



**2007 Research Report**

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Dear members of the Legislature, health care professionals, and concerned citizens of Iowa:

I am happy to provide you with the 2007 research report of the Iowa Registry for Congenital and Inherited Disorders (IRCID). The IRCID performs state-wide surveillance for birth defects, stillbirths, and Duchenne/Becker muscular dystrophy. While taking care to preserve the privacy of families affected by these conditions, the Registry provides important information to state policy makers and public health professionals.

The IRCID also works closely with researchers who are focused on identifying the causes for many birth defects, and it is this work that is the focus of this year's report. The IRCID is a key partner with the Iowa Center of Excellence for Birth Defects Research and Prevention, which is a collaborative enterprise between the Colleges of Medicine and Public Health at The University of Iowa. Its other partners include the Iowa Department of Public Health, the Iowa Chapter of the March of Dimes, and The University of Iowa Center for Health Effects of Environmental Contamination.

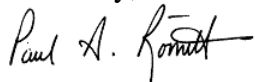
There are nine such centers across the country, and each of them, including the Iowa Center, participates in the National Birth Defects Prevention Study (NBDPS). The NBDPS is the largest population-based study ever conducted in the United States to examine the causes of birth defects. The IRCID identifies children that are eligible for this study and secures permission from their parents before any research is performed with their information. Those who choose to join the study participate in research on a wide variety of conditions and risk factors.

The IRCID is also an active member of the National Birth Defects Prevention Network (NBDPN), an organization of individuals and programs that are concerned with birth defect monitoring, research, and prevention. The IRCID often participates in collaborative research projects sponsored by the Network. Recent studies have included a project that used state data to estimate the nation-wide prevalence for selected birth defects.

The research performed by Iowa investigators has the potential to positively affect the lives of Iowans. Current studies by Iowa investigators are focused on the relationships between birth defects and agricultural chemicals, fertility treatments, and compounds in drinking water. An area of focus is the interaction of genetic and environmental factors that might affect risk for cleft lip and palate.

A strong state-wide birth defect monitoring program is a valuable resource for the state of Iowa. Not only does it provide irreplaceable information for state leaders, it allows for important research on the causes and prevention of birth defects. We are pleased to perform this important work on behalf of the citizens of Iowa.

Sincerely,



Paul A. Romitti, Ph.D.

Director and Associate Professor of Epidemiology

In the United States, the Centers for Disease Control and Prevention (CDC) recognize three types of surveillance systems, each rated differently for completeness of patient ascertainment:

- Vital Records: Use of birth and fetal death certificates provided by the state's Department of Health (Rating: Poor)
- Passive Reporting: Use of medical reports submitted by staff from hospitals, clinics, or other facilities (Rating: Fair to Good)
- Active System: Use of trained personnel who systematically review records in hospitals, clinics, or other facilities (Rating: Excellent)

The IRCID conducts active surveillance to identify information about congenital and inherited disorders that occur in Iowa and to Iowa residents. The IRCID has collected information for over 44,000 children with various birth defects. This information has been used by health care providers and educators to provide treatment and support services. It is also used by researchers to study risk factors for birth defects and to evaluate treatments for birth defects. The IRCID also performs surveillance for Duchenne/Becker muscular dystrophy and has identified 78 children with that neuromuscular disease. In addition, the IRCID is collaborating with the Metropolitan Atlanta Congenital Defects Program to develop approaches to active surveillance for stillbirths.

#### Surveillance for Birth Defects

The term “defect” refers to abnormal development related to body structure, body function and metabolism, or an error in body chemistry. Typically a defect is present at birth (congenital), but a recognizable defect may be diagnosed during pregnancy (prenatal) or following birth (postnatal). Examples of two major categories of birth defects are structural and metabolic defects. Metabolic defects often involve the inability of cells to produce a protein in the correct amount to regulate the chemistry of the body. Structural defects typically involve a body part that is missing or malformed. Examples include heart defects, spina bifida, and cleft lip and palate.

The IRCID has traditionally focused on structural defects rather than metabolic conditions. (The Iowa Neonatal Metabolic Screening Program does an excellent job monitoring for those conditions.) Starting with 2003 deliveries, the IRCID adopted the recommendations of the National Birth Defects Prevention Network (NBDPN) to focus on a core set of 45 defects (see Table 1). Prior to this change, the IRCID included many “minor” conditions, so this change represents a reduction in the number of conditions that it monitors.

