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Bioactive Compounds in Health and Disease

Is vegan diet advisable for children?

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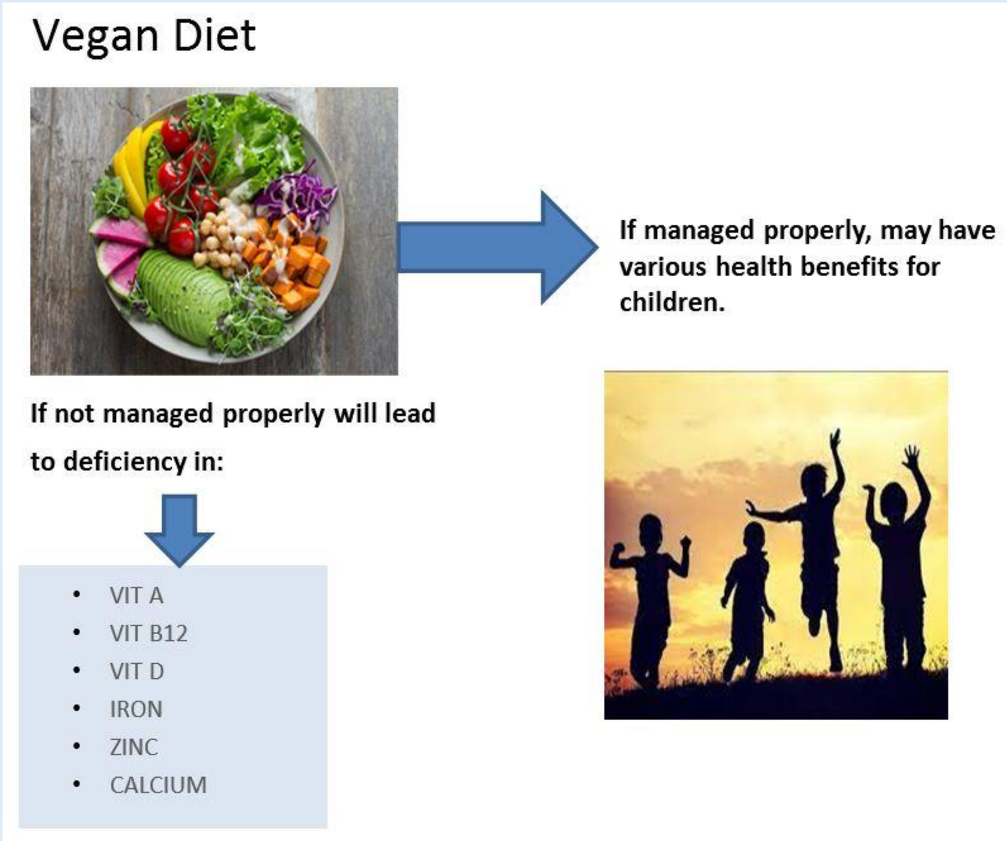
ABSTRACT

Vegan diet (VD) is a diet that consists of only plant-based foods. This diet completely excludes all animal products; meat, fish, poultry, and food gotten from milk, oil, and honey. Vegan diet differs from vegetarian diet, although they are similar; some vegetarians include egg (ovo-vegetarians), milk from animals (lacto-vegetarians) or fish (pescovegetarian) in their diet. VD is believed to be healthier than diets containing animal produce and generally have a higher diet quality than non-vegan diets. VD has many health benefits and may also reduce the risk of certain conditions such as hypertension, diabetes, and cancer. However, these benefits seen in adults may not be the same case for toddlers and young children. Their diet directly affects their height, weight, and psychomotor and neurocognitive development. VD may not supply all the nutrients necessary for development and may lead to nutrient deficiency. Vegan children are at a risk of insufficient supply and deficiency of some critical nutrients such as protein, long chain fatty acids, cholesterol, iron, zinc, iodine, calcium, and vitamin A, B_{12} and D. Deficiency of these nutrients could lead to various developmental and sometimes irreversible disorders. Apart from nutrition, VD also seems to alter the metabolomics and gut microbiota constitution of a vegan. Overall VD may have health benefits for children if it is properly fortified and supplemented. VD in children will also have to be carefully monitored to ensure the diet is healthy, nutritious and promote healthy growth and development.

Keywords: children, vegan diet, nutrition, metabolomics, inborn errors of metabolism



INTRODUCTION

In a vegan diet, all food products obtained from animals including meat, fish, milk, egg, honey, and seafood are completely excluded [1]. The practice of this kind of diet is known as veganism and those who practice it are known as vegans [2]. Reasons for being a vegan maybe ethical, religious, or ecological [3] or to improve health, prevent non-communicable disease or could be as a result of general concern for welfare of animals [4-5]. It must be put into account that although vegan diet and vegetarian diet are basically almost the same, they have some differences. While vegans exclude all animal products from their diet, some vegetarians may choose to eat egg (ovo-vegetarians) or milk (lacto-vegetarians) from animals like goat and cow or both and egg from animals (lacto-ovo vegetarians). Some vegetarians may also have fish contained in their diet (pescovegetarian) [6]. Vegan diet is made up of plant sources such as fruits and vegetables, legumes such as peas, beans, and lentils, nuts and seeds, bread, cereals, olive, meat substitutes, potatoes, vegetable oils, breads, brown rice, pasta, and also dairy alternatives such as soymilk, coconut milk, and almond milk [7-9]. About 1%-5% of the populations in the western countries follow a vegan diet and this diet is common among people between 15-34 years [10-11].

There are different guidelines regarding vegan diets for children, some believe that a vegan diet lacks essential diets needed for growth and development in children while some suggest that a well-balanced vegan diet with adequate amount of vital nutrients like calcium, zinc, iron, supplemented with Vitamins B_{12}, D and polyunsaturated fatty acid docosahexaenoic acid (DHA) is appropriate for children [12-13]. The American Dietetic Association approves vegan diets for all age groups including children provided they are properly planned while the German Nutrition Society does not support children taking vegan diet [14]. According to Weder et al. [1], there was no significant difference in the rate of growth of children who consume vegetarian, vegan, and omnivore diets. Vegan diets are believed to be healthier than diets containing animal products and generally have a higher diet quality than non-vegan diets. Vegan diet has been found to have many health benefits and may also reduce the risk of certain conditions such as hypertension, type-2 diabetes, obesity, non-alcoholic fatty liver disease and cancer [15-16]. According to some data from the Seventh-Day Adventist Health Study, it was reported that vegan diet had positive effects against the development and progression of obesity, hypertension, diabetes, and cardiovascular related diseases [17]. Veganism has been widely recommended and accepted as a model of healthy diet associated with gut microbiota [18-19], cardiovascular diseases [20], diabetes, obesity, cancer, chronic kidney disease, and metabolic syndrome [21-23]. The higher fiber, low energy density, lower saturated fat, antioxidants, potassium, and sodium contents in vegan diet can contribute to a lower body mass index (due to the reduced protein intake). This is because the vegan diet is high in fiber, omega-6 polyunsaturated fatty acids but low in cholesterol, total fat and saturated fatty acids as compared with omnivorous diet [22]. With a lower cholesterol level, this further helps to regulate the blood pressure.

Diets rich in fruits, vegetables, and whole grains, which lead to an increase in blood antioxidant capacity, could reduce blood pressure in hypertensive patients. Due to the consumption of more fruits and vegetables, children who consume vegan diet have lower cholesterol levels, lower rates of obesity and overweight and high levels of antioxidants in their blood. Atherosclerosis begins in the early stage of life and gradually progresses into risk factors of cardiovascular disease in the adult life. Since vegan diet has been shown to reduce the risk factor of cardiovascular disease (CVD), this could potentially improve the cardiometabolic health from childhood to adulthood [24].

In a trial involving obese and hypercholesterolemic children, vegan diet in children was discovered to be more effective than the American Heart Association-recommended diet in reducing the adult risk factors of CVD [24-25]. Vegan diet reduces high blood pressure via several mechanisms, such as improving blood viscosity, vasodilation and insulin sensitivity; by altering the baroreceptors, renin-angiotensin and sympathetic nervous system; by its anti-oxidant and anti-inflammatory properties and by changing the colony and strain of gut microflora. Individuals who consume vegan diets have lower systolic blood pressure, diastolic blood pressure and reduced risk of hypertension compared to those who consume omnivores diet [26]. Vegan diet has also been discovered to be associated with increased lifespan and cancer protection and this is due to the low level of methionine found in this diet [27]. When compared with the omnivores diet, vegan diet has been discovered to be associated with lower bone mineral density which is linked with higher risk of bone fracture [28-29] and this could be because of the deficiency in nutrients and minerals like Vitamins D, B_{12}, A, iodine, zinc, folate, selenium, and calcium which are important for proper bone health [30-31]. Restricted intake of whole food groups in vegan children could however be of great concern due to the fact that their nutrient and energy needs are higher, and the growth might be impaired due to nutrient deficiency at some sensitive points of development [32].

