Starvation linked to greater risk of cardiac complications

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Russians born during the Leningrad Siege in World War II, which was responsible for some of the greatest losses of civilian life in history, are giving scientists new strategies to identify people who experienced intrauterine growth restriction (IUGR) and starvation during childhood at greatest risk of developing long term heart complications. The abstract study[1], presented at the Frontiers in CardioVascular Biology (FCVB) meeting, in London, UK, 30 March to 1 April 2012, makes use of a unique population of people exposed to extreme starvation both as foetuses and during childhood.

The cellular changes identified, investigators suggested, might be used to target treatments to children at greatest risk of developing heart complications. In a second study [2], also presented at FCVB 2012, Spanish investigators elucidated structural changes occurring in the heart as a direct consequence of IUGR. Monitoring reversal of these changes, suggested the authors, might offer a "fast track" approach for testing effectiveness of new therapies.

"Together, these innovative studies demonstrate the impact that basic research can have on the development of new approaches to heart treatments," said Sian Harding, FCVB 2012 chairperson of the Core Scientific Committee. "New treatments preventing heart changes associated with poor nutrition would benefit those exposed to IUGR and also children who've experienced reduced calorie intakes, either due to food shortages or extreme dieting."

Intrauterine growth restriction (IUGR), defined as a birth weight below the 10th percentile for gestational age, currently has an incidence estimated to be 8.1% of births in developed countries, and 6 to 30% of births in developing countries. Common causes include chronically malnourished mothers, maternal health problems during pregnancy (such as diabetes) and placentas that fail to transfer adequate nutrients from mother to foetus.

The connection between IUGR and development of subsequent heart disease was first recognised in 1989 when David Barker, from the MRC Unit at the University of Southampton, UK, showed that the lower the weight of a baby at birth and during infancy, the higher the risk of developing cardiovascular disease (CVD) and other chronic conditions in later life [3]. IUGR newborns show signs of CV remodelling and dysfunction, including reduced myocardial velocities, dilated hearts and increased thickness of artery walls.

Studies have shown that children with IUGR have a distinct cardiac morphology, with "less elongated and more globular" cardiac ventricles. "As a consequence IUGR hearts are not as efficient in generating the normal stroke volumes, which results in the need for an increased heart rate to maintain cardiac outputs. The overall result is less efficient hearts," explained Iratxe Torre, one of the investigators, from The Hospital Clinic of Barcelona, Spain.

No treatments are currently available to reverse the structural heart changes resulting from IUGR.

Telomere length provides CVD insights in survivors of Leningrad Siege.

In abstract P190 investigators from the Almazov Federal Heart, Blood and Endocrinology Centre, St Petersburg, Russian Federation, studied the telomere length of survivors from the siege of Leningrad (1941 to

1944), which was responsible for citizens being subjected to some of the most extreme levels of starvation known in history [1].

"For workers the bread ration was 250g, which amounted to just 300 calories, with around half that for the rest of the population," said Olga Freylikhman, one of the study investigators. The diet, she added, contained virtually no protein. By the end of the siege out of a population of 2.9 million, including 0.5 million children, over 630,000 people had died from hunger related causes.

Telomeres are the DNA-protein complexes that encase the ends of chromosomes. Often likened to the plastic caps on shoelaces, they serve the function of promoting chromosome stability. Consistently shortened telomere lengths have been associated with health risk and disease - one study showed that mean telomere lengths (measured in blood DNA) predicted the 15 year risk of CVD mortality, and others identified shorter telomeres among subjects who smoked, had elevated blood pressure, and premature myocardial infarctions (MIs).

Identification of survivors for the study was made possible by the fact that after World War II, inhabitants of Leningrad (now St Petersburg) who survived the siege were invited to join special support societies. From these societies, still in existence today, investigators have been able to recruit 40 subjects born during the siege, and 260 born before the siege who had lived through the deprivations as children. Survivors were compared to age matched controls born during the same period (1930 to 1943) and now living in St Petersburg, but who had not been exposed to siege conditions. All subjects were asked to fill in questionnaires regarding lifestyle factors and take part in a range of tests including blood pressure measurements, fasting lipids and glucose tests, carotid ultrasound, arterial stiffness, and cognitive function, as well as measurements of their telomere lengths by quantitative PCR.

While measurements of telomere length for all subjects are now in progress, preliminary results (presented in the abstract) comparing the telomere length of survivors of the siege (n=106), with controls (n=27) show that survivors had significantly shorter telomere lengths (p