Global burden of neural tube defects, risk factors, prevention, and the role of folic acid

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Outline

- Definition of birth defects
- Global burden
- Neural tube defects
  - Global burden
  - Risk Factors
  - Prevention strategies with folic acid
  - SEARO/CDC collaboration
Defining Birth Defects

- Structural or functional abnormalities that are present from birth

- Potential for serious adverse effect on health, development, or functional ability

- Can be caused by single gene defects, chromosomal disorders, multifactorial inheritance, environmental teratogens or micronutrient deficiencies

- Often also referred to as congenital anomalies or congenital malformations
Burden of Birth Defects

- 1 in 33 infants has a birth defect (~3%)
  - 4.8 million infants globally

- 1 in 260 infants dies because of a birth defect
  - 0.6 million infants globally

- Underestimated
  - Spontaneous abortion
  - Stillbirths
  - Elective Termination of Pregnancy for Fetal Anomaly (ETOPFA)
Birth Defects: Overall Global Burden

3.0% = 4,800,000 Globally

Data of Total Births 2010 from WHO Statistics Website

- "There is a **paucity of data** on the birth prevalence of birth defects in middle- and low-income countries"

- Why?
  - Constrained diagnostic capability
  - Poor health-related statistics
  - Lack of birth defect surveillance and registries
  - Reliance on hospital-based rather than population-based studies

- Systematic underestimation of the toll of birth defects
Prevalence of Birth Defects (MoD estimates)

Prevalence of Birth Defects (MoD estimates)

Estimated number (per 1,000 – per year) of infants with birth defects (BD, Chrom, Single Gene, Genetic-Haemolysis/Jaundice)

- Congenital heart defects: 1,000,000
- Neural tube defects: 350,000
- Down syndrome: 220,000

Under 5-year Mortality due to BDs by WHO regions: Rate, Percentage and Absolute Numbers

**Rate U-5y-M per 1,000**
- **AFRICA**: 5.3
- **EAST-MEDITER**: 4.0
- **SOUTH-EAST-ASIA**: 3.8
- **AMERICAS**: 3.2
- **EUROPE**: 2.6
- **WEST PACIFIC**: 2.0

**Number of Deaths Under 5y**
- **AFRICA**: 263,000
- **SOUTH-EAST-ASIA**: 143,000
- **EAST-MEDITER**: 71,000
- **WEST PACIFIC**: 56,000
- **AMERICAS**: 49,000
- **EUROPE**: 29,000

**Globally**
- **3.9 per 1,000**
- **611,000**
- **6.2%**

2010 Data from WHO Statistics Website
Overall Under 5-year Mortality (line) and % of Deaths due to BDs (bars) by WHO Region and Country Income

**Legend**
- Countries income: 1= High, 2=Upper-Middle, 3=Lower-Middle, 4=Low
- WHO Regions: AFR=Africa, AM= Americas, EM=Eastern Mediterranean, EU=Europe, SE=South East Asia; WP=Western Pacific

World Health Statistics 2010 data
http://apps.who.int/gho/data/node.main.1?lang=en

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Neural Tube Defects

- Serious birth defects of the brain and spine
- Form in the first month of pregnancy
- Most common are anencephaly and spina bifida
Global Burden of Neural Tube Defects

More than 300,000 neural tube defects each year worldwide*

- Occur widely
  - Different geographical areas
  - Countries of varying levels of economic development
  - Among diverse populations

- Remain a significant, preventable cause of mortality and morbidity worldwide

Global Burden of Neural Tube Defects


Objectives

- To assess the extent to which neural tube defects are a global public health problem
- Summarize prevalence estimates of NTDs at the greatest population representation available
- Assess differences in NTDs prevalence by WHO regions and country income level (low, medium and high)
- Identify gaps in information

Methods

- Search
  - Database search of PubMed, Google Scholar, EUROCAT, ICBDSR registries
  - Observational studies and reports published during 1990-2014
  - Observational studies and registry reports and databases

- Included studies
  - NTD diagnosis, reported number of cases and total number of births
  - Reported at least spina bifida or total NTD cases
  - Registries were pre-identified

- Excluded: studies
  - No reported # NTD cases, mortality reports only, ≤ 5,000 live births per year

- **Preliminary Results**
  - Records identified through database searching (n = ~11,000)
  - Records screened ~1,100
  - Full articles revised ~ 100
  - Records included – 173 (multiple records/ country)
  - Countries by WHO region
    - AFRO 9
    - EMRO 11
    - EURO 28
    - PAHO 14
    - SEARO 4
    - WPRO 9
  - Global NTD Prevalence Range
    - 4.5 – 199.4 per 10,000 live births
Risk Factors for Neural Tube Defects

- Nutritional (Folate insufficiency; Vitamin B-12 deficiency)
- Environmental (hyperthermia)
- Behavioral (medications e.g. valproic acid, some narcotics)
- Maternal conditions (Obesity, diabetes)
Folic Acid and Neural Tube Defects Prevention

- Role of folic acid in preventing neural tube defects is well known
  - The majority of neural tube defects can be prevented with 400 micrograms (mcg) of folic acid daily before and during early pregnancy

- Globally many women of reproductive age do not consume enough folic acid for prevention
Approaches to Increase Folate/Folic Acid Intake

Diet... natural foods such as vegetables, fruits, beans, yeast, liver

Pills... folic acid-containing dietary supplements

Fortification ... folic acid added to foods - flour, rice, pasta, breakfast cereals

Neural Tube Defects Prevalence Changes: Before and After Folic Acid Fortification

<table>
<thead>
<tr>
<th>Country</th>
<th>Before Fortification</th>
<th>After Fortification</th>
<th>Decrease</th>
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<tbody>
<tr>
<td>US</td>
<td>10.8</td>
<td>6.9</td>
<td>-36%</td>
</tr>
<tr>
<td>Canada</td>
<td>15.8</td>
<td>8.6</td>
<td>-46%</td>
</tr>
<tr>
<td>Chile</td>
<td>17.1</td>
<td>8.6</td>
<td>-50%</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>14.1</td>
<td>9.8</td>
<td>-35%</td>
</tr>
<tr>
<td>South Africa</td>
<td>15.8</td>
<td>9.8</td>
<td>-31%</td>
</tr>
</tbody>
</table>

Rate per 10,000 births

Sources:
# Fortification: Cost Effectiveness

<table>
<thead>
<tr>
<th></th>
<th>Year of Fortification</th>
<th>Return on Investment</th>
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<tbody>
<tr>
<td>South Africa</td>
<td>2003</td>
<td>30 to 1</td>
</tr>
<tr>
<td>Chile</td>
<td>1998</td>
<td>12 to 1</td>
</tr>
<tr>
<td>US</td>
<td>1996</td>
<td>150 to 1</td>
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</tbody>
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Sources:
Birth Defects COUNT
Countries and Organizations United for Neural Tube Defects Prevention

- CDC is working with partners to advance neural tube defects prevention globally through folic acid food fortification and supplementation
- Contribute to the achievement of the Millennium Development Goal 4 (reduce under-5 mortality)
- Support the 63rd World Health Assembly resolution on birth defects
- Focus on regions where prevention opportunities will have greatest impact
  - South-East Asia and Africa
WHO-SEARO and Member States working together to move forward birth defects prevention and surveillance

Regional Strategic Framework for Birth Defects Prevention and Control
- 8 countries have held national meetings to adapt into national action plan
Thank you

For more information please contact Centers for Disease Control and Prevention

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Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov  Web: http://www.cdc.gov

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