COHORTS STARTING BEFORE CONCEPTION; WHY IS THE ARCTIC AREA OF INTEREST

>Jørn Olsen

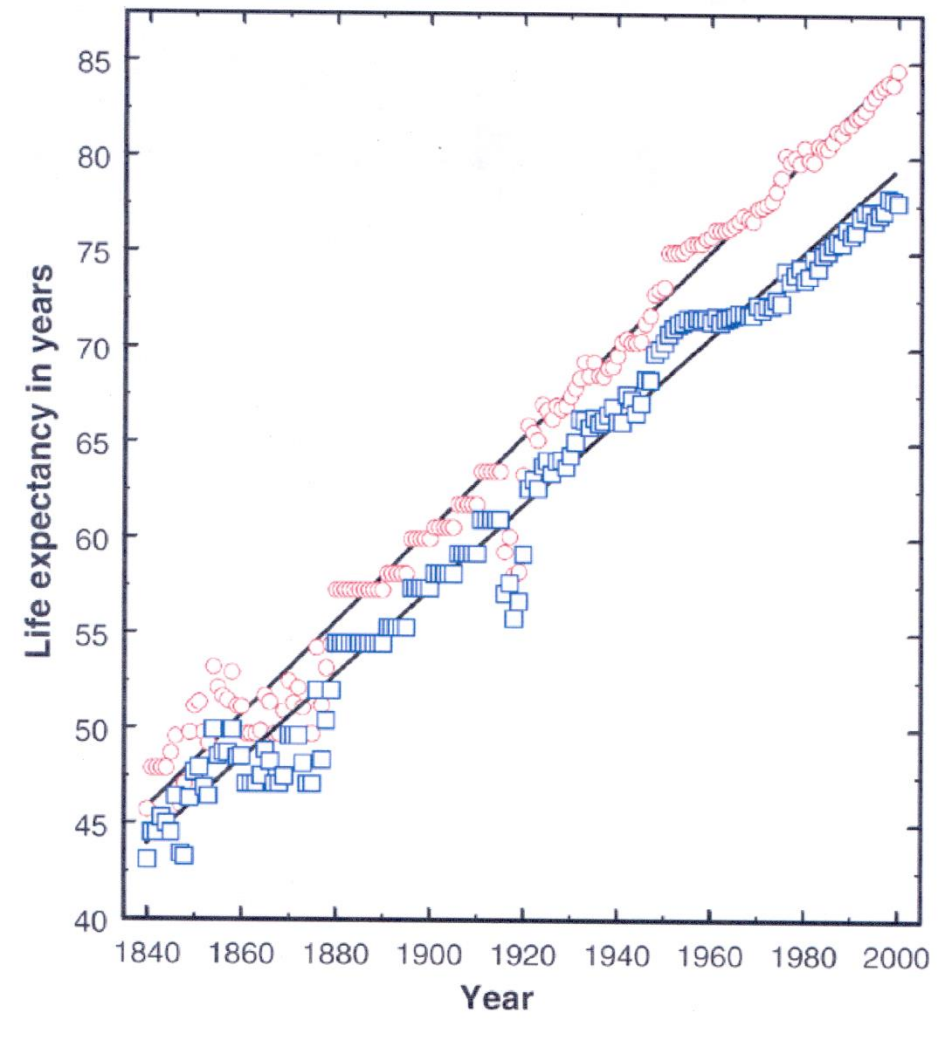
Arctic health workshop 17-18 april

It is well-established that the time of organ development is of importance for understanding causes of some chronic diseases.

It is not unexpected that it is possible to modify how organs function at the time when they are formed, especially since we know that epigenetic changes and gene expression are partly under environmental control.

Development in life expectancy

Figure 2. Male (blue squares) and female (red circles) life expectancy in the record-holding country, based on the annual data shown in supplementary table 1. For males the fitted line has a slope of 0.222 and $r^2 = 0.980$



Oeppen J, Vaupel JW. Science 2002; 296(5570): 1029-1031. (Supplementary material.)

