

# Preconception Health & Health Care: A Life-Course Perspective

---

**Michael C. Lu, MD, MPH**

Associate Professor

Department of Obstetrics & Gynecology  
David Geffen School of Medicine at UCLA  
Department of Community Health Sciences  
UCLA School of Public Health

August 3, 2010

# Why Preconception Care?

# Why Preconception Care?

---

- Early prenatal care is too late.
-

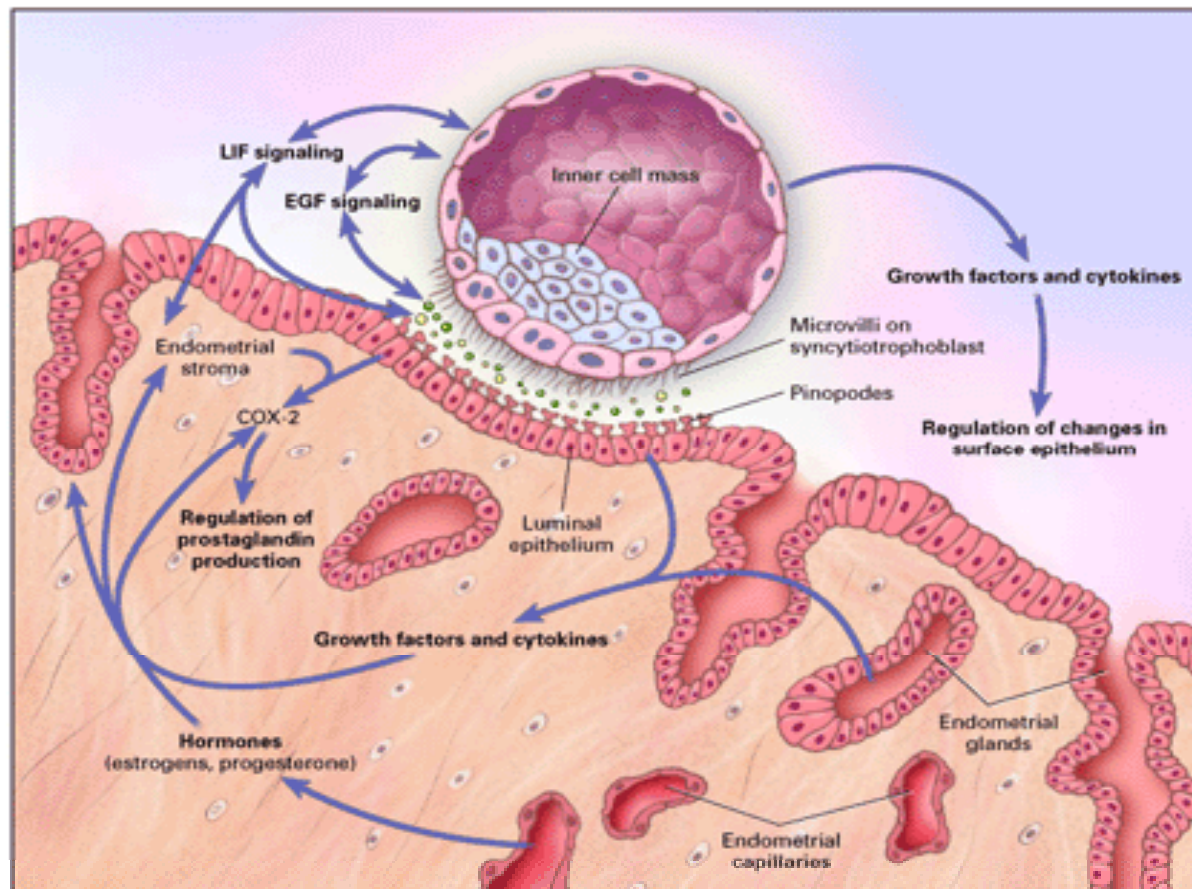
# Early Prenatal Care Is Too Late

## To Prevent Some Birth Defects

---

- ❑ The heart begins to beat at **22** days after conception
  - ❑ The neural tube closes by **28** days after conception
  - ❑ The palate fuses at **56** days after conception
  - ❑ Critical period of teratogenesis – **Day 17 to Day 56**
-

# Early Prenatal Care Is Too Late To Prevent Implantation Errors



Norwitz ER, Schust DJ, Fisher SJ. Implantation and the survival of early pregnancy. *N Engl J Med*. 2001 Nov 8;345(19):1400-8.

# Early Prenatal Care Is Too Late from A Life-Course Perspective

---

- A way of looking at life not as disconnected stages, but as an integrated continuum
-

