Preconception Health & Health Care:
A Life-Course Perspective

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Why Preconception Care?

Why Preconception Care?

- Early prenatal care is too late.

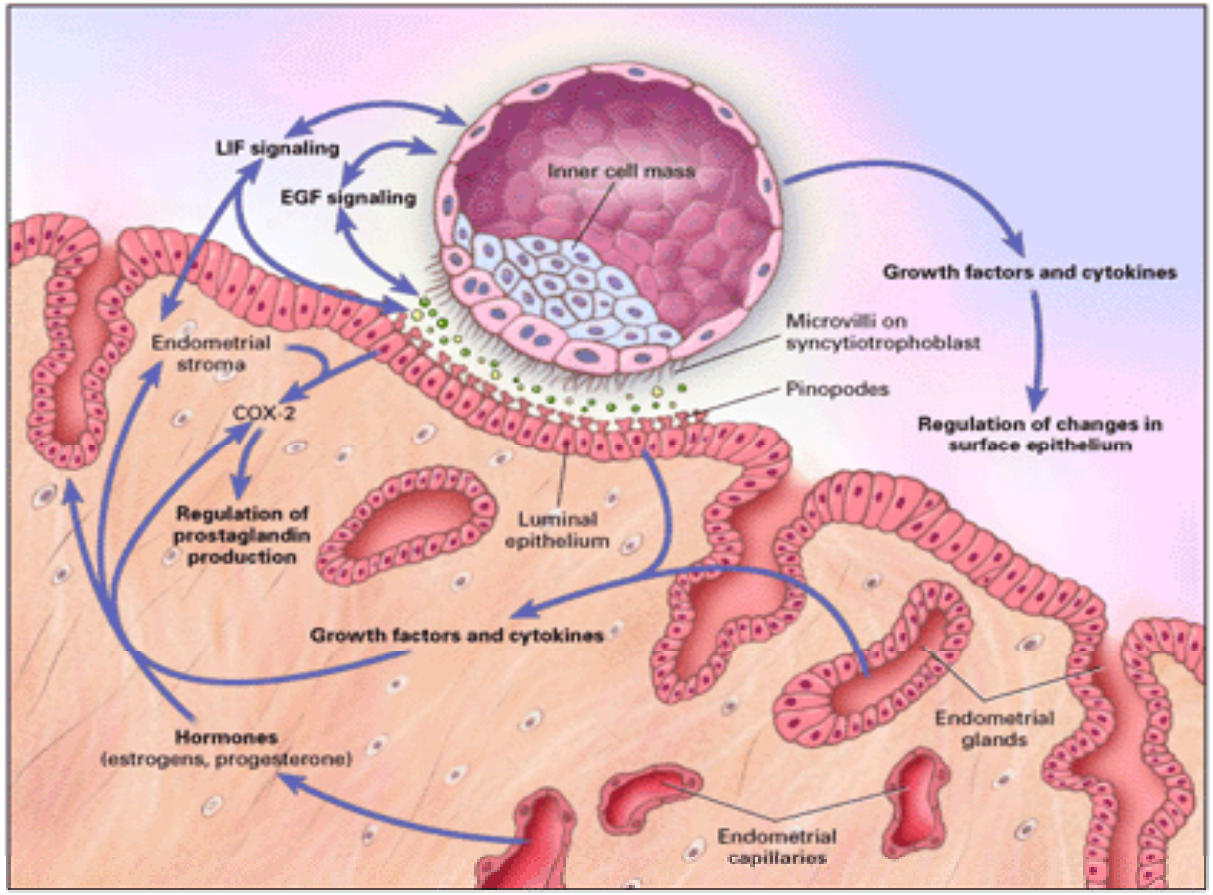
Early Prenatal Care Is Too Late

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

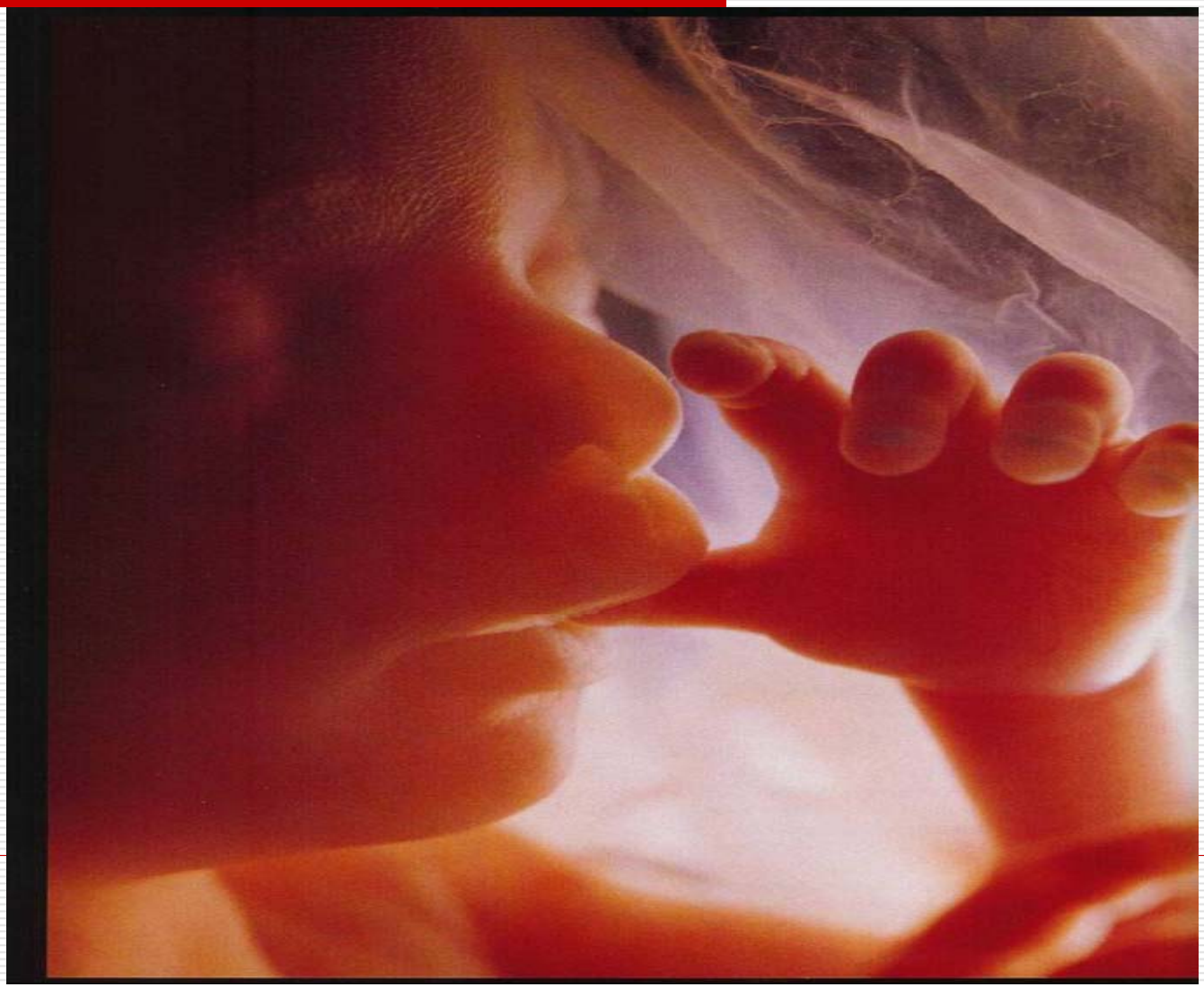


Norwitz ER, Schust DJ, Fisher SJ. Implantation and the survival of early pregnancy. N Engl J Med. 2001 Nov 8;345(19):1400-8.