- Life expectancy Greenland
  - Males: 64,6
  - Females: 70,4

Table 1 **Dietary factors and lifespan of male mice**

Group	*Pregnancy diet (% protein)*	*Lactation diet (% protein)*	*Weaning diet*	*Average age at death (days)*
Normal chow	20	20	Chow	765 ± 22
Normal cafeteria	20	20	Cafeteria	715 ± 21
Catch-up chow	8	20	Chow	568 ± 36
Catch-up cafeteria	8	20	Cafeteria	517 ± 35
Postnatal low-protein chow	20	8	Chow	814 ± 25
Postnatal low-protein cafeteria	20	8	Cafeteria	807 ± 28

The different dietary regimes are summarized in the first three columns ($n = 24$ mice per group). Lifespans are expressed as mean ± standard error and were analysed by two-way analysis of variance followed by Duncan's post-hoc testing where appropriate. Effect of early diet: $P < 0.001$; effect of obesity, $P < 0.01$.

Ozanne SE, et al. Nature 2004;427:411-12.

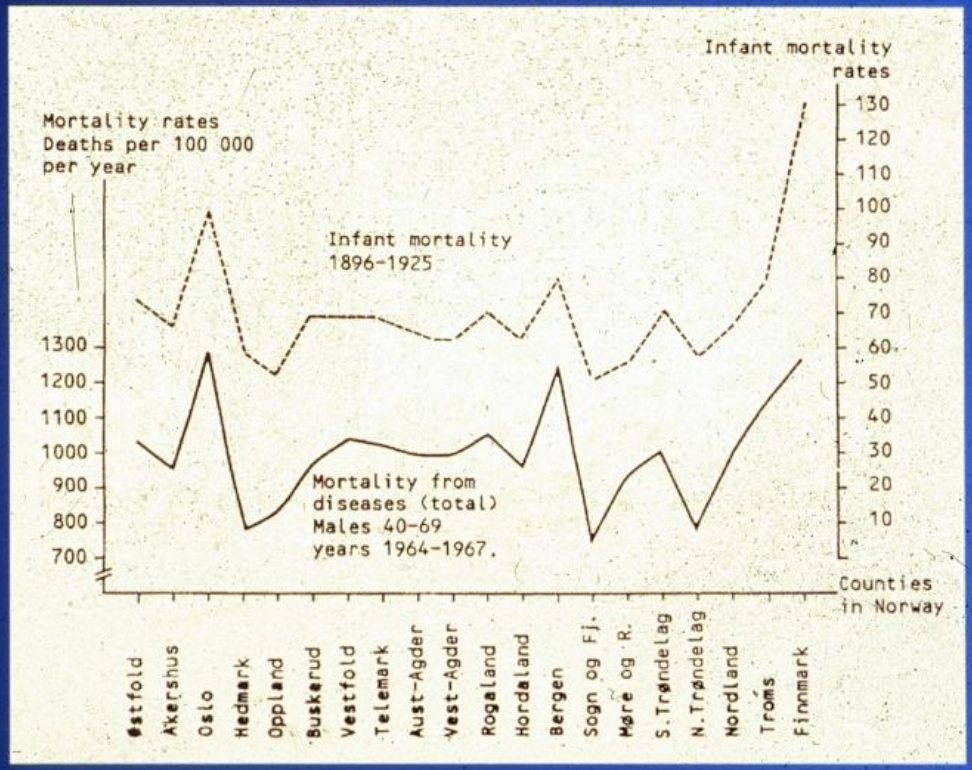
- Early nutrition or stress?

Risk for Schizophrenia for Years 1956 Through 1965 in Wuhu and Surrounding Counties

Year	Cases	No. of births	Adjusted RR (95 % CI)
1956	483	59 088	
1957	455	68 210	
1958	307	49 037	
1959	197	36 261	0.89 (0.78-1.03)
1960	192	13 748	2.30 (1.99-2.65)
1961	191	16 339	1.93 (1.68-2.23)
1962	536	75 365	0.95 (0.87-1.04)
1963	779	81 674	
1964	762	78 437	
1965	695	83 536	

St. Clair D, et al. JAMA 2005; 294(5):557-562

General mortality for Norwegian males aged 40-69 years during the time period 1964-7, and the infant mortality around the time of their birth 1896-1925 by county. Forsdahl (1988, personal communication).



