Improving Birth Outcomes by Reducing the Risk of Birth Defects

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Prevalence and Impact of Birth Defects

In the United States:

• Every 4 ½ minutes baby born with birth defect
• 1 in 33 births
• 2X as likely to be premature
• Leading cause of infant mortality (more than 1 of every 5 infant deaths)
• Illness and long term disability
• Every couple has 3-5% chance of having baby with birth defect or genetic condition

Ohio Infant Mortality Rates

Prepared by Richard Thomas, MPH ODH

Infant Mortality Rates by County, Ohio, 1990-2010

Congenital Anomaly Infant Mortality Rates by County, Ohio, 1990-2010

Infant Mortality
(Standard Deviations)

- Less than 2.0 (less than -2.5)
- 2.50 - 3.50 (-2.50 to -1.50)
- 3.50 - 4.50 (-1.50 to -0.50)
- 4.50 - 5.50 (-0.50 to 0.50)
- 5.50 - 6.50 (0.50 to 1.50)
- 6.50 and above (above 1.5)

Congenital Anomaly Infant Mortality Rate
(Standard Deviations)

- Less than 0.39 (less than -2.5)
- 0.40 - 0.88 (-2.50 to -1.50)
- 0.89 - 1.38 (-1.50 to -0.50)
- 1.39 - 1.87 (-0.50 to 0.50)
- 1.88 - 2.37 (0.50 to 1.50)
- 2.38 and above (above 1.5)

Source:
Birth and death statistical files prepared from Vital Statistics data, Ohio Department of Health.
Prepared by Richard Thomas, MPH, Epidemiology Section, Division of Family and Community Health Services, Ohio Department of Health.

Notes:
1. Rates are calculated from infant mortality rates per 1,000 live births. Records without a county of residence were excluded.
2. Infant mortality rates for the State of Ohio 1990-2010: 8.12 per 1,000 live births. The mean of the county infant mortality rates on which the standard deviations were based (map key) was 7.79 per 1,000 live births.
3. Infant mortality rates based on less than 26 observations may be unstable.
4. Infant mortality rates per 1,000 live births. Records without a county of residence were excluded.
5. Congenital anomalies were enumerated if the leading cause of death was coded for a congenital anomaly. Records without a county of residence were excluded.
6. Congenital anomaly infant mortality rate for the State of Ohio 1990-2010: 1.60 per 1,000 live births. The mean of the county congenital anomaly infant mortality rates on which the standard deviations were based (map key) was 1.63 per 1,000 live births.
Prematurity is the Second Most Common Cause of Infant Mortality

Could Prematurity Have a Genetic Basis?

- Causes heterogeneous
- Numerous genes suspected as having role
- Complex interplay between mother, fetus, & their respective environments
- Multiple pathways involved; each pathway will have genetic and environmental factors that play a role
- Risk for preterm birth increased if had previous preterm birth or if pregnant woman, her mother or her sister were born prematurely
Potential Genetic Causes of Prematurity

• Race/ethnic disparities
• Genes that contribute to formation of amniotic membranes may make them more susceptible to rupture
• Genetic susceptibility to infection, inflammation, autoimmune disorders
• Genetic differences affecting uterine clock and cervical length
• Mother and/or fetus have genetic condition or genetic variation that affects membranes (collagen) ex. Ehlers-Danlos
Preventing Birth defects

Goals in prevention:
- Preventing occurrence
- Preventing recurrence
- Identification and early treatment to prevent/reduce morbidity and mortality

Prevention is challenging:
- Can’t prevent unless know cause
- Prevention is a difficult message
- Prevention is a sensitive message
- Behavioral changes are challenging
- Can’t prevent all birth defects

What we can do:
- Identify causes and educate
- Individuals can take steps to reduce their risks
- Changes in perception of preconception care
- Life course perspective to health
- Reproductive life plan
Causes of Birth Defects
Congenital Heart Defects

- Most common birth defect (1 in 100 births)
- #1 cause of infant mortality
- >15% associated with known genetic conditions
- About 20% to 30% have other physical problems and/or developmental delays
- Repair exceeds $2.2 billion a year

