The relationship between diet, energy balance and fertility in men

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Abstract: Research conducted in recent years provides more and more evidence that diet can have a significant impact on male fertility. The aim of the study was to analyze the relationship between diet, energy balance and fertility in men. A comprehensive literature search of published studies in various languages, was carried out in electronic databases. The direct analysis included 96 works published between 2008 and 2018, including 12 randomized controlled trials and 23 systematic reviews and meta-analyses. A strong adherence to a healthy dietary pattern is positively correlated with total sperm count, progressive motility and total motile sperm count (all $p < 0.05$). However, attention is drawn to the fact that foods that are considered “healthy” can sometimes contain a significant amount of pollution, which negatively affect the semen parameters. An adequate intake of antioxidants or their supplementation have been quite effective in the prevention and treatment of male infertility. The improvement of pregnancy rate after antioxidant therapy ranged in various studies from 11% to 41%. An important problem, however, may be choosing the right dose of the supplement or finding an appropriate combination of antioxidants that may be more effective than any single antioxidant. The normalization of men's body weight is beneficial for the quality of sperm and the concentration of male reproductive hormones. Further, long-term studies require the assessment of the impact of drastic weight loss after bariatric surgery on male fertility.

Keywords: male fertility, dietary patterns, nutrients, antioxidants, Body Mass Index

Introduction

The prevalence of infertility among couples of reproductive age ranges, according to various sources, from 8% to 25% [1–3]. Male infertility is the only cause of infertility in 20–30% of cases and a factor contributing to infertility in 50% of all infertility cases [4]. The assessment of male fertility usually includes medical examination and comparison with the reference values of the following semen parameters: volume, total sperm count, concentration, motility and morphology (Table 1) [5]. Low sperm count and/or quality is present in 90% of couples with fertility problems [6]. In the assessment of fertility, the concentrations of male reproductive hormones are also analyzed. More recently, the molecular composition of sperm cells, assessed by evaluating the degree of DNA fragmentation or oxidative stress [7] has been increasingly taken into account. Several studies use the DNA fragmentation index (DFI) as an indicator of pregnancy success. According to Evenson and Wixon, DFI ranges from 3 to 5% in healthy men, while a DFI of $\geq 30\%$ is associated with reduced fertility [8]. Currently

defined genetic factors, including both chromosomal aberrations and monogenic changes, account for only about 10–15% of cases of male infertility [9]. The cause for fertility problems may also be environmental factors. The aim of the study was to analyze the relationship between diet, energy balance and fertility rates in men.

Strategy of literature search

A comprehensive literature search of published studies in various languages, was carried out in electronic databases, including: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Database of Systematic Review and Google Scholar. Randomized controlled trials, observational and qualitative studies published between 2008 and 2018 (up to and including March) were included. The following keywords related to male infertility, diet, nutrients and their combinations (made by applying operators AND and OR) were used in the search: ‘male infertility’, ‘sperm quality’, ‘idiopathic

Table 1. Reference values of the World Health Organization for human semen parameters (WHO 2010).

Semen parameter	Reference limit (95% confidence intervals)
Semen volume	1.5 ml (1.4–1.7)
Total sperm count	39 million per ejaculate (33–46)
Sperm concentration	15 million per ml (12–16)
Vitality	58% live (55–63)
Progressive motility	32% (31–34)
Total (progressive + nonprogressive) motility	40% (38–42)
Morphologically normal forms	4.0% (3.0–4.0)

oligozoospermia', 'astenoazoospermia', 'oligoastenoteratozoospermia', 'sperm DNA damage', 'nutritional status', 'BMI', 'obesity', 'diet', 'nutrition', dietary pattern', 'food', 'nutrient', 'fatty acids', 'antioxidant', 'supplementation', 'vitamin C', 'vitamin E', 'vitamin A', 'folate', 'zinc', 'selenium', 'L-carnitine', 'glutathione', 'coenzyme Q₁₀', 'N-acetylcysteine', 'lycopene'. Reference lists of studies extracted from the primary electronic search were used to identify additional relevant studies.

Dietary patterns and food groups

The analysis of dietary patterns is increasingly used to assess the relationship between diet and the risk of many diseases and health problems [10]. This approach allows one to achieve a more accurate description of a diet and a more comprehensive illustration of its complexity when compared to studies about the intake of isolated nutrients. Dietary patterns also accurately reflect global changes in dietary behaviors in different populations. Studies on the association between dietary patterns and semen quality among men are sparse (Table 2).

