## The Role of Nutrition and Supplements in the Development and Treatment of

# Female Infertility: A Review of Literature

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### ABSTRACT

**Purpose:** Approximately 10% to 15% of couples have difficulties conceiving, or conceiving the number of children as they anticipate, and many seek specialist fertility care at least once during their reproductive lifetime. The objective of this literature review was to examine the potential roles of nutrition in the development and treatment of female infertility.

**Methods:** Peer-reviewed journal articles regarding nutrition, lifestyle, and infertility were gathered electronically through the PubMed database. The search was further limited to articles within the last 20 years and those written in English.

**Results:** While vitamin D, healthy and balanced diet, and some herbal supplements such as chaseberry may be beneficial to female fertility, obesity, smoke, and early exposure to phytoestrogens may have unfavorable effects on women reproductive health.

**Conclusions:** Nutrition and lifestyle may play a role in the development and treatment of female infertility.

#### INTRODUCTION

According to the article, *Evaluation and Treatment of Anovulatory and Unexplained Infertility*, "With an average monthly fecundity rate of only 20%, human beings are not fertile compared with other mammals. Overall, 10% to 15% of couples have difficulties conceiving, or conceiving the number of children they want, and many will seek specialist fertility care at least once during their reproductive lifetime." [1] In the United States, the infertility rates continue to increase each year with approximately 1.5 million of married women aged 15 to 44 that were infertile [2]. Infertility is an emotionally stressful problem for many couples. Treatment methods for female infertility vary; however a [3]many of them are expensive in nature and not covered by most insurance. With considerably emotional strain and expense involved in Western medicine approach, the question serves to be answered, are there more conservative, less invasive treatment options available? The objective of the current literature review was to examine the potential roles of nutrition in the development and treatment of female infertility. This review will provide recommendations for health care practitioners when giving nutritional consultations to female patients seeking infertility treatment.

#### METHODS

Peer reviewed journals were obtained through the PubMed database. Key search words used were "female infertility", "infertility", "conservative treatment of female infertility", "omega-3 fatty acids and infertility", "chasteberry and infertility", "coq10 and infertility", "vitex agnus castus", "l-carnitine and infertility." The search was further limited to articles within the last 20 years and those written in English. Only articles relevant to the topic of choice were included in the literature review. The articles chosen were then reviewed and summarized in an organized manner. The sources obtained were all intended to determine if there is a more conservative method such as nutrition and lifestyle for the treatment of female infertility.

#### **REVIEW OF LITERATURE**

#### *Causes of female infertility*

Has there actually been an increase in infertility amongst U.S. couples or are there just more women/couples reaching out for infertility help due to technology and its success.Changing times and social norms are catalysts for the increasing discussion of infertility. Over the years, women have chosen to take their early twenties and build careers instead of staying at home and making babies. This choice plays a significant role in the rise of subfertile and infertile women. The availability of options and the disappearance of the taboo-esque nature of infertility might also play a role in the apparent rising nature of the condition of infertility. It is suggested that the increased demand in Western countries for infertility services is likely due to a number of causes including women delaying childbearing for careers which decreases the interval of time of fecundability of the female, an increase of effective treatments by assisted reproductive techniques (ART's) and awareness of effective ART's [4]. The causes of infertility are further categorized to female , male , male and female combined , or unexplained factors [4]. The majority of infertility causes are due to female factor making up about 30% [4], which is the focus of this review.

#### Obesity and fertility

Another aspect of our culture that has a profound effect on female fertility is obesity. The number of people categorized as obese has risen dramatically over the last several years. This prevalence stems from a combination of reduced exercise, changes in dietary composition and an increase in overall caloric intake [5]. In the United States, statistics show that 60% of women are overweight, 35% are obese and 6% are morbidly obese. With the small percentage of women who are underweight, this leaves only 35% of women in the United States who are considered of normal weight. Research shows that overweight and obese women tend to have a lower probability of a healthy live birth due to lower implantation rates, lower pregnancy rates and increased complications during pregnancy for both the mother and the fetus [5]. A research study using artificial insemination looked at the rates of successful conceptions in women who were of normal weight, women who were overweight and women who were underweight. The percentage of women who became pregnant decreased with increasing waist-hip ratio from 63% to 32%. Only 22 women in this particular study were obese and just four of the 22 women became pregnant which suggests a direct relationship between weight and fecundity [6]. Obese women are three times more likely to suffer from infertility and to fail to conceive through both natural and assisted reproductive procedures [5].

