Pediatric Perspectives on International Adoption

Growth, Puberty and Long-Term Medical Risks
Nutrition Issues Specific to International Adoption

- Growth in children exposed to early deprivation.
- Growth suppression and recovery
  - Trajectories
  - Mechanisms
- Factors determining final height
- Long-term risks
  - Mental health
  - Chronic diseases
  - Life-span
Growth Failure in Institutionalized Children
Growth Failure in Institutionalized Children

Z-Score

Height
Weight

Rutter Johnson Mason L. Miller Johnson Albers L. Miller L. Miller BEIP B. Miller
Profound Growth Failure In Institutionalized Children

- 2 to 20 years: Boys
  - Stature-for-age and Weight-for-age percentiles

- 2 to 20 years: Girls
  - Stature-for-age and Weight-for-age percentiles

n=262 133(f) 3-19 y
Nutrition and Institutional Growth Failure

- Available diet
  - Energy requirements are 20% higher in premature infants due to:
    - Higher basal metabolic rate
    - Lower coefficient of absorption for fat and carbohydrates
- Ability and desire to feed
  - Indifference (hospitalism)
  - Neuromotor problems, orofacial malformations
- Opportunity to feed
  - Not cue-based feeding—"efficiency-based"
- Inability to absorb substrate.
Summary: Growth Failure in Institutionalized Children

- All growth parameters affected
- Overall suppression rather than dose-dependent related to degree of deprivation.
- Underlying medical issues (LBW, FAS) exacerbate growth suppression.
- Mechanisms are somewhat age-dependent and involve nutrition and hypothalamic-pituitary-end organ suppression.
Catch-Up Growth
Post-Placement Catch-up Growth

Eastern European Growth Study, U of MN
Summary
Post-Placement Growth

- Rapid- Essentially Complete after 12 Months
- Most Dramatic Catch-up Growth
  - Younger at the Time of Arrival
  - Smaller at the Time of Arrival
  - Higher Quality Care after Arrival
    - Positive Regard
    - Sensitivity
  - Better Caloric Intake after Arrival
  - Recovery of the GH-IGF-1 axis
- Who Lags Behind at 6 Months?
  - Those most growth suppressed at arrival.
  - Older Children
Long Term Recovery
Follow-up Height and Weight

Z-Score vs. Age at Follow-up

- Height
- Weight
Why is Final Height Impaired?

- Parental Size???
- Prenatal growth impairment
- Postnatal growth impairment
- Earlier puberty (particularly girls)
Sex Differences

- **Boys**
  - In Utero Differentiation
  - Early Postnatal Surge
  - Dormant in Infancy
  - Pubertal Activation
    - Later than in Girls
    - Testosterone
    - Genital Changes
    - Pubic Hair
    - Testicular Size
  - Precocious Puberty < 9 years

- **Girls**
  - Minimal Activity in Utero
  - Ovarian Activity Persists through Infancy
  - Pubertal Activation
    - Earlier by 2 years
    - Estradiol and Progesterone
  - Breast Changes
  - Pubic Hair
  - Menses
  - Precocious Puberty < 8 years
Age of Pubertal Changes in International Adoptees vs. Danish Girls

IA's, N = 276
Control, N = 1,100

9.5 (7.1-12.0)
16% < 8 yrs
1.3 years earlier

10.8 (8.4-13.2)

12.1 (10.2-14.0)
16% < 8 yrs
1.3 years earlier

13.4 (10.8-16.0)

Management of Early Puberty

- LHRH Agonists
  - LHRH Agonists eliminate pulsatility
  - Lupron
    - Depot Lupron, 3.75 to 11.25 mg im monthly
    - Desensitizes the HPG Axis
    - Does not impede Adrenal Androgen Production
  - Supprelin LA Depot
    - Surgical implantation of a small plastic rod
    - Releases LHRH agonist daily over 12 months
    - Can be either removed or replaced
LHRH Agonist Treatment

