Getting to the Roots: Early Life Risk Factors for Obesity and Chronic Disease

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"Giving every child the best start in life is crucial to reducing health inequalities across the life course. The foundations for virtually every aspect of human development-physical, intellectual and emotionalare laid in early childhood. What happens during these early years (starting in the womb) has lifelong effects on many aspects of health and well-beingfrom obesity, heart disease and mental health, to educational achievement and economic status. To have an impact on health inequalities we need to address the social gradient in children's access to positive early experiences."

Fair Society, Healthy Lives: Strategic Review of Health Inequalities in England Post-2010

Childhood Trauma Predicts Adult Health

Children born in Helsinki, Finland between 1934-44

320 were evacuated abroad during WW II—separated from their parents

- Average age at evacuation: 4.8 years old
- Average duration of evacuation: 1.7 years

60 years later, compared with children not evacuated, evacuees were much more likely to have:

- Heart disease (OR 2.0) and hypertension
- Type 2 Diabetes (OR 1.4)
- Depressive symptoms (OR 1.7)

 "This study is among the first to show that early life trauma predicts higher prevalence of cardiovascular disease and type 2 diabetes in late adulthood..."

Ann Med 2009;41:66-72, Am J Epidemiol 2007;166:1126-33, Am J Hum Biol 2008;20:345-51

Early Life Experience and the Brain

 Developing brain is remarkably shapeable and adaptable

"The brain's exquisite sensitivity to experience in early childhood allows traumatic experiences during infancy and childhood to impact all future emotional, behavioral, cognitive, social, and physiologic functioning."

Child Adolesc Psychiatr Clin N Am 1998;7(1):33-51

Brain Development



FIGURE 8-1 Human brain development. SOURCE: Charles A. Nelson, University of Minnesota. Reprinted with permission.

From Neurons to Neighborhoods: the Science of Early Child Development. National Academy of Sciences, 2000, p. 188

For diabetes risk, it matters what's happened...

- To us as adults
 - Diet and exercise choices
 - Food of poor nutritional quality: another stimulus to overeat
 - Stress and trauma
- To us as children
 - Nutrition and Stress
- To us in the womb
 - Nutrition and stress
- To our parents
 - Nutrition and stress
- To our grandparents
 - Nutrition and stress
- "It is through epigenetic marks that environmental factors like diet, stress and prenatal nutrition can make an imprint on genes that is passed from one generation to the next." *Time* 1/18/10



International Diabetes Federation Conference on Type 2 Diabetes Etiologies 2002

- **1.** Genetics
- 2. Fetal Origins
- 3. Lifestyle
- 4. Stress

1. Genetics

Genes Inherited

It does matter what genes we inherit

- But proportion of predisposition explained for type 2 DM (5-10%) and BMI (1%) is *small* NEJM 2010;363:2339-50
- Only 15% of genes in cells "turned on" at any given time

Genes Expressed

- "Epigenetics": the "on/off switches" for genes
 - reaction to the environment
 - not always reversible if at key developmental stage of life
 - heritable—some are passed to next generation
 - How the experiences of one generation help prepare the next
 - we know the body's "on/off switches": DNA methylation, histone acetylation, microRNA

JAMA 2005;294:2221-4 and NEJM 2008;359:61-73

Epigenetics

■ No longer "nature vs. nurture"—nurture *affects* nature

- Rat pups raised by nurturing mothers
 - Gene which affects stress hormone receptors "turned on"
 - Grow up to be stress resilient
- Rat pups raised by neglectful mothers
 - Gene which affects stress hormone receptors "turned off"
 - Grow up to be very stress reactive
- Same process has now been shown in humans

Nature Neuroscience 2009;12:342-348

Epigenetics and Diabetes

Epigenetic mechanisms play important role in DM predisposition

- Gene imprinting comes from <u>both</u> parents *Diabetes Care* 2010;33:1823-1828
- Risk of dying from diabetes strongly related to grandparents' nutritional status Eur J Human Genetics 2007;15:784-790 and 2002;10:682-688

2. Fetal Origins



Alcohol/Drugs Nutrition Smoking Maternal Diabetes Toxic/Infectious Exposures Maternal Low Birth Weight Maternal Stress/Mental Health Mother's own Childhood Current/Prenatal

Low Birth Weight (SGA) and Preterm

Babies can be either/both SGA and Preterm
 they <u>both</u> are strongly associated with that baby's later risk for chronic disease

Diabetes 2009;58:523-526

Maternal stressful life events during 1st trimester
 <u>↑ risk</u> of preterm birth (OR 2.4) and SGA

Am J Obstet Gynecol 2010;203:34.e1-8



FIG. 7. The physiological mechanisms underlying the programming of the separate and combined elements of the metabolic syndrome



Mcmillen IC, *et al. Physiol. Rev.* 85: 571-633 2005; doi:10.1152/physrev.00053.2003