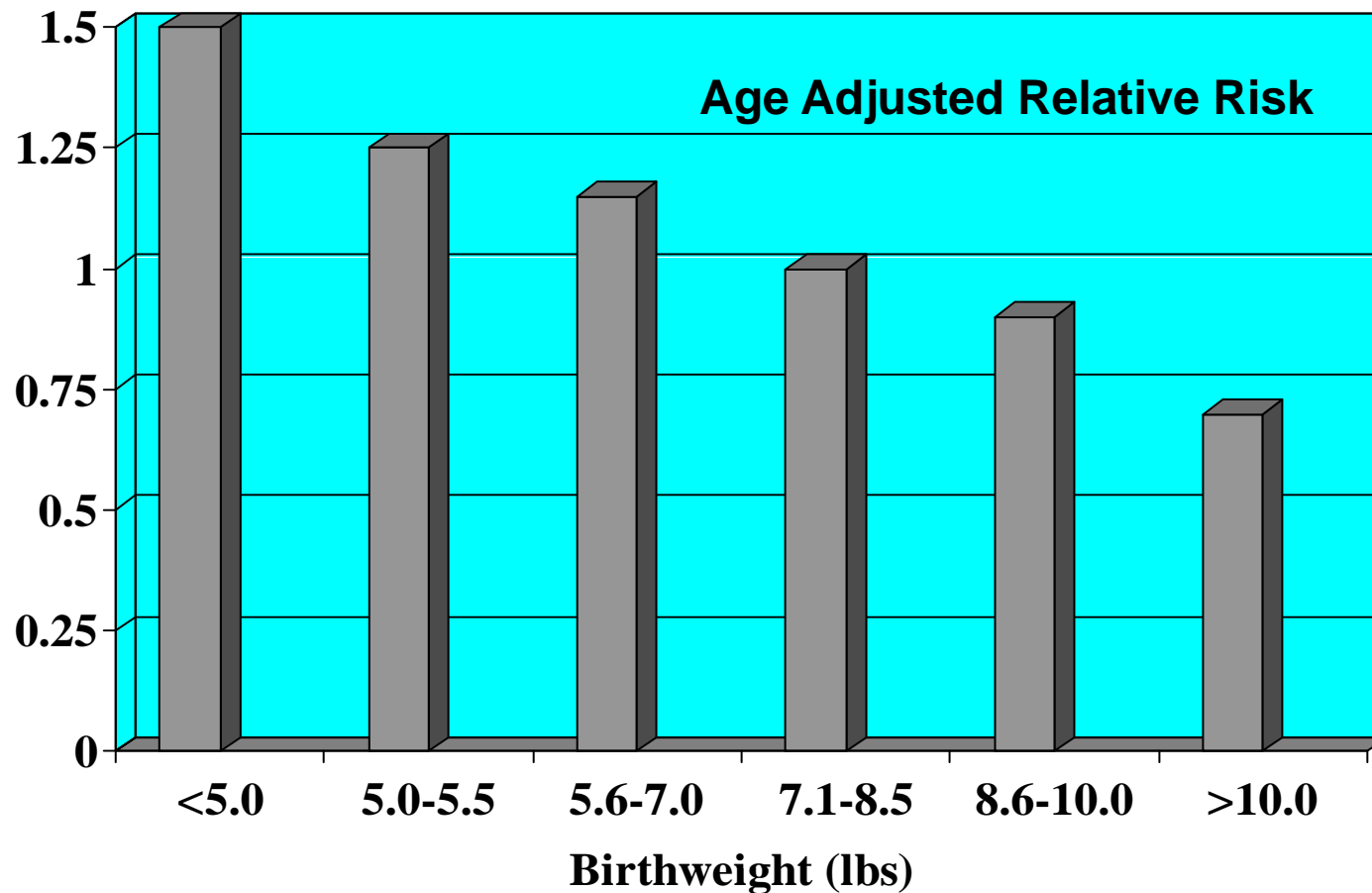
# Early Programming

---



# Barker Hypothesis

## Birth Weight and Coronary Heart Disease

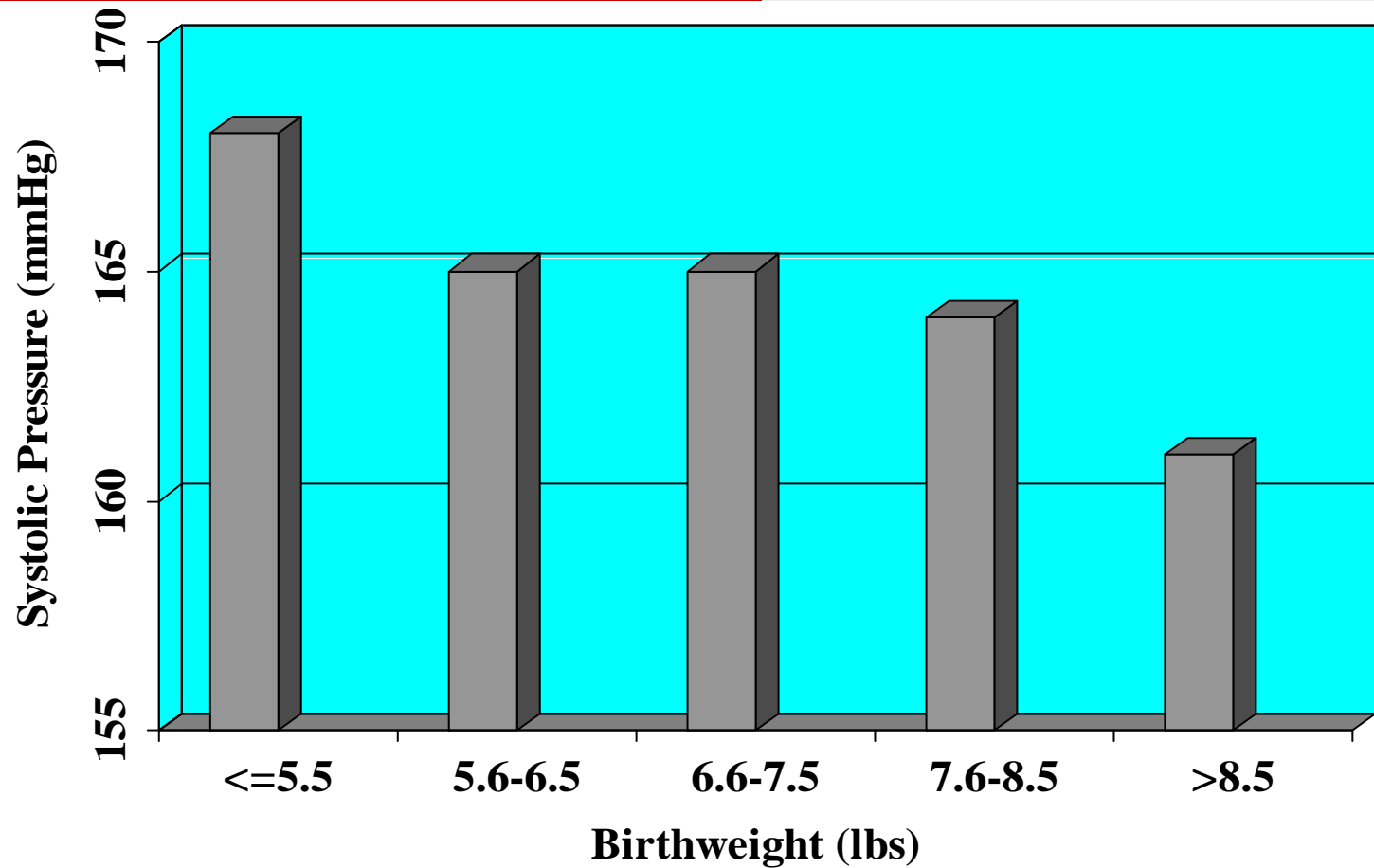


Rich-Edwards JW, Stampfer MJ, Manson JE, Rosner B, Hankinson SE, Colditz GA et al. Birth weight and risk of cardiovascular disease in a cohort of women followed up since 1976. *Br Med J* 1997; 315:396-400.



# Barker Hypothesis

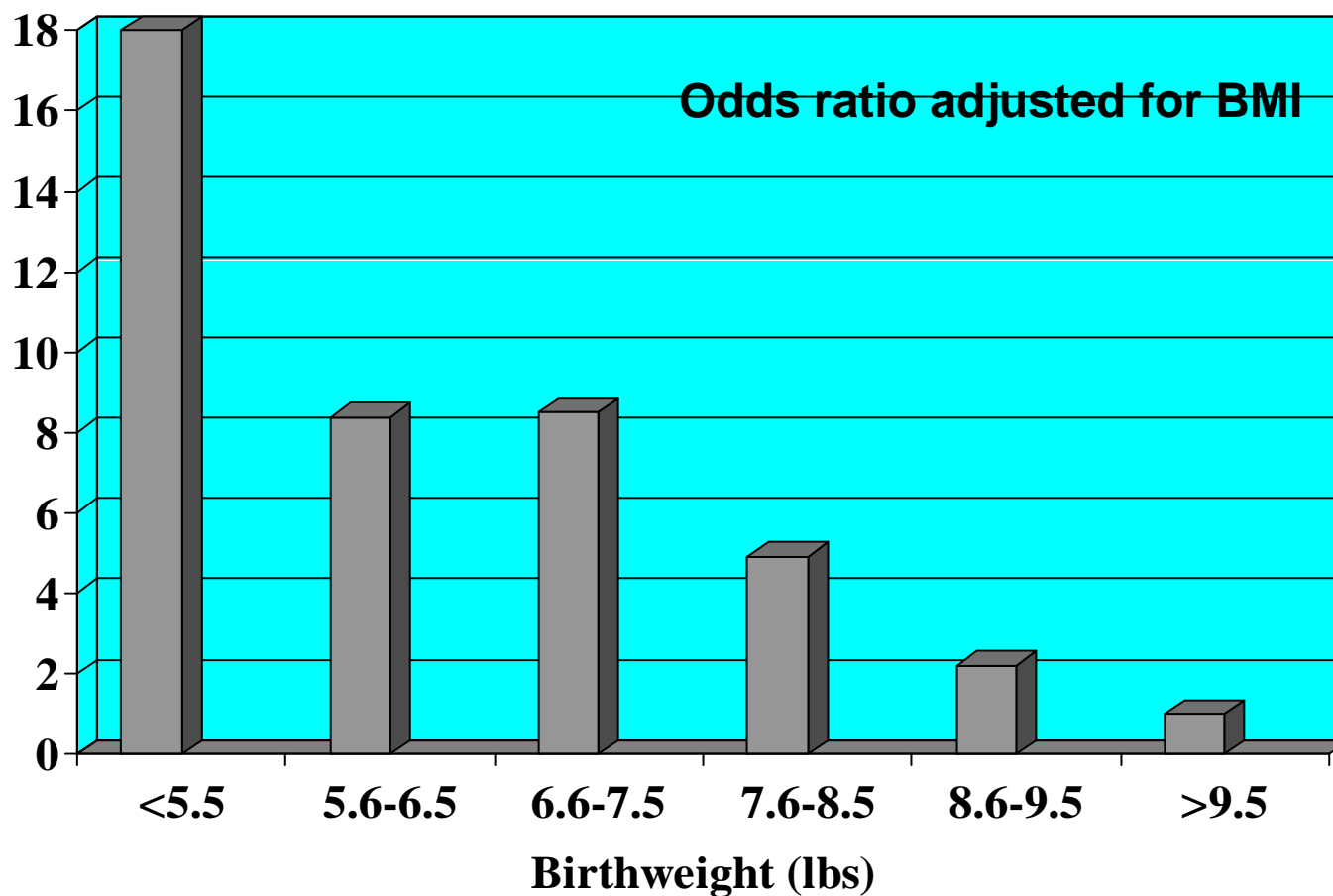
## Birth Weight and Hypertension



Law CM, de Swiet M, Osmond C, Fayers PM, Barker DJP, Cruddas AM, et al. Initiation of hypertension in utero and its amplification throughout life. *Br Med J* 1993;306:24-27.

