Optimising the balance between metabolic capacity and metabolic load for lifelong health

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Life-long health

Maternal health
  - Pregnancy and childbirth

Growth and development

Cardio-metabolic disease
  - Heart disease
  - Diabetes
  - Stroke
Chronic disease: typical onset in adulthood

Image source: UConn Rudd Center for Food Policy & Obesity
A life-course perspective

Critical windows

Plasticity

Development

Lifestyle

NCD risk

High

Low
Thrifty phenotype hypothesis

- Reduced investment in organs (pancreas, liver) = ‘survival phenotype’
- Less tolerant of ‘nutritional excess’ in later life (obesity, inactivity, rich diet)

Hales & Barker, Diabetologia 1992
Stunting and later body composition

Wells et al., Eur J Clin Nutr 2018
Birth weight and later heart disease

Barker Hypothesis

Age Adjusted Relative Risk

Birthweight (lbs)

<5.0  5.0-5.5  5.6-7.0  7.1-8.5  8.6-10.0  >10.0

Rich-Edwards 1997

Rich Edwards et al., BMJ 1997
Dose-response associations

• Most of association lies within ‘normal’ birth weight range

• Every additional unit of birth weight reduces chronic disease risk

• Risk tracks growth patterns
The process of growth

Growth

Hyperplasia

Age

Hypertrophy
Development and structure

Growth

Hyperplasia

Metabolic capacity

Metabolic load

Hypertrophy

Age
Metabolic capacity

- Characteristics of organ structure and function
- Confer homeostatic capacity
- Contingent on fetal/infant growth

Wells, Am J Hum Biol 2011
Birth weight and metabolic capacity

Lean mass

Ethiopian cohort

Coronary artery diameter

Nephron number

Jiang et al., Pediatr 2006; Dezateux et al., Thorax 2004; Manalich et al., Kidney Int 2000
More sophisticated models

Organ/tissue physiology

Gene expression

Metabolic /hormonal set-points

Gut biota
Challenging homeostasis

Allostatic load
- Stress response
- HPA axis
- Cortisol

Metabolic load
- Fuel homeostasis
- Metabolism
- Insulin

McEwen and Stellar, Arch Intern Med 1993
Metabolic load

- Lipogenic diet
- Smoking
- Obesity
- Sedentary behaviour
- Infectious disease
- Psychosocial stress

- Signalling perturbations
- Fuel perturbations
- Haemodynamic perturbations

Homeostatic metabolic capacity

Wells, Am J Hum Biol 2011
Metabolic load

• Diet: fat or carbohydrate?

• Activity: active good, or sedentary bad?

• Obesity: BMI, central fat or metabolism?
Load/capacity and disease risk

Wells, Am J Hum Biol 2011
Capacity and disease risk

Wells, Am J Hum Biol 2011
Load and disease risk

Wells, Am J Hum Biol 2011
Load/capacity and disease risk

Metabolic risk
- Diabetes
- Heart disease
- Stroke
- Hypertension

Tertiles of metabolic load
- Obesity / Childhood weight gain
- Tissue masses
- High dietary glycaemic index
- Physical inactivity

Tertiles of metabolic capacity
- Birth weight or infant weight
  - Nephron number
  - Cardiac structure
  - Pancreatic B-cell mass

Wells, Am J Hum Biol 2011
Supporting evidence: diabetes

Li et al., BMJ 2015
Supporting evidence: hypertension

Li et al., BMC Med 2015
Social rank and metabolic capacity

Victora et al., Ann Hum Biol 1987
Social rank and metabolic load

National Obesity Observatory

Obesity prevalence

Level of deprivation

Most Deprived

Least Deprived

%
Ethnicity and metabolic capacity

Kelly et al., J Public Health 2009
Ethnicity and metabolic load

Fat Mass Index (kg/m²)

Lean Mass Index (kg/m²)

Constant BMI values

Europeans
South Asians

Wells et al, Frontiers Public Health 2016
Maternal nutrition as a critical period

Load

Capacity

Life-course health
Maternal nutrition as a critical period
Inter-generational linkages

Maternal obesity → Child obesity

Cnattingius et al., 2012 Int J Obes
Inadequate capacity for load

Maternal obesity

Low birth weight

3 * risk child obesity

Cnattingius et al., 2012 Int J Obes
Infancy as critical period

- Elevate load
- Constrain capacity

Target of growth:

- Fetal life
- Infancy
- Childhood
- Adolescence
The double burden and childbirth

Normal growth + Stunting → Gestational diabetes

→ Normal BMI + Obesity

Wells, Anat Record 2017
Supporting evidence: cesarean risk

India 2015-2016 survey

Wells et al, Frontiers Public Health 2018
Supporting evidence: cesarean risk

India 2015-2016 survey

Wells et al, Frontiers Public Health 2018
Promoting capacity not load

RUTF supplementation, n = ~1600

Longitudinal measures of Lean mass and Fat mass

Benefits in lean not fat

Fabiansen et al., PLoS Med 2017
Thanks for listening