Fig 1. Vegan diet [33]

It is also important to note that most of the studies supporting these benefits are observational. How the diet directly performs its actions and the mechanistic basis for these observations are unclear. The direct action of metabolism, in addition to systemic effects such as regulation of hormonal actions and antioxidation, serve as a link between diet and health [14].

Owing to differences in protein composition in these diets, amino acid intake and plasma levels may account for one of the main differences between vegan and vegetarian diets as some vegetarians may consume egg, milk from animal, fish and even meat occasionally.

Vegan Diet and The Gut Microbiota: The human gut microbiota is made up of numerous microorganisms like viruses, bacteria, fungi and protozoa [34]. The bacterial composition and diversity can be altered continuously by diets, lifestyle habits, environmental factors, stress, infant transitions, use of probiotics, prebiotics and antibiotics, intestinal and metabolic diseases [19, 34-35].

High-fat, low-fiber and high-protein diets have been reported to increase intestinal inflammation by modifying the translocation of bacterial populations and metabolites involved in modulating inflammatory response [36]. An imbalance in the activity and composition of the microorganisms in the gut is referred to as 'gut microbiota dysbiosis' [37] and it is associated with disorders like chronic kidney, hepatic and gastrointestinal diseases (Ulcerative colitis, Crohn's disease), colorectal cancer, allergy, autoimmune disease, obesity, type 2 diabetes and CVD [34,38-39].

Long term nutritional patterns can change both function and diversity of the gut microbiota and fibers, fats and proteins are commonly involved in the metabolic pathways in the gut microbiota [40-41]. Vegan diets are sources of nutrients for microorganisms while an omnivorous diet greatly alters the human gut microbiota which is made up of bile-tolerant potentially harmful microorganisms due to the fact that omnivores diet has increased levels of fecal bile acids [35]. These bile acids alter the composition of the gut microbiota through metabolic and inflammatory pathways [42-43].

Dietary fibers serve as substrates for bacterial metabolism in the intestine and the end products of the metabolism such as short chain fatty acids (SCFAs), which play a major role in immunoregulation [34,44], providing anti-inflammatory activities in the intestine [45], improving glucose tolerance, blood lipid profiles and insulin sensitivity, absorption of water and sodium, inhibiting cancer cell proliferation [37-38, 46], reduction of body weight [47] and also protection from inflammatory bowel disease, type 2 diabetes and immune diseases [19].

Vegan diet which is low in fats contains monounsaturated and polyunsaturated fats thereby altering the intestinal microbial composition [44] while animal saturated fats promote inflammation leading to metabolic disorder [19] and this has been discovered to be the driving force in CVD as a result of high levels of total serum cholesterol and LDL [45].

Dietary proteins in vegan diet cause an increase in the level of SCFAs in the intestine while animal proteins are involved in inflammatory bowel disease and are also associated with CVD [45].

Vitamins like vitamin K, biotin, cobalamin, riboflavin, thiamin are involved in bacterial metabolism and can be synthesized by the gut microbiota [48].

Metabolic Profile of Vegan Diet In Children: Adequate knowledge of the metabolic concerns of a strict vegan diet is still limited [49]. Children who consume vegan diet have been discovered to have a unique metabolic profile characterized by modification in biosynthesis of bile acids including increased levels of unconjugated primary bile acids and reduced taurine to glycine conjugation ratio of bile acid. It is also unknown whether the differences in the bile acid biosynthesis have any impact on endocrine functions, digestion, absorption and gut microbiome [14]. Low levels of polyunsaturated fatty acid docosahexaenoic acid (DHA), HDL-C and LDL-C, total cholesterol, variations in the level of circulating amino acids, low levels of vitamins A and D, low level of circulating leucine/isoleucine, phenylalanine, valine/betaine, and aspartate and higher levels of alanine, arginine, and glycine and lower protein intake were also observed [50].

A study was conducted in Finland to assess the difference in the metabolomics of omnivores, vegetarian and vegan children and to check if vegan diet is sufficient to support normal growth and development of vegan children. The aim of this exercise was also to assess the effect of vegan diet in dietary management of childhood disorders. At the end of the study it was found that vegan children had a distinct metabolic profile from that of omnivorous children. This distinction was characterized by lower levels of circulating fatty acids, lower levels of cholesterol and low density and high density lipoproteins, change in circulating amino acids, almost devoid of DHA and EPA and also lower levels of vitamin A and D. In the study, the low sufficiency of vitamin A and even lesser DHA could be a cause of concern in the visual health of vegan children. Vegan children also had higher folate intake and serum concentration than omnivorous children while some vegan children had higher folate levels than the recommended range. Although there have not been much adverse effects of high folate and low vitamin B12 levels as seen in some vegans, this might nevertheless pose a problem in neurocognitive health of the child [50].

The most striking alteration of pathway however was that of the bile acid. In vegan children, there were higher levels of unconjugated primary bile acids and significantly lower levels of conjugated primary bile acids as compared to omnivores. Although this is so, it is uncertain how exactly this alteration affect the usefulness of bile acid in digestion and absorption [50].

Vegan diet has also been shown to influence the gut microbiota composition in vegans as compared to omnivores. Plant based diet like the vegan diet seems to be beneficial by enhancing the development of a more diverse and stable microbial system [19].

Nutrients of Interest: Children need proper nutrients to grow up and stay healthy and strong. The dietary requirements for children are quite different from adults, they require more nutrients and energy to ensure normal growth and development of the brain, immune and endocrine systems [51]. Nutrition for children can also help establish a foundation for healthy eating habits and nutritional knowledge that children can apply throughout life. There are various nutrients required for health and growth of children. All the classes of food, which include; carbohydrates, protein, fat and oil, minerals and vitamins, have important functions in growth, health protection and energy metabolism and must be present during the growth of a child and if not present, will result in malnutrition or even death in worst cases. Below are some nutrients and their functions in the body:

Table 1. Nutrients of interest in vegan diet, their functions, and sources.

NUTRIENT	FUNCTION	SOURCES
PROTEIN	Protein which is made up of amino acids is necessary for growth. These amino acids are either essential or non-essential. Essential amino acid can't be made or stored in the body; therefore these amino acids have to be present in the diet. The nine essential amino acids are: histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan, and valine. Essential and nonessential amino acids both produce energy and build proteins, and some form neurotransmitters and hormones. Amino acids such as tryptophan, tyrosine, histidine, and arginine are used by the brain for the synthesis of various neurotransmitters and neuromodulators [53].	Essential amino acids are found in animal sources in sufficient quantities while food such as vegetables, grains, and nuts, are lower in essential amino acids. But they can be combined to create complementary proteins that do provide enough essential amino acids [52].
CHOLESTEROL	Cholesterol can be biosynthesized in the body and ingested through diet. It is synthesized mainly by the liver and also other cells of the body as it has very essential biological functions. Some uses of cholesterol are: building of cell membrane which is highly essential in growing children, cell transporters and signaling molecules, production of hormones, assist in metabolism and production of vitamin D, production of bile acids necessary for digestion of fat and absorption of essential nutrients. It also serves as precursor for several biochemical pathways [54]. Cholesterol is carried around the body by low density lipoprotein (LDL) and high density lipoprotein (HDL). Although cholesterol has several biological functions, excess cholesterol may increase the risk of cardiovascular diseases.	Cholesterol in diet is mainly gotten from animal sources like meat, milk and egg [55].
CALCIUM	Calcium, the most abundant mineral in the body is the basic component of bone and needed for healthy bone and teeth in adult and particularly children. Calcium must be in optimum supply because children are still in the growth phase. Calcium plays a role in muscle movement, cardiovascular health (as it plays a key role in clot formation in blood) and is necessary for maintaining communication between the brain and other body parts [56].	Major sources of calcium include cheese, yogurt, milk and other diary food, fish. It can also be obtained from leafy greens and soybean [57].