# Barker Hypothesis

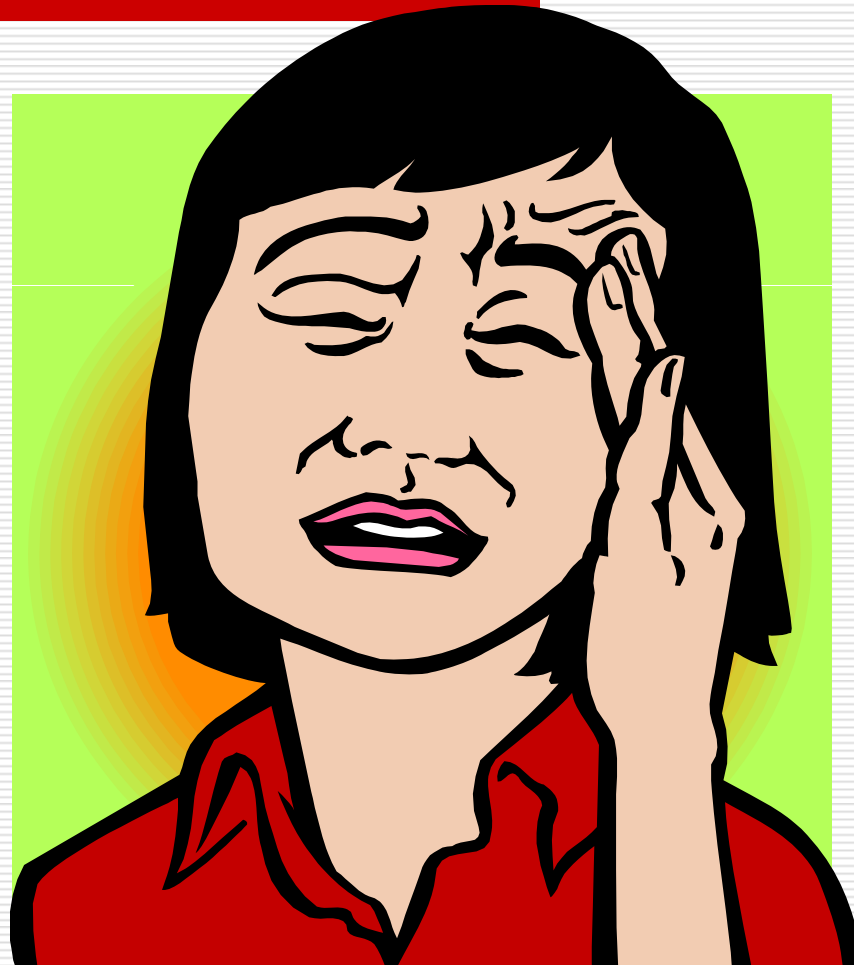
## Birth Weight and Insulin Resistance Syndrome



Barker DJP, Hales CN, Fall CHD, Osmond C, Phipps K, Clark PMS. Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (Syndrome X): Relation to reduced fetal growth. *Diabetologia* 1993;36:62-67.

# Maternal Stress & Fetal Programming

---

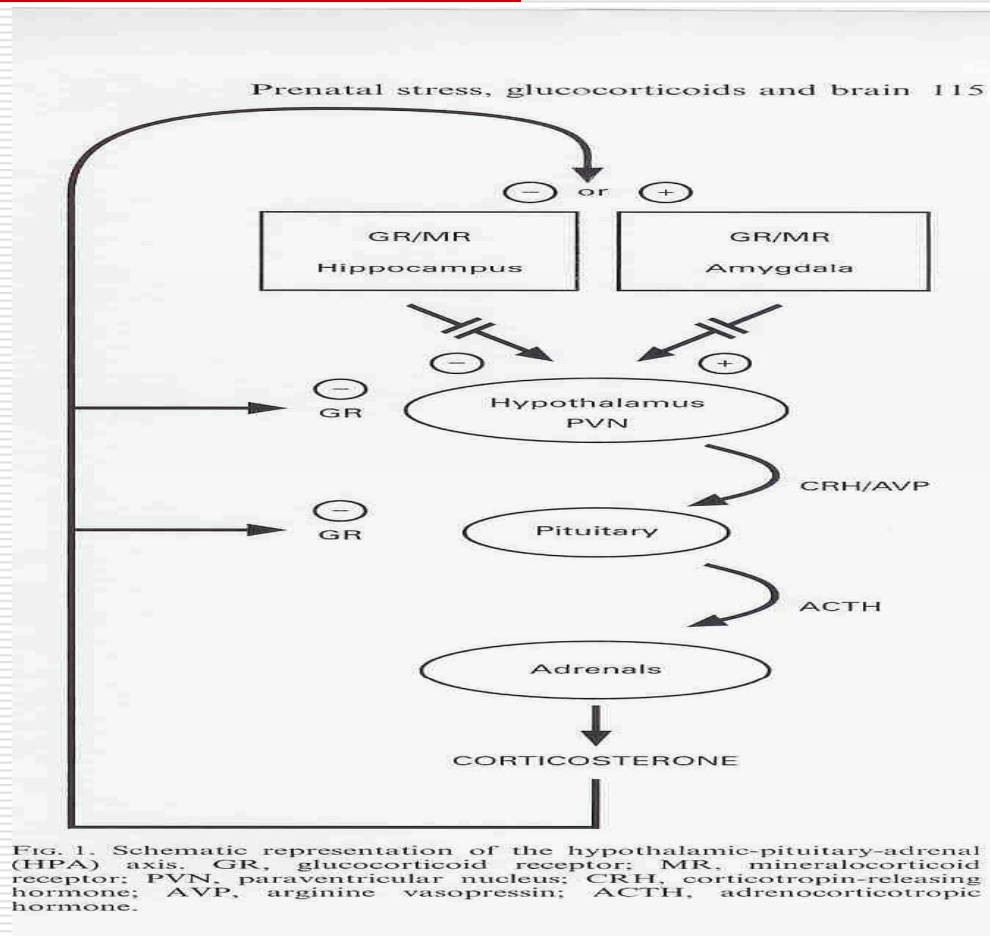


# Prenatal Stress & Programming of the Brain

---

- Prenatal stress (animal model)
  - Hippocampus
    - Site of learning & memory formation
    - Stress down-regulates glucocorticoid receptors
    - Loss of negative feedback; overactive HPA axis
  
  - Amygdala
    - Site of anxiety and fear
    - Stress up-regulates glucocorticoid receptors
    - Accentuated positive feedback; overactive HPA axis

# Prenatal Programming of the Hypothalamic-Pituitary-Adrenal Axis



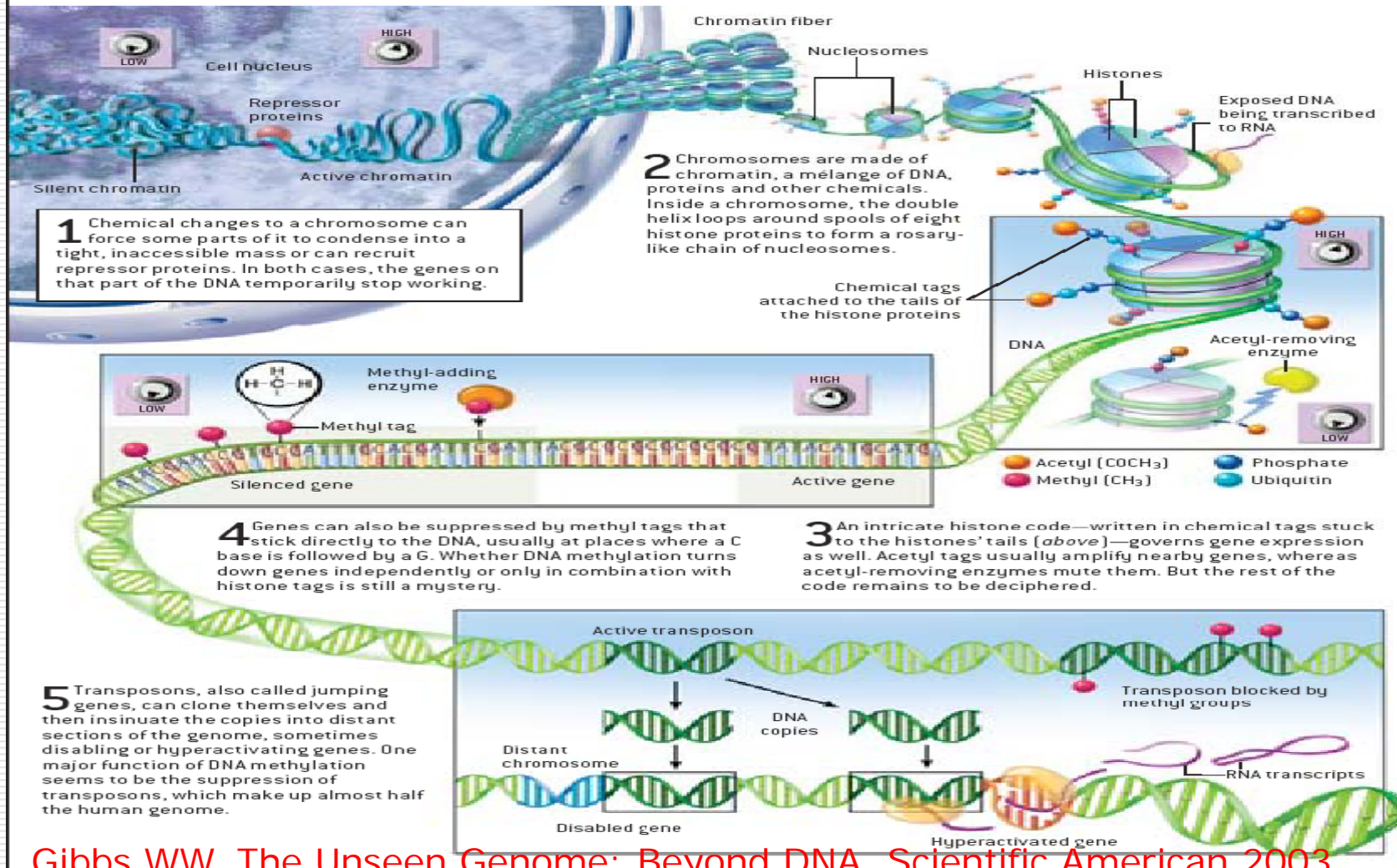
Welberg LAM, Seckl JR. Prenatal stress, glucocorticoids and the programming of the brain. J Neuroendocrinol 2001; 13: 113-28.