CDC, ODH
Prevention of Congenital Heart Defects

Identify cause

- **Genetics** (aneuploidy, microdeletions, single genes, multifactorial)
- **Environmental**
  - Alcohol
  - Medications (Accutane, some anti-seizure medications, Lithium)
  - Maternal Conditions (Diabetes, PKU, Lupus)
  - Rubella (German measles)
  - Maternal Obesity
  - Smoking
- **Unknown**

Planning and risk reduction

- remove teratogen, take folic acid, healthy weight, diabetes control, alternative family planning (such as adoption, PGD)
- Educate family members at risk
Positive Steps in Birth Defect Prevention

Healthy Steps Bookmark

Educational tool developed by Ohio Department of Health

“HEALTHY STEPS TODAY...”

Positive Steps in Birth Defect Prevention

“HEALTHY LIVES TOMORROW”

Are you thinking about having a baby?

NO... Not right now!

Step 1: Every woman and teenage girl should...
- Take a multivitamin with folic acid every day (pill or capsule).
- Exercise regularly.
- Eat a variety of whole grains, vegetables and fruits, and make sure meat, eggs, poultry and fish are fully cooked.
- Have regular medical and dental checkups.
- Refuse smoke or use illegal drugs.
- Avoid secondhand smoke and other toxic or harmful substances.

Step 2: Talk to your doctor about...
- Your family health history.
- Whether your vaccinations are up to date.
- The safety of over-the-counter prescription medications or holistic supplement you take.
- Sexually transmitted infections. If you are or have been sexually active, learn how to protect yourself from these diseases.

Step 3: Until you are ready...
- Take action to get ready.
- If you are not yet ready, choose to delay.
- Limit yourself to one or two drinks daily.

Did you know???
- More than half of all pregnancies are not planned.
- Important growth of the baby occurs very early in pregnancy, before most women know they are pregnant.
- Being healthy before pregnancy helps women have healthy babies.

Steps for Every New Mom to Take
- Talk with your doctor about your family's health history.
- Over-the-counter prescription medications and herbal supplements you take.
- What kind of exercise is safe for you and your baby.
- The benefits of stress limiting.

March of Dimes

Healthy Lives Tomorrow

Are you thinking about having a baby?

YES... I'm ready!

Step 1: Be informed...
- Important growth of the baby occurs very early in pregnancy, before most women know they are pregnant.
- Being healthy before pregnancy helps you have healthy babies.
- If you drink alcohol, STOP! No amount of alcohol is safe for the unborn baby.

Step 2: Make sure you...
- Talk with your doctor about updating your health history.
- Take a multivitamin with folic acid every day (pill or capsule).
- Have regular medical and dental checkups.
- Avoid secondhand smoke and other toxic or harmful substances.
- Eat a variety of whole grains, vegetables and fruits, and make sure meat, eggs, poultry and fish are fully cooked.
- Limit Yourself to one or two drinks daily.
Attaining and Maintaining Optimal Maternal Health

- Physical and emotional health
- Immunizations up-to-date (chickenpox, MMR, flu)
- Infection prevention (CMV, toxoplasmosis, STD’s)
- Preconception health care visits - for every woman of childbearing age, a healthcare visit is a preconception visit!!
Maternal Health Conditions That May Place Baby At Risk

- Diabetes
- High blood pressure
- Epilepsy
- Recurrent infections
- Lupus
- Hypothyroidism
- Heart condition
- Clotting disorder
- PKU
- Other health problems

***proper management before, during and after pregnancy is critical***
Over-the-Counter and Prescription Medications

- Accutane/isotretinoin (acne)
- Warfarin/coumarin by-products
- ACE inhibitors (enalapril, captopril) and ARB’s to treat blood pressure
- Lithium
- Androgens and testosterone by-products
- Anticancer drugs
- Folic acid inhibitors such as methotrexate and aminopterin
- Statins (inhibit cholesterol production)
- Some medications to treat epilepsy and mental illness (carbamazepine, phenytoin, valproic acid)
- Tetracycline, doxycycline, kanamycin, streptomycin
- Thalidomide and lenalidomide
- Aspirin
Dietary/Herbal Supplements and Caffeine