The results of the meta-analysis of observational studies confirm that male adherence to a healthy diet could improve semen quality and fecundability rates [18]. Oostingh et al. noted in their prospective study that sperm concentration, total sperm count, progressive motility and total motile sperm count were all positively associated with a strong adherence to the healthy dietary pattern, especially in men with poor semen quality [14]. Analyzing semen quality parameters in male partners of couples attempting fertility, it was found that men in the lowest adherence to the Mediterranean diet score had approximately a 2.6 times higher likelihood of having abnormal sperm concentration, total sperm count and motility, compared to men in the highest adherence of the score [19]. The meta-analysis of observational studies, that has been conducted recently

showed, that individuals in the lowest adherence to the healthy dietary pattern had a significantly lower level of sperm concentration [20]. No significant association was seen between dietary patterns and other semen quality.

The associations between the intake of specific food groups and the semen quality have been analyzed in many studies. There was an inverse relation between processed red meat intake and total sperm count among young men [21]. The risk of asthenozoospermia was also significantly higher in the highest tertiles of processed meat and sweets intake [22]. Fish consumption was related to a higher sperm count and percentage of morphologically normal sperm. The mean total sperm count increased from 102 million in the lowest to 168 million sperm in the highest quartile of fish intake [23]. In increasing quartiles of fish consumption, the percentage of morphologically normal sperm was higher too. The authors found that consuming fish may have a positive impact on semen parameters, particularly when consumed instead of processed red meats. The results of an analysis conducted by Mínguez-Alarcón et al. demonstrated, however, an exposure to mercury (Hg) through fish intake [24]. Men in the highest quartile of high mercury levels had a sperm concentration higher by 50%, a total sperm count higher by 46% and progressive motility higher by 31%, compared to men in the lowest quartile. These associations were stronger in those men who consumed more fish than the median in the studied group.

In a cohort of young, physically active men, dairy food intake was inversely related to sperm morphology and progressive motility [25]. This association was stronger for full-fat dairy foods. A study conducted in Iran demonstrated that the odds of asthenozoospermia were significantly lower with the intake of skim milk, and higher with an intake of total dairy products [22]. It is assumed that dairy food intake has been related to decreased secretion of LH, FSH and testosterone [26]. Moreover, dairy often includes environmental contaminants (pesticides and chlorinated pollutants) [27]. These contaminants have been associated with lower sperm quality and may be responsible for the observed relationship [27–31].

Chiu et al. found that total fruit and vegetable consumption was unrelated to semen quality parameters [31, 32]. The intake of fruit and vegetables with high pesticide residues was unrelated to semen quality in healthy young men, whereas low-to-moderate pesticide residues was associated with a higher sperm concentration and total sperm count [32]. The consumption of high pesticide - residue on fruits and vegetables was inversely associated with a lower percentage of morphologically normal sperm, total sperm count and ejaculate volume among men attending a fertility clinic [31]. The intake of low-to-moderate pesticide- residue produce was positively related to sperm morphology.

Table 2. Main characteristics of studies on relationship between dietary patterns and fertility parameters in men.