VITAMIN D	Vitamin D is a fat-soluble vitamin produced by the body after being exposed to sunlight. Vitamin D can also be taken through food but the body might not get sufficient amounts of vitamin D through diet alone. Vitamin D is necessary for maintaining healthy bones and teeth. It promotes the absorption of calcium and phosphorus by the body and it is important to maintain a proper immune system [58].	Vitamin D is necessary for maintaining healthy bones and teeth. It promotes the absorption of calcium and phosphorus by the body.
VITAMIN A	Vitamin A is another one of the four fat soluble vitamins. Vitamin A helps in the growth and maintenance of healthy teeth, skeletal and soft muscles, skin and also maintains the integrity of the mucus. Vitamin A promotes good eyesight especially when there is insufficient light [59].	There are two types of vitamin A present in food; Preformed vitamin A which is found in animal products like meat, beef liver, fish, poultry, egg, and dairy food. The most abundant natural source of vitamin A is cod liver oil which is pressed from the liver of cod fish. Provitamin A is found in plant sources such as fruit like carrots and minerals. Provitamin is also usually called beta carotene which is a powerful antioxidant and can alleviate the risk of cancers [60].
IODINE	Iodine is a trace element necessary for the production of thyroid hormones T3 and T4. Iodine is needed for proper growth and also for proper development of the brain. It also aids the regulation of body temperature, metabolism and heart rate [61].	The most abundant sources of iodine are egg, seaweed, fish such as cod and tuna, shrimp, and basically mostly seafood. Iodine can also be found in iodized salt, dairy products such as milk, yogurt and cheese [62].
ZINC	Zinc is a trace mineral associated with very numerous cellular functions in the body. It is required in the catalytic activity of many enzymes and plays a role in immune function, protein synthesis, wound healing, DNA synthesis and cell division [63]. Zinc must be provided through the daily diet since the body does not have a specialized zinc storage system.	The most abundant source of zinc in diet is oyster which contains high amount of zinc. Other food sources high in zinc are meat, poultry, crab, crab, clams, lobster, pork, beans, nuts, whole grains, fortified cereals and dairy products [64].
VITAMIN B_{12}	Vitamin B_{12} is a water-soluble vitamin that plays a key role in the functioning of brain and nervous system, as well as formation of red blood cells. It is involved in the metabolism of every cell in the body. It helps to create and regulate DNA [65]. It also affects fatty acid and amino acid metabolism.	Sources of Vitamin B_{12} are beef, pork, ham, poultry, lamb, fish, dairy products, eggs and fortified cereals. Vitamin B_{12} is found in plants but an unrealistic amount needs to be consumed in order to meet the body requirement [66].
FOLATE	Folate is essential for thymidine synthesis and thus for DNA formation and any cell division hence its role in the formation of red blood cells and healthy cell growth and function [67]. It is also an important nutrient involved in bone protection [69-71].	Main sources of folate include dark green leafy vegetables, beans, peas and nuts. Fruit like oranges, lemons, banana, melons and strawberries are also rich in folate [68].
IRON	Iron is a trace mineral needed for proper formation and functioning of hemoglobin [72].	The best source of iron which is bioavailable are beef, liver, canned clams, ground beef, chicken, mussel, fortified cereal, white beans, dark chocolate, oyster, tofu, chickpeas [73].

Impact of Vegan Diet in Children Nutrients and Metabolomics: Plant-based diet is becoming more prevalent in recent times especially in European and western countries. Families or individuals who choose to adhere to vegan diet may do so for various reasons. Choosing vegan or vegetarian diet may be due to ecological, ethical health related or religious reasons [74]. This diet has been shown to have many positive effects on health in adults, and even children could benefit from this diet, however, veganism in children must be paid close attention, as there are many factors to consider [15]. Adults require different set of nutritional values compared to children because children require more energy and nutrients per body weight [75]. The more restrictive the diet and the younger the child is, the greater is the risk of nutritional deficiency [76].

Toddlers, children and teens who are still growing and developing require nutrient in sufficient qualities to ensure proper growth and development, in not only height and weight but also neurocognitive and psychomotor development. The influence of diet on the gut microbiota can also impact the emotional, epigenetic development and cognitive aspects of an individual [77-78]. Proper development of endocrine, neural and immunological systems need to be considered [79]. Vegan diet may not provide all the necessary nutrients needed for growth and development of a child which may lead to deficiencies if not properly checkmated.

Nutritional Composition of a Vegan Diet Cholesterol: Cholesterol, saturated fatty acids, LDL and HDL altogether are low in vegan diet. Vegan diet has very low amount of cholesterol due to the fact that most cholesterol in diet is consumed from animal source. This results in various health benefits such as reduced body fat, reduced risk of heart disease, reduced risk of blood pressure to name a few. This is also true for children however; children are still growing and cholesterol has many roles in the growth of children. As mentioned above cholesterol is needed in formation of cell membrane and is also a precursor for several steroidal hormones. Progesterone, glucocorticoid, mineralocorticoid, androgens and estrogens are produced from cholesterol [80]. Although cholesterol is produced in the body and isn't necessarily needed from diet, cholesterol is needed in higher levels in children development therefore children may need cholesterol from diet. Therefore, although not as much as animal sources, plant sources of cholesterol such as nuts and seeds, olive oil and coconut oil must be included in the diet of vegan children [81].

Polyunsaturated fatty acid (DHA and EPA): EPA (Eicosapentaenoic acid) and DHA (Docosahexaenoic acid) are omega-3 fatty acids. They are needed in infants for proper development of brain, eyes, and nervous system. It also has been identified to ease depression and improve heart functioning. Vegan diet is very low in EPA and DHA due to the fact that they are majorly found in oil fishes like cod liver, herring, mackerel, salmon, menhaden and sardine. Though the body produces EPA from an essential fatty acid known as alpha-linolenic acid (ALA), the efficiency of conversion of ALA to EPA is much lower than obtaining EPA and DHA from the diet [82]. This is because EPA is a precursor of DHA. Therefore, maintaining the levels of EPA and DHA in the body will be more difficult because of the extra metabolic work needed for the body to produce EPA then use part of it to metabolize DHA. It is advisable that vegans consume food rich in ALA such as flaxseed, walnut, canola oil, soy products and hemp seed. EPA and DHA can also be derived from seaweed algae and omega-3 supplements [83].

Energy and essential amino acids: Vegan children have lower protein intake when compared with omnivorous children. The percentage of energy from protein is considerably lower which is usually portrayed in both vegan adults and children in form of lower body mass and lower BMI although it is still in normal range [84]. A study has found that vegan children tend to be smaller than non-vegan children, and have a deficit in calorie intake [1]. Another study shows that there is an overall reduced level of circulating essential amino acids in the blood pool. It is unclear whether lower levels of several essential amino acids could have adverse or beneficial effects as this has not yet been fully studied and there are no specific guidelines for healthy blood levels of individual amino acids especially for infants and children [50]. In some vegan children, growth velocity was discovered to be lower compared to the omnivorous children although not statistically significant. The vegan children also had similar levels of Insulin-growth factor-1 (IGF-I) and Insulin-like growth factor binding protein-3 (IGFBP-3) with the omnivorous children [85]. Vegans get protein in their diet from beans, soy beans, lentils, tofu, hempseed etc. Several of the vegetable products are characterized by low digestibility; plant cells and some substances like tannins, enzyme inhibitors, phytates can inhibit digestibility of protein [86]. Appropriate combination of vegan food can provide all the essential amino acids needed by the body [87]. In a study by Weder et al. [1], there was no difference in the total energy intake between children on vegan and omnivores diet, with the omnivorous children getting their caloric intake particularly from protein, added sugar and fats while the vegan children got theirs mainly from fibers.

Bone health: The vegan diet may cause an intake of calcium below recommended levels. In a study by Weikert et al. [88], the rate of calcium excretion and serum level of parathyroid hormones (PTH) in vegans were measured. A low rate of calcium excretion and increased PTH level were observed which is the physiological result of low calcium intake. Vegan toddlers fed on breast milk may not experience the problem of not getting their calcium requirements because the calcium from the mother's bones will enrich the breast milk [89]. Lower calcium levels were observed in vegan infants not exclusively breastfed when compared with omnivores infants. Therefore, infants who are not breastfed should not be administered with inadequate plant-based food because the majority of them will lack sufficient calcium supply [90]. As they grow older it will be imperative to monitor their calcium intake and make sure they get adequate calcium supply because it is necessary for the healthy growth of their bones and is needed at higher levels during development [91]. Vegan adults and vegan children alike have higher risks of bone fractures due to lower intake of calcium from their diet. The calcium in their diet also faces the problem of bioavailability. Some sources of bioavailable calcium for vegans are Choy, Chinese cabbage, kale and collard [92]. Vegan diet has been discovered to prevent the children from attaining ideal height or bone mineral status [32]. Consuming non-dairy drinks enriched with calcium is recommended for vegan children in order to derive a good level of calcium in their body [93].

Fiber: Vegans usually tend to consume plenty amounts of fiber. Consumption of fiber might be beneficial because it aids bowel movement and can make up the bulk of food and pass through the system with little to no absorption by the body. However excess consumption of fiber especially in vegans will cause loss of nutrients because the fiber might hinder the absorption of nutrients such as fats, iron, and calcium from food [94]. Therefore, it is imperative that less fiber is consumed in the diet for vegan children. Due to the high fiber content in vegan food, there is premature satisfaction and fullness which can lead to an insufficiency in the energy uptake especially in children [95].