- **Home remedies or herbal supplements** (many have not been tested for safety during pregnancy)

- **Caffeine** (<200mg/day = one 12oz cup of coffee)
Exposures

Alcohol
- Fetal alcohol spectrum disorders

Drugs
- Birth defects
- Neonatal Abstinence Syndrome (opiates)

Smoking (including secondhand exposure)
- Birth defects
- Low birth weight
- Preterm delivery
- Placental abruption
- SIDS

Workplace and Household Exposures (second-hand smoke, carbon monoxide, solvents, lead-based paint)
Healthy Weight

Overweight/obesity before and during pregnancy increases risk of:

- Gestational diabetes
- Thrombotic events
- Hypertension and preeclampsia
- Childhood obesity in offspring
- Birth defects
  - NTDs
  - Heart defects
  - Limb defects
  - Oral clefting
  - Anorectal atresia
  - Hydrocephalus
  - Hypospadias

2. Stothard KJ JAMA 2009;301:363-650
All women of childbearing age should take folic acid
Before and during pregnancy
Can prevent some**:
  - Neural Tube Defects
  - Congenital Heart Defects
  - Cleft Lip and Palate
  - Limb Defects
  - Preterm Births

**may have teratogenic, single gene, syndromic or other cause
Life Course Perspective to Health Care and Reproductive Medicine

Early life events, starting in the womb, shape an individual’s health trajectory.

Life should not be viewed as disconnected stages, but as an integrated continuum.

Interplay of risk and protective factors contribute to health outcome across lifespan, beginning at conception:
- genetics
- socioeconomic status/social factors
- toxic environmental exposures
- mental health/health behaviors
- stress
- nutrition

Birth outcomes are not exclusively shaped by the 9 months in the womb; they are influenced by the entire life course of the mother leading up to the pregnancy!
Early Programming

- Early experiences can “program” an individual’s future health and development
  - **Prenatal programming** (exposures in-utero)
  - **Intergenerational programming** (health of mother prior to conception that impacts health of her baby and developing child)

- Adverse programming can:
  - Result directly in birth defect/disease/condition
  - Make individual more susceptible to birth defect/disease/condition
Reproductive Life Plan

- Personal goals about having or not having children based on personal values and resources
- Determining when/if having children fits into your life plan
- Taking steps to achieve optimal physical health, emotional well-being and financial independence and stability PRIOR to starting a family

http://www.cdc.gov/preconception/reproductiveplan.html
Reproductive Life Plan

1. How do you feel about having (more) children some day?
2. How are you keeping healthy for yourself and for the possibility of a child in the future?
3. If you plan on having children, what are your feelings about an ideal family size?
4. When do you want to start a family/have another child?
5. How much space do you think would be best between pregnancies?
6. What are your plans/what goals would you like to reach before having children/another child?
7. If you don’t want children/another child yet, what steps are you taking to wait until you are ready?
8. What can I do to help you achieve your overall plan?
Considerations in Making a Reproductive Life Plan

- Age
- Educational goals
- Career plans
- Living situation
- Financial situation
- Social support

- Relationship with partner
- Readiness to become a parent
- Current health status
- Hereditary risk factors
- Health behaviors
Keys to success

• Identify motivation for current behaviors and desired changes
• Help choose small goals in which they are likely to succeed, then build on that success
• Preparation and motivation can compensate for lack of confidence or willpower
Universal Carrier Screening

- Mendelian conditions collectively affect 13 million people in the United States
  - Account for 20% of infant mortality and 18% of pediatric hospitalizations
- More than 7,000 known disorders with Mendelian inheritance
  - More than 1,009 are autosomal recessive with established molecular basis
- On average, we each harbor 2.8 known recessive severe childhood disease mutations
- Identify carriers of genetic conditions prior to childbearing
- Provide education and genetic counseling for carriers or carrier/carryer couples
Universal Carrier Screening

- Analyze DNA from saliva or blood samples
- Test for +100 Mendelian disorders
- Aim to identify carriers of autosomal recessive or X-linked disorder before pregnancy
- Inform couples of possible genetic risks to future offspring
Universal Carrier Screening

