Genetic Contributions to Infant Mortality: Prevention Strategies for Better Birth Outcomes

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Summit County Infant Mortality Summit: Every Baby Matters

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Leading Causes of Infant Mortality

10 Leading Causes of Infant Deaths
United States, 2006

- Birth Defects: 5,819
- Low Birth Weight and Prematurity: 4,841
- SIDS: 2,323
- Maternal Complications: 1,683
- Accidents (unintentional injuries): 1,147
- Complications of placenta, cord and membranes: 1,140
- Respiratory distress of newborn: 825
- Bacterial sepsis of newborn: 807
- Neonatal hemorrhage: 618
- Diseases of the circulatory system: 543

Source: CDC, NCHS

Five Leading Causes of Infant Deaths
United States, 2008

- Birth Defects: 5,681
- Low Birth Weight and Prematurity: 4,757
- Sudden Infant Death Syndrome: 2,350
- Maternal Complications: 1,775
- Accidents (unintentional injuries): 1,314

2008 live births = 4,247,726; All causes = 28,075 infant deaths
Birth Defects and Infant Mortality

• Birth defects are the leading cause of infant mortality (more than 1 of every 5 infant deaths)
• 1 in 33 babies born with birth defect
• Survivors have greater chance of illness and long term disability
• Every couple has 3-5% chance of having baby with birth defect or genetic condition
Infants with birth defects are:

1. 2X as likely to be born premature
2. 5-10X more likely to die within first year of life

Types of Birth Defects Contributing to Infant Mortality


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Ohio 2010

Types of Birth Defects as Cause of Infant Death

- Congenital Heart defects
- Chromosome
- Musculoskeletal and Limb
- Other
Ohio Infant Mortality Rates

Infant Mortality Rates\(^1\) by County, Ohio, 1990-2010

Infant mortality rates for the State of Ohio 1990-2010: 6.12 per 1,000 live births. The mean of the county infant mortality rates on which the standard deviations were based (map key) was 7.16 per 1,000 live births.

Prepared by: Epidemiology Section, Division of Family and Community Health Services, Ohio Department of Health.

* Rates based on less than 29 observations may be unreliable.
* County infant mortality rates are per 1,000 live births. Records without a county of residence were excluded.

Congenital Anomaly Infant Mortality Rates\(^1\) by County, Ohio, 1990-2010

* Rates based on less than 20 observations may be unreliable.
* County congenital anomaly infant mortality rates are per 1,000 live births. Congenital anomalies were enumerated if the leading cause of death was selected as a congenital anomaly. Records without a county of residence were excluded.

Congenital anomaly infant mortality rates for the State of Ohio 1990-2010: 1.65 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 1.62 per 1,000 live births.

Data compiled October 38, 2012
Prepared by: Epidemiology Section, Division of Family and Community Health Services, Ohio Department of Health.
Congenital Heart Defects

• #1 cause of all infant mortality in United States
• Most common birth defect (1 in every 100 babies born with CHD; about 40,000 births per year)
• At least 15% associated with genetic conditions
• About 20% to 30% have other physical problems or developmental disorders

CDC
OHIO (2010)

Congenital Heart Defects responsible for 22% of all infant deaths caused by birth defects
Causes of Congenital Heart Defects

- Rubella (German measles)
- Alcohol
- Medications (Accutane, anti-seizure medications, Lithium)
- Genetics
- Maternal Diabetes
- Maternal PKU
- Maternal Lupus
- Smoking
- Unknown factors
Chromosome Abnormalities

- Risk increases with advancing maternal age
- Translocations can be familial
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)
Third Most Common Cause of Infant Mortality: Sudden Infant Death Syndrome

- Variable etiologies
- Ion channel genes
- Arrhythmias (long QT)
- MCAD
- May be treatable
Preventing Birth Defects

Goals:

• Preventing occurrence
• Preventing recurrence
• Identification and early treatment to prevent or reduce morbidity and mortality
Preventing Birth Defects

Problems:

• Can’t prevent unless cause is known
• Prevention is a difficult message
• Behavioral changes are challenging
What can we do?

With what we know now:

1. Individuals can take steps to reduce their risks
2. Changes in perception of preconception care
3. Taking on a life course perspective to health
4. Having a reproductive life plan
9 things to consider before baby

We want to ensure women are informed before they decide to become, or unexpectedly become, pregnant.
Crucial development occurs before women know they are pregnant
1. Maternal Health Conditions

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

- Maintain physical and dental health
- Preconception health care visit
- Immunizations up-to-date (chickenpox, MMR, flu)
- Infection prevention (CMV, toxoplasmosis, STD’s)
- For any woman of childbearing age a healthcare visit is an opportunity for a preconception visit!!
2. Monitor Use of Medications

- Taking over-the-counter or prescription medicine?
  - Accutane
  - Warfarin
  - ACE inhibitors and ARB’s to treat blood pressure
  - Coumadin
  - Statins
  - Some medications to treat epilepsy and mental illness
  - Aspirin
- Using home remedies or herbal supplements?
- Ingesting too much caffeine? (<200mg/day = one 12oz cup of coffee)
3. Consume Enough Folic Acid