Iron: Sources of iron in vegan diet is generally not as bioavailable as non-vegan sources and this can lead to a lower iron status and this was observed in a study by Desmond et al. [32] involving children who consume vegan diet. Bioavailability of non-heme iron is also reduced due to the presence of phytates and dietary fiber in vegan diet. If the iron is not sufficiently absorbed this may lead to an iron deficiency. Non-heme iron found in plant food is less easily absorbed than heme-iron found in animal food [96]. This however might not pose a problem because vegans often consume large amounts of vitamin C rich foods and vitamin C improves the absorption of non-heme iron. In addition to consuming vitamin C rich foods, vegans can also consume calcium fortified food and supplements [89].

Zinc: Vegans are often considered to be at risk for zinc deficiency. Zinc aids the immune system and is a cofactor necessary for the proper functioning of numerous enzymes such as carbonic anhydrase, phosphatases, nucleases, peptidases and many others in the body. Zinc is an essential trace element and needs to be provided in the diet, however, phytic acid found in beans, legumes, seeds, nuts and grains bind the present zinc and inhibit the absorption. Therefore, zinc is not easily absorbed from plants sources while animal sources supply about half of the zinc intake in omnivores [89]. For vegan children this might pose a serious problem on their well-being as their immunity might not be as strong as that of adults. Therefore, extra attention needs to be paid to zinc serum levels in vegan children. However, despite the low zinc availability to the body, vegans do not necessarily show reduced immunological competence. This suggests that the body may have a compensatory mechanism for zinc absorption, but this is yet to be explored. Low plasma zinc levels could however lead to iron deficiency due to its involvement as a catalyst in iron metabolism [97].

Vitamin B_2: Large quantities of Vitamin B_2 are found in foods from animal origin, while the supply of this vitamin from plant-based food is low, as observed in some studies conducted in Finland, France and Germany (Berlin) where it was discovered that the amount of vitamin B_2 absorbed in vegans is lower compared to omnivores because the absorption of vitamin B2 from plant-based food is low [88, 98-99].

Vitamin D: Vitamin D is essential in regulating calcium and phosphate metabolism. Vegans are at higher risk of Vitamin D deficiency. Vitamin D occurs in two forms: vitamin D_2 (ergocalciferol) and vitamin D_3 (cholecalciferol). Vitamin D_2 found in plant sources is less bioavailable than vitamin D_3. Vitamin D_2 can also be produced by ultraviolet radiation in plants [87]. Vitamin D_3 is obtained from animal or plant sources [100]. The body also produces vitamin D_3 from cholesterol. Cholecalciferol is synthesized by the body through exposure to sunlight which stimulates the conversion of 7-hydrocholesterol to vitamin D_3 in the skin [101]. Although the body can synthesize its own vitamin D_3, it is important that it is present in the diet as the amount produced by the body may not be sufficient. It is essential for vegan children to have sufficient vitamin D supply because it is necessary for bone maintenance. Lower bone mineral content was observed in vegan children when compared with omnivore children and this could result from their low calcium, protein, vitamin D and vitamin B_{12} intake [32]. Vitamin D can also be obtained from food supplements although, not all vitamin D_3

supplements are acceptable by vegans as most of them are made from cholecalciferol derived from lanolin which is extracted from sheep's wool. In a study by Hovinen et al, [50], low vitamin D status was reported in vegan Finnish children when compared with children consuming omnivores diet despite the daily intake of Vitamin D supplements.

Vitamin B_{12} (cyanocobalamin): Vitamin B_{12} deficiency is one of the greatest problems occurring in veganism. This is because sufficient vitamin B_{12} can only be obtained from animal sources and is produced solely by microorganisms in the herbivorous animals [30]. Plants do not have reliable sources of Vitamin B_{12} [102]. Vitamin B_{12} is bound to animal protein sources like meat. Upon reaching the stomach the stomach acid, HCL (Hydrochloric acid) separates vitamin B_{12} from the protein which it is bound to. After the separation, a protein secreted by the parietal cells of the stomach known as intrinsic factor, a glycoprotein, binds to the vitamin B_{12} and activates it by removing the cyano group attached to the cobalt atom then it can be absorbed into the body. Children who practice veganism are at a very high risk of being affected by vitamin B_{12} deficiency because they need B_{12} for brain development and also for proper formation of red blood cells [103]. The lack of vitamin B_{12} leading to deficiency could bring about several problems such as growth, reflex and memory problems, tremors, numbness, dementia, depression and megaloblastic anemia characterized by improper formation of red blood cells. It could also cause permanent nerve and brain damage [104]. In some vegans among the Indian and Hong Kong population who rarely include supplements in their diets, high prevalence of vitamin B_{12} deficiency have been reported [20]. In order to receive an adequate supply of Vitamin B_{12}, supplements of Vitamin B_{12} should be taken along with the vegan diet because inadequate vitamin B_{12} status was observed in some children who consume vegan diet without supplementation [32, 105].

The problem of Vitamin B_{12} deficiency is not only restricted to vegan toddlers and children. Even Veganism in pregnant mothers can affect the fetus if it is not getting enough Vitamin B_{12} from the mother. The growth and development of the fetus might be impaired. Therefore, it is compulsory for vegan toddlers, children, pregnant women and adults to rely on fortified food like soy milk, cereals and also supplements [106]. Infants breastfed by vegan mothers have also been reported to have vitamin B_{12} deficiency which could be accredited to the depletion of vitamin B_{12} in their mother's body. Symptoms such as reduced growth rate, reduced bone mineral density, anorexia, weak muscles, delayed speech development, involuntary movement, enlarged liver and spleen, megaloblastic anemia are usually observed in those infants [107-108]. Impaired DNA synthesis and cell function is also associated with vitamin B_{12} deficiency [109].

Vitamin B_{12} is involved in the metabolism of methionine, fatty acids and amino acids, regulation of homocysteine concentration and formation of blood cells. Low serum level of vitamin B_{12} is associated with high plasma level of homocysteine, and this is considered to be a risk factor of cardiovascular disease [110]. According to a study by Pawlak [111], the individuals on vegan diet had very low level of serum $B_{12,}$ low status of Vitamin B_{12} biomarkers like methylmalonic acid (MMA) or holotranscobalamin II (holoTC) and very high level of homocysteine (Hcy). Due to the deficiency of vitamin B_{12} in vegan diet [110], vegans are on an increased risk of suffering from hyperhomocysteinemia.

Vegan Diet and Children's Immune System: Vegan diet has often been related to lowered levels of both white blood cells and red blood cells. The decline in protein and calories adversely affects the immune system. In growing children, nutrition directly affects the development of the immune system. Malnutrition, especially in vegan children will lead to an impaired immune system. However, nutrients that have critical roles in the maintenance of the immune function are best obtained from fruit, vegetables, nuts, whole grains and seeds which are the bulk of vegan diet. Also, the vegan diet is rich in phytochemicals which improve the immune function [112].

Despite the consistent reduced number of white blood cells found in vegans, the antioxidants provided by their food might be helpful in compensating the lack in leucocytes. Therefore, a very well planned and supplemented vegan diet may be beneficial to the immune system. Although there is a high antioxidant content in the vegan diet which may offer some immunity enhancing benefits, vegans don't necessarily exhibit a better immune system than omnivores [113].

Vegan Diet and Inborn Errors of Metabolism: Inborn errors of metabolism are rare disorders caused by inherited (genetic) factors or spontaneous mutations of genes necessary for the conversion of food into energy. Inborn errors of metabolism are heterogeneous and very diverse in nature [114]. Although specific inborn errors in metabolism are quite rare, they are more common when all different types are considered. Inborn errors in metabolism have been observed in 1 out of 2500 births [115]. It is imperative to consider the impact of vegan diet on the infants and children with these conditions.

Vegan diet in children can represent a new means to develop various strategies for dietary management of childhood disorders.

Phenylketonuria: Phenylketonuria is an autosomal recessive inborn metabolic disorder characterized by the inability of the body to metabolize phenylalanine due to the absence of its metabolizing enzyme phenylalanine hydroxylase [116]. This leads to hyperphenylalaninemia which is the accumulation of phenylalanine in the blood, resulting in a series of health problems including retardation, poor skin pigmentation, growth impairment, convulsion and hypersensitivity [117]. In order to manage this condition, phenylalanine intake must be kept to the barest minimum. Phenylalanine is found mainly in high protein food such as meat, pork, chicken, egg and milk. Some other foods containing phenylalanine are beans, grains, nuts, fish, tofu, cheese and soybeans. Also, other food like soda containing aspartame, an artificial sweetener is made with phenylalanine. Consumption of low protein foods such as fruits, vegetable, juices, potatoes, peas, low protein bread and pasta will be more suitable for a child with phenylketonuria. Vegan diet may not be able to completely manage this condition but it serves as a good start.

