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From Famine to Osteoporosis

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ABSTRACT

Throughout history, populations have been exposed to periods of severe food shortages. Parallel to the progress of civilisation, famine has had a direct effect on morbidity and longevity. In addition to famine occurring consequent to uncontrollable climate events and insect infestations, it has also been applied as a political tool and used during wartime as a weapon of mass extermination. Irrespective of the origin of famine, infants born to women who experienced malnutrition during pregnancy are at an increased risk for certain health conditions and there is evidence that musculoskeletal disorders may originate from the intrauterine conditions. Foetal programming is likely to increase the risk of future osteoporosis when the intrauterine environment lacks essential minerals and vitamins and is termed Primary Famine Osteopathy. A brief overview is given and illustrated with details of individual clinical cases of so called Secondary Famine Osteopathy induced by extreme starvation/malnutrition in adolescence or adulthood.

Keywords: *Famine, Intrauterine, post-natal metabolic disturbances.*

HISTORICAL BACKGROUND

Famine on a massive scale is mentioned in Biblical texts and antiquity treatises. Roman historian Josephus Flavius first presented credible reports of a famine causing 20,000 deaths in 441 BCE. [1] The last three mediaeval centuries of the first millennium, named the *Warm period*, were followed by 3-4 centuries of the European *Little Ice Age*, with cold descending from the north, freezing crops and causing famine. Calamities such as flood, drought and earthquakes exacerbated those conditions [2-5].

THE EFFECT OF FAMINE ON HUMAN LONGEVITY:

At the start of the Common Era (CE/AD) the average male Roman lifespan in the Middle East was reported as 25-30 years and that estimate remained unchanged for the next 500 years, when it increased to an average of 32 years. With the availability of increased caloric intake life expectancy increased slowly throughout the second millennium, almost doubling between the end of the 19th century and the present, from 40-60 years to 81-83 years by the year 2000. [4-7, 8].

The longest lifespan exists in ten first world countries (Japan, Italy, Switzerland, Singapore, Israel, Iceland, Spain, Australia, Hong Kong, Sweden), while the average lifespan in Central African countries, with a less reliable food supply, has remained at 49-54 years.[4,5].

THE EFFECT ON FAMINE ON MORTALITY

Devastating global famines in the 20th Century resulted in malnutrition and death in catastrophic numbers, illustrated in Figure 1[3,4] Some were the consequences of political interventions, as for example the Chinese Famine in 1907 (25 million deaths); the Russian Famine of 1921 (5 million deaths); the Soviet Famine of 1932-33 (10 million deaths); the Bengal Famine of 1942 (7 million deaths), the Vietnam Famine (Japanese invasion WWII, 2 million deaths); and another subsequent Vietnam Famine (2 million deaths).

Following WWII, extensive famine emerged in multiple regions of Africa and Asia: Bangladesh 1.5 million victims, Cambodia 2 million, Ethiopia 1 million and Somalia and the Sudan each with 0.5 million. In Ethiopia the Mengitsu policy in the 1960's led to approximately 2 million deaths. More recently, between 1995-99, there was extensive famine in North Korea with a reported 3.5 million deaths [7].

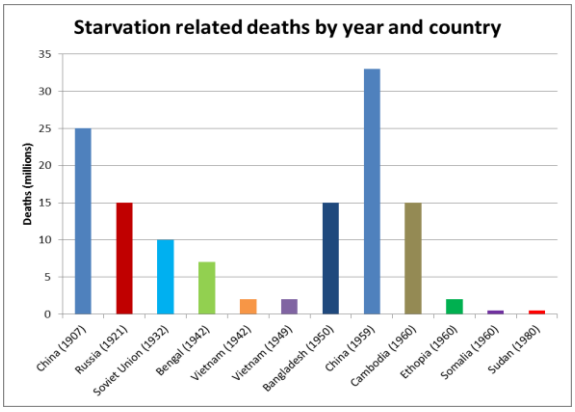

Figure1. *Death (in millions) by country*

However, by far the most catastrophic figures surfaced from China, decades after the event termed The Great Leap Forward (1959-61), during which 33 million people died due to economic and social policies, making it the largest record of famine induced death in history [7]. The social economist Stephen Devereux stated in 1988: *despite a satisfactory global food supply, it remains the twentieth century's shame that over 75 million people perished as a result of famine* [5, 7, 8].

