Developmental origins of long-term health - public health implications

Mark Hanson
Annual General Meeting today at 2 pm

Lunch provided!!
Non-communicable disease

- Cardiovascular disease, diabetes, chronic lung disease, allergy, some cancers, cognitive decline, osteoporosis, sarcopenia, affective disorders
- World’s biggest killers – 35m deaths/year, 60% of all deaths globally. In developed countries but also -
- 80% in low- and middle income countries, especially as they undergo socio-economic improvement following reductions in infectious disease
- WHO projects an increase of 17% in NCDs over next decade globally

- Preventable
- Prevention strategy currently absent from Millennium Development Goals

Adapted from WHO Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases; Dr Ala Alwan, 2008
• All children are affected by their early developmental conditions, with long-term phenotypic consequences

• Biomedical implications

• Policy implications
The normative nature of the phenomenon

Prevalence of NIDDM and IGT (%)

Birth weight (lbs)

Variation in maternal nutrition has phenotypic effects in childhood independent of birth weight

An evolutionary perspective on DOHaD

• Fitness (i.e. reproductive success), longevity and health are *not* the same
• Selection acts to protect or promote (Darwinian) fitness

• Infant and child mortality have fallen dramatically
• Human longevity has increased dramatically
• Fitness is primarily affected by life history traits (e.g. age of puberty)
• We are changing our reproductive behaviour
• We now generally live in evolutionarily novel environments
  – nutritional, social etc.
An evolutionary mismatched or novel environment
The individual has been exposed to an environment beyond their evolved capacity to adapt, or to a novel environment or challenge

- Energy-dense nutrition;
- Unbalanced macro- & micronutrient diet
- Decreased energy expenditure
- New physical environment (eg myopia/artificial light)
- New social pressures
- Change in the symbiotic environment
Demographic change means that mismatch is exaggerated by increased fetal constraint as well as by a more obesogenic environment

- More primigravida
- More elderly primigravida
- More multiple births
- High rates of teenage pregnancy
- Dieting
plus the impact of gestational diabetes and maternal obesity

- Rising incidence
- Offspring have high morbidity
- Biology not understood
- Several pathways
  - Hyperinsulinemia
  - Maternal obesity and normal/large offspring
  - Maternal obesity and small offspring
  - Weight gain in pregnancy
- Toxic or adaptive?
- Need for clinical and experimental studies
Again this is becoming “normal”

Obesity (BMI ≥ 95th percentile) at age 4 years according to maternal first-trimester BMI

...... and the processes interact:
mean % body fat from skinfold thickness in 276 men & women aged 28-31 years

Parity $p=0.004$
Mother’s BMI in early pregnancy $p<0.001$

Reynolds & Godfrey et al
The consequences become multi-generational

- Premature death and morbidity
- Obesity
- Insulin resistance
- Gestational diabetes
- Large babies

Women malnourished
Low pregnancy weight gain

Very poor postnatal environment
Stunting

Suboptimal fetal development

Enriched postnatal environment due to nutritional transition

Obesity
Insulin resistance

Maternal morbidity

Premature death and morbidity

Gluckman and Hanson 2005
• All children are affected by their early developmental conditions, with long-term phenotypic consequences

• Biomedical implications

• Policy implications
DOHaD does not fit conventional models of disease:

• We are healthy until we ‘catch’ a disease
• Genetic variants are most important determinants of risk of disease
• Adult lifestyle interventions are the answer
• Effort should be focussed on screening in young middle-aged people
Even homozygous twins respond very differently

100 days overfeeding (+ve energy balance)

TWIN A
$r = 0.55$
$F = 3.4 \ (p < 0.02)$

TWIN B

Same diet – more exercise (-ve energy balance)

Twin A
$r = 0.74$
$F = 6.8 \ (p = 0.01)$

Twin B

The major achievement in public health
Life course approach – medical models of disease

