

Uterine Fibroids and Nutrition — Possible Links

By Megan Tempest, RD

Four years after giving birth to her son, Janet began to experience abdominal pain and heavier-than-normal bleeding during her monthly periods. Her physician performed a routine pelvic exam and discovered a fibroid tumor the size of a walnut as well as six others of various sizes. As time passed, she experienced such heavy bleeding during her periods that she didn't dare leave her home for fear of having an accident. Within nine months, she was anemic and in desperate need of medical care that would eventually require major surgery.

Uterine fibroids will affect as many as three in four women at some point in their lives.¹ Known as leiomyomas, myomas, or fibromyomas, uterine fibroids are benign tumors that grow within the smooth muscular tissue of the uterus. Women in their 30s and 40s are the most affected, but fibroids can develop at any age.²

In some women, fibroids cause few symptoms and may go unnoticed. In others, fibroids can cause symptoms so severe, as in Janet's case, that their quality of life is compromised. Symptoms include heavy and prolonged menstrual periods, bleeding in between periods, abdominal and lower back pain, frequent urination, constipation and, in rare cases, miscarriage and infertility.

Krystene DiPaola, MD, a reproductive endocrinologist and infertility specialist at the University of Cincinnati Academic Health Center, emphasizes the significance of this condition. "Uterine fibroids are something OB/GYNs take very seriously, as does the American College of Obstetricians and Gynecologists. There's also a large push at the National Institutes of Health [NIH] to do a lot of research on the subject of fibroids because they cause so much suffering in a multitude of ways across multiple ethnicities, in particular African Americans."

In fact, the NIH has held three international congresses, "Advances in Uterine Leiomyoma Research," for the purpose of fostering an exchange of scientific information among members of the leiomyoma research community.

Uterine fibroids vary widely in size, shape, and location within the uterus and in the symptoms they cause. They can grow inside the uterine cavity, within the uterine musculature, on the outer walls of the uterus or they can attach to the uterus in a mushroomlike stalk. Some fibroids are as small as a walnut and cause minimal to no symptoms. Others can grow large and multiply in number, causing a woman's abdomen to become enlarged or distended. A particularly large fibroid can cause the uterus to expand to the size of a six- or seven-month pregnancy.³

A routine pelvic exam initially can detect the presence of fibroids, which can be confirmed by diagnostic testing procedures such as ultrasonography or MRI.³

This continuing education activity will provide an overview of uterine fibroids and discuss risk factors, symptoms, and common treatments. Recent studies demonstrating a link between diet and the development of uterine fibroids will be examined so that nutrition professionals can discuss with patients the current state of research on diet and uterine fibroids.

Common Treatments

For women with asymptomatic fibroids, the treatment approach may involve watchful waiting to monitor the condition's progression. Fibroids can be routinely checked at annual gynecological exams to determine if they're increasing in size. For women with small or asymptomatic tumors or who are approaching menopause (when fibroids tend to shrink on their own), no treatment is necessary.⁴ However, for women suffering from burdensome symptoms, more aggressive pharmaceutical and surgical treatment options may be considered.

Medications

Primary attempts to treat symptomatic fibroids may involve hormone-based treatments, such as hormonal contraceptives, gonadotropin-releasing hormone antagonists, and a hormone-releasing intrauterine device. These treatments can be effective in slowing fibroid growth and alleviating heavy bleeding and pelvic pain, but they come with a downside: Aside from possible side effects such as high blood pressure or blood clots, evidence shows that fibroids likely will return after these hormonal treatments end.³

Surgery

Hysterectomy is the surgical removal of the uterus and may or may not include removal of the ovaries. The procedure is generally considered when other less invasive treatment approaches haven't worked or if a woman's fibroids are very large and highly symptomatic.⁴ According to the American College of Obstetricians and Gynecologists, hysterectomy is the only treatment for fibroids that eliminates the possibility of recurrence.⁵ Given that hysterectomy also eliminates a woman's ability to have children, other surgical techniques such as myomectomy are available to women who aren't ideal candidates for hysterectomy or would like to preserve fertility.