Maple Syrup Urine Disease: Maple syrup urine disease is an inherited disorder characterized by the inability of the body to metabolize some amino acids properly. Isoleucine, leucine and valine cannot be metabolized due to the deficiency of the enzyme complex branched-chain alpha-keto acid dehydrogenase. This causes the accumulation of these amino acids in the body which leads to neurological problems, vomiting and dehydration. To avoid accumulation of these amino acids in the body, it is imperative to reduce the amount of them consumed in the diet. Foods that are high in protein should be avoided. Vegan diet is an advisable diet in managing this condition [118].

CONCLUSION

Vegan diet has a wide range of health benefits both in adults and children. It can be useful in managing some inborn errors of metabolism and other health conditions. However veganism in children must be closely monitored to prevent malnutrition. Depending on the severity of the malnutrition it could lead to impaired growth both bodily and cognitive, in worse cases it could even lead to death. In some cases of malnutrition owing to poorly planned vegan diet, the child was rushed to the hospital and diagnosed with vitamin D deficiency, anemia, failure to thrive and an overall poor health condition. There was also a case of a father and mother who lost custody of their child due to malnutrition because the child was fed with poor vegan diet.

This shows that for a child who is fed with vegan diet, the composition of the diet has to be well planned and accordingly supplemented with some vitamins, minerals and trace elements. Supervision of a nutritionist and pediatrician is advisable and also regular checkups to ensure that the vegan children are getting all their needs [119].

According to the Academy of Nutrition and Dietetics and also the American Dietetic Association, well-planned vegetarian and vegan diets supplemented appropriately are suitable for all life stages, but the German Nutrition Society include strong recommendations to parents that vegan diet should not be adopted by children without medical and dietetic supervision [120].

Also, if a child proposes to go on a vegan diet, the parent or guardian should find out why the child wants to go on a vegan diet. While some choose the vegan diet for a healthier diet and all its health benefits, some might not. Without knowing the reason for choosing a vegan diet, eating disorders like anorexia nervosa can easily be hidden by a vegan diet [121].

List of Abbreviations: DHA: Docosahexaenoic acid, VD: Vegan diet, CVD: Cardiovascular diseases, SCFAs: Short chain fatty acids, HDL-C: High-density lipoprotein-cholesterol, LDL: Low-density lipoprotein, ALA: Alpha-linolenic acid, PTH: Parathyroid hormone, EPA: Eicosapentaenoic acid, MMA: Methylmalonic acid, holoTC: holotranscobalamin II, Hcy: Homocysteine, HCL: Hydrochloric acid.

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REFERENCES

1. Weder S, Hoffmann M, Becker K, Alexy U, Keller M. Energy, macronutrient intake, and anthropometrics of vegetarian, vegan, and omnivorous children (1–3 years) in Germany (VeChi Diet Study). Nutrients. 2019; 11(4): 832. https://doi.org/10.3390/nu11040832.
2. What is the difference between veganism and vegetarianism? Medical News Today. [https://www.medicalnewstoday.com/articles/325478]. Retrieved, 2019.
3. Janssen M, Busch C, Rödiger M, Hamm U. Motives of consumers following a vegan diet and their attitudes towards animal agriculture. Appetite. 2016; 105: 643-51. https://doi.org/ 10.1016/j.appet.2016.06.039
4. Poore J, Nemecek T. Reducing food's environmental impacts through producers and consumers. Science. 2018; 360(6392): 987-92. https://doi.org/10.1126/science.aaq0216
5. Willett W, Rockström J, Loken B, Springmann M, Lang T, Vermeulen S, Garnett T, et al. Food in the Anthropocene: the EAT–Lancet Commission on healthy diets from sustainable food systems. The Lancet. 2019; 393(10170): 447-92. http://doi.org/10.1016/S0140-6736(18)31788-4
6. What's The Difference? Healthline. [https://www.healthline.com/nutrition/vegan-vs-vegetarian]. Retrieved 2016. Retrieved February 28th, 2022

7. What Is A Vegan diet. WebMD Medical. Retrieved from [https://www.webmd.com/diet/vegan-diet-overview]. Retrieved 2019.
8. Papier K, Tong TY, Appleby PN, Bradbury KE, Fensom GK, Knuppel A, Perez-Cornago A, et al. Comparison of major protein-source foods and other food groups in meat-eaters and non-meat-eaters in the EPIC-Oxford cohort. Nutrients. 2019; 11(4): 824. https://doi.org/10.3390/nu11040824
9. Salvador AM, García-Maldonado E, Gallego-Narbón A, Zapatera B, Vaquero MP. Fatty acid profile and cardiometabolic markers in relation with diet type and omega-3 supplementation in Spanish vegetarians. Nutrients. 2019; 11(7): 1659. https://doi.org/10.3390/nu11071659
10. Radnitz C, Beezhold B, DiMatteo J. Investigation of lifestyle choices of individuals following a vegan diet for health and ethical reasons. Appetite. 2015; 90: 31-6. https://doi.org/10.1016/j.appet.2015.02.026
11. Kersting M, Kalhoff H, Melter M, Luecke T. Vegetarian diets in children?-an assessment from pediatrics and nutrition science. Dtsch Med. Wochenschr. (1946). 2018; 143(4): 279-86. https://doi.org/10.1055/s-0043-119864
12. Schüpbach R, Wegmüller R, Berguerand C, Bui M, Herter-Aeberli I. Micronutrient status and intake in omnivores, vegetarians and vegans in Switzerland. Eur. J. Nutr. 2017; 56(1): 283-93. https://doi.org/10.1007/s00394-015-1079-7
13. Baroni L, Goggi S, Battaglino R, Berveglieri M, Fasan I, Filippin D, Griffith P, et al. Vegan nutrition for mothers and children: Practical tools for healthcare providers. Nutrients. 2019; 11(1): 5. https://doi.org/10.3390/nu11010005
14. Allen AE, Locasale JW. Metabolomics: insights into plant-based diets. EMBO Mol. Med. 2021; 13(2): e13568. https://doi.org/10.15252/emmm.202013568
15. Schürmann S, Kersting M, Alexy U. Vegetarian diets in children: a systematic review. . Eur. J. Nutr. 2017; 56(5): 1797-817. https://doi.org/10.1007/s00394-017-1416-0
16. Gallego-Narbón A, Zapatera B, Álvarez I, Vaquero MP. Methylmalonic acid levels and their relation with cobalamin supplementation in Spanish vegetarians. Plant Foods Hum. Nutr. 2018; 73(3): 166-71. https://doi.org/10.1007/s11130-018-0677-y
17. Le LT, Sabaté J. Beyond meatless, the health effects of vegan diets: findings from the Adventist cohorts. Nutrients. 2014; 6(6): 2131-47. https://doi.org/10.3390/nu6062131
18. Wong MW, Yi CH, Liu TT, Lei WY, Hung JS, Lin CL, Lin SZ, et al. Impact of vegan diets on gut microbiota: An update on the clinical implications. Tzu Chi Med. J. 2018; 30(4): 200. https://dx.doi.org/10.4103%2Ftcmj.tcmj_21_18
19. Tomova A, Bukovsky I, Rembert E, Yonas W, Alwarith J, Barnard ND, Kahleova H. The effects of vegetarian and vegan diets on gut microbiota. Front. Nutr. 2019; 6: 47. https://doi.org/10.3389/fnut.2019.00047
20. Woo KS, Kwok TC, Celermajer DS. Vegan diet, subnormal vitamin B-12 status and cardiovascular health. Nutrients. 2014; 6(8): 3259-73. https://doi.org/10.3390/nu6083259
21. Cramer H, Kessler CS, Sundberg T, Leach MJ, Schumann D, Adams J, Lauche R. Characteristics of Americans choosing vegetarian and vegan diets for health reasons. J Nutr Educ Behav. 2017; 49(7): 561-7. https://doi.org/10.1016/j.jneb.2017.04.011
22. Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian, vegan diets and multiple health outcomes: a systematic review with meta-analysis of observational studies. Crit Rev Food Sci Nutr. 2017; 57(17): 3640-9. https://doi.org/10.1080/10408398.2016.1138447
23. Sebastiani G, Herranz Barbero A, Borrás-Novell C, Alsina Casanova M, Aldecoa-Bilbao V, Andreu-Fernández V, Pascual Tutusaus M, et al. The effects of vegetarian and vegan diet during pregnancy on the health of mothers and offspring. Nutrients. 2019; 11(3): 557. https://doi.org/10.3390/nu11030557
24. Desmond MA, Sobiecki J, Fewtrell M, Wells JC. Plant-based diets for children as a means of improving adult cardiometabolic health. Nutr. Rev. 2018 ; 76(4): 260-73. https://doi.org/10.1093/nutrit/nux079
25. Macknin M, Kong T, Weier A, Worley S, Tang AS, Alkhouri N, Golubic M. Plant-based, no-added-fat or American Heart Association diets: impact on cardiovascular risk in obese children with hypercholesterolemia and their parents. J. Pediatr. 2015; 166(4): 953-9. https://doi.org/10.1016/j.jpeds.2014.12.058
26. Orlich MJ, Fraser GE. Vegetarian diets in the Adventist Health Study 2: a review of initial published findings. Am. J. Clin. Nutr. 2014;100(suppl_1): 353S-8S. https://dx.doi.org/10.3945%2Fajcn.113.071233
27. Sanderson SM, Gao X, Dai Z, Locasale JW. Methionine metabolism in health and cancer: a nexus of diet and precision medicine. Nat. Rev. Cancer. 2019; 19(11): 625-37. https://doi.org/10.1038/s41568-019-0187-8
28. Iguacel I, Miguel-Berges ML, Gómez-Bruton A, Moreno LA, Julián C. Veganism, vegetarianism, bone mineral density,

and fracture risk: a systematic review and meta-analysis. Nutr. Rev. 2019; 77(1): 1-8. https://doi.org/10.1093/nutrit/nuy045