Reference	Participants	Semen quality parameters	Dietary pattern (DP)	Conclusion/key findings
Vujkovic et al. [11]	Men of subfertile couples undergoing in vitro fertilization treatment (N = 161)	sperm volume, concentration, motility, morphology and DNA fragmentation index (DFI)	The Health Conscious DP characterized by high intake of fruits, vegetables, fish and whole grains. The Traditional Dutch DP characterized by high intakes of meat, potatoes and whole grains and low intakes of beverages and sweets.	An inverse association was demonstrated between the Health Conscious DP and DFI ($\beta = -2.81$; $p = 0.05$). The Traditional Dutch DP was positively correlated with sperm concentration ($\beta = 13.25$; $p = 0.01$).
Gaskins et al. [12]	Men aged 18–22 (participants in the Rochester Young Men's Study) (N = 188)	sperm concentration, progressive motility and morphology	The Western DP was characterized by high intake of red and processed meat, refined grains, pizza, snacks, high-energy drinks and sweets. The Prudent DP was characterized by high intake of fish, chicken, fruit, vegetables, legumes and whole grains.	Men in the highest quartile of the Prudent DP had 11.3% higher % progressively motile sperm compared with men in the lowest quartile (P-trend = 0.04). The Prudent DP was unrelated to sperm concentration and morphology. The Western DP was not associated with any semen parameter.
Jurewicz et al. [13]	Men who attended the infertility clinic for diagnostic purposes and who had normal semen concentration of 20 to 300 mln/ml or slight oligozoospermia (semen concentration of 15–20 mln/ml) (N = 336)	sperm concentration, motility, morphology, sperm chromatin structure (DNA fragmentation index - DFI), high DNA stainability; the level of reproductive hormones	The Prudent DP (high intakes of fish, chicken, fruit, cruciferous vegetables, tomatoes, leafy green vegetables, legumes, and whole grains). The Western DP (high intakes of red and processed meat, butter, high-fat dairy, refined grains, pizza, snacks, high energy drinks, mayonnaise, and sweets). The other men were classified as the Mixed DP	Higher consumption of a Prudent DP was associated with higher sperm concentration ($p = 0.05$) and higher level of testosterone ($p = 0.03$). Sperm chromatin structure was inversely related to higher consumption of a Prudent DP ($p = 0.05$).
Oostingh et al. [14]	Men aged on average 35 (± 6 SD) years old with BMI of 26.4 ± 4 kg/m ²	ejaculate volume, sperm concentration, total sperm count, progressive motility, immotile sperm, and total motile sperm count (TMSC)	The Healthy DP (high intakes of cereals, fruits, legumes, vegetables, and olive oil). The Unhealthy DP (high intakes of dairy, margarines, mayonnaise, sauces, snacks and sweets).	Sperm concentration ($\beta = 0.278$; $p < 0.05$), total sperm count ($\beta = 1.369$; $p < 0.05$), progressive motility ($\beta = 4.305$; $p < 0.05$), and TMSC ($\beta = 0.319$; $p < 0.05$) were positively associated with the Healthy DP. No significant associations with strong adherence to the Unhealthy DP.
Liu et al. [15]	Healthy Taiwanese men aged 18 years or older who participated in a standard medical screening program (N = 7282)	sperm concentration (SC), normal sperm morphology (NSM), total sperm motility (TSM), progressive motility (PRM)	The Healthy DP contained three different foods in total: light-color vegetables, dark-color vegetables and fruits. The Western DP was characterized by high intake milk, cheese, yogurt, meat, seafood, salad and fried food. The High-carbohydrate DP included three foods: refined grains, whole grains and root vegetables. High sweet snacks & sugar sweetened drinks DP included three types of food: cake or cookies, additional sugars and sweetened beverages. The High-sodium DP involved three food items: processed canned food, instant noodles and condiments	A high intake of a Western DP resulted in statistically linear declines of SC ($p < 0.001$) and NSM ($p < 0.001$). Similarly, a greater intake of High sweet snacks & sugar-sweetened drinks" was associated with a lower SC ($p = 0.001$). Increased intake of a High-carbohydrate DP was related to higher prevalence of abnormal TSM ($p = 0.012$) and PRM ($p = 0.025$). A greater intake of a High-sodium DP was correlated with an elevated prevalence of abnormal NSM ($p = 0.035$).

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Table 2. (Continued)

Reference	Participants	Semen quality parameters	Dietary pattern (DP)	Conclusion/key findings
Eslamian et al. [16]	107 incident asthenozoospermic men and 235 age-matched controls	Asthenozoospermia risk - semen quality data were analyzed according to the fifth edition of the World Health Organization guidelines	A Prudent DP (characterized by high intakes of leafy green vegetables, yellow vegetables, other vegetables, tomatoes, fish and other seafood, fruits and natural fruit juices, legumes, whole grains, poultry, tea and coffee, low-fat dairy products, and vegetable oils). A Western DP (characterized by high intakes of organ meats, red and processed meats, sugar, soft drinks, confectionary, snacks, pasta, rice and refined grains, potatoes, French fries and fast foods, high-fat dairy products, hydrogenated fats, mayonnaise and fatty sauces)	Participants in the highest tertile of the Prudent DP scores had 54% lower risk of asthenozoospermia compared to those in the lowest (P-trend = 0.003). Being in the highest tertile of the Western DP was positively associated with asthenozoospermia risk (OR = 2.86; 95% CI 1.83–2.97).
Cutillas-Tolin et al. [17]	Healthy male university students aged 18–23 years (N = 215)	Total sperm count, semen volume, concentration, morphologically normal sperm (%), total motile sperm, testicular volume, the level of reproductive hormones	A Mediterranean DP (characterized by high intakes of vegetables, fruits and seafood). A Western DP (characterized by high intakes of processed meats, French fries and snacks)	The Mediterranean DP was positively associated with total sperm count (P-trend = 0.040). The Western DP was positively related to the percentage of morphologically normal sperm (P-trend = 0.008). An inverse association was found between adherence to the Western DP and sperm concentration among overweight or obese men (P-trend = 0.040).

Robbins et al. found that in a group of healthy young men, 75 g of walnuts/day added for 12 weeks to a Western-style diet improved sperm vitality, motility, and morphology [33]. In a cross-sectional study, it was found that the intake of soy foods was inversely proportional to the concentration of sperm [34]. It was observed that these compounds were stronger among men with normal or high sperm concentrations than in men with low sperm concentration and in men with overweight and obesity, compared to those with normal weight. The authors suggest that the phytoestrogens contained in soy may affect spermatogenesis by binding membrane estrogen receptors and in this way they can induce transcriptional activity to the same extent as estradiol. The study did not show the effect of soy food intake on sperm motility, morphology or ejaculate volume. Beaton et al. showed that consumption of soy protein of low or high isoflavone content had no negative effect on sperm parameters among healthy adult males [35]. The meta-analysis carried out in 2010 did not confirm the relationship between the consumption of soy foods and isoflavone supplements by men and measurements of bioavailable testosterone concentrations [36].

