Pregnancy in the Context of a Woman’s Lifespan

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Definition of Health and Health Determinants

Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity…. a resource for everyday life, not the objective of living. ¹

Determinants of health:
Who we are (genetics)
Where we live (environment)
How we live (behavior/culture)

¹. Preamble to the Constitution of the World Health Organization
Which ‘lifespan’ are we talking about?

OR
Case 1

Angela:
15 yo G0 presents for PNC at 24 weeks
Underweight, occ drug/EtOH use, + chlamydia
Immigrated to US age 2 with parents (Central America)
Quit school
US Pregnancy trends


Source: National Center for Health Statistics
# “Obvious” Risks and Implications

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  - Preg HTN, anemia, ↑ mortality
  - Lower education
  - Repeat pregnancy
  - Lower wages over time
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- **Neonatal/Baby risks**
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  - ↑ mortality by yr 1
  - ↑ health issues
  - ↑ cognition issues
  - ↑ risk childhood abuse
  - ↑ poverty, lower educ
Not so obvious...risks and implications

Maternal
Future chronic disease risks
Mental health issues
Relational issues
Nutritional deficiencies - osteoporosis
↑ risk adverse outcomes subsequent pregnancy?
↑ risk premature death?

Neonate/Child/Later
Adult
Obesity
HTN
Cardiovascular disease
Diabetes

???????
Future maternal (physical) health implications

Certain pregnancy-related complications predict future chronic disease occurrence;
Pregnancy is a stress test for conditions considered to be precursors to NIDDM, CVD, and the adult insulin resistance syndrome.
The Fetal Origins or “Barker” Hypothesis

- Pioneered by David Barker in the early 1990s
  - Painstaking development of historical birth cohort studies in England
- Part 1: Impaired fetal growth causes adult disease
- Part 2: “Thrifty phenotype” - impaired fetal growth permanently changes the body’s structure and physiology
  - Adaptive for compromised nutrition
  - Maladaptive for over-nutrition
- Potential mechanisms include blood pressure, fibrinogen concentration & glucose tolerance

Crude and SES adjusted rate ratios for mortality from ischaemic heart disease by birth weight: Cohort from Uppsala, Sweden.

Birth weight (kg)

<table>
<thead>
<tr>
<th>Birth weight (kg)</th>
<th>&lt;3.25</th>
<th>3.25-3.7</th>
<th>3.75-4.24</th>
<th>&gt;4.25</th>
<th>P value for trend</th>
</tr>
</thead>
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<tr>
<td>Crude</td>
<td>1.0</td>
<td>0.8</td>
<td>0.7</td>
<td>0.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Adjusted *</td>
<td>1.0</td>
<td>0.9</td>
<td>0.7</td>
<td>0.7</td>
<td>0.01</td>
</tr>
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</table>

*adjusted for SES-related factors

More gestational weight gain associated with higher BMI at 3 y

Oken et al., Am J Obstet Gynecol 2007; 196:322e1
The Embryonic-Fetal Supply Line
“Fetal nutrition”

Mom’s own intrauterine and childhood experiences

Mom’s peri-conceptional health

Diet during pregnancy (+ other behaviors)

Utero-placental blood flow, placental function

Fetal metabolism
The thrifty phenotype hypothesis.

*Source: Adapted from Hales and Barker (2001)*
Fetal health leading to adult health

- Consistent evidence - markers of fetal growth are inversely associated with the later development of CVD, NIDDM, and IRS;
- Good evidence of nutritional fetal programming from animal studies;
- Good evidence of an interaction between birth weight and adult measures of obesity;
Case 2

Evelyn
30 yo G2P0010
+ smoker; EtOH abuse
Lives in a poor urban area (previously industrialized)
“Obvious” Risks and Implications

**Maternal risks**
- CVD
- Hypertension
- Lung and oral cancer
- PPROM, abruption

**Fetal risks**
- LBW
- Prematurity
- Fetal alcohol syndrome
- Stillbirth
- SIDS
Not so obvious risks and implications

**Maternal**
- ↑ risk type 2 diabetes
- Early menopause
- Infertility/subfertility
- Cervical cancer, other cancers

**Neonate/Child/Later Adult**
- Obesity
- Environmental toxicant effects
- Less tolerance to future stress (chronic elevation of stress hormones)?
- ↑ risk chronic diseases?
- ↑ risk cancer?
- ↑ infertility/subfertility
Body Mass Index by Maternal Smoking Status

Suzuki K, Int J. Obesity, 2010
...especially in this environment
Epigenetic programming

- Development is an active interaction between the embryo and the environment. During zygotic development, intrauterine experiences are recorded in the EPIGENOME.