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

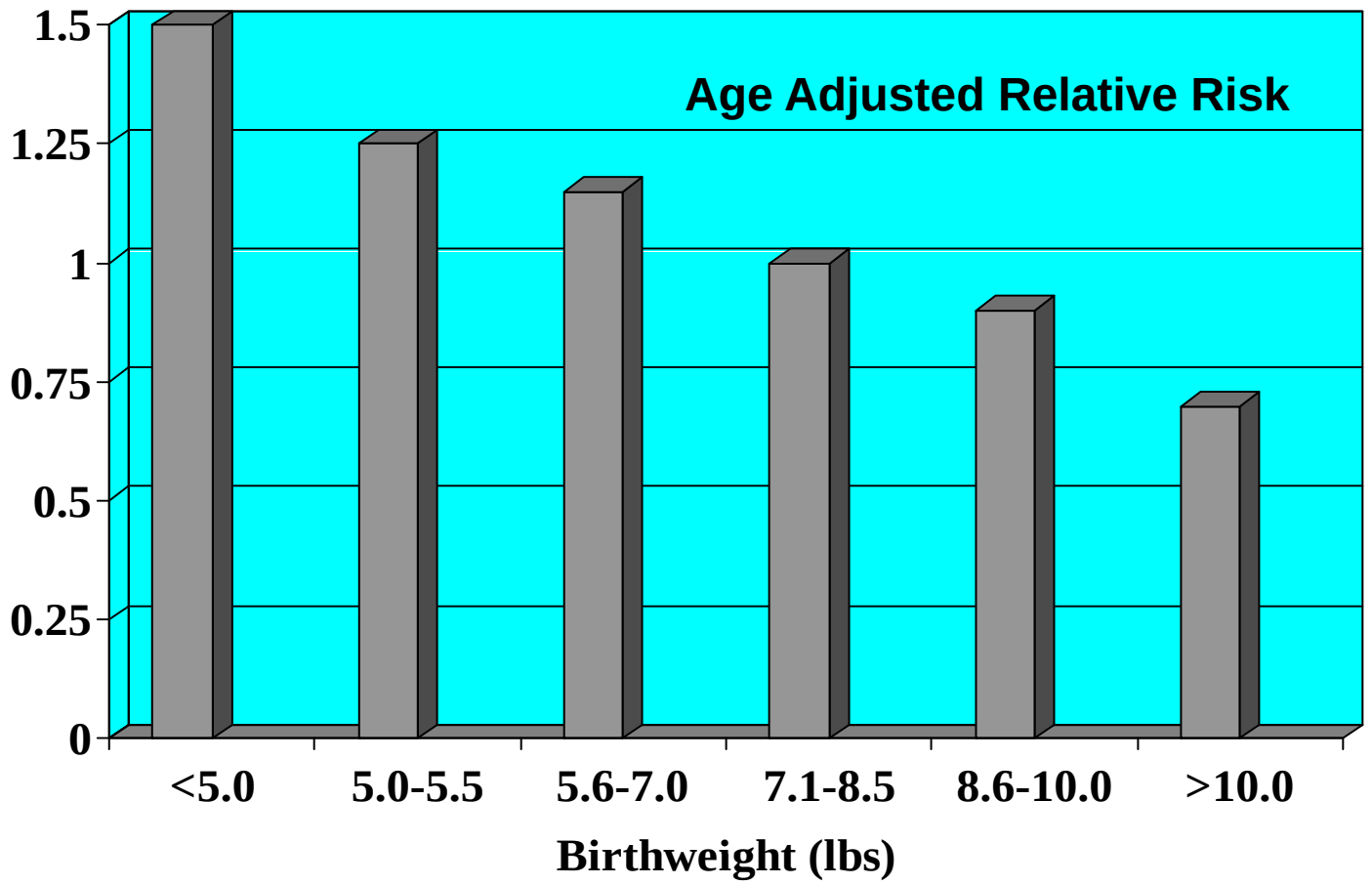
- A way of looking at life not as disconnected stages, but as an integrated continuum

Early Programming



Barker Hypothesis

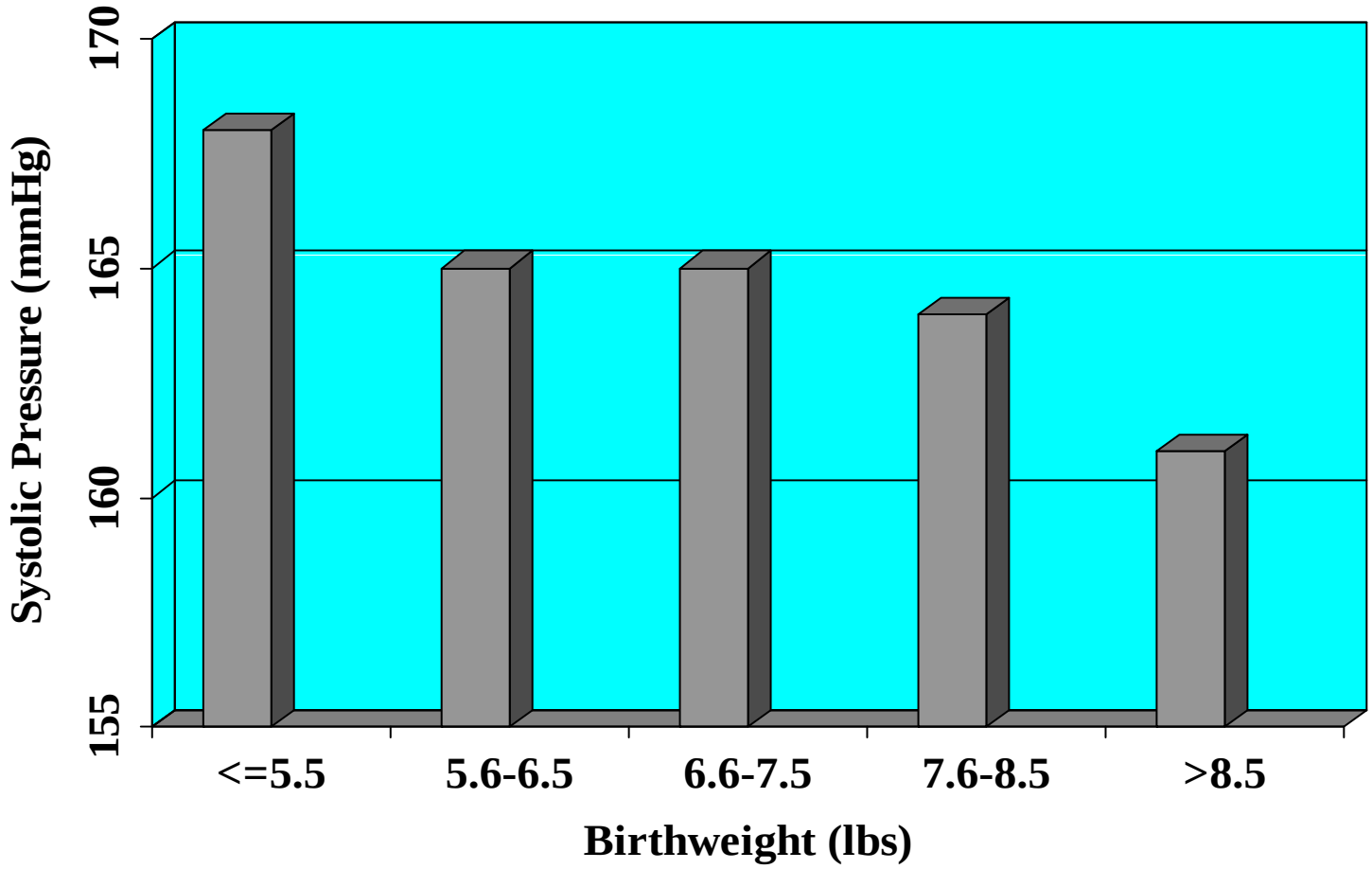
Birth Weight and Coronary Heart Disease



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 Jr 1997;315:396-400.