Table 1  
Prevalence for birth defects in Iowa, 2000-2004 deliveries

Condition	Total	Prevalence Rate <sup>†</sup>
<b>Brain/Spinal Cord</b>		
Anencephalus	61	3.21
Encephalocele	16	0.84
Hydrocephalus without Spina Bifida	202	10.64
Microcephalus	172	9.06
Spina bifida without anencephalus	103	5.42
<b>Eye</b>		
Aniridia	5	0.26
Anophthalmia/ microphthalmia	50	2.63
Congenital cataract	43	2.26
<b>Ear</b>		
Anotia/microtia	66	3.48
<b>Heart</b>		
Aortic valve stenosis	74	3.90
Atrial septal defect	533	28.06
Coarctation of aorta	104	5.48
Common truncus	23	1.21
Ebstein's anomaly	23	1.21
Endocardial cushion defect	121	6.37
Hypoplastic left heart syndrome	53	2.79
Patent ductus arteriosus	536	28.22
Pulmonary valve atresia and stenosis	210	11.06
Tetralogy of Fallot	64	3.37
Transposition of great arteries	106	5.58
Tricuspid valve atresia and stenosis	20	1.05
Ventricular septal defect	868	45.70

<sup>†</sup> Prevalence per 10,000 live births.

*Continued on next page...*

Table 1 (continued from previous page)

Condition	Total	Prevalence Rate <sup>†</sup>
<b>Oral/Facial</b>		
Choanal atresia	44	2.32
Cleft lip with and without cleft palate	241	12.69
Cleft palate without cleft lip	165	8.69
<b>Digestive</b>		
Biliary atresia	13	0.68
Esophageal atresia/ tracheoesophageal fistula	52	2.74
Hirschsprung's disease (congenital megacolon)	46	2.42
Pyloric stenosis	627	33.01
Rectal and large intestinal atresia/stenosis	93	4.90
<b>Genital/Urinary</b>		
Bladder exstrophy	9	0.47
Hypospadias and Epispadias *	134	7.06
Obstructive genitourinary defect	527	27.75
Renal agenesis/hypoplasia	140	7.37
<b>Muscle/Skeletal</b>		
Congenital hip dislocation	161	8.48
Diaphragmatic hernia	24	1.26
Gastroschisis	99	5.21
Omphalocele	49	2.58
Reduction deformity, lower limbs	54	2.84
Reduction deformity, upper limbs	106	5.58
<b>Syndromes</b>		
Down syndrome (Trisomy 21)	301	15.85
Edwards syndrome (Trisomy 18)	51	2.69
Patau syndrome (Trisomy 13)	22	1.16
<b>Other</b>		
Amniotic bands	29	1.53
Fetus or newborn affected by maternal alcohol use	6	0.32

<sup>†</sup> Prevalence per 10,000 live births.

\* Includes epispadias and/or second or third degree hypospadias. Excludes hypospadias NOS and first degree hypospadias.

## Birth Defects Research

Approximately 1 in 33 newborns are affected by a major birth defect, making such conditions disturbingly common. These conditions come with personal and monetary costs, both for the families of these children and for society. Nearly 20% of all infant deaths are caused by birth defects. Hospitalizations associated with such conditions are longer than hospitalizations for other conditions. More than \$8 billion is required to provide lifetime care for the children born with birth defects each year.

Because the causes of up to 70% of birth defects are unknown, research is a critical part of any strategy to prevent these conditions. For this reason, in 1996 the United States Congress directed the CDC to establish regional “centers of excellence” in birth defect research and prevention. Furthermore, interest in fostering collaboration among state birth defect registries led to the formation of the National Birth Defects Prevention Network in 1998.

### *National Birth Defects Prevention Network*

The National Birth Defects Prevention Network (NBDPN) is a nationwide association of birth defect programs and individuals. The IRCID is an active member of the NBDPN and participates in many of its projects. For example, the NBDPN provides a set of guidelines to help birth defect registries around the country organize their work in a consistent manner. The NBDPN also provides educational materials to birth defect abstractors as well as informational resources to promote Birth Defects Prevention Month each January. Another goal of the NBDPN is to encourage scientific collaboration. Recent projects have been focused on such issues as preterm births, ventral wall defects, and neural tube defects. It has also provided national prevalence estimates for selected, common birth defects.

