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Functional Foods in Health and Disease

The blockade of Artsakh causing long-term food, nutrition shortage and starvation: How functional food education can help resolve health related conditions

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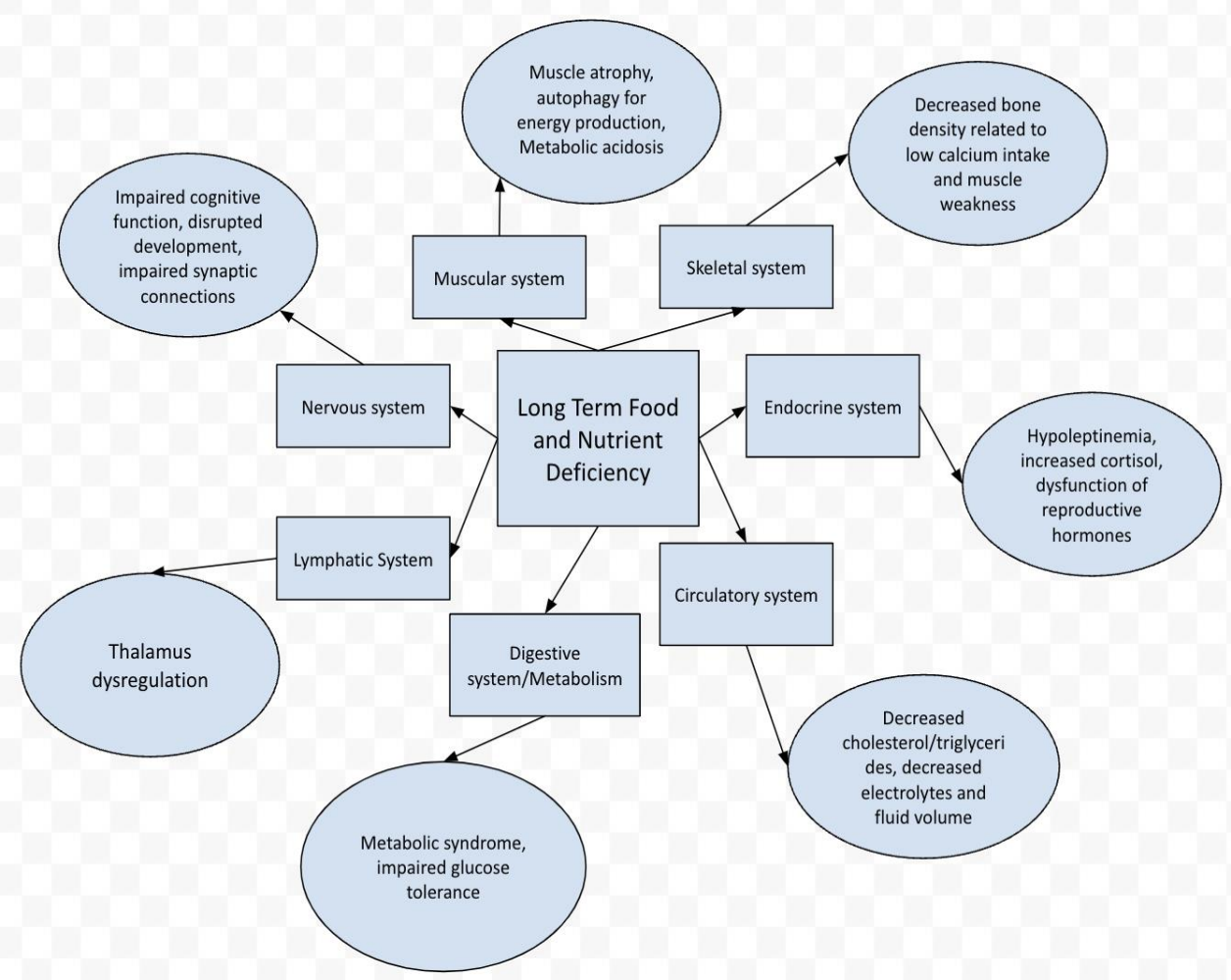
ABSTRACT

