DOHaD ANZ

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The effects of the early environment can last a lifetime

Early environment (diet, microbes, toxins, stress)

The basis of ‘DOHaD’ a new health discipline
(Developmental Origins of Health and Disease)

Risk of later disease (NCDs)
(heart disease, obesity, dementia, diabetes, allergy, asthma)
Examples of NCDs that are developmentally programmed

- Food allergy, eczema
- Asthma, allergic rhinitis
- Obesity and metabolic disease (diabetes)
- Autism, learning and behavioural disorders
- Depression and anxiety
- Infertility
- Breast cancer
- Cardiovascular disease
- Osteoporosis
- Prostate, lung cancer
- Alzheimers, Parkinosns

Early conditions influence the **development** and **function** of all organ systems with both **early** and **latent** long term effects.
Modern lifestyles

- Diets, behaviour, microbial patterns, pollutants

- Mood, behaviour, development, degeneration
- Cardiovascular responses
- Gastrointestinal inflammation

Multisystem effects
- Tissue damage, oxidative stress and tissue repair
- Genetic susceptibility

Increased NCD risk

Molecular Mechanisms
Common risk factors
For many modern diseases

- Microbial diversity
- Dietary profile
  - ↑ Saturated fat
  - ↓ Dietary fibre
  - ↓ n3/n-6 PUFA
  - ↓ Fresh foods
- Sunlight
- Stress
- Physical activity
- Pollutants
  - Smoking
  - Toxins & POPs
  - EM radiation?

Means common and collaborative solutions
Need for a more integrated collaborative approach

- To move beyond medical ‘specialty’ silos
- More *integrated* approach:
  - to health and disease,
  - risk factors and solutions

Strategies to promote early ‘immune’ and ‘metabolic’ health will have multisystem benefits
THE CYCLE OF OBESITY

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What is the Raine Study?
Our children predicted to have shorter life expectancy

WA kids (Raine Study)

- 29% of all 14 year olds at elevated risk for heart and metabolic disease

Huang RC et al. *Diabetes Care*. 2009;32:4
Influence of early life events on risk of MS at 8 years

• Maternal smoking during pregnancy
  – OR=1.82 (95% CI=1.05 to 3.2)

• Kilogram of weight gain between 1 and 8 years
  – OR=1.4 (95%CI=1.3 to 1.5)

• Breast feeding ≥4 months
  – OR=0.60 (95%CI=0.37 to 0.97)

Early Life Programming

Suboptimal antenatal + Suboptimal postnatal

Adult Disease

- Obesity
- Metabolic Syndrome
- Hypertension
- Insulin resistance
- Dyslipidemia
Longitudinal Measures

• Adiposity z-scores
  – 8 times
  – birth-14 years

• Growth trajectories
  – semi-parametric mixture modelling.
Longitudinal Measures

• Adiposity z-scores
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• Growth trajectories
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Optimum Trajectory Model

Huang RC et al. Diabetes Care. 2011;34:1019-1025
Optimum Trajectory Model

Legend
1--- Stable high (6%)
2--- Rising to high (12%)
3--- Falling to moderate (18.2%)
4--- Rising to moderate (11%)
5--- Reference Group (Optimal normal growth) (31.2%)
6--- Moderately low stable (18.5%)
7--- Very low stable (3.1%)

Huang RC et al. *Diabetes Care*. 2011;34:1019-1025
Effect of Trajectories on DOHaD outcomes
A New Initiative
The ORIGINS Project

Driven by both:

- Community engagement – focus groups: key issues
- Comprehensive multidisciplinary input to data collection

Goal: Harmonised

Goal: Utilise new ‘omics technologies & data capacity

Goal: Translation - Observational and intervention arms
The ORIGINS Project

~3,000 deliveries per year at JHC, and over a 5 year period, we aim to recruit:

• **>10,000+ mothers**: data linkage study - to data collected during standard clinical care linked to health outcomes.

• **>5,000+ participants**: active follow-up process (over the 5 year period).
~3,000 deliveries per year at JHC, and over a 5 year period, we aim to recruit:

• >10,000+ mothers: data linkage study - to data collected during standard clinical care linked to health outcomes.

• >5,000+ participants - active follow-up process (over the 5 year period).

‘All’ will be also screened for eligibility for nested clinical trials.
Data linkage Capacity:

Western Australia is second to none

In-built advantage over other centres starting new birth cohorts
Examples of detailed early environmental data

Goal: Harmonised across all new pregnancy studies

- Maternal health and pregnancy data
- Diet and physical activity pattern
- Environmental pollutants, smoking
- Physical activity, time outdoors, screen time
- Infections, vaccines, medications, IVF (ART)
- Work patterns, and sleep patterns
- Stress, social & economic circumstances
Examples of detailed early biological measures

Also harmonised across studies
(blood, urine, cord blood, placenta, stool samples)

Driven by:
- New questions, new issues
- New technologies and new capacity

Goal: Utilise new ‘omics technologies & data capacity

Inbuilt capacity to anticipate the future
Examples of detailed outcome measures

- Growth and adiposity
- Brain, behaviour, learning and development
- Metabolic and cardiovascular
- Sleep
- Asthma
- Dental health
- Eczema & food allergy
- Musculo-skeletal health

Driven by both:
- Community engagement – focus groups: key issues
- Comprehensive multidisciplinary input to data collection
Examples of potential early interventions:

**Interventions for ‘a healthy start to life’**

- Fresh foods and healthier dietary patterns
- Healthier gut biodiversity
- Physical activity, time outdoors
- Education, training, engagement
- Improve social infrastructure
- Reduce pollutants and toxins
- Reducing stress

May target specific risk groups

WE INVITE PROPOSALS
Examples of potential early interventions:

Interventions for ‘a healthy start to life’

May target specific risk groups

WE INVITE PROPOSALS
THE ORIGINS STUDY UPDATE - OCT 2015:

- **The full protocol** finalised (core visits, questionnaires, samples)
- **Business case and Governance:** November 2014
- **Ethics submission:** November 2014
  - For core cohort
  - For first clinical trial
- **External funding:** secured for the first 2 years (pending larger $)
- **Pilot recruitment:** from ≈April 2015
- **Full recruitment:** aiming for early 2016

Contacts: Susan Prescott and Desiree Silva

WE INVITE PROPOSALS

Study Manager: Lyn.Colvin@telethonkids.org.au
HOW CAN YOU GET INVOLVED?

**Basic Science:**
- Mechanistic studies using biological samples

**Intervention or clinical studies**
- Propose new clinical trials or interventions

**Data linkage / data analysis**
- Accessing data on various exposures and outcomes

**New observational studies (additional samples / data)**
- New proposals (separate ethics)

WE INVITE PROPOSALS

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Summary and conclusion
A healthy start
to the human race

Developmental Origins of Health and Disease

2015 DOHaD conference
Melbourne, April 17-19, 2015

DOHaD ANZ – 2015
DOHaD ANZ

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