29. Menzel J, Abraham K, Stangl GI, Ueland PM, Obeid R, Schulze MB, Herter-Aeberli I, et al. Vegan Diet and Bone Health—Results from the Cross-Sectional RBVD Study. Nutrients. 2021; 13(2): 685. https://doi.org/10.3390/nu13020685
30. Richter M, Boeing H, Grünewald-Funk D, Heseker H, Kroke A, Leschik-Bonnet E, Oberritter H, et al. For the German Nutrition Society (DGE).(2016). Vegan diet. Position of the German Nutrition Society (DGE). Ernahrungs umschau. 2016; 63(04): 92-102. https://doi.org/10.4455/eu.2016.021
31. Palermo A, Tuccinardi D, D'Onofrio L, Watanabe M, Maggi D, Maurizi AR, Greto V, et al. Vitamin K and osteoporosis: Myth or reality?. Metabolism. 2017; 70: 57-71. https://doi.org/10.1016/j.metabol.2017.01.032
32. Desmond MA, Sobiecki JG, Jaworski M, Płudowski P, Antoniewicz J, Shirley MK, Eaton S, et al. Growth, body composition, and cardiovascular and nutritional risk of 5-to 10-y-old children consuming vegetarian, vegan, or omnivore diets. Am. J. Clin. Nutr. 2021; 113(6): 1565-77. https://doi.org/10.1093/ajcn/nqaa445
33. Plant based vegetarian and vegan diets. Heart Foundation. [https://www.heartfoundation.org.nz/wellbeing/healthy-eating/nutrition-facts/plant-based-vegetarian-vegan-diets]. Retrieved 2021.
34. Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GA, Gasbarrini A, Mele MC. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms. 2019; 7(1): 14. https://doi.org/10.3390/microorganisms7010014
35. Milanović V, Osimani A, Cardinali F, Litta-Mulondo A, Vignaroli C, Citterio B, Mangiaterra G, et al. Erythromycin-resistant lactic acid bacteria in the healthy gut of vegans, ovo-lacto vegetarians and omnivores. PloS one. 2019; 14(8): e0220549. https://doi.org/10.1371/journal.pone.0220549
36. Karl JP, Margolis LM, Madslien EH, Murphy NE, Castellani JW, Gundersen Y, Hoke AV, et al. Changes in intestinal microbiota composition and metabolism coincide with increased intestinal permeability in young adults under prolonged physiological stress. Am. J. Physiol. - Gastrointest. 2017; 312(6): G559-71. https://doi.org/10.1152/ajpgi.00066.2017
37. McBurney MI, Davis C, Fraser CM, Schneeman BO, Huttenhower C, Verbeke K, Walter J, et al. Establishing what constitutes a healthy human gut microbiome: state of the science, regulatory considerations, and future directions. J Nutr. 2019; 149(11): 1882-95. https://doi.org/10.1093/jn/nxz154
38. Klement RJ, Pazienza V. Impact of different types of diet on gut microbiota profiles and cancer prevention and treatment. Medicina. 2019; 55(4): 84. https://doi.org/10.3390/medicina55040084
39. Li BY, Xu XY, Gan RY, Sun QC, Meng JM, Shang A, Mao QQ, et al. Targeting gut microbiota for the prevention and management of diabetes mellitus by dietary natural products. Foods. 2019; 8(10): 440. https://dx.doi.org/10.3390%2Ffoods8100440
40. De Angelis M, Garruti G, Minervini F, Bonfrate L, Portincasa P, Gobbetti M. The food-gut human axis: the effects of diet on gut microbiota and metabolome. Curr. Med. Chem. 2019; 26(19): 3567-83. https://doi.org/10.2174/0929867324666170428103848
41. Attaye I, Pinto-Sietsma SJ, Herrema H, Nieuwdorp M. A crucial role for diet in the relationship between gut microbiota and cardiometabolic disease. Annu. Rev. Med. 2020; 71: 149-61. https://doi.org/10.1146/annurev-med-062218-023720
42. Ramírez-Pérez O, Cruz-Ramón V, Chinchilla-López P, Méndez-Sánchez N. The role of the gut microbiota in bile acid metabolism. Ann. Hepatol. 2018; 16(1): 21-6. https://doi.org/10.5604/01.3001.0010.5494
43. Just S, Mondot S, Ecker J, Wegner K, Rath E, Gau L, Streidl T, et al. The gut microbiota drives the impact of bile acids and fat source in diet on mouse metabolism. Microbiome. 2018; 6(1): 1-8. https://doi.org/10.1186/s40168-018-0510-8
44. Graf D, Di Cagno R, Fåk F, Flint HJ, Nyman M, Saarela M, Watzl B. Contribution of diet to the composition of the human gut microbiota. Microb. Ecol. health dis. 2015; 26(1): 26164. https://doi.org/10.3402/mehd.v26.26164
45. Singh RK, Chang HW, Yan DI, Lee KM, Ucmak D, Wong K, Abrouk M, Farahnik B, et al. Influence of diet on the gut microbiome and implications for human health. J. Trans.l Med. 2017; 15(1): 1-7. https://doi.org/10.1186/s12967-017-1175-y
46. Daliri EB, Wei S, Oh DH, Lee BH. The human microbiome and metabolomics: current concepts and applications. Crit Rev Food Sci Nutr. 2017; 57(16): 3565-76. https://doi.org/10.1080/10408398.2016.1220913
47. Hjorth MF, Blædel T, Bendtsen LQ, Lorenzen JK, Holm JB, Kiilerich P, Roager HM, et al. Prevotella-to-Bacteroides ratio predicts body weight and fat loss success on 24-week diets

varying in macronutrient composition and dietary fiber: results from a post-hoc analysis. Int J Obes. 2019; 43(1): 149-57. https://doi.org/10.1038/s41366-018-0093-2