Throughout history, regimes have utilized starvation as a form of genocide. Genocide is defined by Rafael Lempkin as an intentional effort to annihilate a national group. The purpose of this research is to analyze the physiological immediate and lasting effects of starvation in the human body. In the current conflict in Artsakh (Nagorno-Karabakh), ecologists from Azerbaijan are preventing fuel, medicine, and food from entering the Armenian border at the Berdzor (Lachin) Corridor since December 12, 2022. Russian peacekeepers are simultaneously stationed at the Berdzor Corridor, which connects Artsakh and Armenia. In this article, observations are presented on the effects of starvation and recovery on the human body as they relate to historical genocides. Short and long-term effects of starvation can be severe, especially in minority populations and small territories. Although prolonged starvation has more profound impacts on the body, metabolic processes and increased stress levels can cause serious harm to someone who hasn't consumed food for even only a few days. The predominant physiological shift during a short period of starvation is the transition from gluconeogenesis as a form of fuel production to lipid oxidation as fuel production, resulting in formation of ketone bodies. This switch ultimately leads to metabolic acidosis and the beginning of further complications if trends continue. A prolonged lack of food can lead to an altered mental state, cardiac dysrhythmia, loss of bone density and various other abnormal physiological processes. Many of these findings are potentially reversible via proposed treatments for recovery, although some are not. The blockade of Artsakh has the potential to cause both severe short and long-term physical and

psychological damage as discussed below. The blockade began more than 80 days ago, thus certain damage has already occurred. We strongly urge the international community to act against this blockade and help prevent a future genocide.

Keywords: food shortage, Starvation, genocide, Artsakh (Nagorno-Karabakh), blockade, Berdzor (Lachin) corridor, bioactive compounds, functional foods



INTRODUCTION: The purpose of this review is to elucidate the detrimental effects of starving the human body. As this has occurred throughout history around the world, it is important to understand what physiological processes developed in this fasted state. Rafael Lempkin, anti-genocide advocate, believed starvation was used as a form of genocide. He stated that "Starvation was a weapon of subjugation and/or extermination" [1]. During World War 2, it was recorded that people of Western Netherlands were consuming an average of 400 kcal/day with a total of 18,000 deaths recorded [1] due to the food embargo Germany initiated in response to Dutch resistance. Under the Nazi regime, another 500,000 died of starvation and disease in Auschwitz alone

[1]. Knowing how the human body is affected in a long-term fasted state helps to understand why this type of genocide is so impactful. The current conflict in Artsakh has the capability of leading to a second genocide by starvation. There has been a long, well-known history of ethnic tension between the Armenian and Azerbaijan republics, however it had been largely within control under Soviet reign [2]. When the Soviet reign began to dissolve, as did the peace. After Nagorno-Karabakh declared independence, war became prevalent between the two republics [2]. In 1993 Armenia had gained control of Nagorno-Karabakh and occupied approximately 20% of Azerbaijan's territory, while nearly a year later a ceasefire was initiated. By 2020, both republics blamed each other for the violated ceasefire orders, leading to the "most intense fighting since 1994, leading to hundreds of casualties along the line of separation" [2]. Despite efforts to regain the ceasefire from Russia, France, and the US, it was not until Russian Peacekeepers were able to end the summer long Nagorno-Karabakh war [2].

On December 12, 2022, this peace was broken [3]. Environmentalists from Azerbaijan created a blockade at the Berdzor (Lachin) Corridor, which prevents fuel, medicine, and food from entering the Armenian border [3-4]. Russian peacekeepers are stationed at the Berdzor Corridor, which connects Artsakh and Armenia.

On February 6th, 2023, the Ministry of Foreign Affairs, Republic of Artsakh, released a statement regarding the current living environments as they relate to territorial gas supply. This statement came as a result of Azerbaijan's decision to effectively remove all gas supply from Armenia to Artsakh via the only existing pipeline [3]. As many as 120,000 residents, including 30,000 children, were without access to hot water during winter conditions [3,5]. In early March, gas was reconnected, however the only power line cannot be restored, thus leaving citizens without electricity [4,6]. These inhumane actions by the Azerbaijan government are leaving people in unbearable living situations [4,6]. Along with the electricity and gas crisis, the Artsakh government has restricted access to food since December 12th, 2022, now only allowing a short supply of food per citizen [5]. Image 2 displays empty shelves at a food store in Stepanakert, demonstrating the severe lack of access to food [4]. The Azerbaijani government is using 'hybrid warfare' with the help of Russian peacekeepers to allow this continued suffering. So, the question begs, how does this lack of food and resources impact our bodies over time? Why is awareness important and relevant in our society? As food shortages become severe, we discuss the ways in which different bodily systems are impacted. In just a few days, we can see a shift from normal body function that can easily turn irreversible if rehabilitation does not begin.

