(Epi)Genetics, Racism, and Pregnancy Outcomes

Michèle G Curtis, MD, MPH, MML
(anticipated JD May 2017)
The Miracle of Life: How does THIS happen?
CENTRAL DOGMA OF MOLECULAR GENETICS

DNA \longrightarrow RNA \longrightarrow PROTEIN SYNTHESIS

REPLICATION \rightarrow TRANSCRIPTION \rightarrow TRANSLATION

Exceptions among viruses – RNA to DNA (retroviruses)
Epigenetics: the communication system b/w environment and DNA

- C.H. Waddington coined the term to mean above or in addition to genetics to explain differentiation.

- DNA is not your final destiny!
Epigenome provides instructions and regulates the functional aspects of all the genes

Epigenetic stimuli establish and maintain genetic marks

Parent’s experiences are passed on to offspring through epigenetic tags

Genetic tags are passed down through generations

When the zygote is formed many epigenetic tags are removed from the chromosomes of the parents, but some remain
The Fetal Origins or “Barker” Hypothesis

- Early 1990s
  - 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

The thrifty phenotype hypothesis. Adapted from Hales and Barker (2001)
Maternal stress and fetal development: pregnancy as a transgenerational event
Birth weight and Risk of Adult Chronic Disease

Maternal Malnutrition

Fetal Malnutrition

- Decreased beta cell mass/function
- Decreased fetal growth
- In Utero metabolic programming

- Impaired beta cell function
- Insulin resistance

Type 2 Diabetes

Relative risk

↑ Cardiovascular disease
↑ Type 2 diabetes mellitus
↑ Metabolic syndrome
↑ High blood pressure

↑ Obesity
↑ Type 2 diabetes mellitus

SGA

Birth weight

LGA

MATERNAL UNDERNUTRITION

Lower 11βHSD Activity

Reduced Nephron Number

Disproportionate Fetal Growth Retardation

Increased Fetal GC Exposure

Impaired Renal Function

Hypersensitivity to GC

HYPERTENSION

- Increased Nephron Number
- Reduced Renal Function
- Normal Fetal Growth
Medical Advances v Disparities 1991-2000

- 176,633 deaths averted due to declines in mortality
- Assume all the decline is due to medical advances

- If the death rates of blacks and whites were identical, 886,202 deaths would have been averted
- 5 deaths could be averted by reducing disparities for every life saved by medical advances
- Eliminating disparities in health would save more lives than current advances in medical technology

Woolf S et al. 2004, AJPH
Costs of Racial Disparities, 2003-2006

- Medical Care Costs = $229.4 Billion
- Lower worker productivity & premature death costs = $1,008 Trillion
- **Total Costs =**
  - $309.3 Billion annual loss to the economy
  - More than GDP of India (12th largest economy)
  - Social Justice can be cost effective
  - Doing nothing is not a viable financial option

LaVeist et al. 2009, Joint Center for Political & Economic Studies
Infant Mortality Rates,* by Race & Hispanic Ethnicity of Mother — US, 2000, 2005, and 2010

*Per 1,000 live births

Racism and Stress: multidimensional social constructs

Racism
3 levels:
Institutionalized
Interpersonal
Internalized

Racism affects health independently of general stress variables  (Williams DR et al. J Health Psychol 1997;2:335-51)
Racism, stress, and biology

- Physiological stress response
- Access to health care
- Health behavior
- Mental health
- Epigenetics
Infant mortality rates, by mother's race, Hispanic origin, and place of birth: Deaths per 1,000 live births, 2010

Racism and Health: Mechanisms

- Restricted SES attainment and group differences in SES and health.
- Pathogenic residential conditions.
- Reduced access to desirable goods and services.
- Acceptance of society’s negative characterization and body/mind impact
- Increased exposure to traditional stressors (e.g. unemployment).
Percent of mothers with a work disability, by age: 2012-2014
Black and White, non-Hispanic mothers living with children in their own households

- White HS or less
- Black HS or less
- White >HS
- Black >HS

Chart by Philip N. Cohen using CPS data from IPUMS.org

2013 Period Linked Birth/Infant Death Public Use File, Centers for Disease Control.
Final path model of relationship between everyday discrimination and birth weight.

Measurement tools for evaluating the impact of racism

- Experiences of Discrimination Scale
- Perceptions of Racism Scale
- Everyday Discrimination Scale
- Perceived Racism Scale

1. Krieger N. Sco Sci Med. 1990; 30(12); 1273-81
Racism & Adverse Pregnancy Outcomes

- Inconsistent results PTD, LBW, and VLBW
- MOST find sig assoc b/w racial discrimination and adverse birth outcomes
- Different instruments
- Sample size
- Different variables
- Self reporting
- Different levels racism measured
- Acute v chronic
“...it’s the skin you’re in. It’s just another part of your life.”

- Enduring impact of childhood experiences
- Perceptions institutionalized and internalized racism; not just interpersonal forms
- Vicarious experiences, esp re: children
- Cumulative impact of pervasiveness and chronicity
- Relationship of sex/gender roles and racism

Future Research Directions

- Better and more sensitive instruments
- Prospective approach
- Broad range of demographics and adequate sample size
- Minimize bias in collection techniques
- Understanding what types of support work best for different dimensions of experiences of racial discrimination
- Develop measures that aren’t limited to self-reporting
- What is protective?
- Develop interventions at multiple levels, including ones specific to HC providers
- More CBPR
- Measure impact of races across ALL races
Chronic disease risk

No/late intervention

Early intervention improves functional capacity & responses to new challenges

With early intervention

Life course

Plasticity

New environmental challenges

(Hanson et al. Progress in Biophysics and Molecular Biology 106 (2011) 272-80)
“The only thing necessary for the triumph of evil is for good men to do nothing.”  

Edmund Burke

Washington DC, Jan. 21, 2017