Myomectomy involves the surgical removal of only the uterine fibroids. Unlike hysterectomy, myomectomy allows for the preservation of the healthy surrounding uterine tissue. "The goal of myomectomy is to remove as many identifiable fibroids as possible and preserve the ability to conceive," DiPaola explains. "The drawback is that, traditionally, myomectomy can be associated with higher blood loss than hysterectomy, and therefore it's reserved as a therapy only for woman of reproductive age. This isn't a technique I'd recommend to a woman in her 50s who's done having children."

A cutting-edge version of this surgery is robotic myomectomy, which DiPaola describes as essentially the same procedure as traditional myomectomy, although it can be performed laparoscopically (thereby avoiding an abdominal incision) and therefore accomplishes better closure of the uterine musculature.

Nonsurgical Treatments

Nonsurgical treatments for uterine fibroids can preserve patients' ability to have children and include the following:

Hysteroscopy is a treatment option for women with fibroids that extend within the uterine cavity. During this procedure, a physician inserts an instrument called a hysteroscope through the vagina into the uterus. Another tool known as a resectoscope—inserted through the hysteroscope—destroys the fibroids with electricity or a laser. Generally, doctors can perform the procedure on an outpatient basis.⁴

DiPaola says one benefit of hysteroscopy is that it doesn't require an incision. "Instead, you physically go through the vagina and into the cervical canal to the uterus to remove the fibroids," she says. This can dramatically decrease bleeding and essentially cure the disease.

Endometrial ablation is a nonsurgical procedure that destroys the lining of the uterus and typically is employed to treat small fibroids.⁴

Uterine artery embolization involves injecting small particles into the blood vessels leading to the uterus, with the goal of cutting off blood flow to the fibroids and causing them to shrink.⁴

MRI-guided ultrasound surgery is a relatively new treatment that uses ultrasound waves to destroy the fibroids. The ultrasound waves are directed at the fibroids through the skin with the assistance of MRI.⁴

What Causes Fibroids?

Despite years of research and the fact that uterine fibroids are among the most common gynecologic conditions in the United States, researchers don't know precisely what causes them.²

Studies have suggested that genetic alterations in the uterine muscle cells may cause fibroids to develop.¹ Fibroids also have been shown to contain more receptors for estrogen and progesterone (the hormones involved in preparing the uterine lining for pregnancy at each menstrual cycle) than normal uterine muscle cells, making them more likely to grow in the presence of these hormones.⁶

Another theory behind their cause is that chemicals in the body, such as insulinlike growth factor (IGF), which help the body maintain normal tissues, may stimulate fibroid development.¹

Risk Factors

Although scientists have yet to pinpoint the cause, the available research has isolated several key risk factors for developing uterine fibroids.

Age: Because fibroids are estrogen-dependent tumors, the greatest risk factor for developing them is believed to be age. Fibroids are most common in premenopausal women in their 30s

and 40s. After menopause, when estrogen levels naturally decrease, fibroids generally shrink or disappear.⁷

Heredity: If a woman's mother or sister has fibroids, she's at increased risk of developing them herself. In fact, a woman whose mother has fibroids has three times the risk of developing them.⁷

Race: African American women are more likely to have fibroids than white women. In addition, black women tend to develop fibroids at a younger age, have more or larger tumors, and develop symptoms faster and with more severity than women in other ethnic groups. Studies have suggested that eight in 10 African American women will develop fibroids at some point in their lives.³

Obesity: Obese women are considered to have two to three times the risk of developing fibroids than women of average weight.⁷

Does Diet Affect Fibroid Development?