Materials and Methods Methodology: A systematic review of published studies concerning the short term and long-term effects of food deprivation was conducted electronically utilizing PubMed®, Google Scholar, George Mason University electronic library system, Loyola University electronic library system, and San Diego University electronic library system. Both review and research papers were included. Eligible articles provided reasonable, scientific evidence on the effects of food deprivation on human health. Articles not available in English were excluded. Keywords for the search included: famine, starvation, blockade, food shortage, nutritional deficiency, malnutrition, undernutrition, digestive system, metabolism, diabetes, insulin resistance, impaired glucose tolerance, metabolic syndrome, nervous system, impaired concentration, impaired comprehension, depression, anxiety, reduced alertness, vitamin B, skeletal system, osteopenia, osteoporosis, rickets, calcium, vitamin D, anencephaly, muscular system, ketones, hypohydration, lymphatic

system, lymphocytes, natural killer cells, endocrine system, leptin, glucose, glycogenesis, acidosis, lipolysis, pregnancy, amenorrhea, miscarriages, stillbirths, folic acid, biotin, circulatory system, electrolytes, potassium, cardiovascular, hypertension, atherosclerosis, food security, microbiome, microecology, choratan, matsun, narine, immune system, selenium, iron, phytonutrients, cultural appropriate, food aid, refugees, bioactive compounds, fermented food, Azerbaijan, blockade of Artsakh, and genocide.

Image 1: Map of the Region, Artsakh (Nagorno-Karabakh) after the Second Karabakh War in November 2020. (Source: Kalj/Golden, Wikimedia Commons)

- Areas captured by Azerbaijan during the 2020 war.
- Areas returned to Azerbaijan per the 2020 ceasefire agreement.
- Areas in Nagorno-Karabakh where Russian peacekeepers operate.
- Lachin corridor and Databank monastery where Russian peacekeepers operate.

Effects of Food Shortage and Starvation on Health: How the Current Situation in Artsakh Could Affect 120,000 Residents Including 30,000 Children:

Digestive System and Metabolism: Adults exposed to famine in the womb, as children, and adolescents have an increased risk of insulin resistance, impaired glucose tolerance, and metabolic syndrome [7-14]. All aforementioned irregularities are adequate indicators of increased risk of Type 2 Diabetes [10-11,15]. In addition, metabolic syndrome is also associated with an increased risk of heart disease, which is concerning as

cardiovascular diseases is the number one cause of death globally [16].

During a retrospective cohort study of the Chinese famine (1959–1961), researchers evaluated over 7,800 subjects, including survivors who had experienced famine as fetuses, infants, and children [10]. The evaluation included a blood panel to measure fasting plasma glucose, plasma triglyceride, and HDL-cholesterol levels. In addition, blood pressure and waist circumference were measured and recorded [10]. Participants who had survived the most severe famine were significantly more likely to have metabolic syndrome than those in less severe areas or those who were not exposed. Furthermore, age played a role in the disposition to inherit this increased risk, as the fetuses and infants were most affected. Subjects who were exposed to severe famine were much more likely to develop metabolic syndrome as adults than those unexposed [10]. Not only does the existence of famine in infancy increase the risk of developing Type 2 Diabetes, but the increase in famine severity appears to increase the risk of Type 2 Diabetes even further [10].

Image 2: Nagorno Karabakh - Empty shelves at a food store in Stepanakert, January 11, 2023. (Source: Azututyan. Retrieved March 6, 2023) [4]

However, infants and fetuses are not the only groups at an increased risk of diabetic issues. Researchers interviewed survivors of the Dutch famine (Winter 1944–1945) [14], and they used this information to determine the severity of the famine in the area as well as control for additional variables. Females exposed to famine during adolescence (ages 11-14) were much more likely to develop diabetes than unexposed females [14,16].

Nervous System: The sympathetic and parasympathetic nervous system play crucial roles in hunger and satiety signaling [18-20]. Proper brain functioning is directly affected by the quality of the nutrition we consume

and/or lack thereof [21-22]. Lack of consumption and subsequent nutrition impacts not only our physiological state but also our mental state and mental health [23-24]. Cognitive functioning can be impacted by short-term nutritional deficiency or supplementation [25-26]. For example, Folic acid supplementation seems to reduce the severity of Alzheimer's effects [26].

Disorders stemming from lack of nutrition can include emotional and cognitive disruptions such as: impaired concentration, impaired judgment, reduced ability to problem solve, impaired comprehension, obsessional thinking, intense negative emotions, depression, anxiety, and reduced alertness [23,27-28]. Starvation predominantly disrupts neural development of crucial structures such as the hippocampus, and the impairment of neurotransmitters including dopamine and serotonin. In particular, Vitamin B deficiency appears to increase the risk of depression [24,27]. Disruptions in the fragility of development of prenatal infants increase vulnerability and exposure to dysregulation including psychiatric disorders, disrupted neuronal migration and impaired synaptic connections [28-29].