Some studies included the influence of saffron, commercially used as a food spice, on the quality of sperm. In infertile men receiving 50 mg of saffron for 3 months, three times a week, an improvement in sperm morphology and motility was found, but no increase in sperm count was noted [37]. In another randomized trial, one group of men with idiopathic oligoasthenoteratozoospermia was given 60 mg/day saffron for 26 weeks, and a placebo in the second group. However, there was no significant improvement in semen parameters and total seminal plasma antioxidant capacity [38].

An analysis of scientific studies show that there are specific dietary patterns in different populations. The synergistic effect of the various combinations of vegetables, fruits and fish consumed, which are the main components of 'healthy' or 'prudent' dietary patterns, was associated with better sperm parameters in men in almost all the studies. A high intake of red and processed meat was associated with poor semen quality in different populations. The results of research on the influence of individual food groups confirm the main observations resulting from the analysis of the impact of dietary patterns on semen quality.

Nutrients

Many studies support the hypothesis that specific nutrients (total fat, saturated fatty acids, polyunsaturated fatty acids, trans fatty acids, vitamin D and antioxidants) can affect semen quality. Men with poor semen quality had a significantly higher intake of proteins and total fat, and a lower intake of carbohydrates and fiber than control subjects [39]. Attaman et al. noted that a high total fat intake was negatively related to total sperm count and sperm concentration [40]. The authors also found that levels of saturated fatty acids in sperm were negatively related to sperm concentration. Jensen et al. detected, on a sample of 701 young Danish men, a dose-response association between the increased intake of saturated fat and total sperm count and sperm concentration [41]. Men in the highest quartile of saturated fat intake had a 41% lower total sperm count and a 38% lower sperm concentration than the men in the lowest quartile. Additionally, the percentage of spermatozoa with a normal morphology was lower among men with a high percentage of energy from monounsaturated fat. In a study conducted in the Iranian population, chances of having normal semen volume increased by 27.5% for each additional 1 g of fat consumed, and with each additional 1 g of saturated fat in the diet, the chance of achieving a normal sperm volume decreased by 38% [42].

Dietary supplementation of omega-3 fatty acids for 32 weeks increased the total sperm cell count, sperm cell concentration and the total percentage of sperm with normal morphology [43]. In one study a supplementation with nutritional levels of DHA and EPA, carried out for 3 months, in idiopathic infertile patients, did not significantly change the conventional sperm parameters [44]. Semen volume was also higher among men with a high intake of n-3 polyunsaturated fatty acids [41]. A higher intake of n-3 fatty acids was also related to a more favorable sperm morphology [40]. Kollahdooz et al. found that black cumin seed oil (*Nigella sativa* L.) may be able to improve the sperm quality of infertile men [45]. They showed that sperm count, volume, motility and morphology were significantly improved in the *N. sativa* oil treated group compared with the placebo group after 2 months. In the authors' opinion the beneficial influence of the oil on the quality of the sperm can be contributed, to a large extent, to the influence of dihomogamma-linolenic acid (20:3 n-6).

Trans fatty acid consumption was inversely related to total sperm count in young healthy men [46]. The authors also found a positive association between stearic acid intake and sperm motility and an inverse association between cholesterol intake and ejaculate volume. An adequate intake of certain fatty acids affects semen quality and is necessary for normal spermatogenesis. Polyunsaturated fatty acids are structural components of cell membranes

of spermatozoa and they contribute to maintaining their fluidity and permeability. The excessive consumption of saturated fats and trans fatty acids from unhealthy diets may lead to their accumulation in testicular cells. This may affect the fatty acid composition of the plasma membrane and the process of spermatogenesis, inhibit testosterone production and induce Leydig cells apoptosis [47–50].

Data on the effect of fatty acid intake on the concentration of reproductive hormones in men are scarce. In a population of young healthy Spanish men, the intake of monounsaturated fatty acids was inversely associated with serum blood levels of total and calculated free testosterone [51]. A positive association was also observed between polyunsaturated fatty acid intake (particularly of n-6 fatty acids) and luteinizing hormone (LH) concentrations [51]. Chavarro et al. had reported that men in the highest quartile of trans fatty acid intake had testosterone levels lowered by 15% [52]. Mínguez-Alarcón et al. also confirmed that the intake of trans fatty acids was associated with lower total testosterone concentration and calculated free testosterone concentration [51].