- Successful in stopping central puberty
- Costs $800 to $2,000 per month
- Similar cost between Lupron and Supprelin
- Buys additional years of childhood
- Definite improvement in adult height when started before age 6
- Lack of agreement on when to start or stop
- No impairment of later reproductive function
SGA vs Institutionalized Children

**SGA**
- Growth Impaired early in life.
- Impaired growth hormone secretion/sensitivity
- Catch-up growth
- Early puberty especially girls
- Abnormalities in cortisol secretion
- Metabolic Syndrome
  - Obesity
  - Type II Diabetes
  - Hypertension
  - Cardiovascular disease

**Institutionalized**
- Growth Impaired early in life.
- Impaired growth hormone secretion/sensitivity
- Catch-up growth
- Early puberty especially girls
- Abnormalities in cortisol secretion
- Metabolic Syndrome
  - Higher BMI’s
Stress and Adverse Outcomes
13,494 Adults in Kaiser Permanente HMO

- Exposed to:
  - Psychological Abuse
  - Physical Abuse
  - Sexual Abuse
  - Household substance abuse
  - Household mental illness
  - Mother treated violently
  - Household criminal behavior

- ≥ 4 Categories
  - Alcoholism 7.4
  - Used elicit drugs 4.7
  - Injected drugs 10.3
  - ≥ 50 intercourse partners 3.2
  - Sexually transmitted disease 2.5
  - Ischemic heart disease 2.2
  - Cancer 1.9
  - Stroke 2.4
  - Chronic bronch/emphy 3.9
  - Diabetes 1.6

Stress and Adverse Outcomes
1193 Female Adults in Kaiser Permanente HMO

- Woman who experienced ≥ 4 exposures were 1.5 time more likely to have an unintended first pregnancy.
  - Strongest associations with
    - Frequent psychological abuse
    - Frequent physical abuse of the mother by her partner
    - Frequent physical abuse

Stress and Adverse Outcomes

Adverse Childhood Experiences, Allostasis, Allostatic Load and Age-Related Diseases

- **Brain**
  - Structural alterations in brain regions responsible for executive function, memory and emotional tone

- **HPA Axis**
  - Alterations in cortisol levels, normal diurnal variations and responsiveness

- **Immune System**
  - Elevated inflammation levels and altered response to infections.

Danese and McEwen Physiology and Behavior 2012;106:9-39
Stress and Adverse Outcomes
Meta-analysis of 24 studies including 48,801 individuals

- Neurological Problems
  - Migraines
- Musculoskeletal Problems
  - Arthritis, broken bones
- Respiratory Problems
  - Asthma, bronchitis
- Cardiovascular Problems
  - Heart attack, stroke
- Gastrointestinal Disorders
  - Hernia, spastic colitis
- Metabolic Disorders
  - Diabetes, obesity
- Autoimmune Disorders

Stress and Adverse Outcomes
32 Year Prospective Study of 1037 New Zealanders

- Children exposed to adverse psychosocial experiences (maltreatment, social isolation) during the first decade of life were at elevated risk of depression, high inflammation levels and a clustering of metabolic risk factors [$\geq 3$ overweight, high blood pressure, high total cholesterol, low HDL cholesterol, elevated Hgb-A1C or low maximum oxygen consumption levels]

IAP-Follow-up Height and Weight

Z-Score

Age at Follow-up

-2 -1.5 -1 -0.5 0 0.5 1

Height

Weight
Genome-Environment Interactions

- Telomeres-specialized nucleoprotein complexes located at the end of chromosomes that promote chromosomal stability.
- Telomere length shortens with each successive cellular division.
- Once telomere length reaches a critical point, cell senescence is trigger, cell division ceases and the cell dies.
- Accelerated telomere length shortening has been associated with normative aging as well as cigarette smoking, radiation exposure, oxidative stress and psychological stress including a history of early maltreatment.
Telomere Length and Institutional Care

- Bucharest Early Intervention Project
  - Telomere length at 8 years of age was inversely related to the length of institutionalization.
    - Girls - length of institutionalization at baseline (22 months of age)
    - Boys - length of institutionalization at 54 months of age.
Stress and Adverse Outcomes