Skeletal System: Bone health is assessed by measuring bone mineral content (BMC) and bone density [30]. Low measurements of BMC and bone density may indicate future health complications, such as osteopenia, osteoporosis, rickets, or an increased risk of bone fractures [30-31]. In order to build strong bones and prevent these health conditions, certain nutrients are necessary, such as calcium and Vitamin D [32-33]. Calcium is responsible for a multitude of physiological functioning including muscle contraction, blood pressure regulation, transmission of nerve function, increasing prothrombin time, adequate bone health, and various other vital processes [34-35]. Vitamin D plays a crucial role in the skeletal system as it facilitates the absorption and retention of calcium and phosphorus [36-38]. Additionally, Vitamin D is important to immune health as it diminishes the expression of cytokines, and their notable production of c-reactive protein [39-40].

Although not many studies have been shown in the neonatal period, we can conclude that bone health during infancy is correlated with Vitamin D exposure [33,41-42]. During the neonatal period, infants who experienced low dietary vitamin D intake were more likely to experience anencephaly, a condition defined as a fetus with an underdeveloped brain and an incomplete skull [43-45]. Anencephaly is a fatal condition with over 80% of infants with anencephaly will die on the 1st day, and almost all dying within the first week of birth [46-47].

When children suffer from malnutrition, growth and development are stunted. Growth velocity slows and reduced height and weight for age are observed in comparison to the normal population values [48]. Birthweight is a successful predictor of future bone mineral content in both men and women [49-51], where an even stronger prediction of BMC is observed at one year old [52]. Height in childhood is also an efficient predictor of bone mineral content in women, specifically [52].

Rickets is a medical condition occurring most often in growing children. The osteoid matrix’s growth plate, which forms before the maturation of bone tissue, experiences mineralization. The lack of mineralization causes soft bones, a condition known as Rickets [31,53-54]. Rickets may be caused by low intake of Vitamin D, calcium, and poor sunlight exposure [31]. Rickets can cause long term serious health complications such as pain, muscle weakness, limb deformities, developmental delay of motor skills, poor sleep, and dental irregularities [31,55]. Even in children without rickets, children who

consume inadequate amounts of calcium are more likely to fracture a bone [56-57]. Famine exposure during childhood and adolescence is associated with decreased bone mass, bone fracture, and increased risk of osteoporosis in adulthood [58-60]. This effect size appears to be greater on women [58,60].

Adult women are also a vulnerable group when considering damage to the skeletal system via malnutrition. It is well-researched and established that postmenopausal women are a high-risk group for osteoporosis and subsequently bone fractures [55,61]. Like all older adults, recommended calcium intakes increase with age [54,61-62].For this vulnerable group, both nutrition and adequate medication may be necessary to prevent skeletal system issues[35,62-63]. Due to the current blockade of Artsakh, postmenopausal women do not have access to either.

The blockade of Artsakh is not the first incident of nutrient deprivation for political reasons. In the Jewish ghettos of Nazi Germany, children reported bone fractures which refused to heal [33]. Adult starvation victims' autopsies demonstrated demineralization of the cortex and matrix [33]. In a study of Holocaust survivors, their rate of osteoporosis was 54.8%, much higher than the control group's 25% rate of osteoporosis [33]. Furthermore, the younger the Holocaust victims were at age of exposure, the greater the rate of incidence [33]. It is likely that similar effects will be seen in the victims of the blockade of Artsakh.

Muscular System: As our bodies are deprived of carbohydrates, fatty acids are released from adipose stores and become the primary source of fuel [64]. During this process, ketones are constantly being excreted through the urine. During a 420 kcal per day restriction for ten days straight, individuals who had no mineral intake or supplementation developed ketonuria, indicating slight acidic changes in the body from a pH of 5.6 to 5.1[64-65]. No ketones in the urine were found for the group receiving a 100g carbohydrate and mineral supplementation. This process of lipolysis promotes the increase of ketone bodies [66]. Ketone bodies are essential for brain and body function as there is no circulating glucose in the blood, however, ketosis is a state where the body naturally becomes very acidic - leading to metabolic acidosis. Since ketosis relies on white fat, those in a ketosis state tend to lose a significant amount of fat mass over a longer period [66]. This is seen in muscle catabolism during a restricted energy state. The group not receiving glucose or mineral supplementation in this study developed slight muscle breakdown as indicated in the blood: 7.12-7.48g/100. For the group receiving supplementation, muscle breakdown was not observed.[65]