Numerous studies have shown that vitamin D may be a regulator of fertility and reproductive function in individuals [53]. It was also found that the presence of a vitamin D receptor and/or the vitamin D metabolizing enzymes can be treated as a predictive marker for semen quality [54]. Most of the published papers analyze the relationships between the vitamin D status in the body and the quality of the semen, and only a few of them studied the effect of supplementation on fertility indicators. After 3 months of treatment with oral vitamin D 200 IU/day, in infertile men with idiopathic oligoasthenozoospermia, the improvement of semen quality was observed, especially the progressive sperm motility [55]. A recent randomized study in which the effect of supplementation with vitamin D and calcium on the fertility of men with a known vitamin D deficiency was analyzed, showed that supplementation did not affect the quality of the semen or the rate of live births. However, treatment with vitamin D resulted in a slight increase in semen production and a higher number of live births in couples, in which the male had oligozoospermia compared to men in the placebo group [56]. Lerchbaum et al. studied the effect of vitamin D supplementation on the concentration of sex hormones in healthy men [57]. They found that the administration of 20,000 IU/week of vitamin D₃ for 12 weeks had no effect on the total testosterone levels. Conversely, Canguven et al. found that vitamin D treatment improved testosterone levels and erectile functions at the end of the 12 months' follow-up [58]. Mínguez-Alarcon et al. did not find, however, a correlation between vitamin D consumption and sperm parameters [59].

It appears plausible that certain nutrients may have mediated the effects of dietary patterns and food groups on semen quality. High intake of fats, especially saturated ones, and trans-fatty acids was negatively related to sperm count and concentration. However, the positive effect of polyunsaturated fatty acids, especially n-3 fatty acids on total sperm count, sperm concentration and a more favorable sperm morphology has been noted. Very few papers have been published in which the associations between consumption of proteins as well as carbohydrates, and the quality of semen were analyzed. It is not possible to formulate any conclusions regarding these nutrients. The relationship between the intake of vitamin D supplements and men's reproductive health is for the time being ambiguous and requires further research.

Antioxidants

Free radical processes (related to the formation of free radicals) play an important role in the development of infertility in men. Sperm cytoplasm contains small amounts of enzymes that capture free radicals, which is why they have quite a limited antioxidant protection. In addition, they are sensitive to the detrimental effect of oxidative stress due to the high content of polyunsaturated fatty acids in the cell membrane. Semen pathology induced by oxidative stress involves damage to cell membranes and DNA, leading to asthenozoospermia (reduced number of motile sperm in semen), necroscemia (lack of viability of spermatozoa in the ejaculate), and DNA fragmentation [60]. Tremellen reports that 30% to 80% of cases of reduced male fertility result from the harmful effects of oxidative stress on sperm [61]. The antioxidant system that protects sperm from free radicals, consists of both the enzyme complex, as well as non-enzymatic substances, which include vitamins C, A, E, B vitamins, coenzyme Q₁₀, L-carnitine, glutathione and micronutrients such as zinc, selenium, and copper [62]. The influence of lycopene and N-acetyl-cysteine on the quality of sperm is also of interest. In some studies, the relationships between single antioxidants and fertility rates were analyzed, whereas recently the influence of various combinations of many nutrients has increasingly been studied.

In a meta-analysis published in 2014, it was stated that there is little evidence suggesting that antioxidant supplementation in subfertile males may improve live birth rates for couples attending fertility clinics [63]. Many individual interventional studies conducted among subfertile/infertile men showed, however, a positive effect of supplementation on sperm parameters. In the group of subfertile men who received 2 capsules with zinc sulfate for 4 months (440 mg total), the mean value of semen volume, the

percentage and total normal sperm count and progressive sperm motility were significantly increased [64]. It was also found that zinc supplementation restored the proper range of oxygen sensitivity and catalase activity in the semen of men with asthenozoospermia [65]. Ajina et al. noted that antioxidant treatment based on in vitro supplementation of zinc, increased values of the antioxidant status index in infertile men, however, it did not prevent sperm lipid peroxidation [66]. In one study of 690 infertile men with idiopathic asthenoteratospermia, simultaneous supplementation with selenium, at a dose of 200 µg per day and vitamin E at a dose of 400 IU per day, for at least 100 days was used [67]. In 52.6% of participants, an improvement in sperm motility and/or sperm morphology was observed. In addition, as many as 10.8% of partners of those men became pregnant.

In general, the human trials showed that an intake of 4–8 mg of lycopene supplements a day for 3–12 months, improve sperm parameters and is sufficient to treat male infertility [68]. Devaraj et al. found that a daily dose of 30 mg of lycopene was required for a 9% decrease in DNA damage [69]. In a study conducted by Safarinejad, 287 infertile men with idiopathic oligoasthenoteratozoospermia were treated with coenzyme Q₁₀, with an oral dose of 300 mg twice a day [70]. After 12 months of therapy, a significant improvement of mean sperm concentration (of 113.7%), sperm progressive motility (of 104.8%), and sperm with normal morphology (of 78.9%) was observed. The results of the meta-analysis, carried out by Lafuente et al., confirmed that coenzyme Q₁₀ improves sperm parameters, however, there was no increase in live births or pregnancy rates [71]. N-acetyl-cysteine, administered orally in an amount of 600 mg/d for 3 months, had significant improving effects on the volume, motility, and viscosity of semen, and the serum total antioxidant capacity [72]. All semen parameters significantly improved with N-acetyl-cysteine and selenium treatment. There was also a decrease in the concentration of follicle-stimulating hormone and an increase in serum concentration of testosterone [73].