48. Rowland I, Gibson G, Heinken A, Scott K, Swann J, Thiele I, Tuohy K. Gut microbiota functions: metabolism of nutrients and other food components. Eur J Nutr. 2018; 57(1): 1-24. https://doi.org/10.1007/s00394-017-1445-8
49. Farella I, Panza R, Baldassarre ME. The difficult alliance between vegan parents and pediatrician: a case report. Int. J. Environ. 2020; 17(17): 6380. https://dx.doi.org/10.3390%2Fijerph17176380
50. Hovinen T, Korkalo L, Freese R, Skaffari E, Isohanni P, Niemi M, Nevalainen J, et al. Vegan diet in young children remodels metabolism and challenges the statuses of essential nutrients. EMBO Mol. Med. 2021; 13(2): e13492. https://doi.org/10.15252/emmm.202013492
51. Heird WC. Nutritional requirements of infants and children. Modern. Nutr. Health Dis, (eds). 2012; 11: 712-33. https://www.ncbi.nlm.nih.gov/books/NBK209820/.
52. Layman DK, Anthony TG, Rasmussen BB, Adams SH, Lynch CJ, Brinkworth GD, Davis TA. Defining meal requirements for protein to optimize metabolic roles of amino acids. Am. J. Clin. Nutr. 2015; 101(6): 1330S-8S. https://doi.org/10.3945/ajcn.114.084053
53. Hou Y, Yin Y, Wu G. Dietary essentiality of “nutritionally non-essential amino acids” for animals and humans. Exp. Biol. Med. 2015; 240(8): 997-1007. https://dx.doi.org/10.1177%2F1535370215587913
54. Cerqueira NM, Oliveira EF, Gesto DS, Santos-Martins D, Moreira C, Moorthy HN, Ramos MJ, et al. Cholesterol biosynthesis: a mechanistic overview. Biochemistry. 2016; 55(39): 5483-506. https://doi.org/10.1021/acs.biochem.6b00342
55. Karimi-Maleh H, Arotiba OA. Simultaneous determination of cholesterol, ascorbic acid and uric acid as three essential biological compounds at a carbon paste electrode modified with copper oxide decorated reduced graphene oxide nanocomposite and ionic liquid. J. Colloid Interface Sci. 2020; 560: 208-12. https://doi.org/10.1016/j.jcis.2019.10.007
56. Okuskhanova E, Suychinov A, Rebezov M, Nurgazezova A, Anuarbekova A, Harlap S, Maksimiuk N, et al. Role of calcium, magnesium and phosphorous in human body. Res. J. Pharm. Biol. Chem. Sci. 2018; 9(6): 258-61. https://www.researchgate.net/publication/332846224
57. Vannucci L, Fossi C, Quattrini S, Guasti L, Pampaloni B, Gronchi G, Giusti F, et al. Calcium intake in bone health: a focus on calcium-rich mineral waters. Nutrients. 2018; 10(12): 1930. https://doi.org/10.3390/nu10121930
58. Cardwell G, Bornman JF, James AP, Black LJ. A review of mushrooms as a potential source of dietary vitamin D. Nutrients. 2018; 10(10): 1498. https://dx.doi.org/10.3390%2Fnu10101498
59. Chea EP, Lopez MJ, Milstein H. Vitamin A. (2020). In: StatPearls. Treasure Island (FL): StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK482362/
60. Tanumihardjo SA. Vitamin A fortification efforts require accurate monitoring of population vitamin A status to prevent excessive intakes. Procedia Chem. 2015; 14: 398-407. https://doi.org/10.1016/j.proche
61. HEALTH The Iodine Deficiency Epidemic—How to Reverse It for Your Health. *Tempus*, *4*. [https://draxe.com/nutrition/iodine-deficiency/]
62. Attar T. A mini-review on importance and role of trace elements in the human organism. Chem Rev Lett. 2020; 3(3): 117-30. https://dx.doi.org/10.22034/crl.2020.229025.1058
63. Kaur K, Gupta R, Saraf SA, Saraf SK. Zinc: the metal of life. Compr. Rev. Food Sci. Food. 2014; 13(4): 358-76. https://doi.org/10.1111/1541-4337.12067
64. Swain PS, Rao SB, Rajendran D, Dominic G, Selvaraju S. Nano zinc, an alternative to conventional zinc as animal feed supplement: A review. Anim. Nutr. 2016; 2(3): 134-41. https://doi.org/10.1016/j.aninu.2016.06.003
65. Bonetti F, Brombo G, Zuliani G. The Role of B Group Vitamins and Choline in Cognition and Brain Aging. In Nutrition and functional foods for healthy aging 2017 :139-158. Academic Press. https://doi.org/10.1016/B978-0-12-805376-8.00015-0
66. Gille D, Schmid A. Vitamin B12 in meat and dairy products. Nutr. Rev. 2015; 73(2): 106-15. https://doi.org/10.1093/nutrit/nuu011
67. Mahmood L. The metabolic processes of folic acid and Vitamin B12 deficiency. J Health Res Rev. 2014; 1(1): 5. https://doi.org/10.4103/2394
68. De LC, De T. Healthy food for healthy life. J. Glob. Biosci. 2019; 8: 6453-68. [https://www.webmd.com/healthy-aging/features/longevity-foods].
69. Knurick JR, Johnston CS, Wherry SJ, Aguayo I. Comparison of correlates of bone mineral density in individuals adhering to lacto-ovo, vegan, or omnivore diets: a cross-sectional investigation. Nutrients. 2015; 7(5): 3416-26. https://doi.org/10.3390/nu7053416

70. Dai Z, Koh WP. B-vitamins and bone health–a review of the current evidence. Nutrients. 2015; 7(5): 3322-46. https://doi.org/10.3390/nu7053322
71. Kalimeri M, Leek F, Wang NX, Koh HR, Roy NC, Cameron-Smith D, Kruger MC, et al. Folate and Vitamin B-12 Status Is Associated With Bone Mineral Density and Hip Strength of Postmenopausal Chinese-Singaporean Women. JBMR plus. 2020; 4(10): e10399. https://doi.org/10.1002/jbm4.10399
72. Nairz M, Theurl I, Wolf D, Weiss G. Iron deficiency or anemia of inflammation? Wien Med Wochenschr. 2016; 166(13): 411-23. https://doi.org/10.1007/s10354-016-0505-7
73. Mughal DT. Nutrition and physical health. Physical Health of Adults with Intellectual and Developmental Disabilities. 2019: 249-92. http://dx.doi.org/10.1002/9780470776216.ch10
74. Fehér A, Gazdecki M, Véha M, Szakály M, Szakály Z. A Comprehensive Review of the Benefits of and the Barriers to the Switch to a Plant-Based Diet. Sustainability. 2020; 12(10): 4136. http://dx.doi.org/10.3390/su12104136
75. Lobstein T, Jackson-Leach R, Moodie ML, Hall KD, Gortmaker SL, Swinburn BA, James WP, et al. Child and adolescent obesity: part of a bigger picture. The Lancet. 2015; 385(9986): 2510-20. https://doi.org/10.1016/s0140-6736(14)61746-3
76. Norris ML, Spettigue WJ, Katzman DK. Update on eating disorders: current perspectives on avoidant/restrictive food intake disorder in children and youth. Neuropsychiatr. Dis. Treat. 2016; 12: 213. https://doi.org/10.2147/ndt.s82538
77. Paparo L, Di Costanzo M, Di Scala C, Cosenza L, Leone L, Nocerino R, Canani RB. The influence of early life nutrition on epigenetic regulatory mechanisms of the immune system. Nutrients. 2014; 6(11): 4706-19. https://doi.org/10.3390/nu6114706
78. Prescott SL. Early Nutrition as a Major Determinant of 'Immune Health': Implications for Allergy, Obesity and Other Noncommunicable Diseases. Preventive Aspects of Early Nutrition. 2016; 85: 1-7. https://doi.org/10.1159/000439477
79. Abeshu MA, Lelisa A, Geleta B. Complementary feeding: review of recommendations, feeding practices, and adequacy of homemade complementary food preparations in developing countries–lessons from Ethiopia. Front. Nutr. 2016; 3: 41. https://doi.org/10.3389/fnut.2016.00041
80. Huff, T., Boyd, B., Jialal, I. (2020). Physiology, cholesterol. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK470561. Retrieved 2020.
81. Cholesterol Physiology. News Medical Life Science. [https://www.news-medical.net/health/Cholesterol-Physiology.aspx]. Retrieved 2019.
82. Sheppard KW, Cheatham CL. Omega-6/omega-3 fatty acid intake of children and older adults in the US: dietary intake in comparison to current dietary recommendations and the Healthy Eating Index. Lipids Health Dis. 2018; 17(1): 1-2. https://doi.org/10.1186/s12944-018-0693-9
83. Metherel AH, Bazinet RP. Updates to the n-3 polyunsaturated fatty acid biosynthesis pathway: DHA synthesis rates, tetracosahexaenoic acid and (minimal) retroconversion. Prog. Lipid. Res. 2019; 76: 101008. https://doi.org/10.1016/j.plipres.2019.101008
84. Schmidt JA, Rinaldi S, Ferrari P, Carayol M, Achaintre D, Scalbert A, Cross AJ, et al. Metabolic profiles of male meat eaters, fish eaters, vegetarians, and vegans from the EPIC-Oxford cohort. Am. J. Clin. Nutr. 2015; 102(6): 1518-26. https://doi.org/10.3945/ajcn.115.111989
85. Purwana A, Budiono B, Batubara JR, Faizi M. Association of Growth Velocity with Insulin-Like Growth Factor-1 and Insulin-Like Growth Factor Binding Protein-3 Levels in Children with a Vegan Diet. J. Biomed. Transl. Res. 2020; 6(1): 6-10. https://doi.org/10.14710/jbtr.v6i1.5474
86. Agnoli C, Baroni L, Bertini I, Ciappellano S, Fabbri A, Papa M, Pellegrini N, et al. Position paper on vegetarian diets from the working group of the Italian Society of Human Nutrition. Nutr Metab Cardiovasc Dis. 2017; 27(12): 1037-52. https://doi.org/10.1016/j.numecd.2017.10.020
87. Sakkas H, Bozidis P, Touzios C, Kolios D, Athanasiou G, Athanasopoulou E, Gerou I, et al. Nutritional status and the influence of the vegan diet on the gut microbiota and human health. Medicina. 2020; 56(2): 88. https://doi.org/10.3390/medicina56020088
88. Weikert C, Trefflich I, Menzel J, Obeid R, Longree A, Dierkes J, Meyer K, et al. Vitamin and mineral status in a vegan diet. Dtsch. Ärztebl. int.. 2020; 117(35-36): 575. https://doi.org/10.3238/arztebl.2020.0575
89. Lemale J, Mas E, Jung C, Bellaiche M, Tounian P, Hepatology FS. Vegan diet in children and adolescents. Recommendations from the French-speaking Pediatric Hepatology, Gastroenterology and Nutrition Group (GFHGNP). Arch Pediatr. 2019; 26(7): 442-50. https://doi.org/10.1016/j.arcped.2019.09.001

