The Influence of Infant Health on Adult Chronic Disease

Womb to Tomb

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Introduction

• Many diseases in adulthood are related to growth patterns during early life

• Maternal nutrition important underlying mechanism for programming growth trajectory in the foetus

• Those with a positive maternal forecast will be adapted to good conditions
Barker Hypothesis

- Reduced foetal growth is strongly associated with chronic conditions in later life
- Increased susceptibility results from adaptations made by the foetus to a nutrient poor environment
Thrifty Phenotype

- Smaller body size
- Lowered metabolic rate
- Reduced level of behaviour
- Adaption for offspring to survive in a predicted nutrient poor postnatal environment
Developmental Origins of Health and Disease

• Early life influences can alter the risk of later disease
• Developmental plasticity allows adaptation to the environment during the life course, underpinned by epigenetic mechanisms
• Adaptations are made due to current environmental cues, and using these to predict future environment
Developmental Origins of Health and Disease

• Mismatch between the anticipated and actual mature environment exposes the organism to adverse consequences

• Animal research shows mismatch between pre and post natal environment results in obesity, leptin and insulin resistance, elevated BP, vascular endothelial dysfunction

• Greater the mismatch, greater the risk
Metabolic Programming

• Increasing evidence that environmental and nutritional influences during critical periods in development can have permanent effects on an individual’s predisposition to obesity and metabolic disease

• Three key periods: Foetal life, infancy, early childhood
Metabolic Programming

• Many population based studies confirm association between birth weight (reflecting foetal nutrition) and later diabetes, heart disease, insulin resistance and obesity

Metabolic Programming

• Infancy and early childhood are also critical periods
• Studies show association between rates of weight gain during early childhood and subsequent obesity and metabolic syndrome in childhood, adolescence or adulthood
  • Leunissen RW et al. Timing and tempo of first year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. JAMA 2009;301: 2234
  • Monteiro PO et al. Rapid growth in infancy and childhood and obesity in later life – a systemic review. Obes rev 2005143; 6:
Paediatricians and Adult Chronic Disease

- Currently many sectors of the paediatric population primed for early onset of chronic disease: suboptimal intrauterine growth, poor growth in infancy, overweight and obesity being main drivers
- Background of dire socioeconomic risk factors
Paediatricians and Adult Chronic Disease

• Groups of children at risk:
  • Large for Gestational Age (LGA) including IDM
  • Small for Gestational Age (SGA) infants
  • Failure to thrive
  • Overweight and obese
SGA (<2.5kg) and LGA(>4.4kg) Babies

• Both exposed to suboptimal nutrition in utero

• High and low birth weight associated with increased risk for metabolic syndrome and diabetes in later life (OR 1.36, 1.47)
Large for Gestational Age infants

- Birth weight > 4 kg
- Children who are LGA and exposed to an intrauterine environment of either diabetes or maternal obesity are at increased risk of developing metabolic syndrome in childhood (by 11 years of age) compared to AGA babies

Boney et al. Metabolic syndrome in childhood: association with birth weight, maternal obesity and gestational diabetes mellitus
Pediatrics 2005 Mar; 115(3)e290-6
Small for gestational age infants

- Foetal origins of adult disease: Barkers hypothesis
- Association between IUGR and adult coronary and vascular disease – foetal undernutrition results in changes in vascular development that predisposes to adult disease
- Not universally accepted
Obstetrics v Paediatrics

• Phenotype established during foetal development and modified by epigenetic factors in utero

• Some studies suggest that events in early postnatal life (such as catch up growth) can have more effect on risk of chronic disease

Growth in Infancy and Childhood

• First 2 years of life is the critical window
• Period of Developmental Plasticity
• Susceptible to Epigenetic modification

• Poor growth, inadequate nutrition during this period associated with increased risk
Failure To Thrive

• Most studies support poor growth in early life results in metabolic and physiological programming with life long effects on risk of disease:
  • Cardiovascular disease
  • Abnormal lipid profiles
  • Type 2 diabetes
  • Hypertension
FTT Growth Chart
Early Childhood Nutrition

• Evidence suggests that rapid weight gain in the first two years of life does not increase the risk of chronic disease, except in children born SGA

• Growing evidence that a good birth weight and moderate rates of weight gain in infancy leads to accumulation of lean body mass

• Maternal and child undernutrition: consequences for adult health and human capital

Growth in Early Childhood

- Rapid weight gain and obesity in later childhood associated with increased risk of metabolic syndrome and type 2 diabetes
- Gaining weight in later childhood results in accumulation of fat mass

- Maternal and child undernutrition: consequences for adult health and human capital
“Worst case scenario”

• A baby of low birth weight, who is stunted and underweight in infancy and gains weight rapidly in childhood and adult life, represents the worst case scenario for cardiovascular and metabolic disease.
Growth in Early Childhood

• Lack of controlled trials of early nutritional interventions looking at long term outcomes
• Recent meta analysis “insufficient evidence to recommend prevention of adult disease through strategies to alter infant growth”
• Need to establish the benefits and hazards of weight gain at different ages
What are we doing in Central Australia?

- Exclusive breast feeding for first 6 months
- Use of WHO growth charts
- Healthy Under 5s programme
- Active intervention for growth faltering in the under 2s (GAA)
Challenges Facing Paediatrics

• Appropriate growth trajectories for prems, SGA, LGA and IDDM
• Prevention and management of FTT
• Prevention of rapid weight gain in older children
• Obesity epidemic
• Early detection of insulin resistance, impaired glucose tolerance and type 2 diabetes