### 2006-2007 NBDPN Publications Using IRCID Data

(Names listed in bold designate Iowa investigators)

Canfield MA, Honein MA, Yuskiv N, Xing J, Mai CT, Collins JS, Devine O, Petrini J, Ramadhani TA, Hobbs CA, Kirby RS, for the National Birth Defects Prevention Network. National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999-2001. *Birth Defects Res A Clin Mol Teratol.* 2006; 76:747-756.

Canfield MA, Ramadhani TA, Yuskiv N, Davidoff MJ, Petrini JR, Hobbs CA, Kirby RS, **Romitti PA**, Collins JS, Devine O, Honein MA, Mai CT, Edmonds LD, Correa A. Improved national prevalence estimates for 18 selected birth defects - United States, 1999-2001. *MMWR Morb Mortal Wkly Rep.* 2006; 54:1301-1305.

National Birth Defects Prevention Network (NBDPN). Birth Defects Surveillance Data from Selected States, 1999-2003. *Birth Defects Res A Clin Mol Teratol.* 2006; 76: 855, 915-916.

National Birth Defects Prevention Network (NBDPN). Population-Based Birth Defects Surveillance Data from Selected States, 2000-2004. *Birth Defects Res A Clin Mol Teratol.* 2007; 79:833, 902-903.

*Iowa Center of Excellence for Birth Defects Research and Prevention*

The Iowa Center of Excellence for Birth Defects Research and Prevention was one of eight charter centers established by the CDC to study genetic and environmental (broadly defined) risk factors for birth defects. Iowa Center investigators participate in local (state-wide) projects and also the National Birth Defects Prevention Study (NBDPS). The NBDPS is a population-based study that investigates genetic and environmental risk factors for over 30 major birth defects. As a partner with the Iowa Center, the IRCID identifies cases and secures permission from parents and guardians to share information with researchers. Women with a pregnancy affected by one or more of the defects and women with an unaffected pregnancy are interviewed about their health, diet and lifestyle during their pregnancies. Biologic samples are also collected from each family to study genetic factors that may contribute to these birth defects. At this point, over 25,000 interviews have been completed nationwide, and biologic samples have been collected from more than 13,000 families.

Over 200 research projects are currently underway nation-wide as part of NBDPS. Some of them examine risk factors such as maternal nutrition. Others examine gene and environment interactions. Still others examine maternal behavior during pregnancy. For example, the Iowa Center recently led a project with other centers examining the role of maternal alcohol consumption during pregnancy on the development of cleft lip and palate. The investigators found that the type of alcohol consumed affected the probability that a child would be born with a cleft. Distilled spirits was associated with the greatest risk, followed by wine, and then beer.

2006-2007 Iowa Center Publications Using IRCID Data

(Names listed in bold designate Iowa investigators)

**Avila JR, Jezewski PA, Vieira AR, Orioli IM, Castilla EE, Christensen K, Daack-Hirsch S, Romitti PA, Murray JC.** PVRL1 variants contribute to non-syndromic cleft lip and palate in multiple populations. *Am J Med Genet A.* 2006; 140A:2562-2570.

Bitsko RH, Reefhuis J, **Romitti PA**, Moore CA, Honein MA. Periconceptional consumption of vitamins containing folic acid and risk for multiple congenital anomalies. *Am J Med Genetics A.* 2007; 143A: 2397-2405.

**Damiano PC, Tyler MC, Romitti PA, Momany ET, Canady JW, Karnell MP, Murray JC.** Type of oral cleft and mothers' perceptions of care, health status and outcomes for preadolescent children. *Cleft Palate Craniofac J.* 2006; 43:715-721.

**Damiano PC, Tyler MC, Romitti PA, Momany ET, Canady JW, Karnell MP, Murray JC.** Health-related quality of life among preadolescent children with oral clefts: the mother's perspective. *Pediatrics.* 2007; 120:e283-e290.

**Shi M, Christensen K, Weinberg CR, Romitti PA, Bathum L, Lozada A, Morris RW, Lovett M, Murray JC.** Orofacial cleft risk is increased with maternal smoking and specific detoxification gene variants. *Am J Hum Genet.* 2007; 80:76-90.

The University of Iowa and the Iowa Department of Public Health. *2007 Iowa Health Fact Book.* Iowa City, IA: The University of Iowa College of Public Health. July 2007.

**Warrington A, Vieira AR**, Christensen K, Orioli IM, Castilla EE, **Romitti PA, Murray JC**. Genetic evidence for the role of loci a 19q13 in cleft lip and palate. *J Med Genet*. 2006; 43:e26.