Physiological Reviews 5 1 1

In utero Risks for Later Type 2 Diabetes

Fetuses of obese mothers develop insulin resistance *in utero*

- "...maternal obesity creates a significant risk for the next generations with metabolic compromise already apparent at birth."
 Diabetes Care 2009;32:1076-1080
- Maternal diet during pregnancy epigenetically affects child's adiposity at age 9 yrs
 Diabetes 2011;60:1528-1534
- Inverse relationship between birth weight and risk of diabetes *JAMA* 2008;300:2886-2897

JAMA 2009;301:2234-2242

Low birth weight is related to nephron number and future risk of kidney disease
Kidney Int 2005;68:S68-S77

"Fetal Programming of Type 2 Diabetes"

- "...intrauterine environment may modify gene expression permanently. ...They might also be inherited transgenerationally, affecting the health of future generations. ...During intrauterine life, there are waves of epigenomic modification, intimately associated with growth and development, and opportunities galore for environmental factors to influence these processes. A fetus thus programmed travels a path of limited options." *Diabetes Care* 2007;30:2754-5
- "It is important to understand that the story is not about birth weight but about fetal programming, and that intergenerational prevention of type 2 diabetes (primordial prevention) will need to target maternal nutrition and metabolism. ...Prevention of fetal programming of diabetes will need to concentrate on the health of young girls." *Diabetes Care* 2010;33:1146-8

3. Lifestyle

Overeating as an Adaptive Response

Food Insecurity:

- Prevalence of overweight in women [^]s as food insecurity [^] Journal of Nutrition. 2001;131:1738-1745
- Pregnancy: food insecurity assoc with pregravid obesity, ↑ gest wt gain, and gest diabetes

J Am Diet Assoc 2010;110:692-701

42% of households below poverty level are food insecure, 21% of households w/children

NEJM 2010;363:6-9

- Carbohydrates affect brain serotonin levels Obes Res 1995 Suppl 4:477S-480S
- "Comfort Foods" ↓ HPA axis stress response Proc Natl Acad Sci 2003;100:11696-11701

4. Stress

- Chronic exposure to Intimate Partner Violence almost doubles (OR 1.8) risk of obesity at age 5 years.
 Arch Pediatr Adolesc Med 2010;164:540-546
- Childhood SES associated with later type 2 DM and Obesity
 BMC Public Health 2010;10:525
- Toddlers who showed insecure attachment to their mothers at age 2 had a 30% increased risk of obesity by age 4 ¹/₂

Arch Pediatr Adolesc Med 2011;165:235-242

"As the twig is bent, so the tree inclines" Adverse Childhood Experiences (ACE) Study --Overall Exposure: 86% (among 7 tribes) Non-Native Native **Physical Abuse-M** $40^{\circ}/_{\circ}$ 30% Physical Abuse-F 27 42 Sexual Abuse-M 16 24 Sexual Abuse-F 31 25 Emotional Abuse 11 30 Household ETOH 27 65 Four or More ACEs 6 33

Am J Prev Med 2003;25:238-244

ACEs and Adult Health

■ ACE Score ≥4

- 4-12 x risk for alcoholism, drug abuse, depression and suicide attempt
- 2-4 x risk for smoking, teen pregnancy, STDs, multiple sexual partners
- 1.4-1.6 x risk for severe obesity
- Strong graded relationship at <u>all</u> levels of ACEs for almost all outcomes, including heart disease

Am J Prev Med 1998;14:245-258 and Circulation 2004;110:1761-6

- Nurse's Health Study II: Childhood abuse
 - dose-response associations (HR \leq 1.69) with risk of diabetes in adult women
 - only *partly* explained by their ↑ BMI *Am J Prev Med* 2010;39:529-536

What is the average ACE score of: --the children in your community? --their parents? What is your ACE score?

Stress in Children

Positive

Normal/necessary part of healthy development

■ First day with new caregiver; immunization

Brief increases in heart rate and stress hormones

Tolerable

- More severe, longer lasting stressor
 - Loss of a loved one, natural disaster, injury

 If buffered by relationship with supportive adult(s), brain and body can recover

Toxic

- Strong, frequent, prolonged adversity
 - Abuse, neglect, caregiver mental illness, poverty

 If no adult support, can disrupt brain and organ development longterm

Center on the Developing Child, Harvard Univ.

"Childhood Trauma...

"...is probably our nation's single most important public health challenge...

- ...chronic maltreatment has pervasive effects on the development of mind and brain.
- Developmental trauma sets the stage for unfocused responses to subsequent stress, leading to dramatic increases in the use of medical, correctional, social, and mental health services."

Complex trauma/toxic stress

- e.g. abuse; neglect; exposure to DV, community violence; poverty; caregiver mental health problems
- worse when caregiver is source of trauma or even just if they are unable to help child process traumatic experiences

van der Kolk, 2005. Psychiatric Annals 35(5):374-378

SIDEBAR 1.