- Epigenetic stimuli establish and maintain genetic marks by DNA methylation and histone modification—changes that make GENES either transcriptionally SILENT or ACTIVE.
BPA causes obesity?

Color of agouti mouse coat correlates with epigenetic changes early in development (decrease methylation → yellow)

Fed pregnant mice BPA

↑ obesity, breast/prostate CA risk

BPA causes demethylation that programs the hypothalamus that results to increased appetite

Mice are GENETICALLY identical but EPIGENETICALLY different.

The yellow mouse is exposed to bisphenol A
Pollutant/ Maternal Health Status

Fetal Genes (active) Tumor Suppressor Genes
BRCA1/ p53 breast cancer
p73 brain cancer

De novo methylation

Silent

Susceptibility to cancer

This altered epigenome can be transmitted to the next generations.
Maternal behavior as an epigenetic stimulus

- Epigenetic timing is time and space regulated
- Effects may be reversible
The role of socioeconomic status

Covariates of socioeconomic status

- obesity
- Sub-optimal nutrition
- Other factors
- smoking
- Physical activity
- Prenatal care

Intrauterine growth restriction

Adulthood Chronic Diseases

Maternal Mortality Rates, by Race/Ethnicity, 2007

Total and Preterm-Related* Infant Mortality Rates by Race and Ethnicity of Mother: United States, 2007
Life expectancy for African Americans is nearly six years less than whites

- Disparities in socioeconomic status explain much of this gap.
- Disparities in cardiovascular mortality explain nearly one third of the gap.
- Hypertension represents the single largest contributor to this gap.
Low birth weight versus social class.

Study - OR (95% CI) % Weight

Fairley 21: 2.14 (2.04 to 2.24) 27.4
Maher 22: 1.45 (1.40 to 1.51) 27.5
Pattenden 30: 1.61 (1.50 to 1.72) 27.1
Spencer 27: 2.17 (1.59 to 2.98) 18.0
Overall (95% CI): 1.79 (1.43 to 2.24)

Heterogeneity p value < 0.001

Weightman A L et al. BMJ Open 2012;2:e000964
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Case 3

Phi
45 yo G3P2 immigrant, speaks little English
In US for 20 years
Unintended pregnancy
+ obesity, hypertension, diabetes
Multiple medications
“Obvious” Risks and Implications

**Maternal**
- Maternal age
- Unintended pregnancy
  - ↑ likelihood abortion (spont and elective)
  - ↑ risk ectopic
  - ↑ risk pregnancy complications
  - ↑ risk hepatitis B

**Neonatal/Baby risks**
- ↑ risk genetic and chromosomal abnorm.
- Poss ↑ risk birth defects (not genetic)
- ↑ risk preterm birth, LBW
- ↑ stillbirth
Not so obvious...risks and implications

**Maternal**

↑ risks with smoking
↑ risk preeclampsia/eclampsia
↑ risk gestational diabetes
↑ risk placenta previa
↑ risk twins
↑ cesarean section

Social issues, possible age issues

**Neonate/Child/Later Adult**

Impact maternal health conditions
Impact accumulated maternal environmental exposures
Impact of parental acculturation
Unintended pregnancy

- Delay in seeking prenatal care and having a premature baby
- Higher risk of domestic violence
- Higher level of stress and frequency of depression
- More likely negative attitude toward baby and abuse
Early life risk factors for development of overweight and obesity

- Genetics
- Maternal factors
  - Pregnancy weight gain
  - Pregnancy diet
  - Gestational diabetes
  - Smoking in pregnancy
- Perinatal factors
  - Birth weight (high and low)
  - Breast feeding (protective)
  - Timing of introduction of solid food
Infant and early childhood obesity

Kim et al., Obesity 2006; ~500,000 well child visits in Mass. HMO
How do we put all the context(s) into our care?

"And that's why we need a computer."
Time For a Paradigm Shift!

**From**
- Healthy Mothers
  - Healthy Babies

**To**
- Healthy Women
  - Healthy Mothers
  - Healthy Babies
Life Course Perspective

Life is not a series of disconnected stages, but an integrated continuum
Health outcomes result from a complex interplay of biological, behavioral, psychological, and social protective and risk factors that span a person’s lifetime
Birth outcomes are not the end product of 10 months of pregnancy, but the entire life course of the mother leading up to the pregnancy.
Implications for MCH Practice

Maternal health during pregnancy is directly related to maternal health prior to pregnancy with an emerging emphasis on preconception care and health maintenance meaning:

- Clinical & Public Health Interventions will have to be more Longitudinally and Contextually Integrated
- Providers will need to move from a strictly clinical approach to one that integrates the social determinants of health

It will still take more than one generation to equalize health disparities but each generational change brings us closer to health equity
So I blame you for everything
- whose fault is that?