• When?
• Critical to begin BEFORE pregnancy
• Who?
• ALL women of childbearing age
• Why?
• Because over 50% of all pregnancies are unintended AND the spine forms before most women know they are pregnant
• How much?
• Daily multivitamin (.4mg folic acid) in addition to eating healthy diet including folate-rich foods
• What birth defects can it prevent?
• Can prevent some**:
  • Neural Tube Defects
  • Congenital Heart Defects
  • Cleft Lip and Palate
  • Limb Defects
  • Preterm births
  • ?Autism

**may be part of a syndrome
• Folic acid prior to conception and during spinal cord formation can prevent half of all neural tube defects.

• Anencephaly is fatal and was responsible for 5% of infant mortality from birth defects in Ohio in 2010
# Folic Acid Public Awareness: March of Dimes Polls

<table>
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<tr>
<th></th>
<th>1995</th>
<th>2000</th>
<th>2005</th>
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<tbody>
<tr>
<td>Heard of Folic Acid</td>
<td>52%</td>
<td>75%</td>
<td>84%</td>
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<tr>
<td>Folic Acid Prevents Birth Defects</td>
<td>5%</td>
<td>14%</td>
<td>25%</td>
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<tr>
<td>Took Folic Acid Daily</td>
<td>28%</td>
<td>34%</td>
<td>33%</td>
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<tr>
<td>Knew to Take Folic Acid Before Pregnancy</td>
<td>2%</td>
<td>10%</td>
<td>7%</td>
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Most often cited reasons for not taking (2005 survey):

- 28% forgot
- 16% don’t need
- 9% get nutrients need from food

What would make a woman more likely to take multivitamin?

*Advice of her health care provider*
Number of Providers who knew the Correct Amount of folic acid (0.4 mg) to Prevent Occurrence

Certified Nurse Midwives
64%

Physicians
31%

***Recurrence prevention = 4.0 mg
How many physicians know that over 50% of pregnancies are unintended?

3% not sure
36% think 25%
52% think 50%
9% think 75%
How Many Take Folic Acid Daily?

Physicians
47%

Other health care providers
54%

Why does this matter?
You are more inclined to recommend a behavior when YOU do the behavior and truly believe that it works
Main reason cited for not giving information

Time!!!!!!!!!!!!!
Neural tube defects – etiology

Folic acid deficiency

Family/pregnancy history

Genetic syndromes

Medications - anti-seizure medications (valproic acid Depakene, Stavzor) increase risks – suspected etiology – folic acid antagonists

Diabetes

Obesity

Increased core body temperature
Waardenburg Syndrome

Autosomal dominant
Type 1 chromosome 2q37
PAX3 gene (abnormal migration of cells derived from neural crest)
Hearing loss
Changes in hair and eye pigmentation
Spina bifida
Cleft lip/palate

Not all neural tube defects have folic acid deficiency as basis
Most commonly occur as isolated birth defects but also associated with many inherited genetic conditions or syndromes.

- Genes
- Environment (medications, alcohol, smoking, obesity)
- Folic acid deficiency

Van der Woude syndrome

*Gene map locus 1q32-q41

Cleft lip and/or palate with mucous cysts of lower lip
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
In US 1 in 5 women of childbearing age is obese
In OH 2 in 5 women are overweight or obese before becoming pregnant.

Since over half of all pregnancies are unplanned and since health habits begin young and unhealthy habits are difficult to break, healthy eating and exercise should begin at an early age and become a way of life.
Obesity among women ages 18-44
US, 2000-2010

Obesity is defined as a Body Mass Index of 30 or more. Hawaii did not conduct BRFSS surveillance in 2004 and is not included in the U.S. rate for this year.
5. Smoking, alcohol, Drugs

Alcohol
  > Fetal alcohol spectrum disorders

Drugs
  > Birth defects
  > Neonatal Abstinence Syndrome

Smoking
  > Birth defects
  > Low birth weight
  > Preterm delivery
  > Placental abruption
Smoking increases risk of orofacial clefts

1. Do genetic differences in mother that influence her metabolism of cigarette smoke and its byproducts set in motion developmental changes that cause the cleft in fetus?

2. Or do genetic differences in fetus hinder its ability to metabolize cigarette smoke and cause clefting?
Clefts and Smoking

- Women who smoke and carry fetus whose DNA lacks MAT and PAT copies of gene GSTT1 involved in detoxifying cigarette smoke, increase baby's chances of cleft lip/palate.
- About 25% of babies of European ancestry and 60% of Asian ancestry lack both copies
- If pregnant woman smokes 15 cigarettes or more/day, chances that her GSTT1 deficient fetus will develop a cleft increases nearly 20-fold.

• No known safe amount, no safe time and no safe kind of alcohol.
• Women should not drink if planning to become pregnant or are sexually active and not using effective birth control.
• This is because a woman could become pregnant and not know for several weeks or more.
• Half of all pregnancies are unplanned.
• FASDs are 100% preventable.