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(Names listed in bold designate Iowa investigators)

Alwan S, Reefhuis J, Rasmussen SA, Olney RS, Friedman JM, for the National Birth Defects Prevention Study. Use of selective serotonin reuptake inhibitors in pregnancy and the risk of birth defects. *N Engl J Med*. 2007; 356: 2684-2692.

Botto LD, Lin AE, Riehle-Colarusso T, Malik S, Correa A and the National Birth Defects Prevention Study. Seeking causes: Classifying and evaluating congenital heart defects in etiologic studies. *Birth Defects Res A Clin Mol Teratol*. 2007; 79: 714-727.

Browne ML, Bell EM, Druschel CM, Gensburg L, Mitchell AA, Lin AE, **Romitti PA**, Correa A, and the National Birth Defects Prevention Study. Maternal caffeine consumption and risk of cardiovascular malformations. *Birth Defects Res Part A Clin Mol Teratol*. 2007; 79:533-543.

Canfield MA, Collins JS, Botto LD, Williams LJ, Mai CT, Kirby RS, Pearson K, Devine O, Mulinare J, for the 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; 73:679-689.

Carmichael SL, Shaw GM, Ma C, Werler MM, Rasmussen SA, Lammer EJ, for the National Birth Defects Prevention Study. Maternal corticosteroid use and risk of orofacial clefts. *Am J Obstet Gynecol*. 2007; 197: 585.e1-585.e7.

Carmichael SL, Shaw GM, Laurent C, Olney RS, Lammer EJ, and the National Birth Defects Prevention Study. Maternal reproductive and demographic characteristics as risk factors for hypospadias. *Paediatr Perinat Epidemiol*. 2007; 21:210-218.

Carmichael SL, Shaw GM, Laurent C, Lammer EJ, Olney RS, and the National Birth Defects Prevention Study. Hypospadias and maternal exposures to cigarette smoke. *Paediatr Perinat Epidemiol*. 2005; 19:406-412.

Carmichael SL, Shaw GM, Yang W, Laurent C, Herring A, Royle MH, Canfield MA, and the National Birth Defects Prevention Study. Correlates of intake of folic acid-containing supplements among pregnant women. *Am J Obstet Gynecol*. 2006;194:203-210.

Carmichael, SL, Shaw GM, Laurent C, Croughan MS, Olney RS, Lammer EJ, for the National Birth Defects Prevention Study. Maternal progestin intake and risk of hypospadias. *Arch Pediatr Adolesc Med*. 2005; 159:957-962.

- Cleves MA, Savell VH Jr., Raj S, Zhao W, Correa A, Werler MM, Hobbs CA, and the National Birth Defects Prevention Study. Maternal use of acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs), and muscular ventricular septal defects. *Birth Defects Res A Clin Mol Teratol*. 2004; 70:107-113.
- Honein MA, Rasmussen SA, Reefhuis J, **Romitti PA**, Lammer E, **Sun L**, Correa A. Maternal smoking and environmental tobacco smoke exposure and the risk of orofacial clefts. *Epidemiology*. 2007; 18:226-233.
- Malik S, Cleves MA, Zhao W, Correa A, Hobbs CA, and the National Birth Defects Prevention Study. Association between congenital heart defects and small for gestational age. *Pediatrics*. 2007; 119:e976.
- Rasmussen SA, Olney RS, Holmes LB, Lin AE, Keppler-Noreuil KM, Moore CA, and the National Birth Defects Prevention Study. Guidelines for case classification for the National Birth Defects Prevention Study. *Birth Defects Res A Clin Mol Teratol*. 2003; 67:193-201.
- Rasmussen SA, Yazdy MM, Honein MA, Carmichael SL, Canfield MA. Maternal thyroid disease as a risk factor for craniosynostosis, National Birth Defects Prevention Study, 1997-2002. *Am J Obstet Gynecol*. 2007; 110: 369-377.
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- Shaw GM, Carmichael SL, Laurent C, Louik C, Finnell RH, Lammer EJ, and the National Birth Defects Prevention Study. Nutrient intakes in women and risks of anophthalmia and microphthalmia in their offspring. *Birth Defects Res A Clin Mol Teratol*. 2007; 79: 708-713.
- Shaw GM, Carmichael SL, Laurent C, Rasmussen SA. Maternal nutrient intakes and risks of human orofacial clefts. *Epidemiology*. 2006; 17:285-291.
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- The NS, Honein MA, Caton A, Moore C, Siega-Riz AM, Druschel C, and the National Birth Defects Preventions Study. Risk factors for isolated biliary atresia, National Birth Defects Prevention Study, 1997-2002. *Am J Med Genet A*. 2007; 143: 2274-2284.
- Waller DK, Shaw GM, Rasmussen SA, Hobbs CA, Canfield MA, Siega-Riz AM, Gallaway MS, Correa A, and the National Birth Defects Prevention Study. Prepregnancy obesity as a risk for structural birth defects. *Arch Pediatr Adolesc Med*. 2007; 161: 745-750.
- Werler MM, McCloskey C, Edmonds LD, Olney RS, Honein MA, Reefhuis J. Evaluation of an association between loratadine and hypospadias -- United States, 1997-2001. *MMWR Morb Mortal Wkly Rep*. 2004; 53:219-221.

