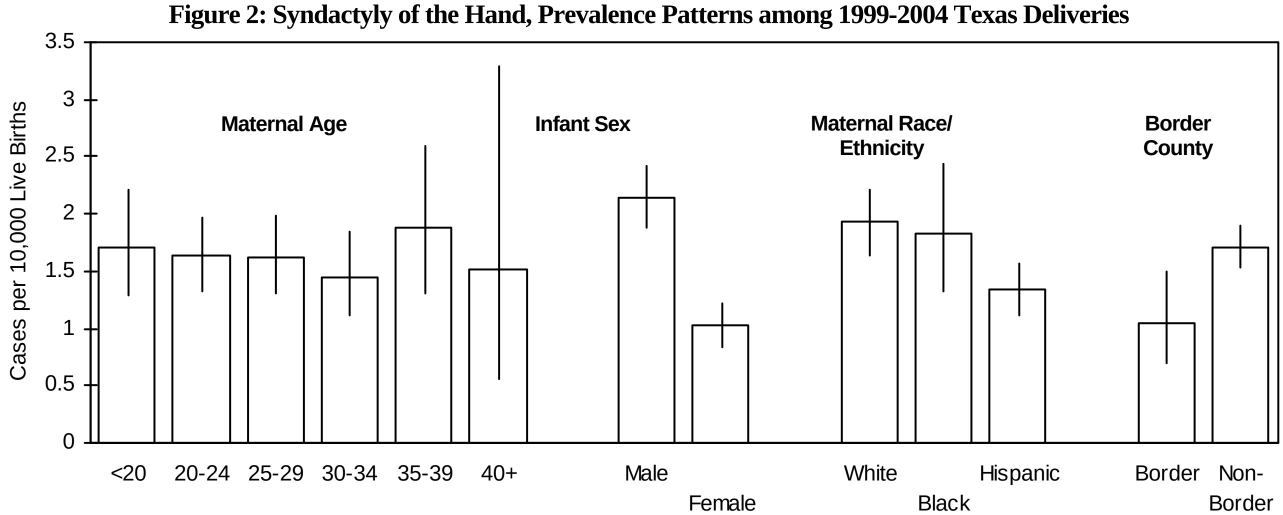


Figure 2: Syndactyly of the Hand, Prevalence Patterns among 1999-2004 Texas Deliveries



the Lower Rio Grande Valley (data not shown), have lower prevalence rates of these defects.

Risk factors associated with these defects include:

- Teenage mother (Chen 2007)
- Maternal smoking during pregnancy (Man 2006, Honein 2001)
- Non-Vietnamese ethnicity (Shaw 2002)
- European plus Carribbean ancestry (Leck 1995)
- Male sex (Lary 2001)
- Vaginal metronidazole plus miconazole use during the second through third months of gestation (Kazy 2005)
- Forestry and logging paternal occupation (Olshan 1991)

In addition, syndactly is found with other defects in syndromes and sequences such as Cornelia de Lange syndrome, Apert syndrome, Holt-Oram syndrome, 10 q sequence and Poland sequence. However, in this analysis, 28% of hand syndactly and 20% of foot syndactly cases were isolated (child had no other identified defects).

References available on request: amy.case@dshs.state.tx.us

DSHS Releases Report on Volume & Mortality Indicators for Pediatric Heart Surgery

In a report entitled *Quality of Children's Care in Texas Hospitals, 2005*, the Center for Health Statistics and Texas Health Care Information Collection analyzed hospital data on pediatric heart surgery. The report shows both the number of times heart operations on children were done at individual hospitals as well as mortality rates at these hospitals for relevant procedures. More information can be found at www.dshs.state.tx.us/THCIC/Publications/Hospitals/PDIReport2005/PDIReport2005.shtm

Remote Access to Hospital Electronic Medical Records

Hospital medical records are increasingly either partially or totally electronic, and can be created in a computerized record keeping system or created on paper and scanned into an electronic system.

When hospitals change from paper medical records to electronic there can be a significant impact on the work of public health surveillance staff. In an active surveillance system such as the Texas Birth Defects Registry, one to as many as 10 staff accessing records in a paper system sit in an area such as a cubicle or conference room, and review dozens to hundreds of records during a visit. When the hospital converts to an electronic system, it typically entails the addition of a limited number of computer terminals which external reviewers and abstractors, as well as hospital staff, use to view the records on-line. This often reduces the number of staff that are able to review records during a visit and can reduce efficiency of the surveillance staff.

However, hospitals with electronic medical records systems may also set up a method for hospital staff (physicians, coders, etc.) to remotely access and view those medical records. In those hospitals, surveillance programs can work with hospital information management personnel to gain remote access for the records they need to review. With the implementation of remote access, registry staff can stay in their offices to review and abstract records rather than traveling to the hospitals and tying up the hospitals limited workstations. This practice has the potential to increase efficiency and lower travel costs for the surveillance programs, although initially adapting to such systemic changes will involve a steep learning curve.

The Texas Birth Defects Registry has been working for several years to implement remote accesses in Texas hospitals and was able to successfully initiate this method of data collection in several facilities in 2007.

Healthcare Information Management personnel interested in exploring this further should contact Dan Driggers, Registry Operations Manager, at 512-458-7232, dan.driggers@dshs.state.tx.us.