Barker Hypothesis

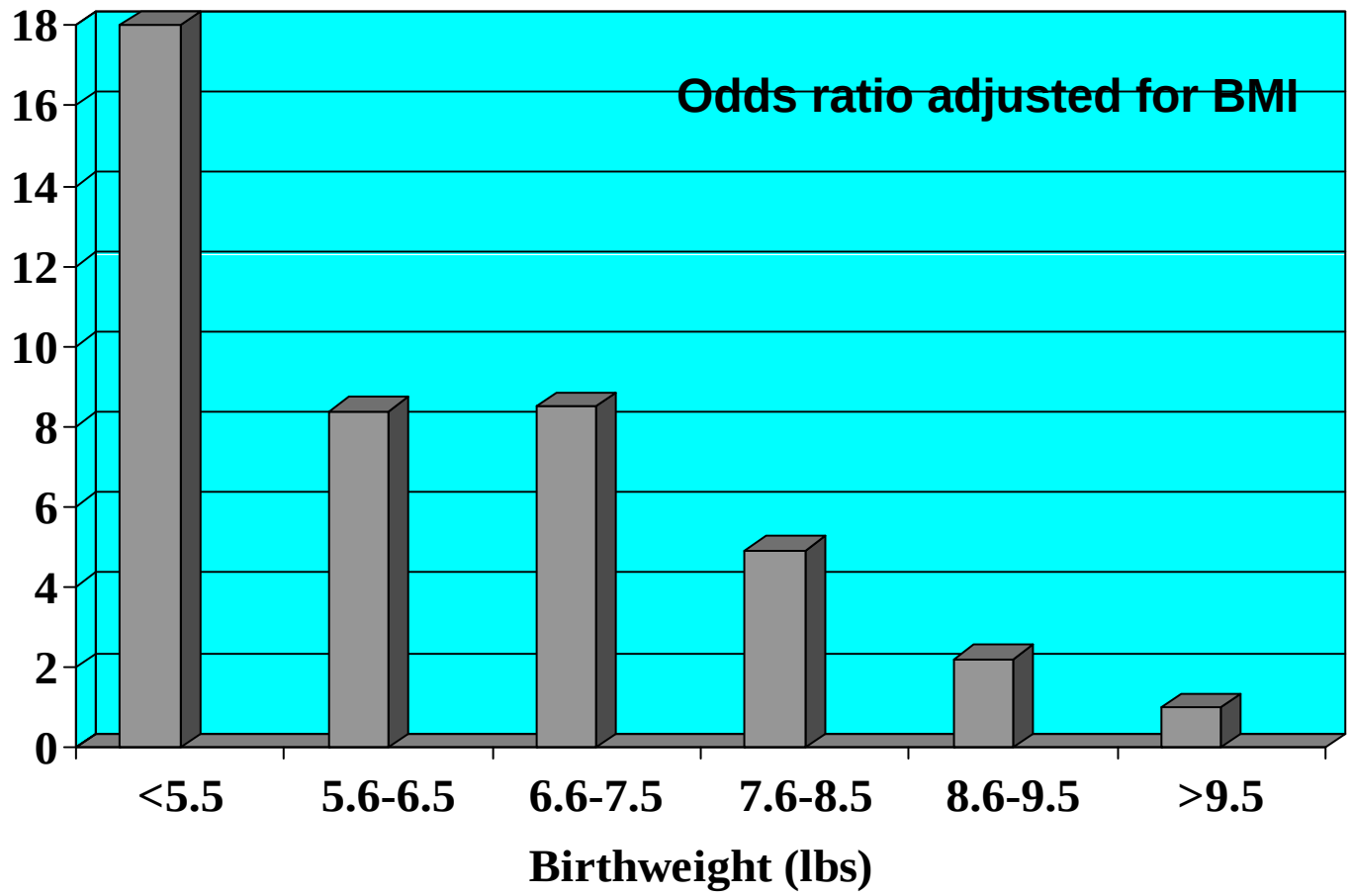
Birth Weight and Hypertension



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.

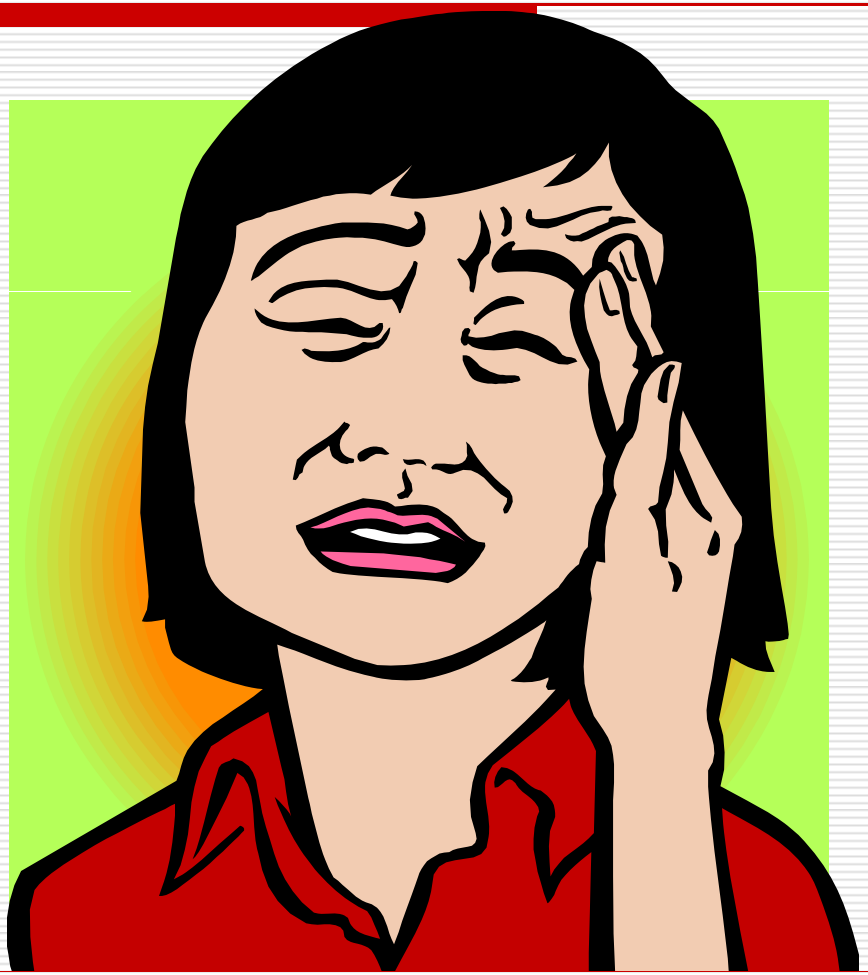
Barker Hypothesis

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

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

Prenatal Programming of the Hypothalamic-Pituitary-Adrenal Axis

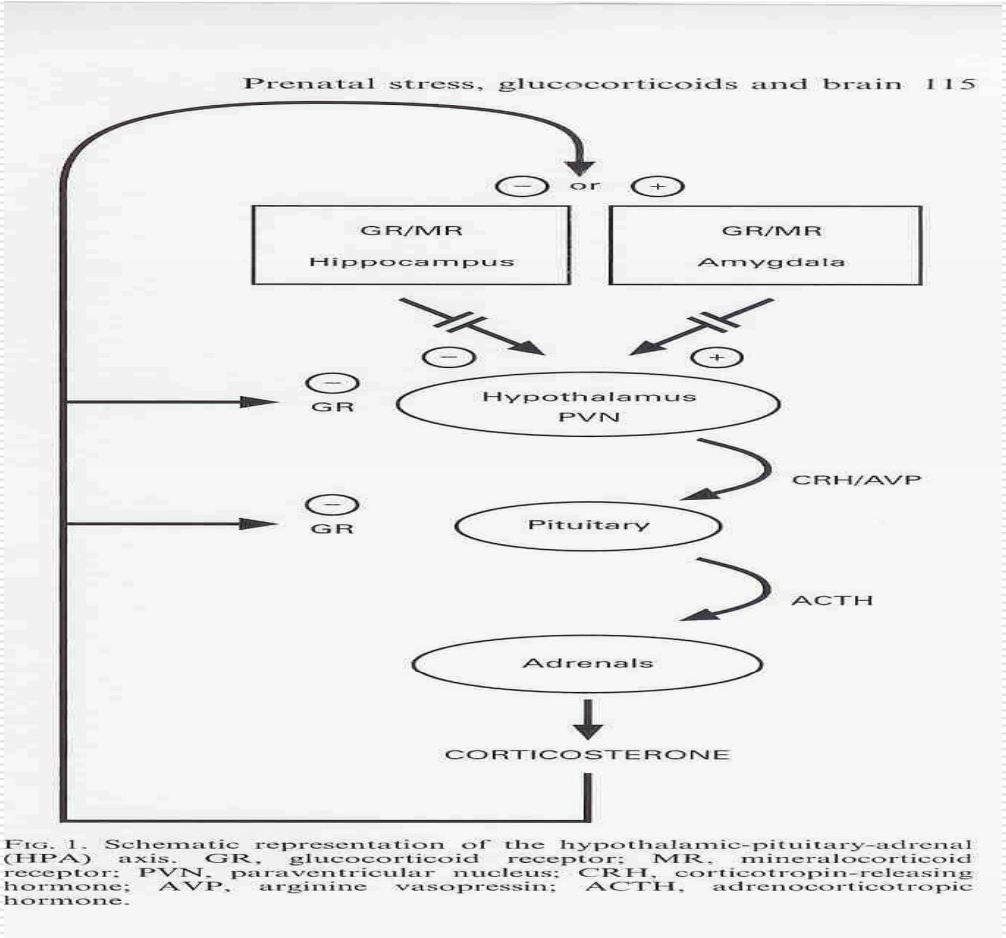
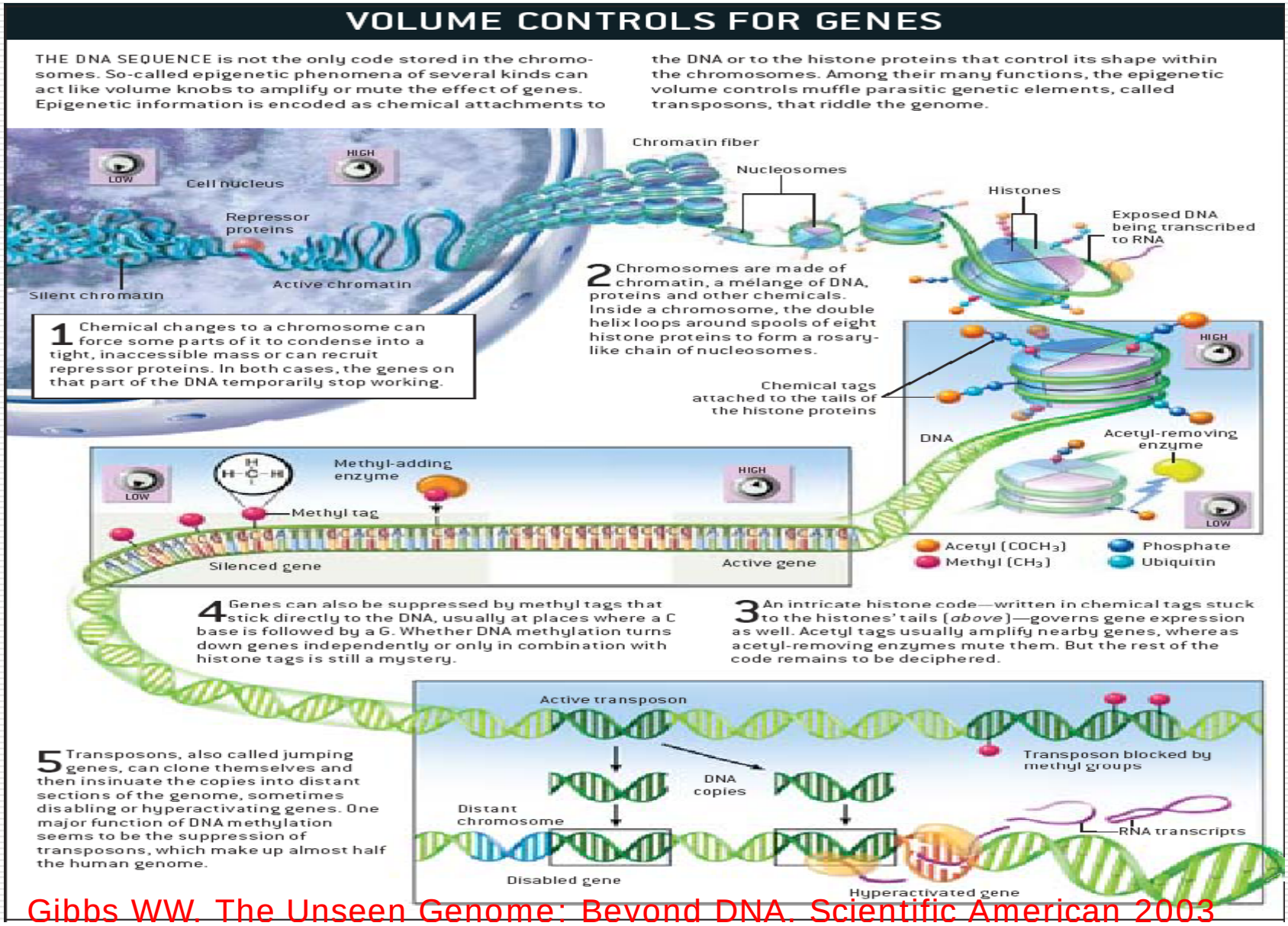