Research has suggested a relationship may exist between diet and the growth of uterine fibroids. More than a decade ago, a study by Chiaffarino and colleagues, published in ***Obstetrics & Gynecology***, reported that uterine fibroids were associated with the consumption of ham and beef. The same study indicated that a high intake of green vegetables has a protective effect against fibroids.⁸

"In the last 15 years, interest has grown concerning the possible influence of diet on the growth of these tumors," says Bala Bhagavath, MD, an endocrinologist at the Center for Reproduction & Infertility at Women and Infants Hospital in Rhode Island. "Italian women with fibroids have been observed to consume more red meat and ham, [and] alcohol consumption has been linked to increased likelihood of fibroids in Japanese women." (see also reference 9)

However, Bhagavath says all the studies published to date are observational and therefore inherently limited: "No interventional study using diet modification has been published to date. It's not known if modification of diet in women with established uterine fibroids will result in resolution of these tumors. Even if they do, the length of time this dietary modification has to be maintained has to be established. It's possible that dietary modification may decrease the incidence of fibroids in women at high risk for developing them. However, even this question of prevention remains unanswered at this time."

That being said, several research studies published in recent years have revealed additional evidence that dietary factors may indeed influence the growth of fibroids, providing further rationale for continued research on this compelling subject.

Dairy

With the knowledge that fibroid rates are two to three times higher in black women than white women, coupled with evidence that black Americans consume fewer servings of dairy foods (and thus have lower mean intakes of calcium, magnesium, and phosphorus) than white

Americans,¹⁰ Wise and colleagues investigated the disparity in dairy intake among these two populations as a potential factor in fibroid growth.¹¹

In the study, published in the January 2010 issue of the *American Journal of Epidemiology*, the team of researchers followed more than 22,000 premenopausal black women in the US Black Women's Health Study over a 10-year period. Self-administered questionnaires on dietary intake were used to assess whether intake of dairy foods such as low-fat and whole milk, cheese, yogurt, and ice cream—and some dairy components like calcium, vitamin D, and butyric acid—may reduce the risk of uterine fibroids. The findings indicated a lower risk of uterine fibroids associated with higher dairy consumption. The perceived protective effect of dairy, according to the researchers, may lie in calcium's ability to reduce fat-induced cell proliferation and in butyric acid (present in milk fat), which is considered a potent antitumorigenic agent that may inhibit cell proliferation and angiogenesis.¹¹

Glycemic Index

Eating foods with a high dietary glycemic index (GI), a measurement of the effects of carbohydrates on blood glucose levels, or a high glycemic load (GL), a ranking of carbohydrate content of various foods based on their glycemic index, is thought to potentially promote tumor growth by increasing endogenous concentrations of IGF-1. Examples of high GI and GL foods include instant white rice, white bread, rice cakes, French fries, donuts, and scones.

In vitro studies have shown that uterine fibroid cells proliferate in the presence of IGF-1. Other studies have shown a positive association between high GL and other hormone-responsive tumors such as ovarian and endometrial cancer. From this standpoint, Radin and colleagues theorized in a study published in the May 2010 issue of the *American Journal of Clinical Nutrition* that a high GI and GL diet may encourage uterine fibroid growth. Based on a prospective analysis of diet questionnaires (collected from the same cohort in the aforementioned study on dairy intake and uterine fibroid risk), they concluded that high dietary GI (but not GL) may be associated with increased risk of uterine fibroids overall, and high GL was associated with increased risk in women younger than 35.¹²

Lycopene

Given that carotenoids have known antioxidants properties and have been associated with lower cancer risk in some studies, Terry and colleagues hypothesized that carotenoids such as lycopene may have a similar effect on uterine fibroids. In a study published in the January 2008 issue of the *American Journal of Obstetrics and Gynecology*, researchers analyzed the nutritional intake (via food-frequency questionnaires) of more than 82,000 premenopausal women over a period of 10 years. Based on the findings, they concluded that total lycopene intake had no association with uterine fibroid risk.¹³

These findings conflict with earlier animal studies by Sahin and colleagues detailed in 2004 in *Nutrition and Cancer*. These researchers reported lycopene supplementation may actually prevent uterine fibroids. Using Japanese quail as subjects (a species in which spontaneously occurring benign oviduct leiomyomas are common), they observed that lycopene supplementation not only decreased the number of fibroids in the birds but also the size of the existing fibroids. Serum levels of antioxidant vitamins A, C, and E were also shown to be

greater in the lycopene-supplemented birds, and serum measures of oxidative stress (malondialdehyde and homocysteine) were lower.¹⁴