BMJ 2001;322:375-376 (17 February)

Editorials

The fetal origins of adult disease

No longer just a hypothesis and may be critically important in south Asia

The Danish National Birth Cohort

The Danish Epidemiology Science Centre

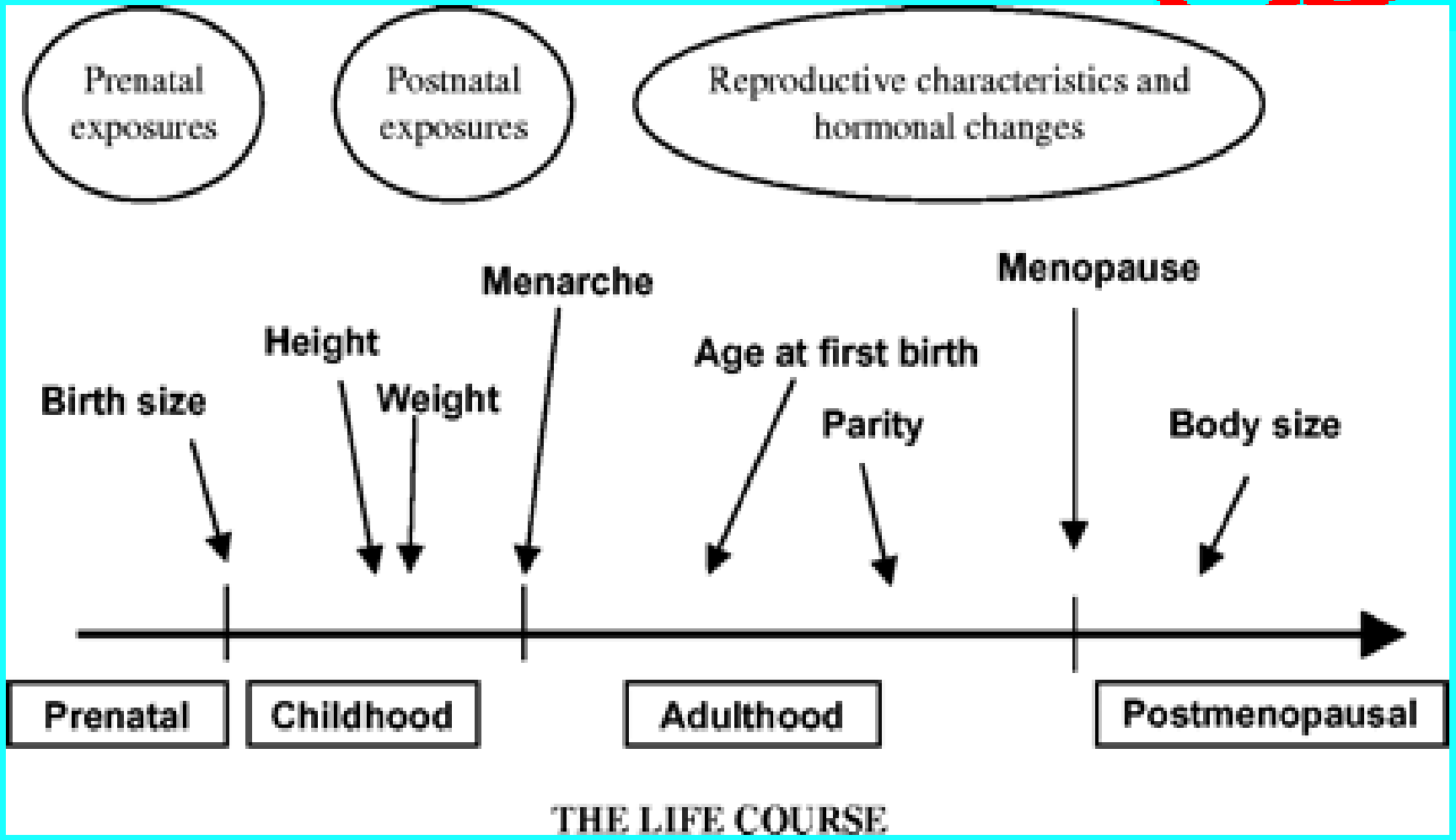
Developmental Origins of Health and Disease: Epigenetic Component?