Although there are confounding arguments as to why women with higher body fat percentages have a more difficult time with fecundity, several theories have developed over time through various research approaches. In the second and third trimesters of pregnancy, often times the complications that occur are due to maternal issues of metabolic syndrome of obesity. In the first trimester however, there appears to be abnormal dialogue between the embryo and the endometrium, suggesting an abnormal uterine environment [5]. The oocyte-embryo complex is

discussed first . Research has shown a lower ovarian response to controlled ovarian stimulation, decreased ooctye retrieval, lower number of mature oocytes, poorer oocyte quality, lower fertilization rates, poorer embryo quality and lower mean number of transferred embryos [5]. Some research has found that the endometrium to be more of a problem. One study examined the ovum donation model, in which eggs were taken from young, healthy, non-obese donors and given to women with different BMIs and success rates of conception were studied. The pregnancy rate per cycle was significantly lower in obese women than in leaner women. These findings suggest that the endometrium and/or it's environment, plays a role in the reproductive outcome of obese women [5].

The increase in assisted reproductive technologies has coincided with the increasing prevalence of obesity over the years. A recent study assessing IVF treatments in obese females found that there appeared to be no affect on the embryo quality but the study did find an increase in both biochemical and clinical miscarriages, decreased implantation rates, decreased pregnancy rates and decreased live birth rates in obese females. As a matter of fact, a logistic regression analysis was performed in this study group finding a significant decrease in pregnancy and live birth rates with each unit of increased BMI [5]. Looking deeper into waist-hip ratio and female fat distribution, a study also examined female fertility and body fat composition found that the cumulative pregnancy rate by insemination for women with waist-hip ratios less than 0.80, often referred to as "pear shape" was significantly higher than that in women with waist-hip ratios greater than 0.80, or "apple shape" [6].

Knowing the consequences of excess weight on fertility doesn't explain why and the reasoning behind it remains unclear. One explanation is that insulin resistance may increase the androgenic microenvironment of the follicle, thereby decreasing egg quality and chances of

conceiving. Another theory is that increased levels of luteinizing hormone (LH), which is responsible for ovulation, may decrease the chance of spontaneous conception and increase spontaneous abortion rates [6]. Along with increasing LH levels and insulin resistance, several other metabolic/endocrine disturbances have been noted in obese females. Other hormones such as leptin, resistin, ghrelin and adiponectin play a role in follicle growth, corpus luteum function, early embryo development, trophoblast function and endometrial receptivity [7]. It has been found that short term weight-loss had a positive effect on oocyte yield and could potentially have an overall beneficial effect on successful pregnancies in this population [8].

#### Smoke and fertility

One of the major causes of infertility in both men and women is smoking. According to the article *Smoking and Infertility: a committee opinion*, approximately 30% of women of reproductive age and 35% of men of reproductive age smoke cigarettes [9]. Women who smoke tend to have lower levels of estrogen (estradiol-17beta) in comparison to their nonsmoking counterparts [10]. Although people generally recognize that smoking has negative health effects, harmful effects on reproductive health do not appear to be common knowledge [9]. The same article *Fertility and Sterility* found that in regards to public knowledge of a variety of health risks and its causal affect with smoking, 99% of the public knew the inherent risk of lung cancer and smoking while only 22% of the public knew of the causal relationship between infertility and smoking [9].