In 2007, the same team reported that dietary supplementation of tomato powder, rich in major carotenoids such as lutein and zeaxanthin as well as lycopene and vitamins A, C, and E, appeared to reduce both the incidence and size of fibroids in Japanese quail subjects.¹⁵

Soy

The scientific evidence behind soy's role in promoting or inhibiting the growth of estrogen-dependent tumors is scattered and conflicted. Soybeans are a rich source of phytoestrogens, specifically isoflavones, that may have an "antiestrogen" effect in the body by competing with estrogen for receptor binding, thereby possibly decreasing the availability of estrogen or altering estrogen biosynthesis.¹⁶

High doses of genistein (an isoflavone abundant in soybeans) have exhibited an inhibitory effect on uterine leiomyoma cell proliferation. In the January 2012 issue of ***Experimental and Molecular Medicine***, Di and colleagues reported that high serum concentrations of genistein downregulate several signaling pathway genes involved in uterine fibroid growth, suggesting that high doses of this isoflavone have an inhibitory effect on uterine fibroids and therefore a potential to be used as a therapeutic agent in their treatment.¹⁷

Conversely, in May 2009, Nagata and colleagues reported in the ***British Journal of Nutrition*** that they observed no statistically significant association between soy isoflavones and uterine fibroids based on a study of 285 premenopausal Japanese women.⁹ Likewise, the aforementioned study on dairy intake and fibroid risk by Radin and colleagues observed no relationship between soy intake and uterine fibroid risk among their cohort from the Black Women's Health Study.¹²

To date, the effects of soy on uterine fibroids is inconclusive. However, future studies will have to be monitored.

Fish

While fish intake is generally associated with good health, one study by Lambertino and colleagues found that fish consumption may have a negative impact on health when it comes to uterine fibroids. The study, published in the May 2011 issue of ***Environmental Research***, found that exposure to polychlorinated biphenyl (better known as PCB) from consuming Great Lakes sport fish such as walleye, lake trout, and yellow perch may increase the risk of uterine fibroids. PCB is a group of persistent, manmade organic pollutants that has been banned from manufacture since 1979 and has been associated with uterine fibroids and other gynecologic conditions like ovarian cysts and endometriosis.^{18,19}

Additional Studies

In the January 2011 issue of ***Fertility and Sterility***, Sharan and colleagues reported that vitamin D inhibits the growth of cells involved in forming uterine fibroids, suggesting that low serum vitamin D levels may be a risk factor for their development.²⁰

Findings from a population-based, cross-sectional analysis of nearly 900 women aged 20 to 49, published by Martin and colleagues in the June 2011 issue of the *Journal of Women's Health*, suggest that higher serum micronutrient concentrations—in particular vitamins A and C—may encourage uterine fibroid development.²

A 2010 animal study by Tuzcu and colleagues, published in *Nutrition and Cancer*, investigated a relationship between dietary supplementation of selenium and uterine fibroid development. Again, using Japanese quail as subjects, the data led the researchers to conclude that selenium appears to reduce the size of existing fibroids.²¹

With evidence from epidemiologic studies suggesting that zinc deficiency is associated with increased cancer risk, Sahin and colleagues investigated the hypothesis that a similar relationship may exist between zinc and uterine fibroid risk in a study published in the December 2009 issue of the *Journal of Medicinal Food*. They reported that dietary supplementation with zinc picolinate reduced the growth of spontaneously occurring fibroids in the oviduct of Japanese quail, suggesting that further studies are warranted to determine whether zinc supplementation may be effective in the treatment or prevention of this condition.²²

In the December 2011 issue of the *American Journal of Clinical Nutrition*, Wise and colleagues published a study investigating the relationship between the dietary intake of fruits, vegetables, and carotenoids and fibroid risk. Again, based on diet questionnaires collected from a cohort from the Black Women's Health Study, they observed a reduced risk of uterine fibroids among women with a greater intake of fruit and retinol, or preformed vitamin A from animal sources such as whole milk and eggs.²³