FIG. 1. Schematic representation of the hypothalamic-pituitary-adrenal (HPA) axis. GR, glucocorticoid receptor; MR, mineralocorticoid receptor; PVN, paraventricular nucleus; CRH, corticotropin-releasing hormone; AVP, arginine vasopressin; ACTH, adrenocorticotropic hormone.

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

Epigenetics



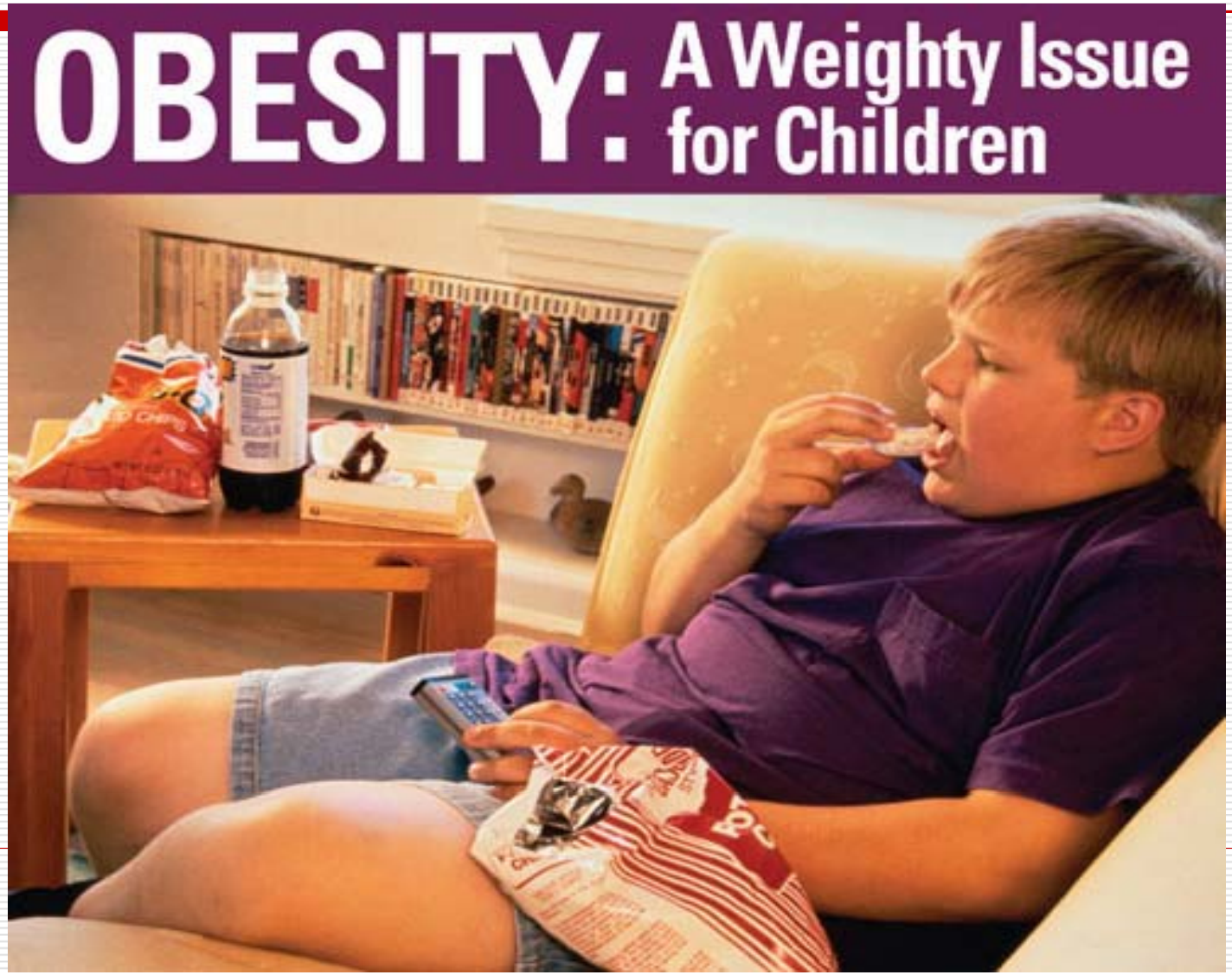
Gibbs WW. The Unseen Genome: Beyond DNA. Scientific American 2003