Famine as Deliberate Instrument of Mass Murder or Military Famine

There are numerous examples of famine caused death consequent on perceived military necessity:

At the start of the 20th Century, there was a locust invasion of the Middle East (today's Lebanon, Israel and Syria). This was aggravated by the Allied navies severing food supply via the Mediterranean as WWI strategy, while the Ottoman Empire imposed its own food restrictions, thereby simultaneously cutting off the land route from the East, those combined actions resulting in 200,000 deaths [8].

During 1932-3, Ukrainian farmers' lack of cooperation with Soviet collectivisation, resulted in food confiscation. The event termed Holodomor, resulted in close to 4 million Ukrainian deaths [9] and was paralleled by the Soviet Famine of 1932-3 with 10 million deaths.

The statement: **If only one man dies of hunger, that is a tragedy. If millions die, that's only statistics"** was attributed to Joseph Stalin in 1947 [10].

During the years 1933-45 Nazi Germany stands out as the most spectacular causative agent of mass starvation both as a side effect of military maneuvers, but more sadly in instigating it as an instrument for the mass murder of people termed sub-humans.

Siege of Leningrad

The German siege, from September 1941 until January 1944, resulted in 800,000 deaths. Some 40 years later, studies conducted in Stockholm's Karolinska Institute on children born to mothers surviving on a daily sustenance of 300-800 calories, found a clear relationship between low weight and small size of newborns and consequent adult metabolic diseases (obesity, hyperlipidemia, cardiac disease and diabetes) [5,11,].

Holland ("Honger winter")

In November 1944, as a reaction to resistance by Dutch partisans, the German occupying army instituted a food embargo over the western Netherlands. By April 1945, with a mere 400 calories/day/person food availability, 18.000 deaths were recorded. Some 40 years later an Amsterdam University study found that small size and low weight at birth were related to adult metabolic aberration (glucose and lipid), obesity, cancer and an increased mortality rate. [12].

The Channel Islands

Occupied by Germany in 1940, the Normandy invasion in 1944 cut off the island's food supply from Europe. Islanders exposed to malnutrition as infants were later found to have delayed onset of puberty and increased cardiovascular morbidity, [7].

Herbert Backe's Hungerplan ("hunger plan")

Herbert Backe, High SS functionary, developed this plan as a policy for the mass murder of Slavic and Jewish "useless eaters", to accord with the *Lebensraum* policy of German expansion to the East. This agriculturalist's plan was to secure food supply for the Wehrmacht,

with the prediction that: ("If we take what we need out of the occupied countries, there can be no doubt that 20-30 millions of people will die of starvation".) Backe stated that, to procure further food for the German army, eventually killings would be required. [13,14]. A total of 4.2 million Russians and 3.3 million Byelorussians and Ukrainians were starved to death. The caloric ration for the population in Nazi occupied territories was racially distributed, down to some 420 calories per day, resulting in thousands of deaths during the harsh winter of 1941-2. The intended food allocation in 1941 compared to pre-war times was reconstructed from by Raphael Lemkin (a Polish jurist), who coined the term Genocide [15]:

Figure2. *Program of gradual nutritional elimination expressed as a percentage of daily requirement.*

	Germans	Poles	Jews
Calories	93	78	20
Meat	100	36	0
Fat	77	18	9.3
Sugar	100	77	27

THE AFTER-EFFECTS OF STARVATION

The immediate effects of starvation on individuals was easily apparent in the Nazi established Ghettos (Warsaw, Lodz, Lwow and others), where it led to devastating morbidity and mortality [16-19]. Its multigenerational consequences are illustrated through the following individual clinical examples[1]:

Case 1: The Effect of Gestational Famine

A pregnant woman, aged 26 incarcerated in the Budapest ghetto was exposed to severe nutritional deprivation. She delivered a premature female weighing only 1.5 kg who was hospitalised at the end of the war for 4 months and placed in an incubator until reaching a satisfactory weight. The infant developed normally and became a mother of two in Australia, where at the age of 51 was diagnosed with hypertension, hyperlipidaemia and osteopaenia, T-1.46; Z-1.6, without fractures. Her son (i.e. third generation) was diagnosed with metabolic syndrome and myocardial ischemia at the age of 39.His bone densitometry at age 41 was a T-score of -1.7. [Normal:-1.5 and +1,5] ***We suggest this case as an early stage bone mineral starvation, namely Primary Osteopathy reflected in the second generation and followed by Secondary Osteopathy in the third generation [17, 18].***

