Diet and men's fertility: does diet affect sperm quality?

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Male contribution to a couple's fecundity is important, and identifying the dietary factors that can influence male fertility potential is of high importance. Despite this importance, there are currently no clear clinical guidelines for male patients seeking fertility treatment. In this review, we present the most up-to-date evidence about diet and male fertility in humans. We focus on the dietary factors necessary for production of healthy functioning sperm with high fertility potential. Based on this review, men may be encouraged to use antioxidant supplements and to follow dietary patterns favoring the consumption of seafood, poultry, nuts, whole grains, fruits, and vegetables. Evidence is strongest for recommending the use of antioxidant supplements to men in couples undergoing infertility treatment—although the specific antioxidants and doses remain unclear—and increasing consumption of omega-3 fatty acids from fish and nuts. (Fertil Steril® 2018;110:570–7. ©2018 by American Society for Reproductive Medicine.)
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Approximately one in six couples who try to become pregnant fail to do so within a year, thus meeting the definition of infertility (1). Although male factor is identified in ~50% of couples seeking medical help with infertility (2, 3), infertility research has primarily focused on female factors. Nevertheless, three meta-analyses have documented collectively downward trends in sperm concentration and total sperm count over the past eight decades (4–6). The most recent meta-analyses, which included more than 185 studies of men without known fertility problems, found that sperm counts have declined in industrialized countries by 50%–60% from 1973 to 2011 (6). Although the underlying causes of this downward trend in semen quality are a matter of both active research and heated debate, concurrent trends in worsening diet quality (7) and increasing obesity (8–10) could to some extent explain these trends.

Although there is strong and consistent evidence that overweight and obesity play a significant role in maintaining semen quality (10) and a couple's fertility (11), there are no clear dietary guidelines to counsel men in couples trying to become pregnant. In the present review, we aim to summarize the growing literature about the role of men's diet on fertility. Most of the literature has focused on the relationship between diet and semen quality. Although conventional semen analysis is a far from perfect fertility proxy for reproductive potential (12–17), it is considered to be the cornerstone of the male fertility evaluation (18) and does provide insight into male reproductive function. We will also consider the relation between diet and serum reproductive hormones as well as the emerging literature on men's diet and couple-based outcomes, including measures of fecundity in studies of pregnancy planners and studies of pregnancy outcomes after the use of assisted reproductive technologies (ART). To facilitate that discussion, we will first review the literature that describes dietary factors that may directly affect semen quality as sperm mature, followed by a discussion of dietary factors that may affect spermatogenesis by altering the reproductive hormonal milieu, and close our discussion by reviewing how those findings fit into overall patterns of diet. We will then end the review by discussing the gaps in this growing literature and the implications for research and clinical practice.

DIET AND THE BUILDING BLOCKS FOR SPERM

Although there are a large number of complex steps in the transformation from spermatogonia to mature sperm, focusing on a few key changes can facilitate the discussion of how nutritional input affects this complex process. First, spermatozoa lose most of their cytoplasm before leaving the testis, and condensation of the sperm

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chromatin occurs after they progress from the caput epididymis in transit to the cauda epididymis. These processes include repeated oxidation reactions (19). The shuttle systems for removing and transferring reducing equivalents into the mitochondria are not operational during these reactions, essentially leaving sperm without intracellular defense mechanisms against oxidative damage. Only enzymatic and nonenzymatic antioxidants in seminal plasma provide cellular protection (20). At the same time, the fatty acid composition of the cell membrane changes, favoring the accumulation of long-chain polyunsaturated fatty acids (PUFAs). Although all three processes are essential for performing the sperm's function, they make sperm exceedingly susceptible to oxidative stress by simultaneously removing most of the nonspecific defense against oxidative damage (by loss of cytoplasm), concentrating the endogenous production of reactive oxygen species (ROS; by increasing concentration of mitochondria relative to cell size), and preferentially incorporating into the cell membrane a highly oxidizable substrate (PUFAs) (21, 22). Second, an adequate supply of substrates for DNA production is essential to meet the constant demands for new DNA of spermatogenesis.