# Epigenetics

## VOLUME CONTROLS FOR GENES

THE DNA SEQUENCE is not the only code stored in the chromosomes. So-called epigenetic phenomena of several kinds can act like volume knobs to amplify or mute the effect of genes. Epigenetic information is encoded as chemical attachments to

the DNA or to the histone proteins that control its shape within the chromosomes. Among their many functions, the epigenetic volume controls muffle parasitic genetic elements, called transposons, that riddle the genome.



Gibbs WW. The Unseen Genome: Beyond DNA. Scientific American 2003

# Epigenetics

## *Same Genome, Different Epigenome*

---



R.A. Waterland, R.A. Jirtle, "Transposable elements: targets for early nutritional effects on epigenetic gene regulation," *Mol Cell Biol*, 23:5293-300, 2003. Reprinted in [the New Scientist 2004](#)

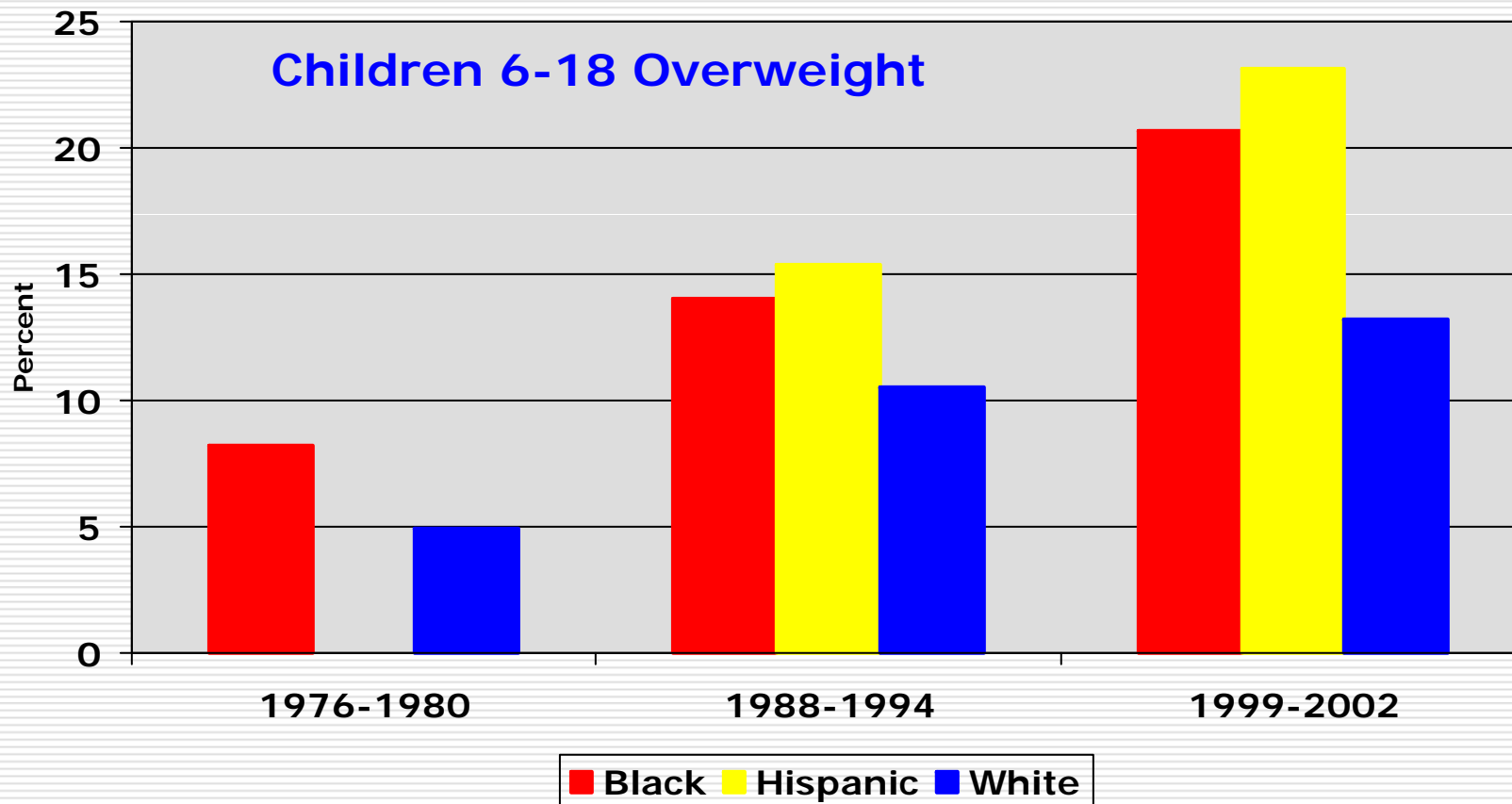
# Prenatal Programming of Childhood Obesity

**OBESITY:** A Weighty Issue  
for Children





# Epidemic of Childhood Overweight & Obesity



Source: National Center for Health Statistics, National Health and Nutrition Examination Survey

Note: Estimate not available for 1976-1980 for Hispanic; overweight defined as BMI at or above the 95<sup>th</sup> percentile of the CDC BMI-for-age growth charts

# Prenatal Programming of Childhood Overweight & Obesity

Matern Child Health J  
DOI 10.1007/s10995-006-0141-8

ORIGINAL PAPER

## Prenatal Programming of Childhood Overweight and Obesity

Jennifer S. Huang · Tiffany A. Lee · Michael C. Lu

© Springer Science+Business Media, LLC 2006

**Abstract** *Objective:* To review the scientific evidence for prenatal programming of childhood overweight and obesity, and discuss its implications for MCH research, practice, and policy.

*Methods:* A systematic review of observational studies examining the relationship between prenatal exposures and childhood overweight and obesity was conducted using MOOSE guidelines. The review included literature posted on PubMed and MDCconsult and published between January 1975 and December 2005. Prenatal exposures to maternal diabetes, malnutrition, and cigarette smoking were examined, and primary study outcome was childhood overweight or obesity as measured by body mass index (BMI) for children ages 5 to 21.

*Results:* Four of six included studies of prenatal exposure to maternal diabetes found higher prevalence of childhood overweight or obesity among offspring of diabetic mothers, with the highest quality study reporting an odds ratio of adolescent overweight of 1.4 (95% CI 1.0–1.9). The Dutch famine study found that exposure to maternal malnutrition in early, but not late, gestation was associated with increased

odds of childhood obesity (OR 1.9, 95% CI 1.5–2.4). All eight included studies of prenatal exposure to maternal smoking showed significantly increased odds of childhood overweight and obesity, with most odds ratios clustering around 1.5 to 2.0. The biological mechanisms mediating these relationships are unknown but may be partially related to programming of insulin, leptin, and glucocorticoid resistance *in utero*.

*Conclusion:* Our review supports prenatal programming of childhood overweight and obesity. MCH research, practice, and policy need to consider the prenatal period a window of opportunity for obesity prevention.

**Keywords** Prenatal programming · Childhood obesity · Overweight · Developmental programming · Fetal programming · Gestational diabetes · Maternal malnutrition · Cigarette smoking

Childhood overweight and obesity is a growing problem in the United States and worldwide. The prevalence of childhood overweight in the U.S. tripled between 1980 and 2000 [1]. Today approximately 1 in 6 (16%) U.S. children are overweight with significant racial-ethnic disparities. For example, nearly 1 in 4 (23%) non-Hispanic black girls ages 6 to 19 are overweight, a prevalence almost twice that of non-Hispanic white girls [1].