Skeletal muscle is expressed as fundamental for normal human processes such as breathing and eating [66]. When the body is deprived of fuel, it uses its own stores to stay alive. Autophagy, or self-destruction, is activated in catabolic conditions when the body is deprived of energy and high of stress. Unfolded protein response and endoplasmic reticulum-stress-related pathways are shown to regulate muscle atrophy.[66] During this phase, we also see mitochondrial dysfunction which further induces oxidative stress and the inflammatory response.[66]. We can see this protein autophagy during the ten-day starvation trial. Men experiencing a 420-kcal diet between the ages of 21 and 52 experienced 535g of protein excretion on average per individual. This was analyzed via excess nitrogen levels excreted daily through urine. Hypohydration is another process during fasting that eliminates minerals in the body. As less fluids and sodium circulate the body during

day 10 of the study, muscle fatigue occurs [65]. This is related to the body's need for sodium and subsequent cellular fluid retention during skeletal muscle contraction. Soldiers and civilians in history who faced caloric restriction or starvation had great physical demands. Soldiers were required to carry loads of equipment along with food intake for up to ten days. Studies were initiated to address the necessary food requirements to maintain adequate functioning [65].

Additionally, As the human brain requires high amounts of energy, it will prioritize itself for the distribution of energy resources. It will even do so at the expense of other vital organs, thus creating the term "Selfish Brain Theory" [67]. As there are not enough nutrients at this point for other vital organs, the brain is top priority decreasing energy demands from other organs in the body. This increase in lactate and pyruvate creates metabolic acidosis, which, when observed all in conjunction, are body processes that occur when someone is depleted of food and water for days[67].

Lymphatic System: The lymphatic system is responsible as a main defense against bacteria, viruses, parasites, and fungi [68]. Mechanisms of action in the lymphatic system include production and circulation of lymphocytes (white blood cells), protection against pathogens, returning fluid from interstitial space, and the aid/transport of dietary lipids/lipid-soluble vitamins [68]. Three major types of lymphocytes include T-cells, produced in the thymus, B-cells produced from stem cells in bone marrow, and NK cells, also known as "Natural Killer" cells, fight against physiologically stressed cells, such as cells with tumors or viruses [68].

Any degree of malnutrition or nutrient deficiency can cause conflict in thalamus regulation. In circumstances of severe malnutrition-related immunodeficiency, the thymus undergoes atrophy [69]. This atrophy is caused by the death of thymocyte cells and subsequent loss of $CD4^+$ and $CD8^+$ cells and although cortical thymus atrophy is also known to occur in bouts of acute infection, it is commonly seen as the key indicator for assessing and diagnosing malnutrition [69]. CD4+ cells are notably referred to as the "T-helper cells," retrieving their name from their role in triggering the immune system to fight off pathogens.

Thymic atrophy is closely associated with zinc and specifically zinc deficiency [70]. Shown in several species along with humans, this decline in condition becomes worsened with lymphopenia, a disorder in which the body doesn't produce adequate lymphocytes, which then leads to a reduction in cell and antibody-mediated responses; ultimately leaving the body more susceptible to pathogens and infectious diseases [70].

Endocrine System: Even at forty hours of fasting, our liver can produce glucose through a process commonly known as glycogenesis. At this time, our body can carry out normal functioning without significant acidosis occurring. From 48-72 hours of starvation with no significant exercise, we see lipolysis begin [71-72]. As stated previously, this is when adipose tissue is being used for energy in the absence of new glucose being produced by the liver as termed gluconeogenesis. Our thyroid hormones promote lipolysis by telling the liver to use fatty acids for gluconeogenesis [72]. Insulin produced by pancreatic beta cells is the vital hormone regulating blood sugar. Insulin is responsible for carrying glucose in the cells, so when sugar is low, so is insulin. Fasting for just 72 hours decreases insulin levels 35% [72]. Lipolysis targets mostly white adipose tissue, with the remaining 15% targeting low density lipoproteins (LDLs) [71]. Furthermore, once we stop consuming adequate energy,

leptin levels begin to significantly decrease. Leptin is a hormone that regulates energy balance - influencing satiety and hunger cues. Studies have shown that starvation will decrease leptin levels by 50% in one day [63]. Conclusions revealed that starvation-induced leptinemia is the adapter to a starvation response. This starvation response is directly correlated with cortisol and ketones - the driver of glucose to lipid metabolism in humans [63].

Another vital hormone for human processing is epinephrine. Epinephrine is our "fight or flight" response that shunts normal processing and gives our bodies a rush of adrenaline. This quickly increases stress responses, working in parallel with cortisol. When the body is in a fasting state, it is constantly in this pivotal mode to keep us alive and alert [63].

The deprivation of calories and nutrients also affects reproductive hormones. During prolonged periods of famine, pregnancy and birth rates decrease [74- 76]. This decrease in birth rate is largely due to amenorrhea, miscarriages, and stillbirths [75]. First, inadequate nutrition and the inherent stress of famine can induce hypothalamic amenorrhea, a condition in which the release of GnRH is ceased predominantly due to stress and lack of energy intake [74-75, 77].