Smoking has been found to affect several different aspects of reproductive health in both men and women including conception delay, ovarian follicular depletion, effects on sperm parameters, mutagenic potential, early pregnancy effects, affects of maternal smoking on male progeny and influence on assisted reproductive outcomes [9]. A meta-analysis looking at smoking and in vitro fertilization found a significant negative effect on smoker's ability to conceive and may need twice as many cycle of in vitro fertilization to become pregnant [10]. Chemicals from cigarette smoke were detected in the serum of women smokers. High concentrations of rhodanate, a smoke exposure marker, were found in follicular fluid of women who were smoking and undergoing IVF. Cotinine, a marker for nicotine exposure was also found in follicular fluid of smoker receiving IVF. The heavy metal cadmium, found in cigarette tobacco was also found in the follicles of smokers [10]. Due to all of the potential negative influences of smoking con reproductive health, it is estimated that approximately 13% of all infertility is smoking related [9].

Little research has been done on how quickly reversal of negative health effects of smoking can occur in regards to fertility. Findings suggest that if a woman is the process ofmanaging infertility and is also a smoker, she should be advised to quit or significantly reduce smoking [10].

#### *Diet and fertility*

One commonly overlooked factor in female infertility and sub-fertility is the preconception diet. Often times a woman's preconception diet is inadequate [11]. What a woman eats determines the amount of micronutrients, vitamins and minerals she is receiving which plays a direct role in her ability to conceive [12]. How much of a role is yet to be determined but some research has been done to attempt to determine the effects different types of diets have on a woman's ability to become pregnant and stay pregnant. Often times, for research

purposes, questionnaires are used to determine the nutritional status of the couple trying to conceive. Vujkovic, et.al examined the consistency of two preconception dietary patterns, "health-conscious, low-processed" and "Mediterranean diet".. The first pattern, "Healthconscious, low-processed" consisted of high intake of fruit and vegetables, whole grains and fish and low intakes of snacks, meat and mayonnaise [12]. The second pattern, "Mediterranean diet" was similar to the first, but slightly different in that it was defined by high intakes of vegetable oils, vegetables, fruits, nuts, fish and legumes, low dairy intake and moderate alcohol consumption [12]. Although the two patterns had significant overlap in the foods included in their category, only the Mediterranean diet increased the chances of pregnancy after IVF treatment [12]. Looking further into the differences between the two diet patterns, it appeared that one significant detail would be the high intake of vegetable oil in the "Mediterranean diet." Vegetable oils are high in linoleic acid, a member of the omega-6 fatty acids, which are precursors to prostaglandins. Prostaglandins play a major role in the maintenance of pregnancy by increasing the chances of implantation due to increased endometrial receptivity [12]. The second major difference that separates the Mediterranean diet from the "Health-conscious, lowprocessed "diet is the notable amount of vitamin B6. Research has shown that vitamin B6, when given to infertile or subfertile women, increases chances of conception by 40% and decreases chances of miscarriage by almost 30% [12]. These findings indicate that couples may experience more success with reproduction when adhering to the Mediterranean diet.

Twigt, et.al. used a food intake questionnaire to determine nutritional status in couples planning to conceive but took a different approach by including preconception counseling as well [11]. The study found that couples who participated in preconception counseling on nutrition and lifestyle and followed the preconception diet had a better chance of ongoing

pregnancy with IVF treatment within six months of initiating changes [11]. The findings suggest that couples diagnosed with "unexplained infertility" should consider nutrition and lifestyle counseling as a first-choice treatment [11].

#### Nutrients/supplements and fertility

Couples seeking treatment for infertility have a multitude of treatment options, including the use of supplementation. In the case of unexplained infertility, issues could be due to hormonal levels, aging reproductive systems and/or nutritional deficiencies .[13] If infertility stems from nutritional deficiencies or hormonal imbalance, nutritional supplementation may play an important role in optimizing chances of reproduction . [14] FertilityBlend is a proprietary, natural nutritional supplement with combined micronutrients and vitamins aimed at improving female fertility. Two research studies focused on this specific supplement and its effect on fertility. FertilityBlend contains chasteberry, green tea extracts, L-arginine, vitamins, (including folate, vitamin B12, vitamin B6, vitamin E), minerals ( including iron, magnesium , zinc and selenium), and L-arginine [14].