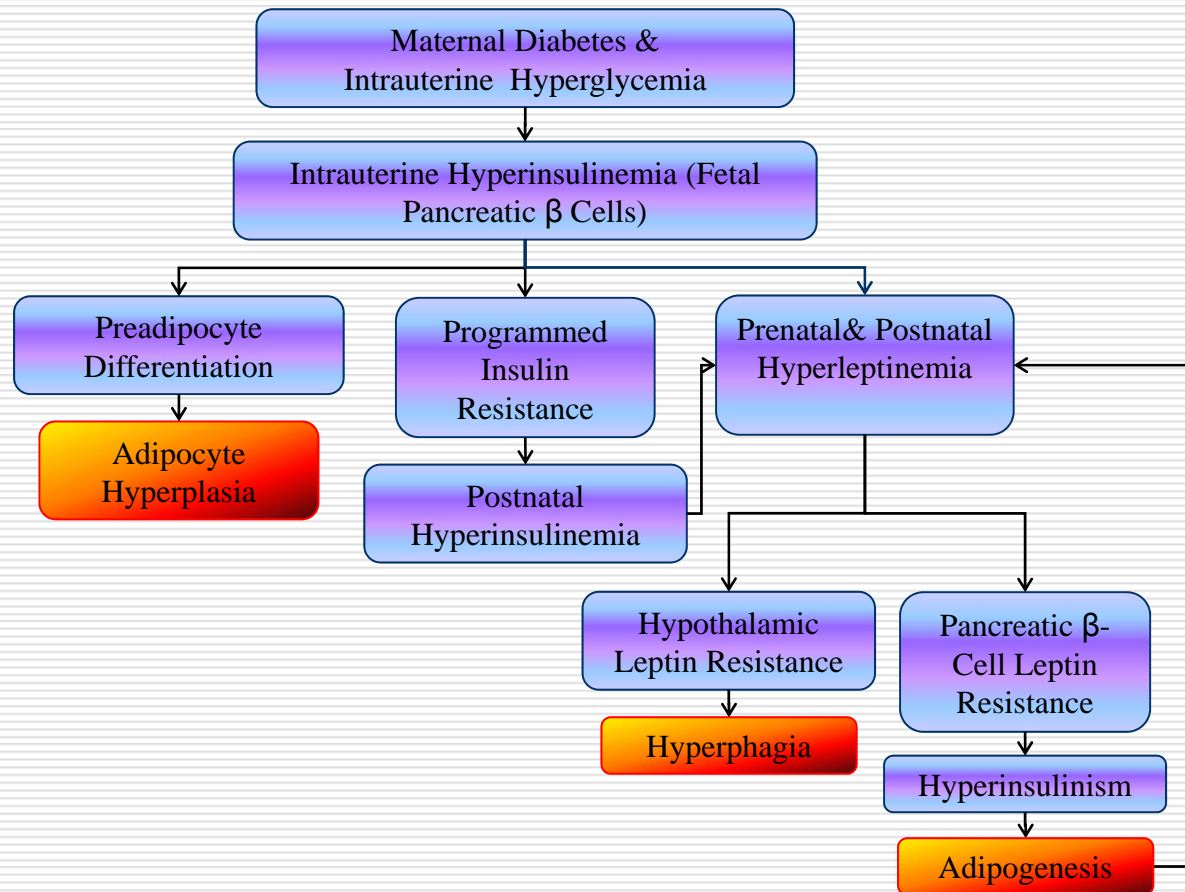
Overweight and obesity has significant lifelong consequences on the health and well-being of children [2, 3]. Childhood obesity is associated with early-onset Type II diabetes mellitus, hypertension, metabolic syndrome, and sleep apnea. It is also associated with cognitive or intellectual impairment and social exclusion and stigmatization as parts of a vicious cycle including school avoidance [3]. Childhood obesity tracks strongly into adulthood [4, 5]; obesity beyond

**Disclaimer:** The opinions expressed in this paper are the authors' and do not necessarily reflect the views or policies of the institutions with which the authors are affiliated.

J. S. Huang · T. A. Lee · M. C. Lu  
Department of Obstetrics and Gynecology,  
David Geffen School of Medicine at UCLA,  
CA, USA

M. C. Lu (✉)  
Department of Community Health Sciences and the Center  
for Healthier Children, Families and Communities,  
UCLA School of Public Health,  
Box 951772, Los Angeles, CA 90095-1772, USA  
e-mail: mclu@ucla.edu

# Prenatal Programming of Childhood Obesity



# Cumulative Pathways



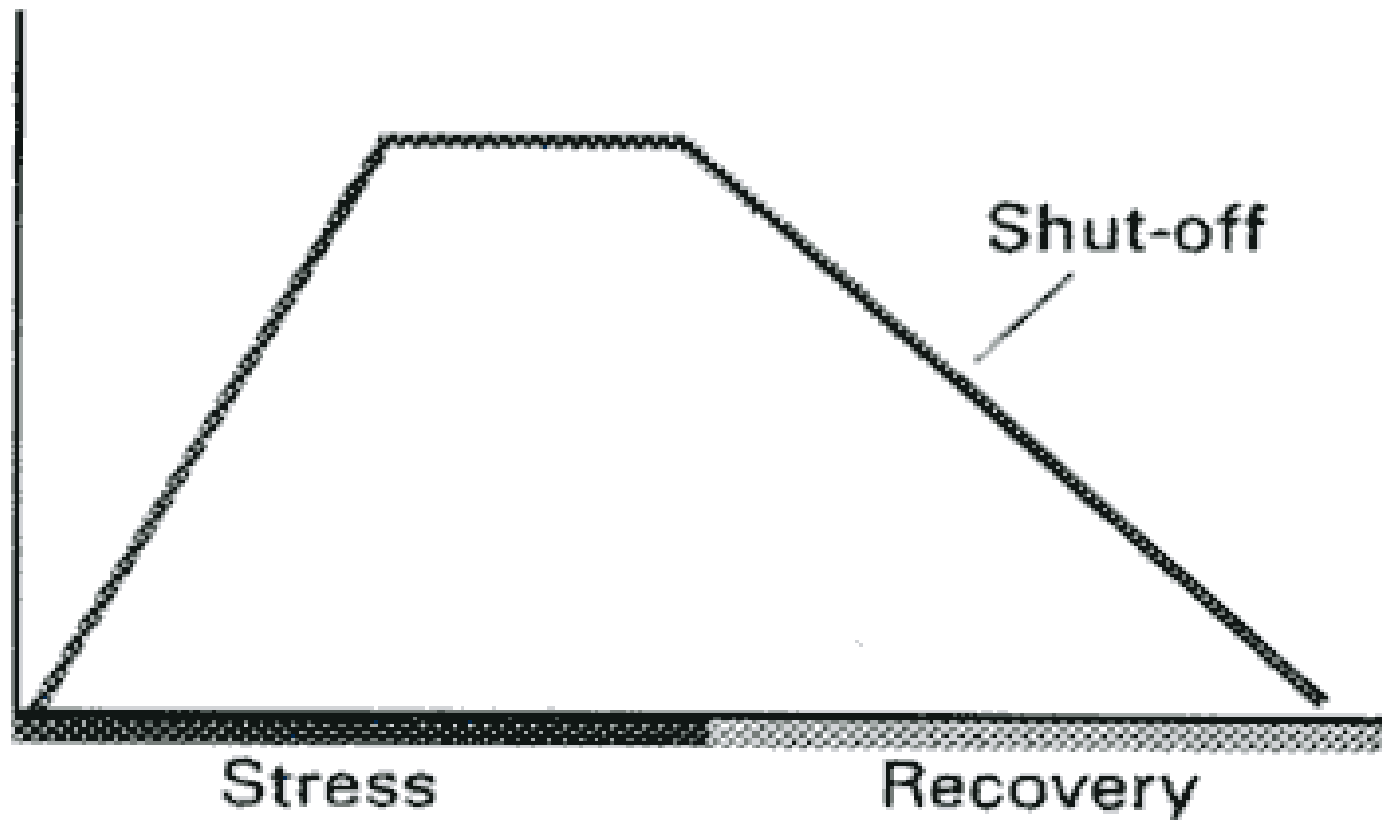
Photo: <http://www.lam.mus.ca.us/cats/encyclo/smilodon/>