Epigenetics

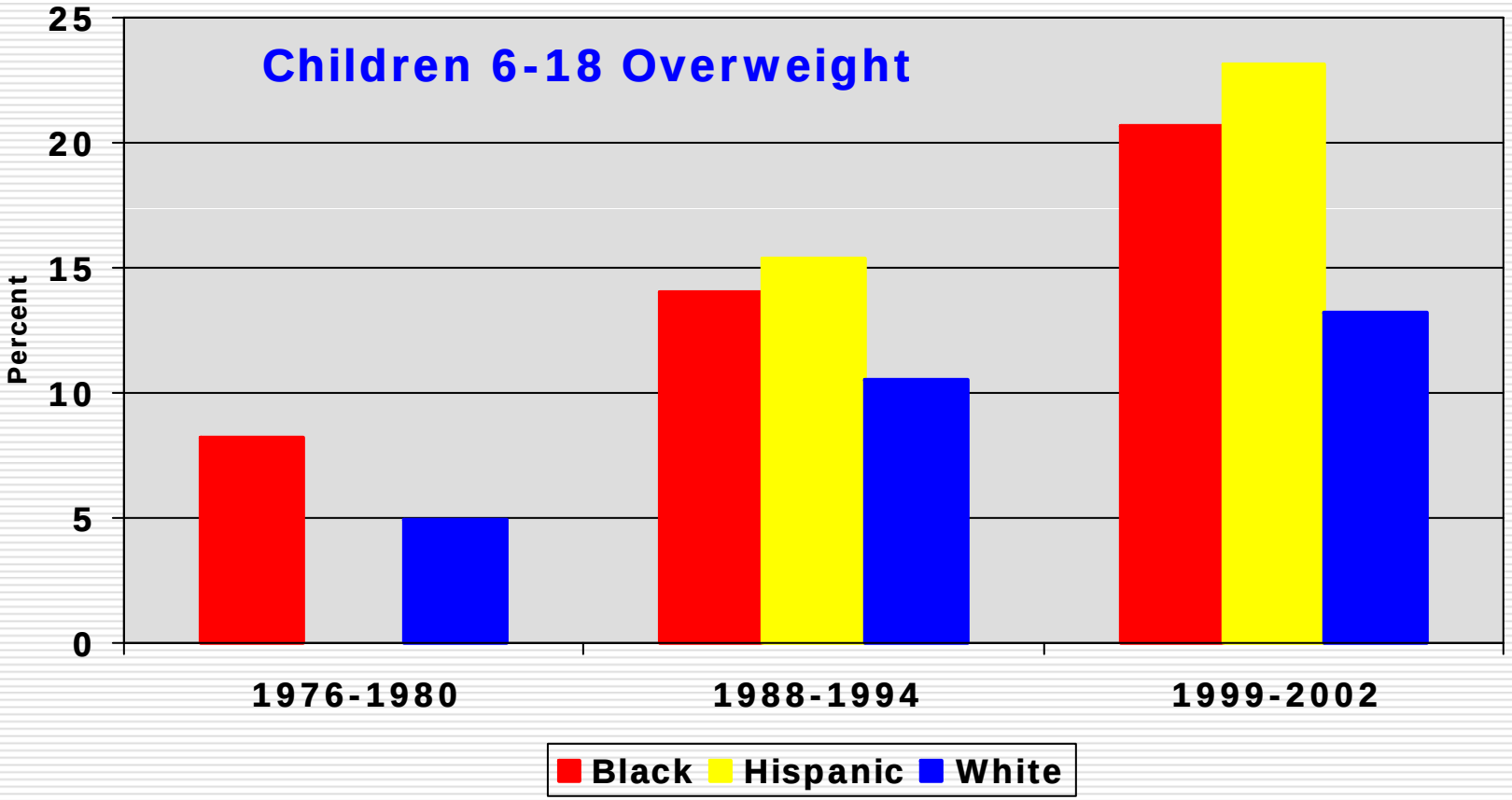
Same Genome, Different Epigenome

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



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 95th percentile ofr 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

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 MDConsult 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.

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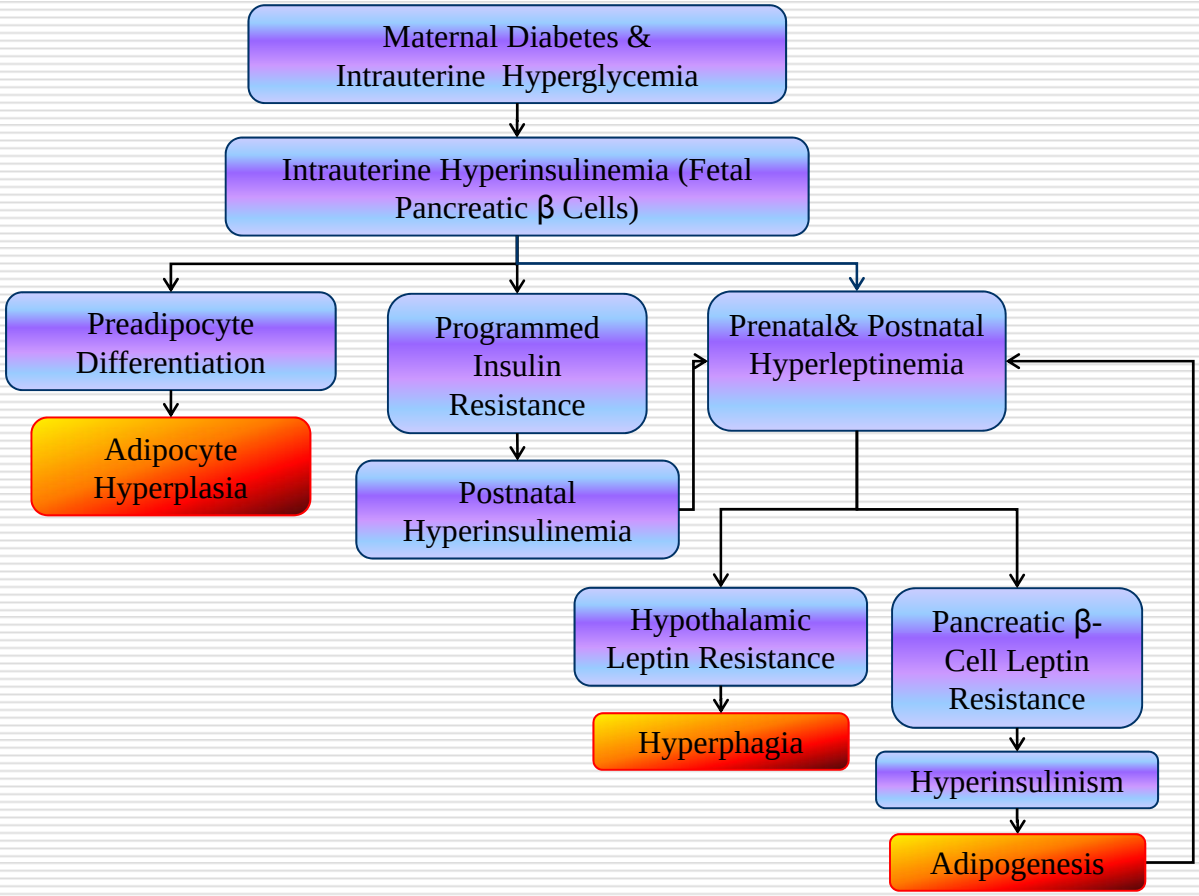
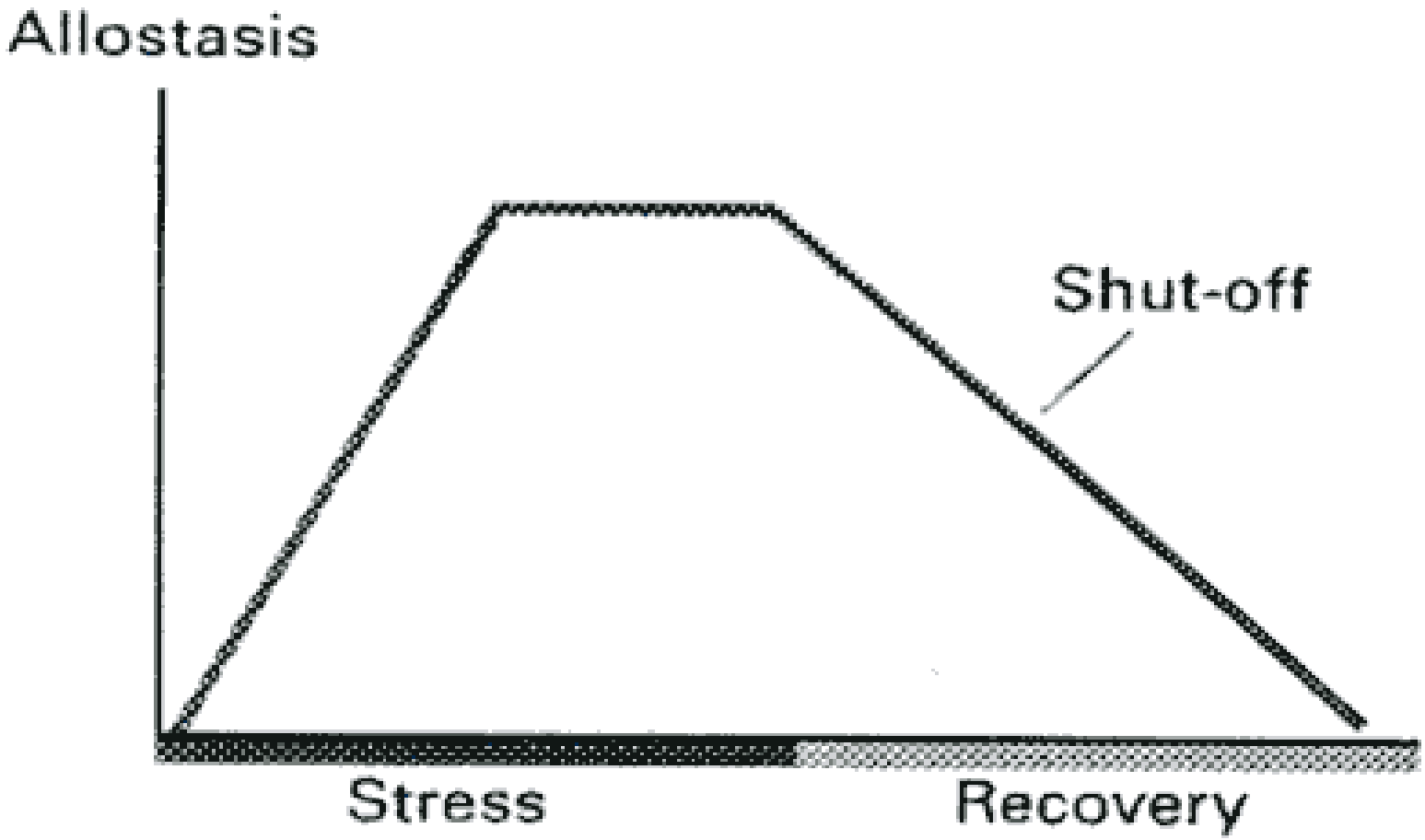
Prenatal Programming of Childhood Obesity