Reproductive options for carrier/carrier couples:

• Adoption
• Pre-implantation genetic diagnosis
• Sperm or oocyte donation
• Refraining from having children/smaller family size
Universal Carrier Screening

- Should be offered to:
  - Couples desiring to start a family - in order to provide individualized risk of conceiving a child affected by a specific recessively inherited disease
  - Couples undergoing in vitro fertilization - testing of couples, pretesting of sperm and egg donors
  - Individuals and populations at high risk of a recessive disorder - populations with genetic bottlenecks and/or higher rate of consanguinity
  - General population testing - voluntary carrier testing of the general population
Public Health Impacts

- Prevention of death or markedly diminished disease severity when curative treatments are available
  - Neonatal diagnosis and treatment for certain forms of CAH, MCAD, galactosemia and other conditions may prevent neonatal death
- Improvement in quality of life in disorders where treatments are available
  - Timely diagnosis allows specific interventions
  - Slow disease progression, lessen symptoms, prevent complications and improve affected organ systems
- Genetic counseling of patients and families about risk for other relatives and offspring
Informed Consent

• Counseling before screening should include:
  • Purpose, voluntary nature of screening
  • Range of symptoms and severity of disease
  • Risk of carrier status and affected offspring
  • Meaning of positive and negative results
  • Factors to consider in decision-making
When and Why to Refer to Genetics
Who provides genetic services?

Clinical Geneticist (MD)
  Physician with fellowship in genetics
Genetic Counselor (MS, LGC)
  Master’s trained licensed medical professional
Other members of the team
  Nurse, laboratory geneticist, support staff
Purpose of Genetics Evaluation

• Determine whether a genetic condition is present
• Educate about the genetic condition in the family
• Provide accurate recurrence risks
• Recommend appropriate medical management
Process of Genetics Evaluation

- Review medical history
- Review family history
- Physical examination when indicated
- Explanation of recommended testing
- Support and counseling
Preconception

• Previous child with a genetic condition, birth defect, or intellectual disability
• Family history of a genetic condition
• Ethnicity-based screening or identified as a carrier from universal screening test or from family history information
• Multiple pregnancy losses
• Consanguinity
Prenatal

- Abnormal screening test (maternal analyte screening, cell-free fetal DNA)
- Ultrasound findings
- Advanced maternal age
- Exposure concerns
- Abnormal carrier screening
Prenatal Diagnosis and the Reduction of Morbidity and Mortality Associated with Birth Defects

- Eliminate or reduce exposure/treat maternal condition
- Fetal surgery
- Change mode of delivery, hospital of delivery, prepare medical staff such as NICU staff, surgeons and other specialists
- Family preparation and birth plans

Fetal Treatment Centers
Pediatrics and Adult

- Birth defects
- Unusual features
- Developmental delay, intellectual disability, and/or autism
- Abnormal genetic test results
- Abnormal newborn screen
- Families concerned about recurrence risk
- Diagnoses often leads to altered and better treatment reducing morbidity and mortality
Where are Genetics Services Provided in Ohio?
# Regional Genetic Centers

<table>
<thead>
<tr>
<th>Region</th>
<th>Center</th>
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<tbody>
<tr>
<td>1  Southwest</td>
<td>Cincinnati Children’s</td>
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<tr>
<td>2  Central West</td>
<td>Dayton Children’s</td>
</tr>
<tr>
<td>3  Northwest</td>
<td>Mercy Children’s and Promedica Toledo</td>
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<td>Cleveland Clinic</td>
</tr>
<tr>
<td>6  Central East</td>
<td>Akron Children’s</td>
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</tbody>
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Prevention of birth defects

Cannot prevent all birth defects
Value of those with birth defects
Learn and educate about causes of birth defects and focus on ones that can be prevented
Educate risk reduction including information regarding family history and carrier screening
Referral to genetic center when suspect an increased risk for a birth defect (family history/previous child, test result increasing risk etc.)
Knowing cause can promote best chance for reduction of morbidity and mortality through planned care and treatment
Planning is essential to overall health and birth defect reduction
Societal change/shift in perspective on health (shift from education and communication to implementation and routinization)