In the group of 50 infertile men with established oxidative stress, treatment lasting 3 months was conducted, consisting of the administration of vitamin C (100 mg), E (400 IU), folic acid (0.5 mg), zinc (25 mg), selenium (26 µg) and garlic (1 mg). The study showed that the therapy applied resulted in a significant improvement of sperm DNA and protamine packaging integrity. In addition, a reduction in apoptosis and seminal production of reactive oxygen species was observed. There were no significant changes in the concentration of male reproductive hormones, as well as concentration, sperm motility and morphology [74]. Lipovac et al. showed that the administration of a combination of eight micronutrients (440 mg of L-carnitine + 250 mg of L-arginine + 120 mg

of vitamin E + 800 µg of folic acid + 80 mg of glutathione + 15 mg of coenzyme Q10 + 40 mg of zinc + 60 µg of selenium) had a significantly higher positive effect on sperm density and overall progressive motility (including fast motility) in comparison with the preparation containing L-carnitine alone [75].

There was a positive association between dietary intake of vitamin C and semen volume and total motile sperm count in young, healthy university students [59]. Total motile sperm count increased also with higher intakes of lycopene, β-carotene and cryptoxanthin. Men with poor semen quality, attending fertility clinics, had a significantly lower intake of vitamin C and lycopene than control subjects [39]. It was demonstrated in subsequent studies that infertile subjects had a significantly lower dietary intake of vitamin C and E when compared to the control subjects [76]. In a population of healthy young men, the intake of lycopene was associated with better sperm morphology, and carotenoid intake with higher sperm motility [77]. The authors also observed a nonlinear relationship between vitamin C intake and sperm concentration. A moderate intake of vitamin C, as well as β-carotene, was associated with the highest sperm concentration, sperm count, and motile count. Nadjarzadeh et al. confirmed positive correlations between the intake of folate and zinc, and sperm concentration and motility [76]. In a study aiming to evaluate the influence of B vitamins intake on semen parameters of men with MTHFR gene polymorphisms, it was observed that sufficient consumption of folates and vitamin B₁₂ improved sperm parameters of men with different MTHFR polymorphisms, especially among men with T allele of MTHFR C677T polymorphism [78]. Only Minguez-Alarcon et al. did not find an association between the consumption of antioxidants such as α-carotene, vitamin E, lutein, zeaxanthin, folate, vitamin B₆, B₁₂, and sperm parameters [59].

The results of many studies have shown that an adequate intake or supplementation of some antioxidants may be effective in the prevention and treatment of infertility in men. The improvement of pregnancy rate after antioxidant therapy ranged in various studies from 11% to 41%. Studies that use different combinations of many antioxidant ingredients are particularly promising. The key problem may be choosing the right dose of the supplement [79, 80]. The improvement of sperm parameters resulting from antioxidant supplementation did not always translate into an improvement in live births or pregnancy rates, indicating the high complexity of this problem.

Caffeine

Drinking coffee within usual levels of intake (3–4 cups a day) has generally a positive influence on a person's health [81]. However, in higher doses, caffeine may change the Sertoli

Cells glycolytic and oxidative profile, disturbing the male's reproductive potential [82]. In a study conducted among Danish men, increased testosterone levels with increasing caffeine intake was observed, but with no adverse effect on semen quality [83]. Consumption of > 800 mg of caffeine per day resulted in a nonsignificant reduction in semen quality [84]. A meta-analysis conducted in 2017 suggests that caffeine intake may negatively affect male reproductive function, possibly through sperm DNA damage [85]. The authors found that evidence from epidemiological studies on semen parameters and fertility is inconclusive. Karmon et al. did not confirm an association between male caffeine intake and semen quality. They only demonstrated that male caffeine intake was negatively correlated with live birth after assisted reproductive technologies [86].

In most studies, semen parameters were not affected by caffeine intake. However, some authors suggested a negative effect of caffeine-containing beverages on count, concentration and volume of sperm. It is also possible that the less healthy lifestyle of men drinking caffeine-containing soft drinks may explain these findings.