Octobe

January 2010

October 2010

- Environment experienced *in-utero* may predispose for diseases and disorders throughout life
- A critical period for exposures



THE LIFE COURSE

- TORCH (Toxoplasmosis, Other, Rubella, Cytomegalovirus, Herpes simplex virus)

- Infections involving CNS – with potential long-term consequences.

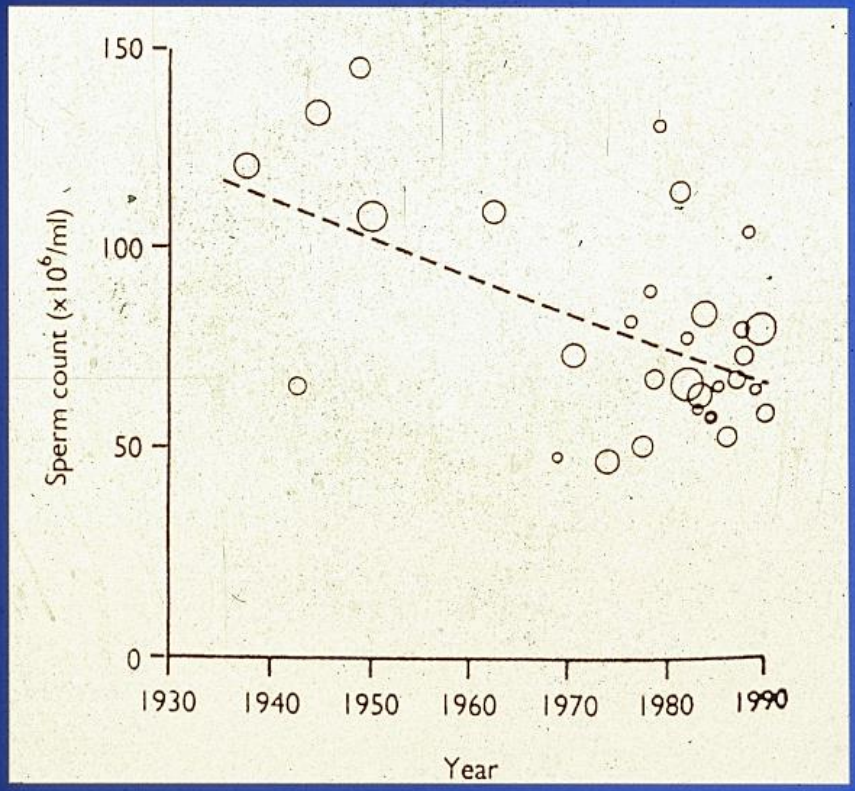
- Molecular mimicry
- Antibodies to infectious agents with common epitopes of developing brain.
- Consequences of a brain lesion is expected to depend on timing of exposure.

- Evidence – growing
- Influenza epidemics and schizophrenia
- Toxo infections and schizophrenia
- Streptococ infections and encephalitis

- Season of birth, crowdiness
- Self-reported data on infections and epilepsy
- Use of antibiotics during pregnancy and epilepsy, autism

- Environmental chemicals with hormonal effects?

Linear regression of mean sperm density reported in 61 publications (represented by circles whose area is proportional to the logarithm of the number of subjects in study) each weighed according to number of subjects, 1938-90



- An Arctic pregnancy pre-conceptual cohort
- Why a cohort in this time period?

- High risk time period
- Infertility 10-20%
- Spontaneous abortion 30-40%
- Mortality first year of life – like 54 year old male
- Congenial malfunctions 4-8%
- Functional defects - unknown

- Long term health problems – unknown
- Best candidates: Childhood cancer, Autism/ADHD/CP
- But also: Obesity, asthma, infections, CVD, mental disorders

- Why in Greenland?
  - Some exposures of interest are frequent
  - Diet – high in fat, especially saturated fat
  - Social conditions
  - Infections
  - Genes
  - Lifestyle