Case 2: The Effect of Adolescent Famine

A 13-year-old boy escaped from the Ghetto Lwow (now Lviv, Ukraine) and wandered through the countryside for 3 years. He was exposed to severe starvation, with only intermittent feeding by farmers or passers-by. He seemed to recover after the war, reached 167 cm, in height, but at the age of 27, following a minor fall, he suffered a fractured neck of femur, a type of injury more typical in the elderly. He was radiologically diagnosed with osteoporosis of the hip, which also helped to explain his repeated cough induced rib fractures. At the age of 59, bone density was measured at T-score -4.4 with significant fracture risk. [17]. **We suggest this case as an adolescent malnutrition induced Secondary Osteopathy**

Case3. The Effect of Adult Famine on Late Morbidity

While treated for a fractured pelvis, aged 90, Miriam recounted to the first author her war time experience. In 1942, she escaped with her husband into the Slovakian Mountains where they lived for close to one year in a deserted shack, during which their food supply, provided fortnightly, consisted entirely of corn, essentially almost a pure carbohydrate diet[2]. After liberation she suffered from severe weakness, cachexia, anemia and a non-viable pregnancy. Nonetheless, she recovered, enjoyed a normal reproductive life, but suffered severe post-menopausal bone loss. Her daughter, at age 51, although asymptomatic, was found with a T-score of -2.2 and Z-score of 1.3, possibly

[1]All clinical cases were those of the author's personal practice. The research cases done on international patients were with direct electronic contact, given voluntarily with permission. Some were presented or published elsewhere and reused with the permission of patients and Journals.

[2]The nutritional values obtained indicate satisfactory survival for restricted period, from 85 calories from corn: 9 cal. from fat, total fat = 1gr; saturated fat = 1gr; cholesterol = 0; sodium = 9; potassium = 165 mg; carbohydrate = 19 gr. fibre =2 gm; sugar = 4 gr; protein = 3gr; vit. A 4%; vit. C = 8%; iron = 2%; Calcium = 0 (from Certified Health information, USA, May 2018)

secondary to her mother's malnutrition during early adult life. **We suggest this a *case of malnutrition induced Second generation Osteopathy. [19].***

Case4. The Effect of Famine on Second and Third Generation Bone Metabolism

A 23 years old Hungarian woman was initially incarcerated in a labour camp, subsequently sent to the Ravensbrück concentration camp and subjected to hard labour with severe nutritional deprivation. After liberation she lived till the age 96, despite severe osteoporosis. She suffered several fractures and was found to have a T-score -4.4. Her three daughters had bone density T-scores of -3.3, -1.7 and -1.5, respectively. The daughter of the*)* first born, (i.e. third generation), at the age 43, still with a normal menstrual cycle, was recorded with a T-score of -2.5. [18**]. We suggest this *case as malnutrition induced Secondary Osteopathy in the Second and Third generation.***

Cases in Group 5:

With WWIl drawing to a close during late 1944- early 1945, 12 pregnant debilitated women, each weighing around 30 kg, managed to survive and gave birth under unbelievably harsh conditions in Auschwitz and other camps. They recovered and lived long, relatively healthy lives, but with possibly related or intensified morbidity. Six mothers were investigated and diagnosed with osteoporosis and various spinal pathologies (compression, scoliosis, kyphosis, spondylolisthesis). Nine mothers lived into their 80's, but three succumbed to malignancies. 11 children were born weighing under 2 kg, and one boy weighed 3 kg [16].

Following liberation the 12 babies were treated with cod liver oil, overcame prematurity and survived. Six tested were found with osteoporosis and similar skeletal problems like the mothers. The *children*, now in their 70s, are alive and are successful professionals [16]. Despite their osteoporosis and deformities diagnosed at an advanced age, **we suggest these cases to represent early malnutrition induced osteopaenia i.e. Primary Osteopathy for the second generation and premature adult Secondary Osteopathy for the third generation. [17]**

The Pathology of Primary Famine Induced Osteopathy

The occupying NAZI regime permitted the existence of a '*Sanitary course for the prevention of infectious diseases*', in particular of typhus, a disease highly feared by the Germans. This course was clandestinely organised by the Jewish physicians in to a Medical School[3], using the facilities of the pre-existing hospitals, teaching never discovered by the authorities. They offered a nocturnal course to some 400 students lasting 15 months, terminated in July 1942 when the Ghetto's remaining inhabitants were deported to death camps [17]. The medical staff within the confines of the ghetto achieved impressive clinical results and recorded scientific observations on the effects of starvation.

