EARLY CAREER RESEARCHERS

Transgenerational effects of famine: initiation of the offsprings' study of Leningrad Siege survivors

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A wide range of intrauterine influences can change the pathway of fetal development. Starving during pregnancy and early life stage is one of the most important reasons of remote cardiometabolic disorders in adulthood¹. Such disorders develop due to plasticity when in a certain environment the most suitable phenotype is expressed². The disease progression in adulthood may result from poor functional capacity of malfunctioning vital organs³.

The long-term nutritional effects during pregnancy can be assessed in human populations born during periods of natural disasters and wars. Given that the genetic composition of a population changes very slowly over many generations, DNA changes can hardly be evaluated to study the response to new environmental conditions⁴. On the contrary, epigenetics, defined as somatically inherited chemical modifications of DNA that do not entail changes in the sequence itself, is plastic and responsive to the environment. Since epigenetic layers respond to external and internal conditions by modulating their pattern of chemical modifications, they are sometimes called “mediators” between the environment and DNA⁴.

The study involving the inhabitants of besieged Leningrad, who suffered a long-term lack of nutrition during Second World War, and their offspring can contribute significantly to this field. The average daily diet for the majority of Leningrad residents during the siege was about 300 calories and contained almost no protein. The longitudinal study of 3905 Leningrad siege survivors carried out by Sparen in 2004 demonstrated that they were more likely to have higher blood pressure, as well as higher rates of mortality from coronary heart disease and stroke⁵. In 1997, the study by Stanner et al showed that intrauterine malnutrition and starvation

in infancy of siege survivors were not associated with metabolic disorder or cardiovascular disease (CVD) in adulthood⁶.

The influence of environmental factors, and starvation in particular, can contribute to epigenetic transgenerational inheritance of phenotype variability⁷. It can increase susceptibility or tolerance to diseases development in next generations. Only few studies involved offspring of Leningrad Siege survivors. Professor Khoroshinina et al. (2017) found that prolonged starvation contributes to higher rates of obesity and death at younger age in Leningrad siege survivors⁸. Professor Rachkov examined the survivors and their descendants who often manifest musculoskeletal, cardiovascular, gastrointestinal and respiratory diseases⁹.

Our cohort study of 305 Leningrad siege survivors was carried out in 2009-2011. We found significantly lower anthropometric features and higher protective type of lipids (HDL) in survivors comparing with controls. The control group did not experience starvation and was comparable by sex and age. Telomere length has been suggested as a biomarker of aging and may be lifestyle related. Being the first study of T/S telomere length in survivors it showed significantly shorter ratio comparing with controls¹⁰.

We are planning to examine the descendants of the Leningrad siege survivors comparing with sex- and age-matched controls. Our study aims at assessing the transgenerational effects of starvation at early stages of development on cardiometabolic disorders along with vascular ageing in 2 generations of survivors' offspring (children, grandchildren). The study is intended to estimate both early vascular ageing (EVA syndrome) and new phenotype SUPERNOVA¹¹. SUPERNOVA patients

demonstrate extremely low vascular stiffness for their age and gender independently of cardiovascular risk factors. The data on cardiometabolic and vascular transgenerational effects of starvation can be used to improve personalized cardiovascular prevention.

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