Life course

CHRONIC DISEASE RISK
Life course approach

- Plasticity
  - Inadequate response to new challenges

Chronic Disease Risk

Life course
Life course approach

CHRONIC DISEASE RISK

Life course

Plasticity

Inadequate response to new challenges
Life course approach

Timely intervention

Inadequate response to new challenges

Plasticity
Population prevalence rates of angina and heart attack (CHD) amongst adults across the deprivation bands in the Republic of Ireland within each sex and age group (2007).
Impact of Type 2 diabetes screening

From a Party manifesto, published in The Lancet, 1 May 2010

• “Preventive health-care routine check-ups will be introduced for all aged over 40 years”
Reproduction & behaviour
Adolescence: a critical juncture
Puberty and adolescence - a good example of life history plasticity, evolutionary mismatch and adverse consequences
The link with puberty: timing of puberty is changing

Secular trend:

Tanner (1978)
Girls who were smaller at birth but larger at 8 years reach menarche earlier

From Sloboda et al. J Clin Endocrinol Metab 2007; 92:46-50
The Problem of Adolescence: White matter and axonal organisation

The fornix, centrum semiovale and corona radiata showed no FA changes with age from 5-30 years.

Brain regions:
- ILF
- Splenium
- Geni
- SFO
- Anterior limb
- SLF
- IFO
- Subcortical white matter in gyri
- External capsule
- Posterior limb
- Thalamus
- Corticospinal tract
- Caudate nucleus
- Globus pallidus
- Putamen
- Cingulum
- Uncinate fasciculus

Age at which brain region is 90% developed (years)

Percent increase of fractional anisotropy from 5-30 years

Fronto-thalamatic pathways

Lebel et al. (2008) NeuroImage
Evidence associating early puberty in girls with psychosocial adjustment problems, mental health problems, advanced drinking & cigarette smoking

• Swiss SMASH ‘02 study, 565 item questionnaire
• 7,488 16–20 year olds, 97.7% of possible sample

Michaud et al. (2006) Mol Cell Endocrinol
Females – early versus average puberty

- Body image concerns: 1.3 times higher
- Functional symptoms: 1.5 times higher
- Victimisation: 1.7 times higher
- Sexually active: 1.9 times higher
- Smoking: 1.4 times higher

All p<0.001
Males – early versus average puberty

- Bad health 1.9 times higher
- Functional symptoms 2.2 times higher
- Victimisation 1.7 times higher
- Sexually active 1.8 times higher
- Smoking 1.8 times higher
- Drunk in last 6 months 1.4 times higher
- Cannabis use 1.8 times higher
- Illegal drug use 2 times higher
- Depression 2.1 times higher
- Suicide attempts 4.9 (3.0-8.1) times higher

All p<0.001
Michaud et al
• All children are affected by their early developmental conditions, with long-term phenotypic consequences

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• Policy implications
Counting the cost

- Not only what populations will spend on healthcare
- But also the value of individual lives and their human capital - resources, knowledge, health etc - (heritable)
**The first economic analysis; benefits of shifting one LBW Infant (<2500g) to non-LBW (2501 g) status**

**H. Alderman and J.R. Behrman, (World Bank) 2004**

<table>
<thead>
<tr>
<th>Benefit</th>
<th>PDV (US$)</th>
<th>%</th>
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<tbody>
<tr>
<td>1. Reduced infant mortality</td>
<td>$92.86</td>
<td>16%</td>
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<tr>
<td>2. Reduced neonatal care</td>
<td>$41.80</td>
<td>7%</td>
</tr>
<tr>
<td>3. Reduced costs of infant/child illness</td>
<td>$38.10</td>
<td>7%</td>
</tr>
<tr>
<td>4. Productivity gain from reduced stunting</td>
<td>$99.34</td>
<td>17%</td>
</tr>
<tr>
<td>5. Productivity gain from increased ability</td>
<td>$239.31</td>
<td>41%</td>
</tr>
<tr>
<td>6. Reduction in costs of chronic diseases</td>
<td>$23.29</td>
<td>4% **</td>
</tr>
<tr>
<td>7. Intergenerational benefits</td>
<td>45.12</td>
<td>8%</td>
</tr>
<tr>
<td>Sum of PDV of seven benefits</td>
<td>$579.82</td>
<td>100%</td>
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**grossly underestimated**
New models will take account of:

