

More on Fetal Programming of Adult Metabolic Disorders in Holocaust Survivors

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This important topic was previously reviewed in the pages of *IMAJ* and elsewhere by Ophir [1], Ben-Shlomo [2], Hazani [3] and Haimov-Kochman [4]. The topic has also been recognized by international researchers [5–8].

Subsequently, in April 2014, Bercovici wrote on the long-term effects of famine in adults born during the Holocaust. This work was a baseline study on Holocaust survivors in Israel [9]. Although the authors described certain shortcomings in their work (statistical bias), the study has clinical value and offers important public health information. The length of exposure to hunger was different in the camps, in ghettos or in hiding, so the extent of starvation, accordingly, was also different. This “exposed” European group was compared with a “non-exposed” population living in Israel during the same period. One must remember, however, that even those in Israel were at times at least partially nutritionally deprived.

There have also been publications on cancer in survivors [10], and reviews of the late effects of starvation while in utero on adults and their offspring [11]. Later, in April 2015, related research was published in *IMAJ* [12]. The authors detected various metabolic disorders in adults born during World War II who were affected by nutritional deficiencies while in utero or in early infancy. This syndrome was also known in non-Holocaust-affected survivors of famine. One aspect not considered in this excellent study, however, was the effect of nutritional deprivation on the development of premature osteopenia/osteoporosis.

In 2013 we published a study of a small group of Australian Holocaust survivors that suggested a close relationship between adult osteoporosis and deficiencies in nutrition in early life [13]. The results of a more detailed study of this topic were presented at the 2013 conference “Medicine and the Holocaust” that was held in Nahariya, Israel. Although statistically non-significant, our small numbers indicated premature metabolic disorders

and premature osteoporosis in adults exposed to famine in their early life.

In 2014 a study conducted from a different point of view investigated siblings in a single family with a history of moderate nutritional deficiency while living in a Hungarian ghetto in 1944–45 [14]. The findings demonstrated various degrees of bone demineralization in these adults, directly related to the duration of starvation during gestation. Three of the siblings had a history of famine during the critical second trimester in utero (when skeletal and muscle tissues are developing) as well as in the less critical third trimester. They all showed osteopenia/osteoporosis in later life, but the youngest sibling (conceived and born after the war) remained with normal bone metabolism despite being some 10 years into menopause.

In the above mentioned 2014 article [14], a call was issued to investigate bone metabolism in a larger number of survivors than those available in distant Australia. This call is issued once again for a study of the effect of the Holocaust on bone mineral metabolism in the much larger population of survivors in Israel. Osteoporosis in female survivors was proven by Marcus and Menczel to be nutrition-dependent [15].

Moreover, the effect of early-life starvation on the second generation has also been raised in a number of publications [3,11], most systematically in *IMAJ* in 2015 [12]. In support of this concept we present the case of a woman who during 1944 was in utero while her mother was experiencing severe starvation in a provincial Hungarian ghetto. As an adult in Australia, she recorded premature menopause and metabolic syndrome in her fifties. More importantly, her son was found to have full metabolic syndrome, arteriosclerotic disease, myocardial infarction at age 39, and borderline osteopenia at age 41. This outcome, albeit in a single case only, is consistent with the theory proposed by Keinan-Boker that fetal starvation caused by the Holocaust or other famine conditions could have effects even on the second generation [11,12].

Israel, with the largest number of rapidly dwindling Holocaust survivors, is now in the last period of being able to assess the survivors’ health problems “programmed” by the Holocaust. Moreover, new immigrants are filtering in from underdeveloped Middle Eastern or East African countries and are being exposed to sudden “catch-up” over-feeding in the

neonatal period. This situation presents yet another important public health problem, namely the need to prevent intra-uterine underfeeding and postnatal overfeeding, as both have been proven to lead to obesity and diabetes in adolescent and adult life. The same applies to sarcopenia and osteopenia [7,16].

More recently two significant publications have appeared, so far online only, adding further information on the present topic. The first one re-affirmed the effect of starvation on bone health in survivors of the Holocaust [17] and the second found conditions in this population similar to anorexia nervosa.

The articles cited represent only part of the Israeli contribution to this extremely important new field of medicine: the metabolic programming of adult diseases [7-9] and its associated life course approach to chronic diseases [2], a contribution also acknowledged by international scientists [18,19].

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