The first study looked at thirty women aged 24-46 years who had tried unsuccessfully to conceive for 6-36 months. After 3 months of supplementation with FertilityBlend, the supplement group showed an increase in mid-luteal phase progesterone levels and a significant increase in the number of days with an elevated basal body temperature >37 degrees Celsius (98 degrees Farennheit) during the luteal phase. The placebo group showed no notable changes in progesterone levels or basal body temperature changes [14]. After 5 months of supplementation, 5 of the 15 (33%) women in the supplement group became pregnant and none of the women in

the non-supplementation group became pregnant. After the research study was completed, a woman from the placebo group began taking FertilityBlend and became pregnant, as well [14].

The second study also looked at FertilityBlend supplementation in 93 infertile/sub-fertile women between the ages of 24-41 years who had unsuccessfully attempted to conceive for 6-36 months. FertilityBlend was taken daily, three capsules per day for three menstrual cycles. The study looked at progesterone levels, changes in basal body temperature, length of menstrual cycle, pregnancy rate (PR) and incidence of side effects. These parameters were monitored for four months, the first being two weeks before the supplement was taken [13]. After three months of supplementing with FertilityBlend, the supplement group demonstrated increased progesterone levels, especially notable in women with low initial progesterone levels [14]. The supplement group also showed an increase in the number of days in their menstrual cycles with basal body temperatures over 37 degrees Celsius. In women with short cycle lengths, the average cycle length increased significantly. The same effect was shown in women with longer average cycle lengths. These women experienced a significant decrease in the number of days in their menstrual cycles. As hypothesized, cycle length did not change in the placebo group [13]. At the end of the three month trial, 14 of the 53 women in the supplement group became pregnant, in comparison to 4 of the 40 in the placebo group. Four of the 40 women in the placebo group started FertilityBlend after the study and became pregnant within the first three months [13]. Of the 21 women who became pregnant, 11 of them had low progesterone levels before the initiation of the study. Thirteen of the 14 women in the supplement group who became pregnant demonstrated an increase in the number of days of increased basal body temperature in the luteal phase of their menstrual cycle [13]. Results from the study suggest that nutritional

supplementation might be able to provide an effective alternative to conventional techniques such as assisted reproductive technologies for women struggling with infertility.

### Vitex and fertility

Chasteberry (Vitex Agnus Castus) has been used for centuries to aid in gynecologic conditions including premenstrual syndrome, cyclical breast discomfort, menstrual cycle irregularities and dysfunctional uterine bleeding [15]. The medicinal properties in Chasteberry include flavenoids, iridoid glycosides and essential oils. Chasteberry has a dopaminergic effect that inhibits basal and thyrotropin releasing hormone stimulated prolactin release [15]. It's therapeutic effects are reflective of it's indirect effect on hormones, most notably prolactin and progesterone [15]. This effect on the hormone levels is dose-dependent meaning that low doses result in decreased estrogen levels and increased progesterone and prolactin levels. It is thought that the increase in progesterone and prolactin could be due to the inhibition of follicle-stimulating hormone (FSH) and stimulation of luteinizing hormone (LH) [15]. In other studies however, higher levels of Chasteberry had no effect on FSH or LH, but showed a decline in prolactin levels suggesting that low doses of the berry may stimulate breast milk production while higher doses might inhibit milk production [15]. Along with gynecologic disorders, Chasteberry has been used in cases of infertility, specifically luteal phase defects [15].