In addition, pregnancy is a well-known time of increased nutritional needs [78]. In order to maintain a healthy pregnancy, certain nutrients must be met such as folic acid, biotin, and collagen[79]. When caloric and nutritional needs are not adequately met, basic progesterone levels are not able to be properly maintained, leading to more miscarriages[80].

Circulatory System: Within the circulatory system, starvation causes changes to the blood, fluids, and heart. At the end of the 10-day calorie restriction discussed above, blood, plasma and RBC volumes were reduced by an average of 23% [81]. Oxygen saturation is important, although the lack of blood volume from dehydration results in hypotension and increased cardiac demands. The group receiving supplementation during the 10-day fast only lost 50% of the components listed [81]. Mineral and glucose supplementation helps to retain cellular fluids thus stabilizing blood volume. Hematocrit levels were also decreased in both groups (44.5 and 44.8% to 40.8% and 41.8%). The values during the rehabilitation phase continued to drop due to rehydration [71].

Weight loss while fasting during the first few days is primarily water. This 10-day study indicated that group 1, who did not receive supplementation, lost an average 1,602g of water while group 2 (supplemented) only lost 404g of fluid [81]. We can observe this further in excreted urine volumes. Abnormal electrolytes and fluid volume has been indicative of abnormal heart rhythms. During starvation, potassium dropped from 5.6-4.5mmol/L. These levels did not return to normal after rehabilitation [81]. Most electrolytes were affected, although there was no significant decrease in vitamin levels. Lastly, they found abnormalities in electrocardiograms in all subjects, indicating the heart is much more susceptible to complications than people originally believed [81].

More recently, analyzed blood components of 109 individuals before and after a 10-day fasting period [82]. Long-term fasting is characterized as 12-24 hours without food consumption, which has been used for improving glucose regulation, fat loss and treating certain pathologies. The study followed a 250-kcal consumption and advised participants to drink plenty of water and tea throughout the day. Systolic blood pressure decreased on average from 131.9 mmHg to 119.7 mmHg after 10 days which indicates a decreased demand on the heart. A statistically significant decrease in triglycerides and

cholesterol was also measured, further decreasing the risk of cardiovascular complications in the future [82]. Although a lack of micronutrients can be harmful short term, this 10-day fast indicates improved cardiovascular function by decreasing risks of hypertension, atherosclerosis, and further secondary complications.

On the other hand, undernutrition from in utero to adolescence is associated with significantly increased risk of hypertension [83-84]. Although famine exposure increases the risk of heart disease, the specific effects and windows of vulnerability appear to vary between the sexes. For instance, females who had experienced the famine of Leningrad from ages 6-8 had higher blood pressure compared to unexposed females of the same age. On the contrary, exposed males ages 9-15 were more likely to experience hypertension later in life, compared to their unexposed counterparts [84]. Males exposed to famine during puberty are more likely to die of ischemic heart disease and stroke. Pathophysiology of this disease results from the lack of blood oxygenating the coronary arteries and brain. This can happen due to many factors - cholesterol buildup mainly as stated previously. Arteries narrow, suppressing oxygenation to the affected organs. Furthermore, Famine-exposed men had an excess risk of dying (from all causes) of 21% [85]. During late childhood (approximately 10 years old), exposure to starvation can still increase risk of heart attacks later in life [86]. The risk of coronary artery disease is doubled in those conceived during famines. Fetuses also experienced coronary artery disease earlier in life [87]. This polarization in findings could be related to growth and development. Analyzing adults versus children and fetuses can have a variety of outcomes. We can see a connection between a lack of nutrients and circulating micronutrients and cardiovascular complications short term.

IRREVERSIBLE EFFECTS OF STARVATION AND IT'S MANAGEMENT BY FUNCTIONAL FOODS AND BIOACTIVE COMPOUNDS:

Irreversible Effects of Food Shortage (and Starvation) - Food and Nutrition Security: According to the USDA, food security is the consistent and equitable access to healthy, safe, affordable foods essential to optimal health. Even in the United States where food access is not limited, we still fall short of a healthy lifestyle under food guidelines [88]. Poor nutrition is the cause of half a million deaths each year, associated with decreased education and financial instability regarding healthy foods. Additionally, undernutrition is the cause of 45% of childhood deaths 5 and below [89]. Artsakh is suffering from access to foods, which is where education can play its role. If this population can understand what foods provide nutrients in these unprecedented times, detrimental effects will be lessened. Within the context of famines, both short-term and long-term, overall health outcome is greatly affected by socioeconomic status and educational status [90]. Even gender roles can make an impact as seen with the Bangladesh famine. Then, parents were more likely to give any food to their sons rather than to their daughters as girls were seen as an economic burden [90]. When addressing the conflict, steps must be taken to ensure that all members of society are given not only equitable access to resources, but education on the best foods to consume for adequate nutrients.