Cumulative Pathways

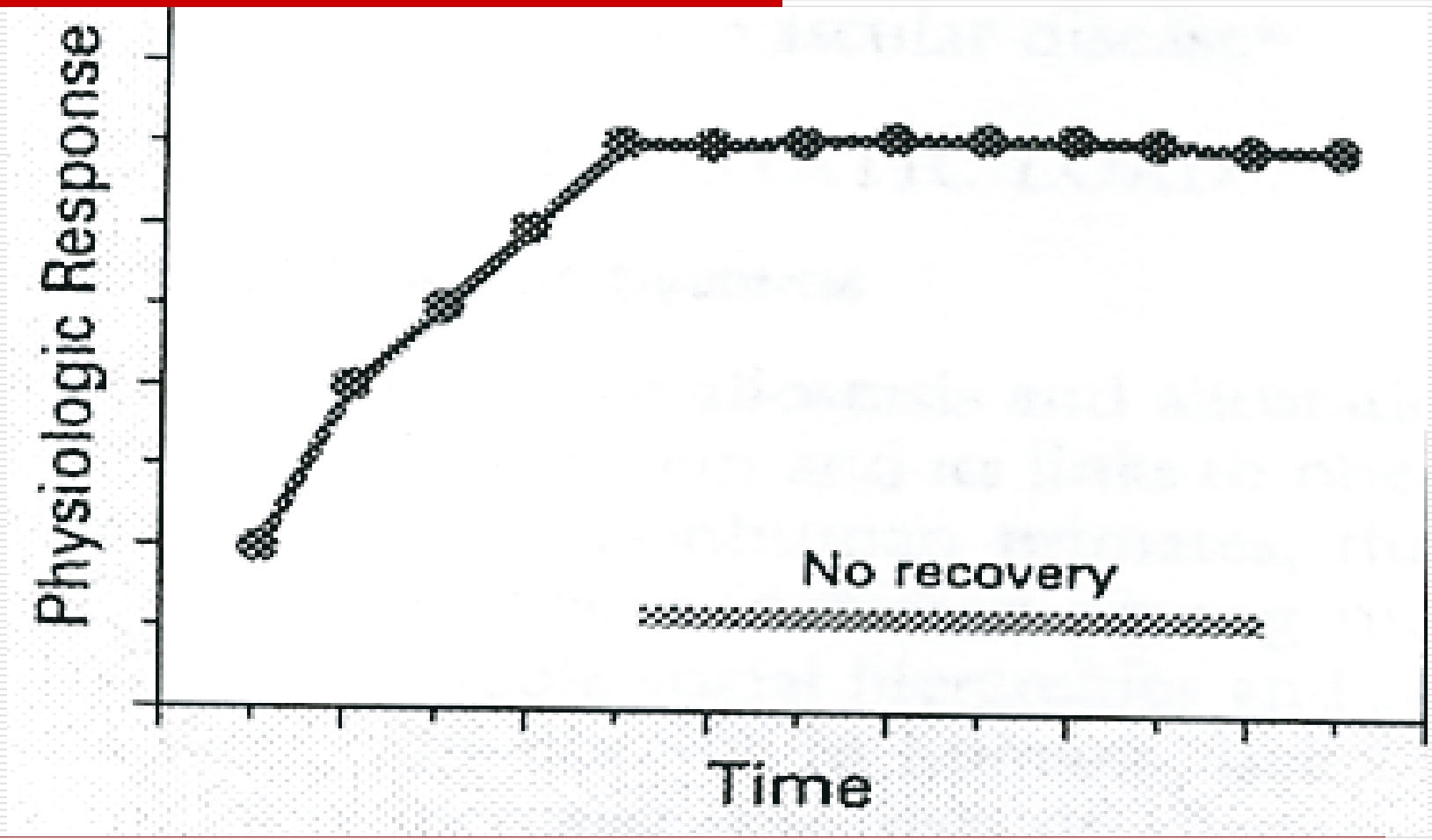

Photo: http://www.lam.mus.ca.us/cats/encyclo/smilodon/

Allostasis:
Maintain Stability through Change



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

Allostastic 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