- Other developmental factors not simply reflected in birthweight
- Effects at high and low ends of spectrum
- Wider range of social, economic and health consequences
- Effects on more that just next generation
WHO’s budgetary allocations and burden of disease: a comparative analysis

Stuckler et al Lancet 372 Nov 1 2008

**Family income gradients in child health status emerge early and widen with age**

![Graph showing income gradients in child health status](image)

Invest 1$.........
START WITH A GIRL
A NEW AGENDA FOR GLOBAL HEALTH
A GIRLS COUNT REPORT ON ADOLESCENT GIRLS

MIRIAM TEMIN
RUTH LEVINE
CENTER FOR GLOBAL DEVELOPMENT

Center for Global Development
Independent research and practical ideas for global prosperity
Altering the equation for girls: A crucial investment

- Girls’ rights first & foremost
- Global health goals
- The prevention imperative
- A lever for economic & social development
Social determinants underlie epidemiology

Child marriage is still common in many regions of the world

Percentage of women (20-24 years) married before 18 years (2008)

Maps designed and prepared by maplecroft
Unhealthy young mothers, unhealthy babies

Mother’s age is a risk factor for children’s health problems


*The analysis also controlled for mothers 20 to 25 years old.

**Conclusion:** Only a small proportion of women planning a pregnancy in UK follow the recommendations for nutrition and lifestyle (folic acid supplement intake, alcohol consumption, smoking, diet, and physical activity)
Influences on diet

- Not smoking
- Watching little television
- Dieting
- Taking strenuous exercise
- Older age
- Not living with children

Education

Prudent Diet
Young Southampton women with a lower level of educational attainment are more likely to eat an unbalanced “imprudent” diet.

<table>
<thead>
<tr>
<th>Educational level</th>
<th>% in the lowest quarter of prudent diet score</th>
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<tbody>
<tr>
<td>No exams</td>
<td>54.7%</td>
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<tr>
<td>Lower level exams</td>
<td>48.5%</td>
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<tr>
<td>Intermediate level exams</td>
<td>33.5%</td>
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<tr>
<td>Advanced level exams</td>
<td>19.4%</td>
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<tr>
<td>Higher National Diploma</td>
<td>12.9%</td>
</tr>
<tr>
<td>University degree</td>
<td>3.5%</td>
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Infant diet relates to diet of the mother

- Infant guidelines score
- Mother’s diet score

Good

Bad
Individual factors

Environmental factors (peer, parent, media)

Health Literacy

Using Social Cognitive theory
- Maganello, 2008
Health Literacy (Nutbeam, D. 2000)

The degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions

1. Basic or functional health literacy
2. Communicative or interactive health literacy
3. Critical health literacy (autonomy and personal empowerment)
• Make health promotion concepts and behaviours culturally relevant and part of child’s environment
• Capabilities develop earlier than often thought
• Children themselves can become agents of change
• Focus not so much on ability to read a health text but on health literacy itself
• Can empower vulnerable and marginalised groups

Steps in knowledge transfer to policy

- The challenges of genetic determinism
- The focus on life-style determinism in adults
- The failure to recognise the developmental sources of individual variation in vulnerability
Steps in knowledge transfer to policy

- The DOHaD approach looks like a “folk biology” model of nurture, motherhood & apple pie
- And focus on empowerment of women may clash with some cultural views
New knowledge from science

Accepted scientific position

Public understanding and acceptance

Cost/benefit

The treasury view

• Cost benefit?
• Relativities?
• The problem of life course discounting
• The lack of a specific intervention
• Politicians think they already invest more than enough in maternal and infant health.

• Political priorities, ideology, voting cycles and public opinion

Courtesy Prof. Sir Peter Gluckman FRS
DOHaD 2011

7th World Congress on Developmental Origins of Health and Disease

September 18-21, 2011
PORTLAND, OREGON  USA
Marriott, Downtown Waterfront

OHSU Heart Research Center
Greater Oregon March of Dimes