Long term consequences of exposure to famine
Lorentz center
Leiden, 3-5 November 2008

Studies of men and women who survived the Siege of Leningrad (1941-1944)

Denny Vågerö, Ilona Koupil and Dmitri B Shestov
Hunger and famines in 20th century Russia/Soviet - resulting in a vulnerable population?

1906 (22% of the pop affected)

1911 (25 million people affected)

1919-24 ($60,000,000 relief from US)

1933 Ukraine and North Caucasus

1941-45 Leningrad, Charkov…

1946-47 Post war hunger (1-2 million deaths)
1990s??

Sorokin (1922/75). Hunger as a factor in human affairs
Pitirim Sorokin (1922)

- The human being is what he has eaten, particularly during the first years of life, as well as what his parents ate during the time of conception and prenatal development.

(Hunger....page 55)
Leningrad siege 1941-1944

- Blockade from September 1941 to January 1944
- Food rationed from July 18th 1941 to February 22nd 1944
- Acute food shortage, severe malnutrition, trauma

- Average daily rations in winter 1941/1942 around 300 kcal.
- Smallest rations from Nov 20th to December 25th (125 g bread for office workers and dependants (< 250 kcal) (Jones 2008)
- Limitations in food availability continued in the post-war period, severe shortage in 1947 (Ellman 2000)

- Birth weights down by 5-600 g (term babies in 1942); One in two less than 2,500 g
- Fertility fell by 90% (Antonov 1947)
- Leningrad blockade hypertension epidemic (Brozek et al 1948)

in contrast with …

- Daily adult per capita rations around 700 kcal during the Dutch Hunger (Elias et al. 2004), daily intake of around 1200 kcal in Guernsey in 1944-1945 (Symons 1946) and of 2700-2800 kcal in Norway in 1943-1945 (Hansen 1947, Strom 1948)
- Food situation improved rapidly after the war
US-Soviet Collaborative Programme of 1973
(Lipid Research Clinics programme)

- **St Petersburg, several subcohorts:**


- Height, weight, blood pressure, lipids measured at a clinic; interview about smoking, alcohol, social characteristics

- Mortality follow-up till end 2005

- “were you in Leningrad during the siege” (about one third said yes)
Long term mortality after severe starvation during the siege of Leningrad: prospective cohort study

Pär Sparén, Denny Vågerö, Dmitri B Shestov, Svetlana Plavinskaja, Nina Parfenova, Valeri Hoptiar, Dominique Paturot, Maria Rosaria Galanti

Conclusions Starvation, or accompanying chronic stress, particularly at the onset of or during puberty, may increase vulnerability to later cardiovascular disease.
Long term mortality after severe starvation during the siege of Leningrad: prospective cohort study

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BMJ
2004;328:11
Relative risk for stroke by (age at) siege exposure. Mortality follow-up 1975-2000

Sparen et al, BMJ 2004
Discussion in the BMJ (2004)...

Long term mortality after starvation during the Leningrad siege

"No evidence that starvation around puberty causes later cardiovascular disease" (MD Croft)

"Crucial confounder was overlooked" (C Bell)

Role of war trauma and stress

Survival of fat people?
Expanding the analyses to include women:

**MORTALITY**

*Blood pressure, hypertension and mortality from circulatory disease in men and women who survived the siege of Leningrad*

Ilona Koupil¹, Dmitri B. Shestov², Pär Sparén³, Svetlana Plavinskaja², Nina Parfenova² & Denny Vågerö¹,⁴
Women who were 6-8 year-old and men who were 9-15 year-old at the peak of starvation had higher systolic blood pressure compared to unexposed subjects born during the same period of birth.

Mean height of women who were exposed to siege at age 6+ years appeared to be greater than that of unexposed women of same age.

No consistent effects of exposure to siege on lipid levels or obesity were detected in men or women.

Koupil et al. 2007
Caloric restriction and cancer: - famine studies suggest a link
Leningrad siege studies

Based on the Leningrad siege cohort:
• **Raised blood pressure and increased circulatory disease mortality** in men exposed around puberty (Sparen et al. 2004, Vågerö et al. 2004)
• Raised blood pressure in women exposed in childhood, **exposed women taller as adults** (Koupil et al. 2007)
• **Increased mortality from breast cancer** in women exposed at age 10-18 years (Koupil et al. In press)

Other:
• No effect of exposure in utero or infancy on glucose tolerance, hypertension, dyslipidaemia or microalbuminuria (Yudkin et al. 1997, Stanner & Yudkin 2001)
• ”**Leningrad blockade hypertension epidemic**” (Brozek et al. 1948... Khoroshinina 2004)
Issues in interpretation of our results

• Misclassification
• Selection bias
• Limited data on behavioural characteristics
• No data on reproductive histories
• Distinction between effects of hunger, cold and stress difficult

Hypotheses:

1. "programming" not restricted to foetal period

2. Hypothalamo-pituitary axis might be programmed by events experienced in adolescence and lead to long term changes in levels of hormones, reproductive function and blood pressure regulation in both sexes.
Thank you

**Funding:** Foundation for Baltic and East European Studies, MacArthur Foundation, FAS Sweden

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Caloric restriction and cancer: famine studies

higher risk of breast cancer
- 1944-1945 Dutch Hunger Winter age 12-27 years (Dirx et al. 1999) and 2-33 years (Elias et al. 2004)
- Occupation of Guernsey in 1940-1945 age 6-20 years (Fentiman et al. 2007)

prostate cancer
- Dutch Hunger Winter age 12-15 years (Dirx et al. 2001)

colon cancer
- Holocaust survivors born during war who immigrated to Israel (Vin Raviv et al. 2006)

lower risk of colon cancer
- men and women exposed to Dutch Hunger Winter at age 12-15 (Dirx et al. 2003)