Alcohol

Studies conducted in earlier years indicated that alcohol consumption changes semen parameters and has an impact on human testicular pathology. It was suggested that these disorders can be associated with hypotestosteronemia, which results from ethanol effects on both the central component of the hypothalamic–pituitary–testicular axis and at the testicular level [87]. These associations have also been confirmed in recent works [88]. Jensen et al. suggest that even modest habitual alcohol consumption of more than 5 units per week had adverse effects on sperm concentration, total sperm count and percentage of spermatozoa with normal morphology [89]. The negative impact of alcohol on the quality of sperm increased with the increase of the amount of alcohol consumed. Men with a typical intake above 40 units/week had a 33% reduction in sperm concentration compared to men with an intake of 1–5 units in a typical week. Recent alcohol intake (for the week preceding the visit) was linked with an increase in serum testosterone and reduction in sex hormone-binding globulin. Analysis of histological samples from deceased men showed that high alcohol consumption (>80 g alcohol/day) was associated with reduced spermatogenesis, including spermatogenic arrest and Sertoli-cell-only syndrome [90]. There is also biological plausibility to support an increased production of spermatozoa with fragmented or degenerated DNA in association with alcohol abuse. Chronic alcohol use significantly increased the sperm DNA fragmentation index to 49.6% compared with 33.9% in nondrinkers [91]. Meta-analysis of cross-sectional studies, which included

more than 16000 men, confirmed the harmful influence of alcohol consumption on the volume of semen and normal morphology [92]. Alcohol consumption did not consistently have an influence on sperm concentration and its motility though.

Most studies confirm the adverse effect of alcohol on the quality of semen. The negative impact of high alcohol consumption was particularly marked with regard to sperm morphology and DNA damage.

Energy balance

A lack of balance between the amount of energy consumed and its expenditure and their health consequences, constitute a growing problem in many populations [93]. The effect of obesity on male fertility is thought to be multifactorial. It may be modulated by genetic, endocrinal and environmental influences. Katib explains that male obesity has a negative impact on fertility through direct changes to sperm function and sperm molecular composition, as well as through changes at hormonal levels [94]. Decreased sperm may be a result of changes to the hypothalamic pituitary gonadal axis through reductions in the levels of total testosterone, free testosterone and sex hormone-binding globulin. Moreover, excess adipose tissue causes an increased conversion of testosterone to estradiol, which may be the cause of secondary hypogonadism, through reproductive axis suppression. Infertility in obese men may also be associated with insensitivity to leptin. The increase in leptin levels, characteristic of obesity, contributes to a significant reduction in testosterone production by Leydig cells. Martins et al. also reported that leptin modulates the function of Sertoli cell that are the nutritional support of developing germ cells [95]. The build-up of suprapubic and inner fat may cause scrotal hyperthermia, which is a probable cause of elevated oxidative stress, and may contribute to decreased sperm quality through an influence on mitochondrial dysfunction [96].

Numerous studies have demonstrated that male obesity is related to an increased incidence of low sperm concentration and low progressively motile sperm count. The incidence of oligozoospermia increased proportionally to increasing BMI and was 5.3% in normal weight men and respectively 9.5% and 15.6% in overweight and obese men. Similarly, the prevalence of a low progressively motile sperm count increased with increasing BMI and was respectively 4.5%, 8.9%, and 13.3% in normal weight, overweight and obese men [97]. However, the results of a meta-analysis conducted by MacDonald et al. did not show an association between increased BMI and semen parameters, but there was strong evidence of a negative relationship for testosterone, sex hormone binding globulin and free testosterone with increased BMI [98]. Sermondade et al. confirmed that

overweight and obesity significantly increases the risk of oligozoospermia and azoospermia [99]. Subsequently, cross-sectional studies showed that BMI had a marginally significant effect on normal sperm morphology, and that overweight and obese men showed no significantly increased relative risk of abnormal semen parameters. However, in a general male population in Taiwan, sperm concentration showed a significantly negative association with BMI [100]. Moreover, the authors noted an inverse association between BMI, waist-to-height ratio and normal sperm morphology.

Regarding the reproductive hormones, significant negative relationships with BMI were found for total testosterone, free testosterone and sex hormone binding globulin [101]. Ejaculate volume showed a linear decline with increasing BMI and waist circumference in men who did not have fertility problems [102]. Similarly, the total sperm count showed a negative linear association with waist circumference. No significant relationship was seen between BMI or waist circumference and semen concentration, motility, vitality, morphology or DNA fragmentation index. Weight loss during the 14-week intervention involving healthy diet and daily exercise in obese men was associated with an increase in semen volume and total sperm count, as well as an improvement of the reproductive hormonal profile, especially in the group with the largest weight reduction [103]. In one of the studies, in three patients that had undergone bariatric surgery to achieve a drastic decrease in body weight, a significant deterioration of semen parameters was observed [104]. The authors suggest that this effect may be triggered by various mechanisms: the suppression of the deleterious effects of obesity, the negative effect of nutrient deficiency or the release of toxic substances.