Results of studies on ***Hunger disease*** were retrieved after the war and published by the few medical staff who survived the ghetto, first in Polish and French and eventually in English through NY's Columbia University: *It remains to be considered as the most detailed scientific study of semi-starvation ever carried out and has had a profound influence on the way that disease is managed [18]*.

The **Hunger Disease** authors left behind precise descriptive observations of the starvation induced metabolic slowdown which occurs for the purpose of energy preservation. They emphasized the need to effect only gradual re-nutrition, to compensate for the discrepancy between a rapid return of metabolic processes with a much slower cardiac recovery, which may result in cardiac decompensation [18].

They also documented the histology of delayed bone fracture healing in starvation induced osteoporosis and osteomalacia, and the consequent ineffectiveness of plating and nailing of those fractures [18-21]. The ghetto doctors found that the effect of famine can be either diminished osteoid/matrix formation in childhood, (viz. osteomalacia) or osteoporosis in adults. Histology obtained from autopsies showed connective tissue replacement of bone marrow.

The Pathology of Secondary Famine Induced Osteopathy

The well-publicised Casuccio classification [22] lists the following pathogenesis:

a) **Primary Osteoblastic Deficiency,** (osteogenesis imperfecta);

[3] There were 14 medical facilities consisting of pre-existing equipped hospitals and clinics within the confines of the ghetto. They were allowed to provide a semi-functioning medical service until the final deportation, albeit with accumulating shortages.

b) **Reduced Osteoblastic activity** secondary to ovarian and testicular agenesis, menopause;

c) **Reduced Osteoblastic activity** secondary to adrenal, hypophysial or thyroid hypersecretion;

d) **Normal Osteoblastic Activity,** but insufficient bone mineral intake [5,6].

In the late 20th century, an additional category was added: e. **Foetal programming** [18]**.**

The "Barker theory" of the occurrence of adult metabolic disease as a consequence of intrauterine conditions was initially applied to glucose and lipid metabolism in the 1980s. The concept of the intrauterine origin of adult skeletal changes was introduced comparatively later in 2013 [22].

During weeks 4-9 of gestation, glucose, vit. K, Zinc and Folic acid availability influence neuron and mesenchymal-cartilaginous tissue development followed by multiplication and growth of existing cells.

During the second trimester osteogenesis (i.e. bone tissue formation) and during the third trimester limb length, head circumference and final birth weight are determined [5,6,17, 23].

During the 1990s Cooper developed the theory that deleterious influences on the early stages of bone development will result in adult bone disease and the earlier in life malnutrition occurs, the greater the likelihood of faulty bone mineralization and demineralization in later life. [24-28]. In 2012 the epigenetic programming of metabolic disorders, including osteoporosis, was described, explaining the previously made empiric observations. [27,28].

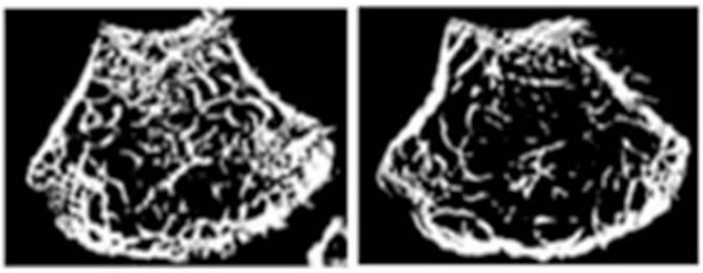

Figure3. *Bone architecture seen radiologically Normal.*

Porosis: Decreased bone mineralisation

CONCLUSION

We condemn the use of famine as a weapon of war (Leningrad), as collective punishment (Netherland) and as an instrument of mass murder (Nazi camps). Clinical case reports of the long term effects of famine on up to three consecutive generations, support the theory that severe malnutrition results in epigenetic inheritable changes, in this instance of metabolic bone disorders [29-31].

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