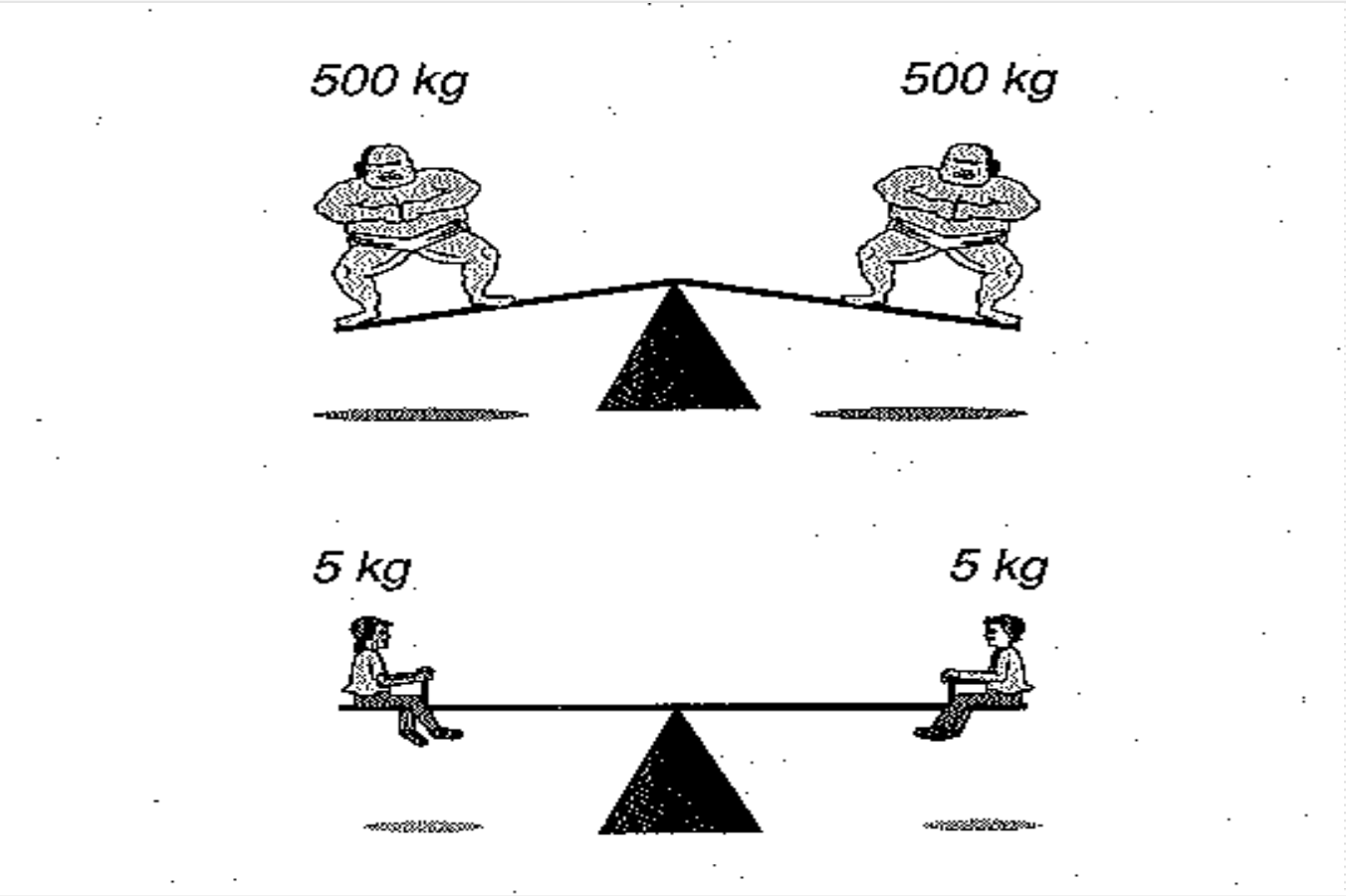
Stressed

- 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

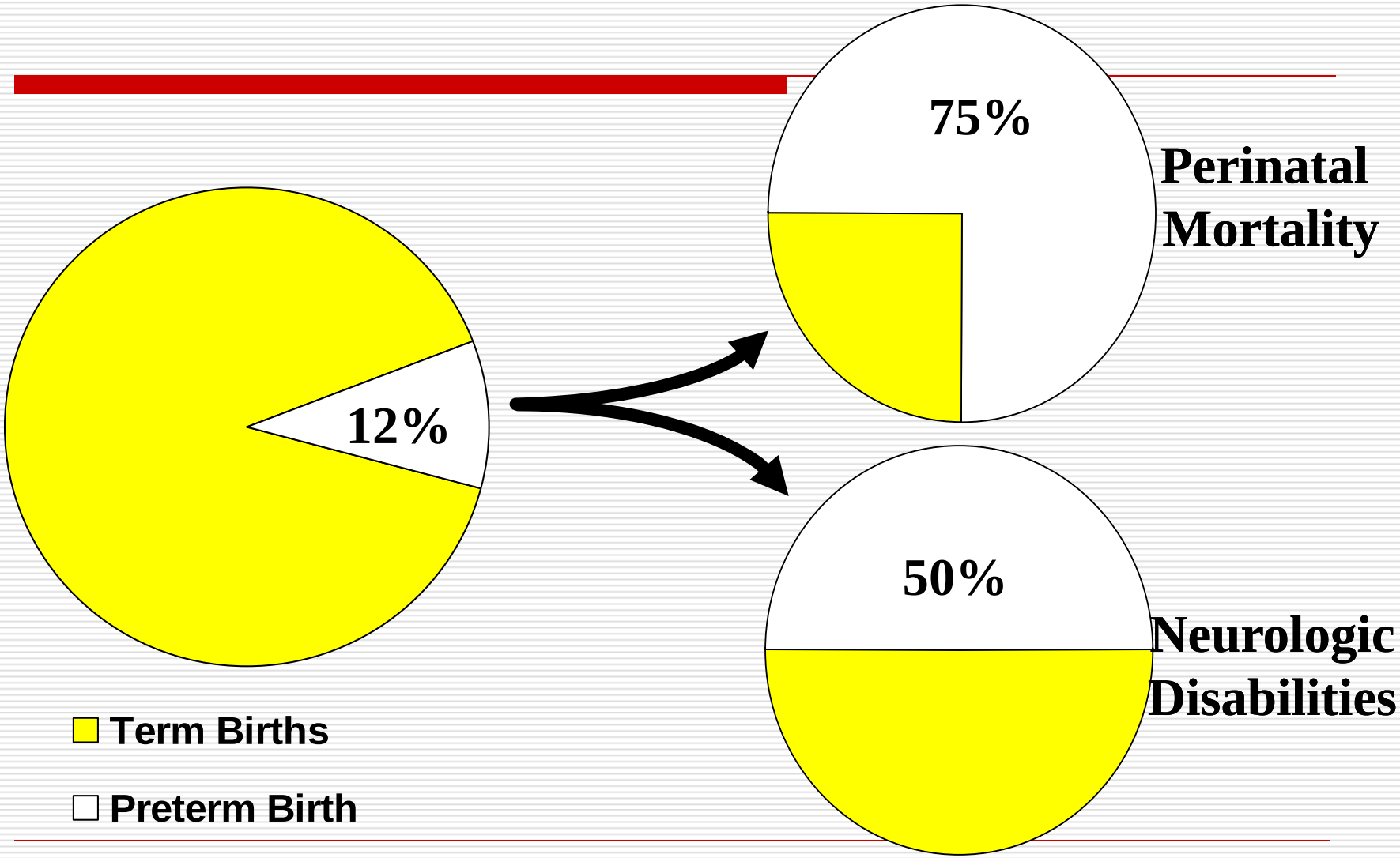
Allostasis & Allostatic Load



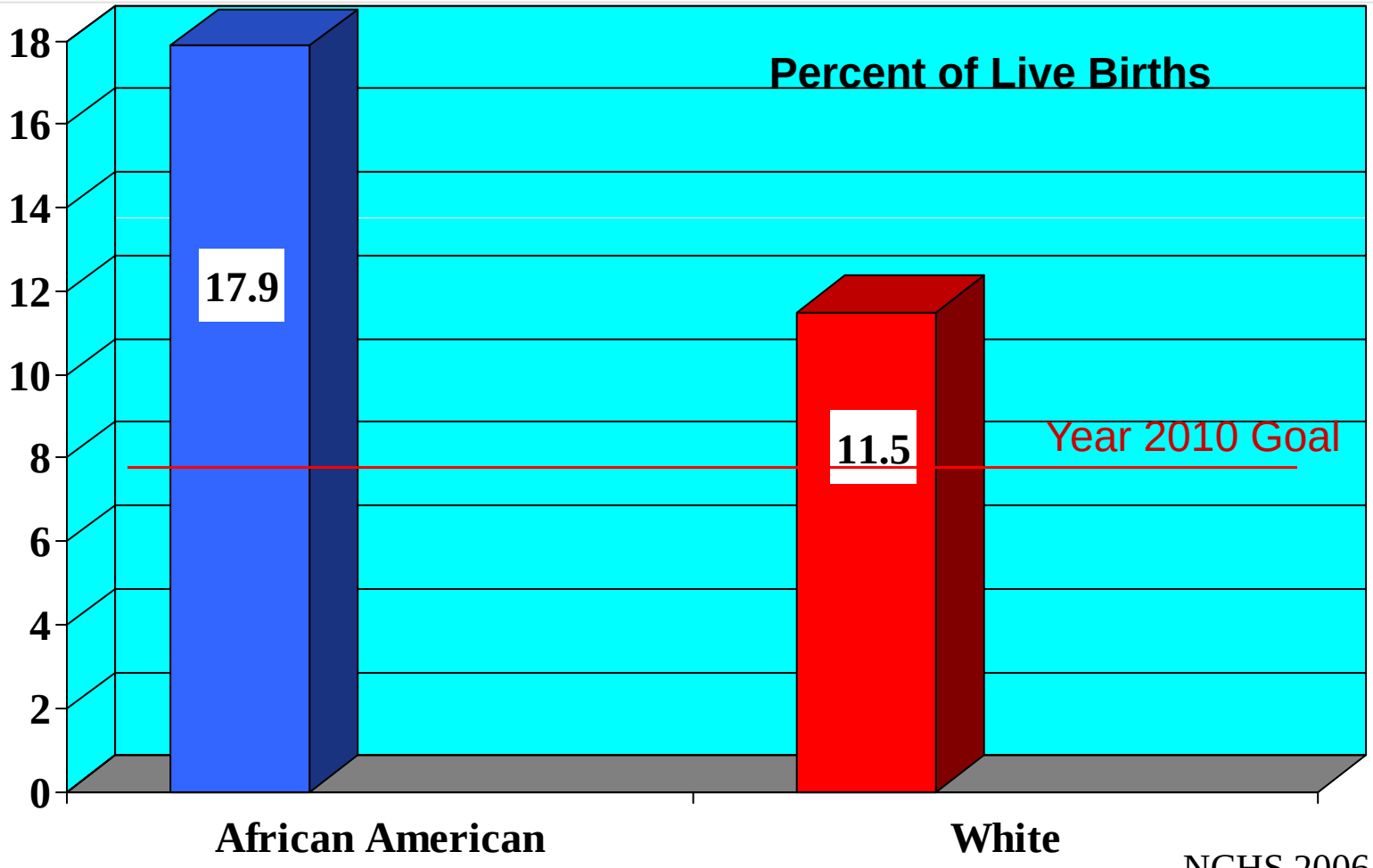
McEwen BS, Lasley EN. The end of stress: As we know it. Washington DC: John Henry Press. 2002