# Allostasis:

## Maintain Stability through Change

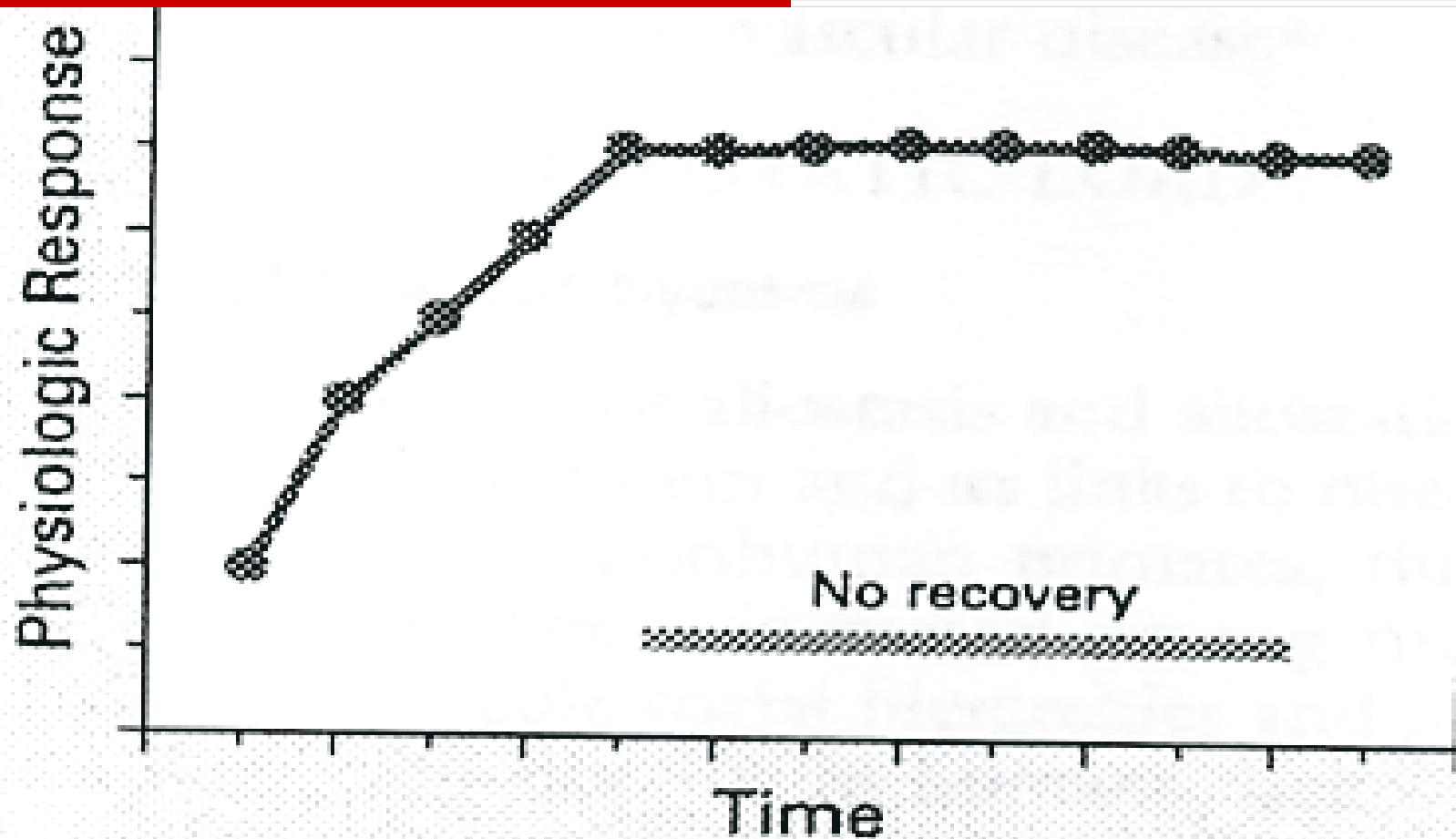
---

Allostasis



McEwen BS. Protective and damaging effects of stress mediators. N Eng J Med. 1998;338:171-9.

# Allostatic Load: Wear and Tear from Chronic Stress



McEwen BS. Protective and damaging effects of stress mediators. N Eng J Med. 1998;338:171-9.

# Stressed vs. Stressed Out

## □ Stressed

- Increased cardiac output
- Increased available glucose
- Enhanced immune functions
- Growth of neurons in hippocampus & prefrontal cortex

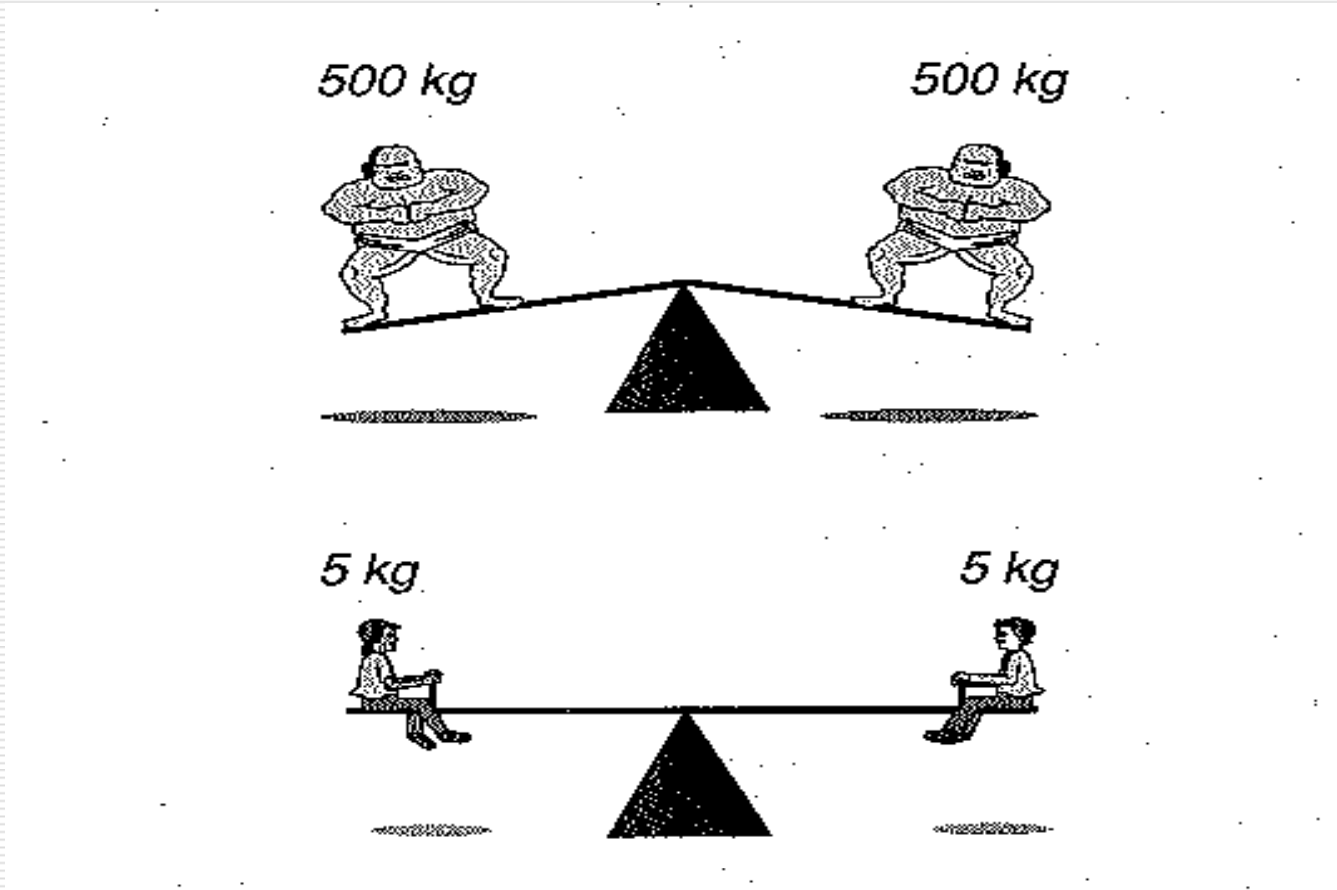
## □ Stressed Out

- Hypertension & cardiovascular diseases
- Glucose intolerance & insulin resistance
- Infection & inflammation
- Atrophy & death of neurons in hippocampus & prefrontal cortex