The study of Bandel et al. indicated that overweight, per se, was not associated with a higher level of sperm DNA damage [105]. Campbell et al. found that obese men had an increased percentage of sperm with abnormal morphology, low mitochondrial membrane potential and DNA fragmentation. They did not find, however, a significant association between obesity and conventional semen parameters [106]. In a study conducted by Taha et al. fertile obese men had significantly lower sperm concentration, sperm normal morphology, progressive sperm motility, and significantly higher seminal reactive oxygen species and sperm DNA fragmentation, compared with other fertile men [107]. Fariello et al. demonstrated that obesity in men was associated with increased DNA fragmentation and decreased progressive motility and mitochondrial activity [108]. Epigenome and small non-coding RNAs alterations in sperm of obese men were also found to have an impact on male fertility potential [50]. In a study in which 4000 men participated, all semen parameters (sperm morphology, volume, concentration, motility and total motile count)

Figure 1. Nutrition-related factors with a beneficial effect on male fertility.

declined with an increasing BMI [109]. The increase in mass was also accompanied by a lowering testosterone concentration and increasing estrogen concentration.

Few studies have included the relationship between mass deficiency and male fertility in their analyzes. Cui et al. showed that men with BMI < 18.5 kg/m² had significantly lower sperm concentration (59.42 ± 8.16 vs. $68.39 \pm 8.54 \times 10^6/\text{ml}$), progressive motility (33.62 ± 11.31 vs. $40.28 \pm 12.98\%$), reduced percentage of normal sperm morphology (7.63 ± 1.33 vs. $12.11 \pm 3.59\%$ normal), higher testosterone concentration (398.24 ± 22.19 vs. 386.58 ± 21.32 ng/dl), as well as estradiol (34.11 ± 8.27 vs. 29.32 ± 7.90 pg/ml), compared to men with normal BMI [110].

In conclusion, it should be noted that not all older studies confirmed the relationship between excess weight and the quantity and quality of semen. Ambiguous results may have been the result of varied age, lifestyle, as well as the overall health of the surveyed men. In recent years, however, it is increasingly noted that obesity negatively affects the sperm parameters. Studies also showed that weight loss had a positive effect on both sperm morphology and on the percentage of DNA fragmentation index (DFI) [111].

Conclusions

The results of research conducted over the last 10 years leave no doubt that diet belongs to modifiable factors that

can have a significant impact on male fertility (Figure 1). A strong adherence to a healthy dietary pattern, which is based mainly on plant foods, fish and chicken is positively correlated with such indicators as: total sperm count, progressive motility and total motile sperm count, and in some studies also with sperm concentration and morphology. However, attention is drawn to the fact that foods that are considered “healthy” (e.g. fruit, vegetables or fish), can sometimes contain a significant amount of pollution, which negatively affect the parameters of the semen. A high intake of red and processed meat, high fat products and confectionery was associated with poor semen quality in different populations.

The results of research on the influence of individual nutrients confirm the main observations resulting from the analysis of the impact of dietary patterns on the quality of semen: high intake of fats, especially saturated ones, and trans-fatty acids is negatively related to sperm count and concentration. However, the positive effect of polyunsaturated n-3 fatty acids on total sperm count, sperm concentration and a more favorable sperm morphology has been noted. The relationship between the intake of vitamin D supplements and men’s reproductive health is for the time being ambiguous and requires further research.

The phenomenon of infertility in men is particularly strongly related to the occurrence of free radical processes. Studies that have been published in the last 10 years have confirmed that an adequate intake of antioxidants or their

supplementation have been quite effective in the prevention and treatment of male infertility. Positive results have been reported in the case of a high intake of vitamin C, E, β -carotene and lycopene supplements, the coenzyme Q₁₀, N-acetyl-cysteine, as well as zinc and selenium. An important problem, however, may be choosing the right dose of the supplement or finding an appropriate combination of antioxidants that may be more effective than any single antioxidant.

Results from epidemiological studies regarding the influence of coffee and beverages that contain caffeine on semen quality and fertility are inconclusive. In most studies, semen parameters were not affected by caffeine intake. Regular consumption of alcohol had adverse effects on sperm concentration, total sperm count, percentage of spermatozoa with normal morphology and increased sperm DNA fragmentation.

Despite some discrepancies in the results of the study, it can also be confirmed that the normalization of men's body weight is beneficial for the quality of sperm and the concentration of male reproductive hormones. Further, long-term studies require the assessment of the impact of drastic weight loss after bariatric surgery on male fertility.

The strength of this work is a comprehensive search of current works, published over the last 10 years, carried out in many electronic databases. However, we cannot exclude that the results obtained by many authors could have been affected by unmeasured confounders, such as physical activity and sedentary behavior, stress, sleep disturbance, occupation, cell phone use and environmental pollution. It is necessary to conduct further, preferably long-term research, as well as carefully designed, placebo-controlled clinical trials to better establish the relationship between diet and fertility in men.

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Authors contribution

E.S. researched the topic and drafted the review. S.G. provided supervision and critically reviewed the manuscript. All authors contributed to and approved the final version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

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