One randomized, placebo-controlled trial looked at 96 women with fertility disorders. Fertility disorders included 38 women with secondary amenorrhea, 31 with luteal insufficiency and 27 with unexplained infertility. The women received Chasteberry supplementation or placebo twice daily for three months. Women with amenorrhea or luteal insufficiency in the supplementation group showed a two-fold increase in occurrence of pregnancy over the placebo

group [15] Another randomized, placebo-controlled trial looked at 52 women with luteal phase defects. The active treatment group demonstrated reduced prolactin release, normalized luteal phases, increase luteal phase progesterone synthesis and increase luteal phase estradiol; however, the effects on fertility were not noted [13, 15]. A double-blind placebo-controlled pilot study also examined the effects of Vitex on fertility in 30 women, 15 of whom were in the active treatment group for five months. The active treatment group showed increased mid-luteal phase progesterone levels and an increase in the number of pregnancies attained [14, 15]. In a study by Loch, et al. [16], researchers found an increase in the number of pregnancies among premenstrual syndrome women taking Vitex. The advantages of taking Vitex over other commonly prescribed fertility medications like Clomid include reduced instance of multiple births and the almost nonexistent side effects from usage [14]. The AHPA Botanical Safety Handbook states that traditional use of Chasteberry can aid in the prevention of miscarriage in the first trimester of pregnancy when the cause of potential miscarriage is low progesterone levels [13].

#### Vitamin D and fertility

Another nutrient that research suggests potentially plays a role in female fertility is vitamin D. While vitamin D is famous for its role in calcium and phosphorous regulation for bone mineralization, it also plays a significant role in many other mechanisms in the body. Although most of the vitamin D that is absorbed in the human body and metabolized and synthesized via the skin, the rest of the vitamin D in the system comes from dietary intake. Provitamin D, found in the skin, is converted to pre-vitamin D3 by thermal conversion and is isomerized into cholecalciferol [17]. Cholecalciferol is bound to vitamin D-binding protein (DBP) and converted to calcitriol through a two-step enzymatic process involving 25hydroxylase of the liver and 1-alpha-hydroxylase of the kidney and extrarenal tissues [17]. The biologically active form of vitamin D is 1,25(OH)2D3, however vitamin D status in the body is assessed by measuring serum 25(OH)D<sub>3</sub>. Presently there is no consensus for optimal levels of vitamin D, but most experts use 25 nmol/L as the cutoff measurement for deficiency of vitamin D. Another source suggested that 25(OH)D values >75 nmol/L favor fertility .[18] Recent evidence demonstrates that women of childbearing age have a surprisingly high prevalence of vitamin D deficiency [17]. Vitamin D receptor (VDR) mRNA and 1-alpha-hydroxylase are expressed in the ovary, uterus and placenta linking serum vitamin D levels and reproductive health in women [19].

Vitamin D may also play an important function in production of female hormone production. 1,25(OH)2D3 stimulated progesterone production by 13%, estradiol production by 9% and estrone production by 21% in human ovarian tissue [19]. Other studies have shown that calcitriol, the active form of vitamin D, promotes calcium transport in the placenta, stimulates placental lactogen expression and regulates HOXA10 expression in human endometrial stroma cells [19]. HOXA10 expression is crucial in the uterine and endometrial development, making the uterus more ideal for implantation [19].

Seasonal conception and birth rates have been seen consistently showing peak conception rates in the summer. Studies have shown a tendency for high levels of serum  $25(OH)D_3$  in summer and autumn and lower levels in spring and winter. In parts of the country where there is an increased seasonal contrast in light, conception rates, ovulation rates and endometrial receptivity are decreased during long, dark winter months with a peak conception rate during summer [19]. The reduction in female fecundity during long, dark winter months might be

explained by an altered hypothalamic-pituitary axis or the role of brain neurotransmitters such as dopamine, melotonin, serotonin and endogenous opiods [19]. It is known through experimental studies that  $1,25(OH)_2D_3$  targets the ovary suggesting that the active form of vitamin D may play a direct role in ovarian function, thus female feritility .[17]

Experimental studies looking at female rats and vitamin D levels found that vitamin D deficiency in these rats led to 75% reduced fecundity. Another study looking at  $25(OH)D_3$  deficient female rats found decreased fertility, decreased litter sizes and dysfunctional mating behaviors .[17] In female mice with 1-alpha-hydroxylase ablation demonstrated abnormal ovarian follicle development, uterine hypoplasia and infertility [17].