# Allostasis & Allostatic Load

---

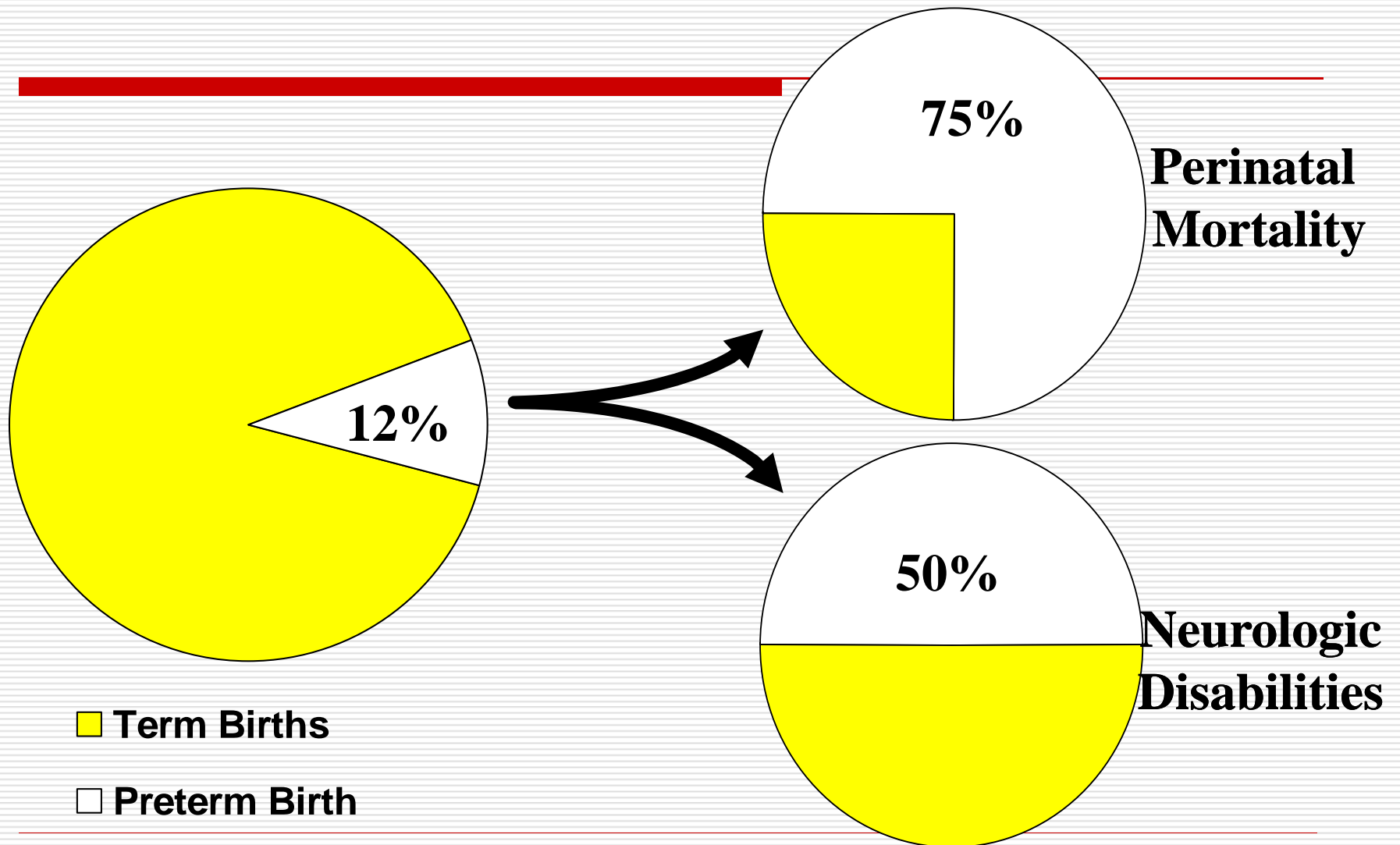


McEwen BS, Lasley EN. The end of stress: As we know it. Washington DC: John Henry Press. 2002