In this paper, we have discussed in detail the detrimental effects of long-term nutrition and food shortages. Already, these effects are emerging in the population, as the Health Ministry of Artsakh disclosed recent data describing the mounting health issues [6]. For heart diseases and its complications, there was a 58% increase. There was a 36% increase in birth

complications, and a 25% increase in medical issues caused by a lack of proper nutrition. Visits to neurologists and psychologists increased by 46% in children and 47% in adults [6]. In only 80 days these effects are profound, and further deprivation of nutrition will continue to exacerbate the situation.

Management Through Functional Foods and Bioactive Compounds: It is stated that the violation of one's own micro ecological system (gut bacteria) is associated with a variety of adverse effects: antibiotic resistance, expansion of microbial diseases, reduced mental well-being, and reduced resistance to infections [91-93]. An altered normal flora has metabolism and immune system deviations that are comparable to issues expressed with starvation above.

Choratan is an ancient Armenian fermented milk proven as a functional and medical food [93-94]. In parallel, Matsun is a fermented milk product that has been used for years as a dietary staple for digestion and human longevity [94]. Additionally, Narine, a fermented milk-based product designed from *Lactobacillus acidophilus*, contains probiotics that have antimicrobial effects against pathogenic bacteria [95]. It is concluded that probiotics contribute to the treatment of chronic diseases such as rheumatoid arthritis, atopic diseases, and blood glucose regulation [93].

During periods of famine, outbreaks of diseases occur [96-97]. These outbreaks have a few main causes: people consuming low quality and spoiled food due to desperation, and the weakening of the immune system due to poor nutrition[90,95,98]. The first issue may be addressed by providing non spoiled food products. The second issue may be remedied by providing foods rich in the necessary vitamins and minerals. For instance, foods rich in zinc are essential for signaling antiviral interferon response[99]. Zinc is available in high amounts in fish, beef, and oatmeal [100].

In addition, selenium is important to effectively use activated T-cells and NK-cells [95,101]. Foods naturally rich in selenium include Brazil nuts, tuna, sardines, halibut, ham, beef, brown rice, cottage cheese, eggs, and oatmeal[102]. In addition, iron contributes to the immune system via the development of immune cells such as lymphocytes[102]. Iron also appears to regulate the inflammatory response and may reduce the risk of atherosclerosis [104-105]. Foods naturally rich in iron include oats, dried apricots, blueberries, and beans [106-107]. We can also use the benefits of phytonutrients in this case, to aid in the immune system, nervous system regulation, and anti-inflammatory properties [108]. On the flip side, technical food additives, industrial poisons, food additives, pesticides and radiation are all factors that violate our normal flora [93].

Food shortage and subsequent starvation is a factor that alters the gut microbiome for an unforeseen amount of time. People aren't feeding their good gut bacteria with the necessary nutrients, thus allowing those vulnerable bacteria to die. Biologically active food supplements, or fermented foods, can help this population regain a healthy gut through the process of rehabilitation [109]. In order to receive adequate nutrients, it is beneficial to use milk products such as yogurt, matsun and kefir [110-112]. Fermenting milk products have prebiotic benefits, while vegetables for the benefit of containing probiotics [107]. If the people of Artsakh use their methods of fermentation using milk and vegetables, ingestion can halt some detrimental effects starvation has on the body. In all, factors that violate our gut microbiome, whether it's related to starvation or a highly processed diet, can lead to a variety of chronic diseases. The use of fermented foods during

these events are shown to keep the quality of gut bacteria at bay [113].

Finally, when recommending food aid, we considered the cultural appropriateness of these ingredients. Past experiences have shown that even in dire situations, people may abstain from food altogether rather than eat something that is not familiar or culturally appropriate [114-116]. Additionally, the amount of fuel and water needed to prepare these items should also be considered, as these resources may also be in low supply [117].

FFC Recommendations for Healthy, Functional Foods and Education:

- Fermented foods: cultured milk, yogurt/matsun, narine kimchi, sauerkraut [91-95]
- Supplements during food restriction: 100g glucose/day, sodium, potassium [81], calcium, vitamin D [33]
- Supply nutrient-rich foods such as beef, oatmeal, walnuts, Brazil nuts, ham, brown rice, cottage cheese, eggs, dried apricots, blueberries, and beans [100-101, 106-107].
- Phytonutrients: seen in plant foods such as vegetables, fruits, and legumes [108, 118-119, 120]. The Functional Food Center recommends educating the public regarding bioactive compounds and functional, healthy foods. The FFC also recommends that targeted instructions for the duration and variety of functional food products may be a practical method to improve the health of Artsakh residents, especially for the vulnerable categories such as pregnant women, children, and the elderly population [121-127].