Research regarding vitamin D and human specimens is limited and far between, but one study looking at IVF success and vitamin D found an association between raised oestradiol levels during gonadotrophin-induced ovarian stimulation and a significant increase in serum 1,25(OH)<sub>2</sub>D<sub>3</sub> levels. Another study looking at IVF and serum vitamin D levels found higher pregnancy and implantation rates with decreased 25(OH)D<sub>3</sub> in follicular fluid of 84 infertile women undergoing IVF treatment . The study found 25(OH)D<sub>3</sub> follicular fluid levels to be an independent predictor to IVF success [17]. Interesting to note, one study looking at glucose and vitamin D levels, found that increased levels of 25(OH)D<sub>3</sub> in follicular fluid and decreased glucose in follicular fluid had a negative impact on embryo quality and therefore, on IVF outcome [17].

Currently, there are no recommendations for vitamin D supplementation for the purposes of infertility. The recommendations from the Institute of Medicine regarding vitamin D are 600 IU for individuals up to 70 years of age and 800 IU for older adults .[18] The tolerable upper

intake is 4000 IU /day [18]. The Endocrine Practice Guidelines Committee(EPGC) suggests 1500-2000 IU/day for adults>18 years and up to 70 years of age. 1500-2000 IU/day are recommended to raise serum 25(OH)D levels . The upper limit according to the EPGC is 10,000 IU/day. Suggested intake did not change for pregnant or lactating women [18].

With such a high percentage of vitamin D deficient women and women suffering from infertility, further research into the supplementation of vitamin D as a first resort of treatment is warranted.

#### Phytoestrogen exposure and fertility

People are naturally exposed to phytoestrogens in their daily lives mainly through diets. The most potent form of phytoestrogen is genistein. Genistein is thought to interact with estrogen receptors in the body [20]. It has been suggested that genistein, due to its estrogenic effects on the human body, may be linked to promotion of hormonally responsive cancers .[20] Other potential effects of phytoestrogens on human reproductive health include altered sexual development, timing of puberty, sex-dependent behaviors, testicular and ovarian endocrine functions, gamete production and lactation [21]. Much research has been done to determine the effects of estrogen exposure in critical periods of development, specifically on the male and female reproductive system. One of the most critical periods for endocrine development is infancy. Exposure to significant levels of phytoestroges during the time can have long-term effects on reproductive health and behavior [21]. The effects of phytoestrogens on the reproductive system was first seen in the 1940's when sheep grazing on red clover, a source of phytoestrogen, demonstrated infertility [22].

The American population is not exposed to soy products as much as other cultures around the world, most specifically the Asian cultures, but one specific source of soy that many Americans are exposed to is soy-based infant formula. Although infants fed breast milk or milkbased formula are also exposed to phytoestrogens, the highest consumption of phytoestrogens is infants fed soy-based formula (SBIF) [23]. It is estimated that approximately 20-25% of infants are fed soy formula which is a common alternative for women who want to breast feed but can't [22]. Research data found that Infants fed SBIFhad 13,000-22,000 times higher concentrations of circulating phytoestrogens than non-SBIF fed infants [21]. Though there is limited data using human studies, one prospective study looked at the long-term biological effects of phytoestrogens on adult reproductive health and found prolonged menstruation and increased discomfort during menstruation from women who were fed soy-based infant formula (SBIF) as infants [24]. Another study looking at 3-month old infants fed SBIF found greater vaginal cell maturation in comparison to infants fed milk-based formula or breast milk [24]. A crosssectional study looked at 2 year olds fed SBIF and found a higher prevalence of breast buds in the second year of life as compared to infants fed breast milk or milk-based formula [21].