2003-2004 Deliveries Now Included in Interactive Database

The Texas Center for Health Statistics maintains an interactive web page which allows the user to retrieve data about birth defects by year of delivery, mother's age, race/ethnicity and geographic location region and county, and sex of infant. In December 2007, this was expanded to include 1999-2004 births: http://soupfin.tdh.state.tx.us/bdefdoc.htm

Research Center News

Recent Publications from the Texas Center for Birth Defects Research and Prevention

Case AP, Ramadhani TA, Canfield MA, Wicklund CA. Awareness and Attitudes Regarding Prenatal Testing among Texas Women of Childbearing Age. J Genet Couns. 2007 Aug 3.

Ester AR, Tyerman G, Wise CA, Blanton SH, Hecht JT. Apoptotic gene analysis in idiopathic talipes equinovarus (clubfoot). Clin Orthop Relat Res. 2007 Sep;462:32-7.

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Langlois PH, Scheuerle A. Using registry data to suggest which birth defects may be more susceptible to artifactual clusters and trends. Birth Defects Res A Clin Mol Teratol. 2007 Nov;79(11):798-805.

Rasmussen SA, Yazdy MM, Carmichael SL, Jamieson DJ, Canfield MA, Honein MA, Maternal Thyroid Disease as a Risk Factor for Craniosynostosis. Obstet Gynecol. 2007 Aug;110(2):369-377.

Suarez L, Brender JD, Langlois PH, Zhan FB, Moody K Maternal Exposures to Hazardous Waste Sites and Industrial Facilities and Risk of Neural Tube Defects in Offspring. Ann Epidemiol. 2007 Aug 4.

Waller DK, Shaw GM, Rasmussen SA, Hobbs CA, Canfield MA, Siega-Riz AM, Gallaway MS, Correa A. Prepregnancy obesity as a risk factor for structural birth defects. Arch Pediatr Adolesc Med. 2007 Aug;161(8):745-50.

(Folic Acid Fortification, Continued from page 1)

First, it is evident that folic acid fortification has made great progress in achieving the stated objective of reducing preventable cases of neural tube defects; which have declined by about one-fifth to one-third since the pre-fortification period (Canfield 2005, Williams 2005, Williams 2002, Honein 2001), an astonishing success by most standards. In addition, there has been a substantial drop in MSAFP (a marker used prenatally to screen for NTDs) levels among pregnant women (Evans 2004).

Among women age 20-39 total dietary folic acid intake increased by 36% when comparing 1988-1994 levels with 1999-2000 (Dietrich 2005). Early gains were also noted in the folate status of women along the Texas-Mexico border, although not as dramatic as those of the larger population (Felkner 2002). It is somewhat surprising, however, that measures of folate levels in women of childbearing age have not risen consistently since fortification. In fact, while there was an increase in these levels in the early post-fortification period, since 2000 blood and serum folate levels have actually dropped somewhat (CDC 2007).

Next, several studies have looked at whether defects other than NTDs have declined in the U.S. since fortification began. Several have noted declines in birth prevalence for oral clefts between the pre- and post-fortification periods (Yazdy 2007, Canfield 2005, Hashmi 2005). Statistically significant decreases in birth prevalence have also been found for transposition of the great arteries, pyloric stenosis, upper limb reduction defects, omphalocele and renal agenesis. In addition, common truncus and upper limb reduction defects have declined among Hispanics (Canfield 2005).

Also of interest is whether other conditions thought to be related to high homocysteine levels (which adequate folic acid attenuates) have declined as well. Some evidence exists that a decline in colorectal cancer may be associated with fortification (Mason 2007), as well as improvements in stroke and other cardiovascular-related mortality (Yang 2006, McCully 2007).

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Canfield M, Collins J, Botto L, Williams L, Mai C, Kirby R, Pearson K, Devine O, Mulinare J. National Birth Defects Prevention Network. Changes in the birth prevalence of selected birth defects after grain fortification with folic acid in the United States: findings from a multi-state population-based study. Birth Defects Res A Clin Mol Teratol. 2005 Oct;73(10):679-89.

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

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CALENDAR

January 28-February 2 Society for Maternal-Fetal Medicine Annual Meeting, Dallas. Contact: 202/863-2476, smfm@smfm.org.

February 8: 35th Annual Texas Human Nutrition Conference, College Station. http://nutr.tamu.edu/THNC2008.htm. Contact: Julie Prouse 979-845-1735.

February 2008. National Birth Defects Prevention Network Annual Meeting, Washington D.C. area. Contact Cara Mai 409-498-3918, cwm7@cdc.gov.

February 20-23, 2008 Inclusion Works! Conference, Renaissance Hotel, Austin. Contact: 800-252-9729, secretary@thearcoftexas.org

February 20-23, 2008: Preventive Medicine 2008, Austin. www.preventivemedicine2008.org/. (202) 466-2044.

March 5-7: Texas Public health Association, 84th Annual Education Conference, San Antonio. Contact: Txpha@aol.com

April 14-19: 17th Annual Texas Children's Hospital International Colloquium, Houston. www.texaschildrenshospital.org/allabout/international/Colloquium08.aspx. Contact: internationalcolloquium@texaschildrenshospital.org,

May 29-31: Third Annual Texas Conference on Health Disparities, University of North Texas Health Science Center, Fort Worth. www.hsc.unt.edu/HealthDisparities/conference.html. Contact: (800)987-2CME.

June 22-24: TxHIMA Annual Convention, The Woodlands. www.txhima.org/ Contact: txhima@txhima.org, 512.392.4715.