Dietary Fats and Their Role in the Sperm Cell Membrane

The fatty acid composition of the sperm cell membrane is highly important for proper sperm function. The sperm cell membrane plays a critical role in key fertilization events, such as capacitation, acrosome reaction, and sperm-oocyte fusion (19). The amount of PUFAs, particularly docosahexaenoic acid (DHA), in the sperm cell membrane increases as the sperm matures (23). DHA represents 20% of the fatty acid content in mature sperm, compared with only 4% in immature germ cells (23). The relative content of DHA is higher in epididymal versus testicular sperm in mice (24). Similarly, human orchiectomy specimens show that the proportion of PUFAs in cell membranes is higher in sperm recovered from the cauda than in sperm recovered from the caput epipidymis (25).

The sperm cell membrane fatty acid composition is partly due to a highly specialized local metabolism. Sertoli cells express Δ6-desaturase (the rate-limiting enzyme in the metabolism of PUFAs) and Δ5-desaturase at levels similar to those in the liver (26). In addition, enzymes involved in the elongation of PUFAs are expressed in a very limited number of tissues, but are highly expressed in the testis (27–30). Furthermore, it has been observed that Sertoli cells can actively convert the 18- and 20-carbon PUFAs into their 22- and 24-carbon metabolites more efficiently than hepatocytes (31–33). Also in Sertoli cells, the enzymes involved in this pathway prefer the conversion of omega-3 fatty acids into 22- and 2four carbon metabolites over converting omega-6 fatty acids (31–33), explaining to some extent the high concentration of DHA in sperm. The proper functioning of this specialized machinery in the testis relies on an adequate supply of metabolic substrates obtained from diet. PUFAs can not be endogenously synthesized by humans and must therefore be obtained from consuming nuts, seeds, and vegetable oils in the case of 18-carbon linoleic (LA) and α-linolenic acids (ALA), or seafood in the case of longer-chain omega-3 PUFAs such as eicosapentaenoic acid (EPA) and DHA.

Consuming these fatty acids or their food sources has been shown to modify the fatty acid composition of sperm and semen quality. Diets supplemented with fish oil, which is rich in EPA and DHA, increase testicular DHA concentrations in rodents (34–36) and sperm membrane DHA in humans (37). Sperm membrane DHA content has, in turn, been associated with higher sperm motility (37–43), normal morphology (37, 43), and concentration (37, 39, 42–45). Moreover, intake of these fatty acids and their food sources has been related to semen quality. In observational studies among fertility patients, higher intake of omega-3 PUFAs has been related to a greater proportion of morphologically normal sperm (46) and fish intake to total sperm count and normal sperm morphology (45). Although in a small trial ($n = 28$) among asthenospermic men, 3 months of DHA supplementation did not improve sperm motility (47), other trials are in agreement with the preponderance of the literature. A trial of long-chain omega-3 fatty acid (DHA + EPA) supplementation (1.84 g/d for 32 weeks) among 211 men with idiopathic oligoasthenoteratospermia resulted in a significant increase in total sperm count, sperm concentration, and percentages of motile and morphologically normal sperm (37). Walnuts, which contain large amounts of plant omega-3 fatty acids, have been related to higher sperm parameters. In a randomized controlled trial of young healthy men consuming a typical Western-style diet, men randomized to walnut supplementation of 75 g/d for 12 weeks had improvements in sperm vitality, motility, and morphology compared with control subjects (48). Recent studies further suggest that the benefit may extend beyond semen quality. In a prospective cohort of couples trying to become pregnant, men's fish intake was related to shorter time to pregnancy and lower risk of infertility (49).

Trans fatty acids and saturated fats, on the other hand, appear to have the effect on spermatogenesis opposite to that of PUFAs. Like PUFAs, *trans* fats—which are primarily found in commercially baked and fried foods—accumulate in the testis (50, 51), but unlike with PUFAs, sperm membrane levels and intake of these fatty acids has been consistently related to poor semen quality, particularly to lower counts (44, 46, 52, 53). In fact, nonhuman models suggest that diets supplemented with *trans* fats result not only in decreased spermatogenesis but can, in a dose-dependent manner, decrease production of testosterone, reduce testicular mass, and promote testicular degeneration (50, 54–56). Of note, the decision by the U.S. Food and Drug Administration to exclude *trans* fats from industrial origin from the list of substances Generally Regarded as Safe as of June 2018 will effectively eliminate this concern from the U.S. once the ruling is fully implemented. Saturated fats, however, will not disappear from the food supply. Given the pervasiveness of *trans* fats in the global food supply, particularly in the developing world, this will, however, remain a concern. Although evidence is thinner, two observational studies have found that saturated fat intake is