While dietary interventions aren't likely to cure uterine fibroids, it's reasonable to assume that scientific studies will continue to explore how dietary interventions may enhance traditional medical treatments. DiPaola says she considers the existing research promising that particular food groups, or a lack thereof, may influence fibroid growth. "I think we're still at the beginning stages of learning whether or not diet strongly influences fibroid growth and development or if dietary changes could affect the presentation or sequela of fibroid growth," she says. "It will be some time before we can tell if certain food groups worsen or [inhibit] fibroid growth."

Margaret Wertheim, MS, RD, LDN, a dietitian at Pulling Down the Moon, an integrative care center for fertility in Chicago who works with women struggling with infertility, believes good nutrition can only help women who suffer from this condition. Given the evidence that vitamin D may inhibit fibroid growth, Wertheim routinely recommends women get their serum vitamin D levels tested and supplement (with medical supervision) as needed to correct deficiency.²⁰ Wertheim also recommends women with fibroids increase their intake of cruciferous vegetables such as cabbage, broccoli, and kale. "This group of vegetables, in particular, contains indole-3-carbinol, which research has suggested may prevent estrogen-driven tumors due to its effect on estrogen metabolism."²⁴

Specific food groups and nutrients aside, dietitians can help women manage fibroids by encouraging weight loss when necessary, according to DiPaola. "We do know that fibroids

respond to estrogen, and that estrogen isn't produced only in the ovaries but also in peripheral fat in the form of estrone," she explains.²⁵ "The estrone can, in higher doses such as in overweight women, affect fibroid growth and cause them to be more symptomatic."

DiPaola believes any nutritional modification that may lower peripheral fat stores, and therefore reduce estrogen production from those fat stores, only helps women with symptomatic fibroids.

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Examination

1. Which of the following therapies aims to treat uterine fibroids while preserving a woman's ability to conceive?

- a. Myomectomy
- b. Endometrial ablation
- c. Uterine artery embolization
- d. All of the above

2. Based on the literature presented, which components of dairy foods may exhibit a protective effect against uterine fibroids?

- a. Calcium
- b. Butyric acid
- c. Vitamin D
- d. All of the above

3. Which of the following characteristics is not associated with an increased risk of developing uterine fibroids?

- a. Being underweight
- b. Having a mother or sister who has uterine fibroids
- c. Being of African American descent
- d. All of the above

4. Which of the following assumptions apply to uterine fibroids?

- a. They're benign, estrogen-dependent tumors.
- b. They usually shrink or disappear after menopause.
- c. Their only proven "cure" is endometrial ablation.
- d. A and B

5. Which of the following are possible symptoms of uterine fibroids?

- a. Heavy menstrual periods
- b. Frequent urination
- c. Constipation
- d. Lower back pain
- e. All of the above

6. Noted drawbacks of using hormone-based drugs to treat fibroids include all of the following except:

- a. increased uterine bleeding.
- b. increased risk of high blood pressure.
- c. possible return of fibroids when hormone treatment ends.
- d. increased risk of blood clots.

7. High dietary glycemic index and glycemic load may increase fibroid risk by increasing endogenous concentrations of which hormone?

- a. Progesterone

- b. Estrogen
- c. Insulinlike growth factor 1
- d. Vitamin D

8. Research studies using Japanese quail as subjects suggest that all but which of the following micronutrients may inhibit growth of existing fibroids?

- a. Selenium
- b. Lycopene
- c. Tocopherol
- d. Zinc

9. Genistein is a type of phytoestrogen found in soybeans that has exhibited an inhibitory effect on uterine fibroids.

- A. True
- B. False

10. A study evaluating the consumption of Great Lakes sport fish concluded that consuming these fish may increase the risk of uterine fibroids because the fish contain which of these environmental pollutants?

- a. Polychlorinated biphenyls
- b. Bacteria
- c. Agricultural fertilizers
- d. All of the above