Rethinking Preterm Birth

Sequelae of Preterm Birth

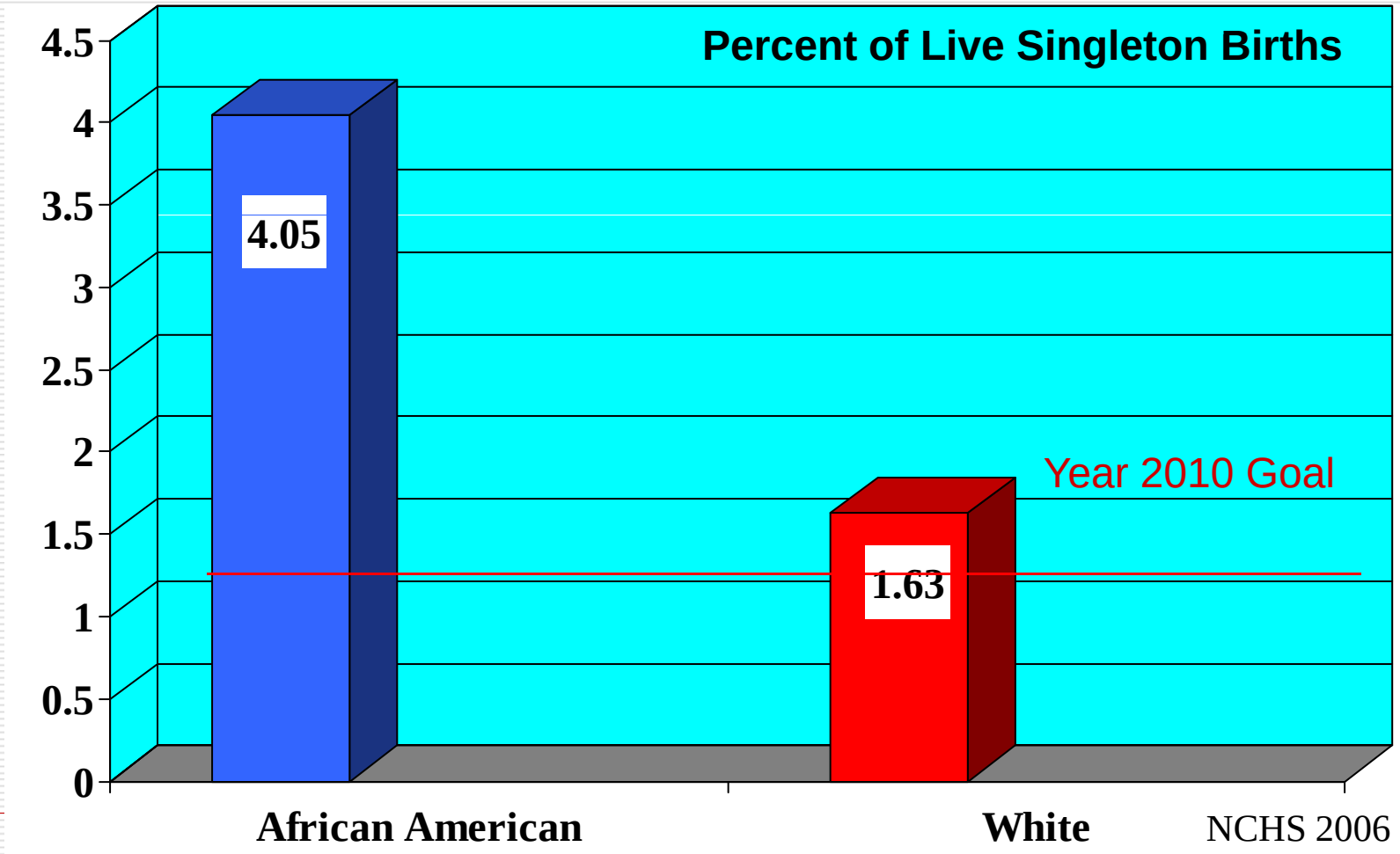


Racial & Ethnic Disparities
Preterm Births < 37 Weeks

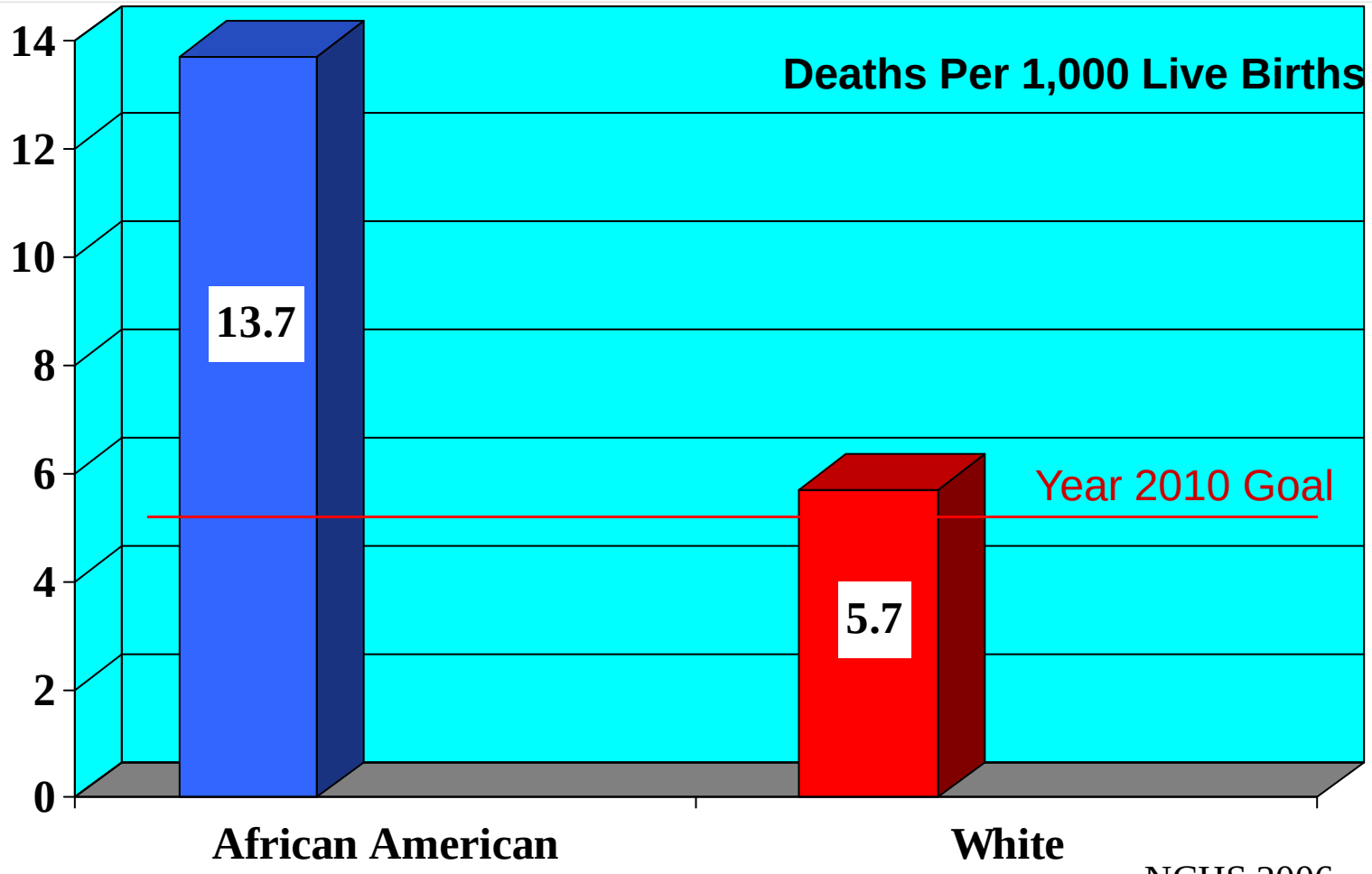


NCHS 2006

Racial & Ethnic Disparities
Very Preterm Births < 32 Weeks



Racial & Ethnic Disparities
Infant Mortality



NCHS 2006

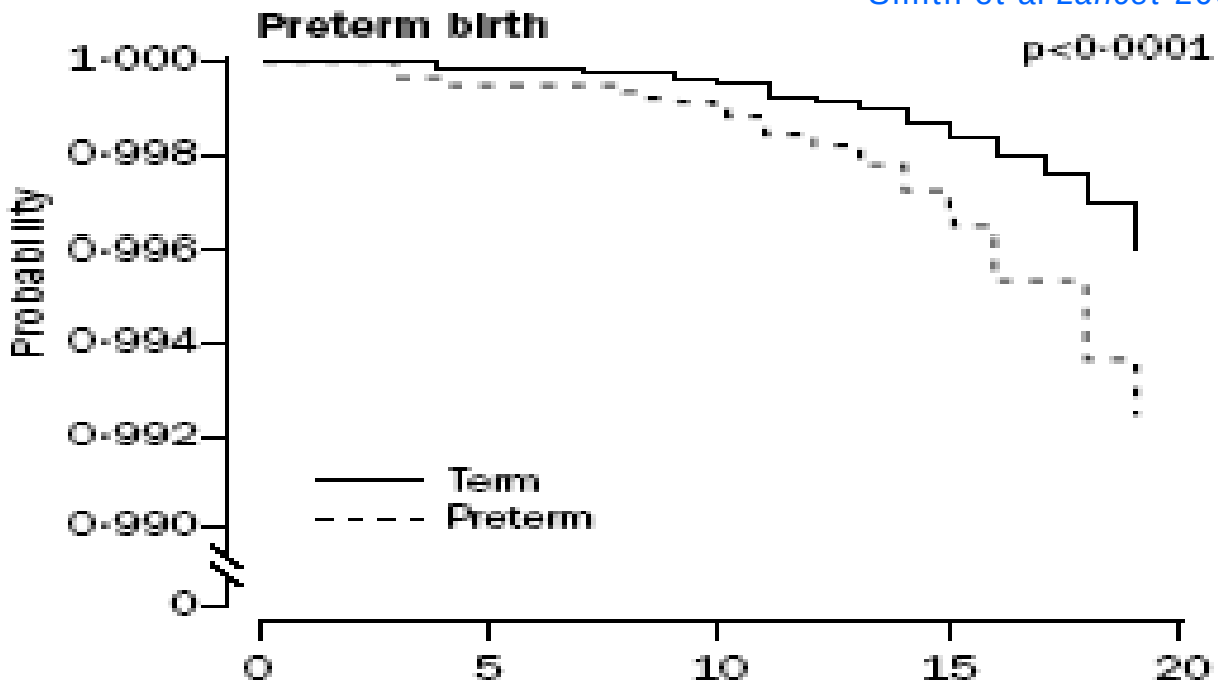
Rethinking Preterm Birth

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