Most studies have been performed on rodents due to the difficulty of gathering information over the life span of the subjects, difficulty of controlling exposures and accuracy of information collected [23]. One study looked at neonatal mouse genistein exposure and observed abnormal estrous cycles and anovulation in these mice . These researchers also suggested that neonatal genistein exposure caused failure of oocyte nest breakdown and development of multi-oocyte follicles [23]. In addition, mice treated neonatally with genistein also demonstrated a 35% increased chance of uterine cancer [23]. Mice with early exposure to soy isoflavones at levels comparable to levels found in human infants experienced reduced

fertility, abnormal reproductive organ structure and changes in estrous cycling [24]. Along with these findings, other studies have found altered ovarian differentiation in female exposed to genistein early in life [22].

A recent meeting of the Center for Evaluation of Risks to Human Reproduction failed to reach a conclusion about the safety of soy-based infant formula for infants due to lack of research data onhuman subjects [21].Applying findings from animal model to humans is complex but may provide some relevant evidence in terms of the unfavorable long-term effects of neonatal soy exposure on reproductive health. [24].

#### DISCUSSION

When it comes to conservative treatment of female infertility, it appears that there is much controversy regarding efficacy of supplementation with vitamin D, combination therapies like FertilityBlend and Vitex Castus Agnus. Research has shown in all three cases that increased chances of conception have occurred with the use of these supplements . In the case of FertilityBlend, of the 53 women in the supplement study, 14 became pregnant along with four in the placebo group who began taking FertilityBlend after the study's completion [13]. Along with increased chances of conception, a greater number of days of raised basal body temperature were reported in women with low progesterone levels prior to the initiation of the study [13]. Vitex has been used for many years to treat hormonal imbalances. Studies looking at fertility and Vitex usage not only demonstrated increased conception rates but also decreased incidence of early miscarriage [15]. Vitamin D deficiency has also been shown to decrease a woman's fecundity due to its active role in ovarian, uterine and placental function [19].

While much controversy exists concerning the efficacy of supplementation, there is little doubt the negative role that smoking, unhealthy diet and obesity play in a woman's fertility. A good diet is necessary for everyone seeking a healthy lifestyle to ensure that we receive the right micronutrients, vitamins and minerals. It is especially important in women seeking to conceive and certain vitamins and minerals have been found to aid specifically in conception. One example is vitamin B6. In one study, vitamin B6 was shown to increase chances of conception by 40% and decrease chances of miscarriage as well [12]. Higher body fat percentage has been linked to decreased oocyte quality and has been shown to have a negative effect on the endometrium, making it harder for implantation to occur [5]. Chemicals from cigarette smoke have been found in the follicular fluid of women who smoke. This finding has been linked to nearly 14% of all infertility [10].

Exposure to phytoestrogens and infertility is still uncertain, but some evidence shows a connection between infants fed soy-based infant formula and reproductive system dysfunction later in life [23]. More research tracking long-term results is necessary to make a conclusive statement.

#### CONCLUSIONS

Although the medical community, through technology, has created many options for women struggling to conceive, these options are often pre-emptive and expensive. Perhaps if each individual took some time to change personal habits and create a healthy environment for conception, extreme measures with potential side effects and financial strain could be avoided. Research is limited and can only provide us with so much information, much of it often inconclusive, but knowing that it might be as easy as increasing the amount of one specific

nutrient, or losing a few pounds, or finally kicking a bad habit might be all it takes gives many a feeling of control over their own fertility and sense of calm knowing they have options.