Domains of Impairment in Children Exposed to Complex Trauma I. Attachment **IV.** Dissociation **VI.** Cognition Problems with boundaries Distinct alterations in states of Difficulties in attention regulation and consciousness executive functioning Distrust and suspiciousness Amnesia Lack of sustained curiosity Social isolation Depersonalization and derealization Problems with processing novel Interpersonal difficulties information Two or more distinct states of Difficulty attuning to other people's consciousness Problems focusing on and completing emotional states tasks Impaired memory for state-based events Difficulty with perspective taking Problems with object constancy Difficulty planning and anticipating II. Biology Problems understanding responsibility V. Behavioral control Sensorimotor developmental problems Learning difficulties Poor modulation of impulses Problems with language development Analgesia Self-destructive behavior Problems with coordination, balance, Problems with orientation in time and body tone Aggression toward others space Somatization Pathological self-soothing behaviors Increased medical problems across Sleep disturbances VII. Self-concept a wide span (eq, pelvic pain, asthma, Eating disorders skin problems, autoimmune disorders, Lack of a continuous, predictable sense Substance abuse pseudoseizures) of self Excessive compliance Poor sense of separateness **Oppositional behavior** Disturbances of body image III. Affect regulation Difficulty understanding and complying Low self-esteem Difficulty with emotional self-regulation with rules Shame and guilt Difficulty labeling and expressing Reenactment of trauma in behavior or feelings play (eg, sexual, aggressive) Problems knowing and describing internal states Difficulty communicating wishes and needs

Cook, et al. 2005. Psychiatric Annals 35(5) p. 392



Reducing Prenatal and Early Life Risk Factors for Obesity and Chronic Disease

Parenting is Key

- 2-3x ↑ risk for anxiety and disruptive behavior disorders and major depression in children of depressed parents
- Treating the mothers' depression reduces symptoms in <u>both</u> mothers and children

JAMA 2006;295:1389-1398

 Maternal warmth buffers the effects of low early-life SES on pro-inflammatory signaling in adulthood. *Molecular Psychiatry* 2010;doi:10.1038/mp.2010.53

Prenatal/Early Life Home Visiting

- One of the key evidence-based interventions proven to improve the life trajectories of low income women and children
 - Positive effects now shown up to age 19 yrs

Arch Pediatr Adolesc Med 2010;164:9-15, 412-418, 419-424

- If home visiting were a medication, it would be malpractice not to provide it
- Tribal Maternal, Infant & Early Childhood Home Visiting Program
 - Administered by ACF
 - 18 tribes/T.O.'s now funded to provide home visiting

Nurse-Family Partnership



Example of an evidence-based home visiting program

 Works with vulnerable first-time mothers living in poverty—starting early in pregnancy thru child's 2nd birthday

Goals: Improve prenatal care, quality of parenting and life prospects for mothers by partnering them with a registered nurse.



Academic Achievement

Grades 1–3, Age 9—Memphis (Born to low-resource mothers)



Source: Reproduced with permission from *Pediatrics*, Vol. 120, e838, Copyright © 2007 by the AAP.

Preschool Language Scale

Age 4—Denver (Born to low-resource mothers)



Source: Reproduced with permission from *Pediatrics*, Vol. 114, 1565, Copyright © 2004 by the AAP.



Days Hospitalized for Injuries

Birth to age 2—Memphis



Between first and second child (by first child's fifth birthday)—Memphis





Source: JAMA, 1997, Vol. 278, 650, Copyright © 1997, American Medical Association. All rights reserved. Source: JAMA, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved.



Months Receiving Welfare Assistance (AFDC) Birth through age 5—Memphis



Source: JAMA, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved. Months Receiving Food Stamps Birth through age 5—Memphis



Source: JAMA, 2000, Vol. 283, 1987, Copyright © 2000, American Medical Association. All rights reserved.

Monetary Benefits





Weaving a safety net so tight that no child slips through'

Map out all the programs/services already in a community—there's more than we think

- Look for gaps
- Look for overlap
- What can be realigned to better cover the gaps?
- What new components are needed?
- All programs need to be talking to each other
 Tribal, federal, state, county, private
 Social services, medical, mental health, schools
 ...and have a common, unifying vision

The start of one tribe's map

Preconception- Pregnancy- Childhood-Adolescence

School Food Programs WIC "Backpack Foods" **Breastfeeding support Teen Pregnancy Support** Zero-to-Three Court Referral Program, Healthy Parenting curriculum Mental Health: Parent Child Interaction Therapy, Parenting groups, Trauma Tx Coping Skills classes: emotions, finances Home Visiting------**Teen Education and Family Nights** Cherokee Choices: Mentoring, coping skills, exercise, healthy foods Head Start/Parents as Teachers Language immersion program------Prenatal Dental Program **Pediatric dentist** Renew tribal traditional pregnancy/child-rearing practices

What can we do—right now?

- Alleviate food insecurity/provide good nutrition
- Home visiting interventions
- Teach parenting and coping skills
- Screen for/treat depression and substance abuse
- Intervene in adverse childhood experiences
- Strengthen traditional values, worldviews and practices
 - Especially to care for pregnant women, children and young parents
 - Take the "long view"—good things that happen now may take several generations to show their full benefit
- Change ourselves
 - See patients more clearly—their resilience is amazing
 - See that *everything* relates to health—and vice versa
 - Need to develop new partnerships to strengthen the "web"

"Dance with Desire to Make the World Well"