Werler, MM, Mitchell AA, Hernandez-Diaz S, Honein MA, and the National Birth Defects Prevention Study. Use of over-the-counter medications during pregnancy. *Am J Obstet Gynecol.* 2005; 193:771-777.

#### *National Down Syndrome Project*

The National Down Syndrome Project (NDSP) is a population-based study to investigate genetic and environmental risk factors for Down syndrome. This study is led by investigators at Emory University and is a combined effort of the Iowa Center and programs in five other states. Iowa women who give birth to an infant affected with Down syndrome and women with an unaffected birth are interviewed about their health, diet and lifestyle during pregnancy. Biologic samples are collected from each family to better understand genetic factors that may contribute to Down syndrome.

#### 2006-2007 NDSP Publication Using IRCID Data

(Names listed in bold designate Iowa investigators)

Freeman SB, Allen EG, Oxford-Wright CL, Tinker SW, Druschel CM, Hobbs CA, O'Leary LA, **Romitti PA**, Royle MH, Torfs CP, Sherman SL. The National Down Syndrome Project: Design and implementation. *Public Health Rep.* 2007; 122:62-72.

## Muscular Dystrophy Research

Muscular dystrophy refers to a group of genetic diseases that cause progressive muscle weakness. The most common form of muscular dystrophy affecting children is Duchenne/Becker muscular dystrophy (DBMD). Duchenne muscular dystrophy is the name that historically refers to the most severe form of this disorder. DBMD usually presents with weakness in early childhood. Weakness is progressive and children lose the ability to walk in late childhood. In the severe form, death occurs in young adulthood.

DBMD is caused by mutations in the dystrophin gene on the X chromosome. Girls rarely have the disease, but they can be carriers of the gene mutation. Approximately 1 in 3,500 boys have DBMD. Approximately one-third of boys with Duchenne muscular dystrophy did not inherit the disorder, but have a genetic mutation that is new in their family.

### *The Muscular Dystrophy Surveillance Tracking and Research Network*

MDSTARnet, the Muscular Dystrophy Surveillance Tracking and Research Network, is a program currently active in five states. Its goal is to identify all people with childhood-onset Duchenne and Becker muscular dystrophies (DBMD). On behalf of MDSTARnet, the IRCID is undertaking surveillance of Iowans born since 1982 with DBMD. This surveillance consists of identification and ongoing medical chart review.

### 2006-2007 MDSTARnet Publication Using IRCID Data

(Names listed in bold designate Iowa investigators)

Miller LA, **Romitti PA**, Cunniff C, Druschel CM, **Mathews KD**, Meaney FJ, Matthews D, **Kantamneni J**, **Feng ZF**, **Zemblidge N**, Miller TM, Andrews J, Fox D, Cifaloni E, Pandya S, Montgomery A, Kenneson A. (2006) The muscular dystrophy surveillance tracking and research network (MD STARnet): surveillance methodology. *Birth Defects Res Part A Clin Mol Teratol.* 2006; 76:793-797.

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- College of Nursing
- College of Public Health
- Craniofacial Anomalies Research Center
- Iowa Cancer Registry
- University Hygienic Laboratory
- UI Governmental Relations Office

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March of Dimes Birth Defects Foundation

KID Coalition

ASK Resource Center

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Iowa Department of Public Health



**Iowa Registry for  
Congenital and  
Inherited Disorders**

*The Iowa Registry for Congenital and Inherited Disorders is a collaborative program of the University of Iowa's College of Public Health and the Iowa Department of Public Health.*