### REFERENCES

- 1. Propst AM, Bates GW, Jr.: Evaluation and treatment of anovulatory and unexplained infertility. *Obstet Gynecol Clin North Am* 2012, **39**(4):507-519.
- 2. Centers for Disease Prevention website. Available at: http://www.cdc.gov/nchs/fastats.
- Crosignani PG, Rubin BL: Optimal use of infertility diagnostic tests and treatments.
  The ESHRE Capri Workshop Group. *Hum Reprod* 2000, 15(3):723-732.
- Forti G, Krausz C: Clinical review 100: Evaluation and treatment of the infertile couple. J Clin Endocrinol Metab 1998, 83(12):4177-4188.
- Bellver J, Ayllon Y, Ferrando M, Melo M, Goyri E, Pellicer A, Remohi J, Meseguer M: Female obesity impairs in vitro fertilization outcome without affecting embryo quality. *Fertil Steril* 2010, 93(2):447-454.
- 6. Zaadstra BM, Seidell JC, Van Noord PA, te Velde ER, Habbema JD, Vrieswijk B, Karbaat J: Fat and female fecundity: prospective study of effect of body fat distribution on conception rates. *BMJ* 1993, 306(6876):484-487.
- Bellver J, Melo MA, Bosch E, Serra V, Remohi J, Pellicer A: Obesity and poor reproductive outcome: the potential role of the endometrium. *Fertil Steril* 2007, 88(2):446-451.
- Chavarro JE, Ehrlich S, Colaci DS, Wright DL, Toth TL, Petrozza JC, Hauser R: Body mass index and short-term weight change in relation to treatment outcomes in women undergoing assisted reproduction. *Fertil Steril* 2012, 98(1):109-116.
- 9. Smoking and infertility: a committee opinion. *Fertil Steril* 2012, **98**(6):1400-1406.
- Feichtinger W, Papalambrou K, Poehl M, Krischker U, Neumann K: Smoking and in vitro fertilization: a meta-analysis. J Assist Reprod Genet 1997, 14(10):596-599.

- Twigt JM, Bolhuis ME, Steegers EA, Hammiche F, van Inzen WG, Laven JS, Steegers-Theunissen RP: The preconception diet is associated with the chance of ongoing pregnancy in women undergoing IVF/ICSI treatment. *Hum Reprod* 2012, 27(8):2526-2531.
- 12. Vujkovic M, de Vries JH, Lindemans J, Macklon NS, van der Spek PJ, Steegers EA, Steegers-Theunissen RP: The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy. *Fertil Steril* 2010, **94**(6):2096-2101.
- Westphal LM, Polan ML, Trant AS: Double-blind, placebo-controlled study of Fertilityblend: a nutritional supplement for improving fertility in women. *Clin Exp Obstet Gynecol* 2006, 33(4):205-208.
- Westphal LM, Polan ML, Trant AS, Mooney SB: A nutritional supplement for improving fertility in women: a pilot study. *J Reprod Med* 2004, 49(4):289-293.
- 15. Hamm, BR. Chasteberry. American Family Physician 2005, 72(5):821-824.
- Loch EG, Selle H, Boblitz N: Treatment of premenstrual syndrome with a phytopharmaceutical formulation containing Vitex agnus castus. J Womens Health Gend Based Med 2000, 9(3):315-320.
- Christesen HT, Falkenberg T, Lamont RF, Jorgensen JS: The impact of vitamin D on pregnancy: a systematic review. *Acta Obstet Gynecol Scand* 2012, 91(12):1357-1367.
- Grundmann M, von Versen-Hoynck F: Vitamin D roles in women's reproductive health? *Reprod Biol Endocrinol* 2011, 9:146.
- Lerchbaum E, Obermayer-Pietsch B: Vitamin D and fertility: a systematic review. *Eur J Endocrinol* 2012, 166(5):765-778.

- 20. Seppen J: A diet containing the soy phytoestrogen genistein causes infertility in female rats partially deficient in UDP glucuronyltransferase. *Toxicol Appl Pharmacol* 2012, **264**(3):335-342.
- 21. Cederroth CR, Zimmermann C, Nef S: Soy, phytoestrogens and their impact on reproductive health. *Mol Cell Endocrinol* 2012, **355**(2):192-200.
- Jefferson WN, Williams CJ: Circulating levels of genistein in the neonate, apart from dose and route, predict future adverse female reproductive outcomes. *Reprod Toxicol* 2011, 31(3):272-279.
- Jefferson WN, Patisaul HB, Williams CJ: Reproductive consequences of developmental phytoestrogen exposure. *Reproduction* 2012, 143(3):247-260.
- 24. Dinsdale EC, Chen J, Ward WE: Early life exposure to isoflavones adversely affects reproductive health in first but not second generation female CD-1 mice. *J Nutr* 2011, 141(11):1996-2002.