Based on the research conducted and observations analyzed, the FFC has offered the following nutritional recommendations to implement during this conflict. The recommendations stated above are based on bioactive compounds and nutrient density. Fermented foods such as cultured milk, yogurt and sauerkraut have the potential to build positive bacteria in the gut [91-95]. Unfortunately, those struggling in Artsakh may not have access to all these products. Knowing the benefits of fermenting milk as opposed to traditional milk, for example, can aid in health promotion during these times. Additionally, Calcium and vitamin D are essential for bone health, which is vital to promote strength for those in Artsakh [32-35]. Sodium and potassium are also essential electrolytes for proper body functioning [81]. Another factor at play for this vulnerable population is the lack of electricity readily available. This makes it extremely difficult for anyone attempting to store and cook food. In this case, supplying nutrient rich foods can be a challenge. The FFC recommends people consume foods such as canned fish, dried fruits, beans and vegetables to promote nutrient levels in the body [100-101, 106-108]. Recent Functional Food Center investigations demonstrated that the supplementation of the bioactive compound squalene could be beneficial, especially for those who are suffering from chronic diseases such as type 2 diabetes [123-127].

CONCLUSIONS: We utilize the aforementioned experimental studies to understand the impact starvation has on the human body. The people of Artsakh are at risk for these effects of food scarcity, along with having no inhabitable living conditions such as electricity, medicine, and gas. Each bodily system is grossly impacted due to the lack of energy consumption, which is rarely a quick fix. Detrimental processes can become irreversible through the development of chronic diseases, such as metabolic disorders and heart failure.

Inability to receive adequate nutrients can also alter the gut microbiota, where we observe that an altered normal flora has been correlated with further complications. The incorporation of recommended functional foods will enhance good gut bacteria, thus decreasing the risk of complications. For example, we can use pickled vegetables and fermented milk products (yogurt, kefir, matsun, choratan, cheese, Narine) as sources of foods to keep the gut microbiome strong.

Supplementation can also decrease hypohydration, metabolic acidosis, abnormal electrocardiogram (EKG) rhythms and more. With famine as a major result of the Artsakh conflict, critical starvation will be the next consequence if a resolution is not found. These populations are struggling on a domestic level, and the first step to advocating for their health is to understand why. Now is the time to break history and protect the lives of these people before damaging outcomes become irreversible.

Call to Action: As outlined, this blockade starves the present population and will irreversibly damage the next. We present this information to encourage world leaders to prevent this act of genocide. As scientists, we implore the World Health Organization (WHO) and the United Nations (UN) to promote a peace treaty and combine resources (medical personnel, medical equipment, and food supplies) in order to address the already existing and continuing damage caused by the conflict [53,128].

At the beginning of this conflict, many organizations and leaders spoke out against this emerging war during a pandemic. Secretary-General of the United Nations, Antonio Guterres, urged countries to call a cease-fire on March 23, 2020. Most countries complied in order to fight the pandemic in unity, except Azerbaijan. Even after many deaths, Azerbaijan continued against UN recommendations [129]. There are several factors to be considered when measuring the war related to covid-19 deaths. Those include compromised sanitary conditions, rapid spread through close contact and equipment, and most importantly, proper medical care [129]. Fast forward to today, not only are these people becoming sicker with lack of food, but they also don't have the resources for quality care [129]. Not only are these people fighting for food, but they are vulnerable to illness and death with their decreased immune symptoms. The continual persecution of an ethnic minority over decades demonstrates a need for emphatic international condemnation. Thus, increasing the overall understanding of this failure could be invaluable to the prevention of future genocides.

Additionally, the aggressing government of Azerbaijan must be held responsible for the loss of life and subsequent damage caused. Not only do government officials need to take action to help this population and avoid the next conflict, it is dire that people around the world recognize the implications of not having access to food. Each body system is affected in a way that can potentially cause irreversible harm. Knowledge is the first step to create change, and the more people who can advocate for Artsakh, the bigger difference they will make.

The Functional Food Center is willing to provide free consultations concerning functional and healthy foods, nutrition, vitamins, and trace elements to protect and promote health in all life stages during this food shortage.

Abbreviations: UN: United Nation, World Health Organization (WHO), electrocardiogram (EKG)

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