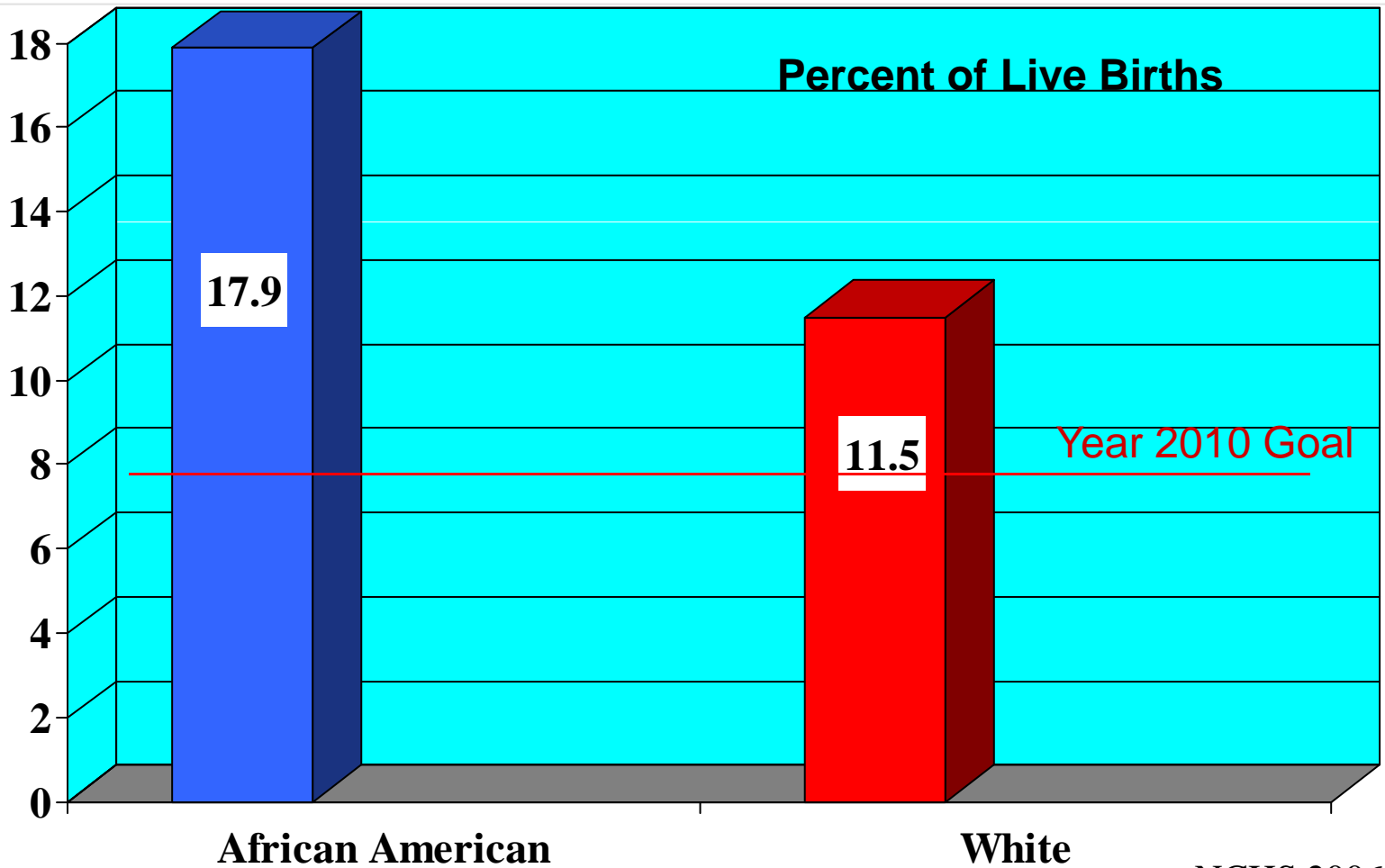
# Rethinking Preterm Birth



# Sequelae of Preterm Birth

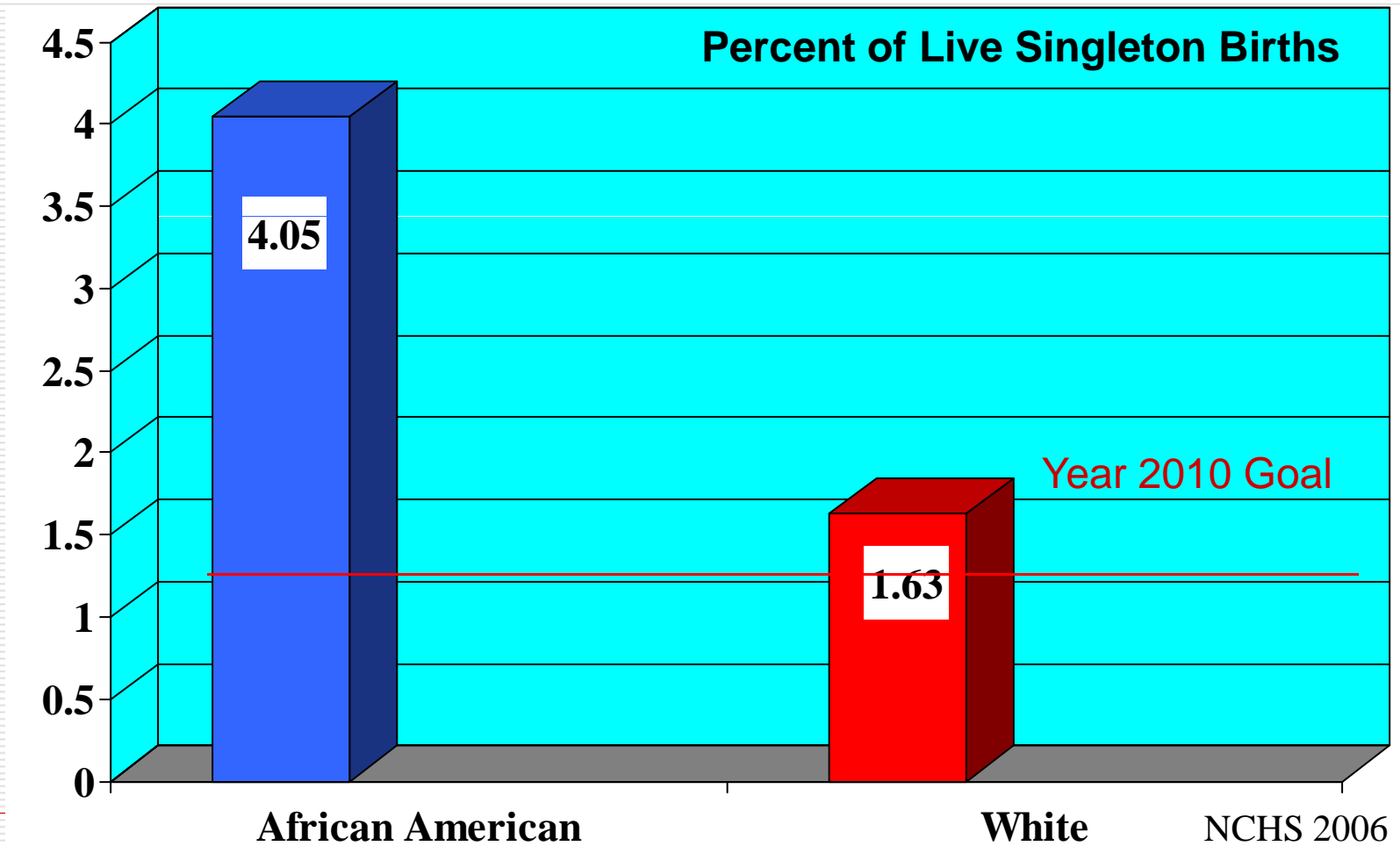


# Racial & Ethnic Disparities Preterm Births < 37 Weeks

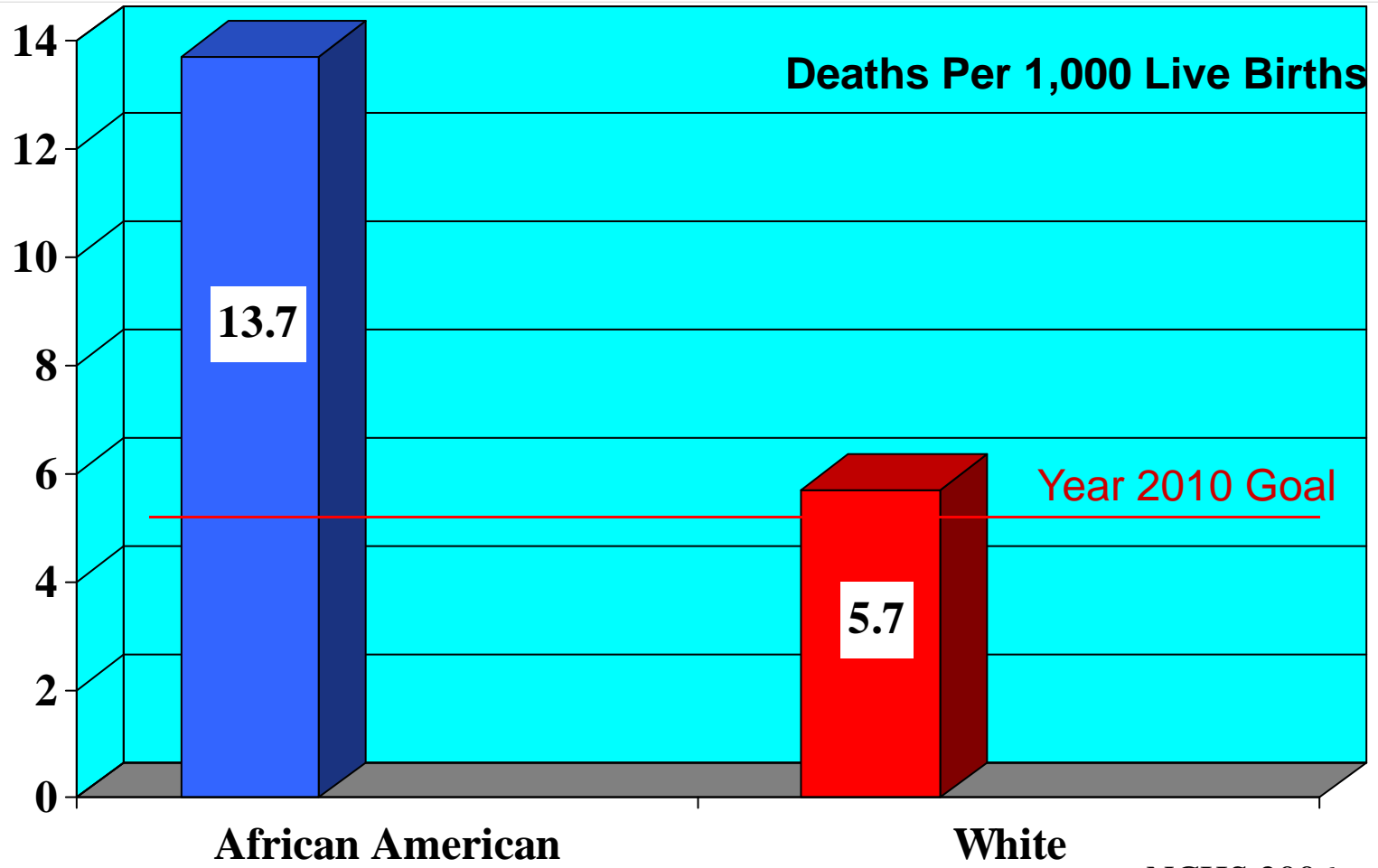


NCHS 2006

# Racial & Ethnic Disparities Very Preterm Births < 32 Weeks



# Racial & Ethnic Disparities Infant Mortality



NCHS 2006

# Rethinking Preterm Birth

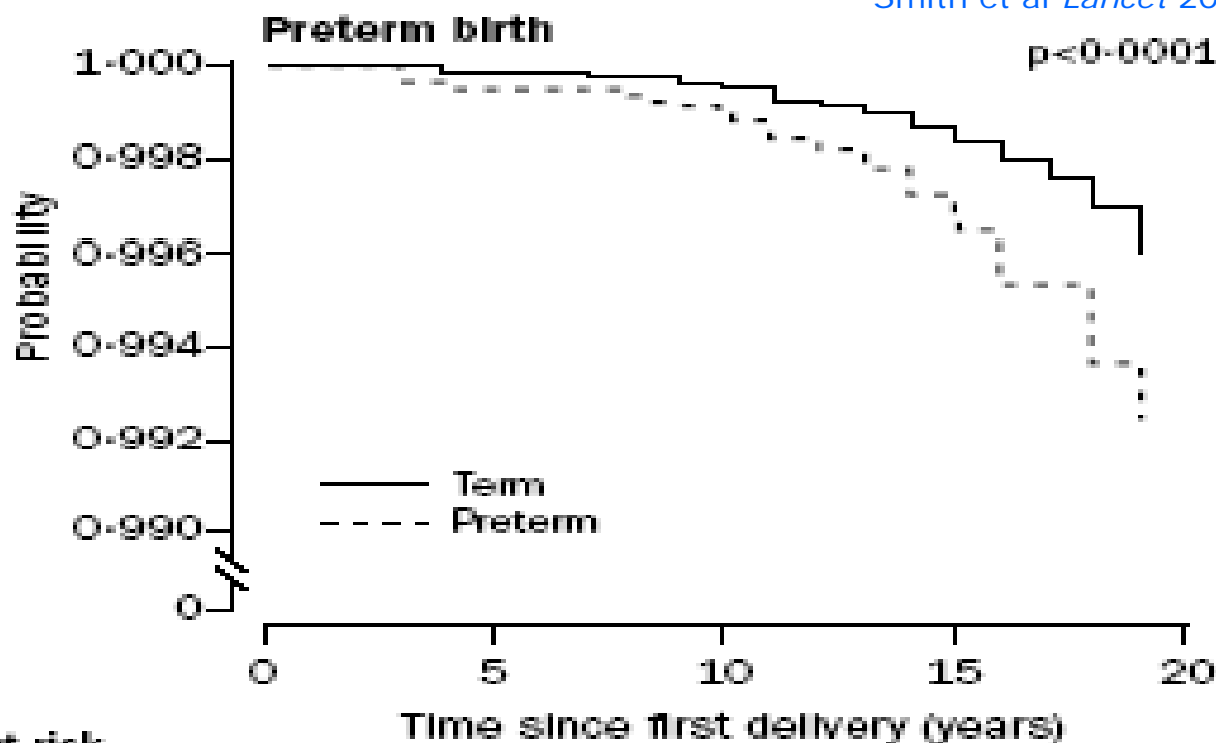
Vulnerability to preterm delivery may be traced to not only exposure to stress & infection during pregnancy, but host response to stress & infection (e.g. stress reactivity & inflammatory dysregulation) patterned over the life course (early programming & cumulative allostatic load)

- 
- An important objective of preconception care is to restore allostasis to women's health before pregnancy
-



# Preterm Birth & Maternal Ischemic Heart Disease

Smith et al *Lancet* 2001;357:2002-06



Number at risk

Term	121975	121813	121518	97169
Preterm	7315	7295	7262	5727

Kaplan-Meier plots of cumulative probability of survival **without** admission or death from ischemic heart disease after first pregnancy in relation to preterm birth

# Why Preconception Care?

## Summary

---

- Early Prenatal Care Is Too Late
    - To prevent some birth defects
    - To prevent implantation errors
    - To restore allostasis quickly enough to optimize fetal programming
-

# **Why Preconception Care?**

# **Before, Between, and Beyond Pregnancy**

**Put the W Back in MCH**

# **INTERCONCEPTION CARE**