Binge alcohol use among women ages 18-44

Percent of women ages 18-44
6. Avoid household and work hazards

- Toxins and exposure to unsafe chemicals at work and home (second-hand smoke, carbon monoxide, solvents)
- Houses built prior to 1978 may have lead-based paint
7. Learn to reduce stress

- May affect ability to become pregnant and may influence birth outcomes

- Healthy eating, exercise, alcohol and tobacco avoidance

- Healthy outlets
8. Wait between pregnancies

- For most women, best to wait at least 18 months after birth before becoming pregnant again.

- Increase risks of preterm delivery and other adverse pregnancy outcomes.
9. Family histories

- Birth defects/genetic conditions
- Inherited health conditions
- Ethnic background
- Prior preterm birth, miscarriages, pregnancy complications or adverse pregnancy outcome
Many genetic conditions occur in absence of family history

Autosomal Recessive Pedigree

Homozygotes (affected)  Heterozygotes (asymptomatic)
Comprehensive (Universal) Carrier Screening

Each individual has 2-3 known recessive, severe childhood disease mutations
Individually uncommon but collectively common
Carrier testing can provide prospective parents with ability to identify and understand risk for conceiving child with autosomal recessive or X-linked condition
Potential to reduce occurrence of many fatal genetic conditions in children
Comprehensive Carrier Screening

- Barriers were technology and cost
- 107 AR, XLR conditions for $99 (includes CF, Tay-Sachs, Fragile X, hemoglobinopathies)
- In process of developing test that screens for 600 conditions for less than $500.00
Redefining when prenatal care begins
Life Course Perspective to health care and reproductive medicine

Early life events shape individual’s health trajectory
Look at life not as disconnected stages, but as integrated continuum
Acknowledge interplay of risk and protective factors that contribute to health outcome across lifespan, beginning at conception:
Conceptualize birth outcomes as end product of not only nine months of pregnancy, but entire life course of the mother leading up to the pregnancy
Reproductive Life Plan

Set of personal goals about having or not having children based on personal values and resources

http://www.cdc.gov/preconception/reproductiveplan.html
What is a Reproductive Life Plan?

- Part of an overall LIFE plan
- Determining when (and 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
Reproductive Life Plan

Questions Prompting a Reproductive Life Plan

1. Do you hope to have any (more) children?
2. How many children do you hope to have?
3. How long do you plan to wait until you (next) become pregnant?
4. How much space do you plan to have between your pregnancies?
5. What do you plan to do until you are ready to become pregnant?
6. What can I do today to help you achieve your plan?
Why is reproductive life planning important?

Lack of planning for pregnancy and pregnancy spacing, management of health conditions affecting pregnancy outcomes, environmental risk factors, and negative health behaviors affecting pregnancy outcomes leads to:

- unintended pregnancies
- increased risk for preterm births
- increased risk for low birth weight births
- increased rates of birth defects
- poorer health status for women
- increased health disparities

Why is unintended pregnancy a concern?

- Increased elective abortion rate
- Increased risk for infant morbidity and mortality; including preterm birth, low birth weight, and birth defects
- Late entry into prenatal care
- Higher rates of smoking prior to pregnancy
- Increased child abuse and neglect
- Increased Medicaid costs
- Increased risk of physical abuse and partner relationship ending for mothers

Benefits of Reproductive Life Planning

Reproductive life planning

Intended pregnancies

Better birth outcomes and healthier women
Reproductive Life Planning

1. Access to health services for preconception/wellness services including, but not limited to, family planning
2. Dialogue between health care providers and patients about a plan for future pregnancy or a plan to prevent pregnancy
3. Revisiting of reproductive life plan as time goes on
Who can provide reproductive life planning?

- Pediatricians
- Primary care providers
- Family practice physicians
- OB GYNs
- Nurses/nurse practitioners/nurse midwives
- Physician assistants
- Health educators
- Social workers
- Community outreach workers
- Dieticians
Getting started: Reproductive life planning

- Thinking about whether or not an individual plans to have children and
- When?
- How many?
- How often?
- And…how they can implement their plan and maintain their health now, their health during pregnancy and their baby’s health
Considerations

- 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 the individual motivation for current behaviors and desired changes
- Help patients choose small goals in which they are likely to succeed, then build on that success
- Preparation and motivation compensate for lack of confidence or will power
Getting started with behavior change

Talk to patient about current behaviors, motivators, and barriers

What changes would you like to make?
Why is this important to you?
What’s keeping you from making changes?
What would make it easier for you to change?
What do you need in order to make the change?
Improving reproductive life planning services at your facility

- Who provides reproductive life planning counseling?
- Who should provide reproductive life planning counseling?
- What should it include?
- Where should it take place?
- When should reproductive life planning counseling be offered?
- What tools are used?
- What tools should be used?
Summary

Birth defects are the leading cause of infant mortality

Prematurity is the second leading cause of infant mortality and genetics may play a role

There are steps that can be taken to reduce risks of infant mortality
Questions?

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