90. Lemale J, Salaun JF, Assathiany R, Garcette K, Peretti N, Tounian P. Replacing breastmilk or infant formula with a nondairy drink in infants exposes them to severe nutritional complications. Acta Paediatr. 2018; 107(10): 1828-9. https://doi.org/10.1111/apa.14437
91. Ambroszkiewicz J, Chełchowska M, Szamotulska K, Rowicka G, Klemarczyk W, Strucińska M, Gajewska J. Bone status and adipokine levels in children on vegetarian and omnivorous diets. Clin. Nutr. 2019; 38(2): 730-7. https://doi.org/10.1016/j.clnu.2018.03.010
92. Bolland MJ, Leung W, Tai V, Bastin S, Gamble GD, Grey A, Reid IR. Calcium intake and risk of fracture: systematic review. Bmj. 2015; 351. https://doi.org/10.1136/bmj.h4580
93. Sanchis-Chordá J, Redondo-Cuevas L, Codoñer-Franch P. Vagan diet in childhood: Benefits and risks. Rev. Esp. Pediatr. 2016; 72(5): 299-303. https://www.researchgate.net/publication/340398725
94. Baroni L, Goggi S, Battino M. Planning well-balanced vegetarian diets in infants, children, and adolescents: the vegplate junior. J Acad Nutr Diet . 2019; 119(7): 1067-73. https://doi.org/10.1016/j.jand.2018.06.008
95. Müller P. Vegan diet in young children. Global Landscape of Nutrition Challenges in Infants and Children. 2020; 93: 103-10. https://doi.org/10.1159/000503348
96. Zielińska-Dawidziak M. Plant ferritin—a source of iron to prevent its deficiency. Nutrients. 2015; 7(2): 1184-201. https://dx.doi.org/10.3390%2Fnu7021184
97. Abdelhaleim AF, Amer AY, Soliman JS. Correction: Association of Zinc Deficiency with Iron Deficiency Anemia and its Symptoms: Results from a Case-control Study. Cureus. 2019; 11(4). https://doi.org/10.7759/cureus.3811
98. Elorinne AL, Alfthan G, Erlund I, Kivimäki H, Paju A, Salminen I, Turpeinen U, et al. Food and nutrient intake and nutritional status of Finnish vegans and non-vegetarians. PloS one. 2016; 11(2): e0148235. https://doi.org/10.1371/journal.pone.0148235
99. Allès B, Baudry J, Méjean C, Touvier M, Péneau S, Hercberg S, Kesse-Guyot E. Comparison of sociodemographic and nutritional characteristics between self-reported vegetarians, vegans, and meat-eaters from the NutriNet-Santé study. Nutrients. 2017; 9(9): 1023. https://doi.org/10.3390/nu9091023
100. Sutter DO. *The impact of vegan diet on health and growth of children and adolescents–Literature review* (Doctoral dissertation, Master thesis, Germany: Universitat Bern). 2017. http://dx.doi.org/10.13140/RG.2.2.30001.68963
101. Wilson LR, Tripkovic L, Hart KH, Lanham-New SA. Vitamin D deficiency as a public health issue: using vitamin D2 or vitamin D3 in future fortification strategies. Proceedings of the Nutrition Society. 2017; 76(3): 392-9. https://doi.org/10.1017/s0029665117000349
102. Rizzo G, Laganà AS, Rapisarda AM, Ferrera L, Grazia GM, Buscema M, Rossetti P, et al. Vitamin B12 among vegetarians: status, assessment and supplementation. Nutrients. 2016; 8(12): 767. https://doi.org/10.3390/nu8120767
103. Tong TY, Key TJ, Gaitskell K, Green TJ, Guo W, Sanders TA, Bradbury KE. Hematological parameters and prevalence of anemia in white and British Indian vegetarians and nonvegetarians in the UK Biobank. Am J Clin Nutr. 2019; 110(2): 461-72. https://doi.org/10.1093/ajcn/nqz072
104. Shubham K, Anukiruthika T, Dutta S, Kashyap AV, Moses JA, Anandharamakrishnan C. Iron deficiency anemia: A comprehensive review on iron absorption, bioavailability and emerging food fortification approaches. Trends Food SciTechnol. 2020; 99: 58-75. https://doi.org/10.1016/j.tifs.2020.02.021
105. Pawlak R, Lester SE, Babatunde T. The prevalence of cobalamin deficiency among vegetarians assessed by serum vitamin B12: a review of literature. Eur J Clin Nutr. 2014; 68(5): 541-8. https://doi.org/10.1038/ejcn.2014.46
106. Melina V, Craig W, Levin S. Position of the Academy of Nutrition and Dietetics: vegetarian diets. J Acad Nutr Diet. 2016; 116(12): 1970-80. https://doi.org/10.1016/j.jand.2016.09.025
107. Black MM. Effects of vitamin B12 and folate deficiency on brain development in children. Food Nutr Bull. 2008; 29(2_suppl1) :S126-31. https://doi.org/10.1177/15648265080292s117
108. Dror DK, Allen LH. Effect of vitamin B12 deficiency on neurodevelopment in infants: current knowledge and possible mechanisms. Nutr. rev. 2008; 66(5):250-5. https://doi.org/10.1111/j.1753-4887.2008.00031.x
109. Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR. Modern nutrition in health and disease. LWW; 2012. https://jhu.pure.elsevier.com/en/publications/modern-nutrition-in-health-and-disease-eleventh-edition. Retrieved 2012.
110. Obersby D, Chappell DC, Dunnett A, Tsiami AA. Plasma total homocysteine status of vegetarians compared with omnivores: a systematic review and meta-analysis. BJN. 2013; 109(5):785-94.

https://doi.org/10.1017/s000711451200520x

111. Pawlak R. To vegan or not to vegan when pregnant, lactating or feeding young children. Eur. J. Clin. Nutr. 2017; 71(11):1259-62. https://doi.org/10.1038/ejcn.2017.111
112. Suardi C, Cazzaniga E, Graci S, Dongo D, Palestini P. Link between Viral Infections, Immune System, Inflammation and Diet. Int. J. Environ. Res. Public Health. 2021; 18(5):2455. https://dx.doi.org/10.3390%2Fijerph18052455
113. Zhang C, Björkman A, Cai K, Liu G, Wang C, Li Y, Xia H, et al. Impact of a 3-months vegetarian diet on the gut microbiota and immune repertoire. Front. immunol. 2018; 9:908. https://doi.org/10.3389/fimmu.2018.00908
114. Roth TL, Marson A. Genetic Disease and Therapy. Ann Rev Path: Mechanisms of Disease. 2021; 16:145-66. https://doi.org/10.1146/annurev-pathmechdis-012419-032626
115. Cano A, Resseguier N, Ouattara A, De Lonlay P, Arnoux JB, Brassier A, Schiff M, et al. Health status of French young patients with inborn errors of metabolism with lifelong restricted diet. . Pediatr. 2020; 220:184-92. https://doi.org/10.1016/j.jpeds.2020.01.059
116. Sarah HL, Singh RH. Protein substitute for children and adults with phenylketonuria. Cochrane Database of Systematic Reviews. 2015(2). https://doi.org/10.1002/14651858.cd004731.pub4
117. Gonzalez-Lopez E, McFalls AJ, Vrana KE. Phenylketonuria (PKU). eLS.:1-8. https://doi.org/10.1002/9780470015902.a0002006.pub2
118. Blackburn PR, Gass JM, e Vairo FP, Farnham KM, Atwal HK, Macklin S, Klee EW, et al. Maple syrup urine disease: mechanisms and management. Appl. Clin. Genet. 2017; 10:57. https://doi.org/10.2147/tacg.s125962
119. Müller P. Vegan diet in young children. Global Landscape of Nutrition Challenges in Infants and Children. 2020; 93:103-10. https://doi.org/10.1159/000503348
120. Sebastiani G, Herranz Barbero A, Borrás-Novell C, Alsina Casanova M, Aldecoa-Bilbao V, Andreu-Fernández V, Pascual Tutusaus M, et al. The effects of vegetarian and vegan diet during pregnancy on the health of mothers and offspring. Nutrients. 2019; 11(3):557. https://doi.org/10.3390/nu11030557
121. Wood D, Knight C. Anorexia nervosa in adolescence. Paediatr Child Health. 2019; 29(9):401-6. https://doi.org/10.1016/j.paed.2019.06.006