Nutrition and Pelvic Health for Women: Pharmacy Contributions to Wellness

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Upon successful completion of this activity, the pharmacist should be able to:

1. Identify the best dietary sources of key essential vitamins and minerals for women.
2. Discuss multivitamin bioavailability concerns and approaches to maximize nutrient absorption.
3. Suggest nutrients and dosages particularly necessary during pregnancy and possible sources.
4. Describe overlapping pelvic and bladder-specific disease symptoms and their etiologies.
5. Interpret the proper first-line and progressive treatment options for chronic bladder disorders.

INTRODUCTION

As recently as the early 1980s, women’s health needs and disease management protocols were based almost exclusively on the results of observations and guidelines obtained from experiences in adult men. As the research focus on women has expanded in more recent decades, the unique concerns of women from puberty through childbearing and menopausal years have become clearer. Rather than experiencing the same disease symptoms and requiring the same medications and dosages as men, women have distinct disease experiences, requirements for treatment options and dosages, and disparate health conditions, particularly in the pelvic floor.

Similarly, women have specialized and age-variable nutrition requirements that are not always clearly understood or properly managed across a woman’s life stages. Lifestyle-related causes of nutritional deficiencies range from high-intensity sports and veganism to pregnancy. Disease states or iatrogenic effects of medications, dietary changes for disease management—including adjustments for constipation, blood pressure, and heartburn control—can alter nutrient requirements as well.

VITAMINS AND MINERALS FOR WELLNESS Overview

More than 40 percent of the U.S. adult population consumes a daily multivitamin. Women are twice as likely as men to comply with regular multivitamin use. The variety of multivitamin products available on the market reflects consumer concerns and uncertainties about which vitamins and minerals are truly important for proper wellness according to sex, age, activity level, and disease prevention needs. Although all multivitamin products contain some combination of the 13 vitamins and 10 trace elements identified by the Department of Agriculture as essential for optimal body functions, these supplements are not held to medication standards regarding the reporting of quantity or quality of contents. In addition, nutrition experts and researchers have expressed doubt that multivitamin products are useful in the majority of healthy adults, and high intake of certain vitamins and minerals may actually be detrimental to health. Given these conflicts, pharmacists’ knowledge about specific nutritional needs can guide patients to the best dietary or marketed vitamin and mineral sources providing a valuable counseling service. Women in particular can benefit from directed selection of supplements to meet nutrient requirements before, during, and after pregnancy; dosage planning to avoid adverse effects and maximize supplement benefits; and specialized formulation selection of multivitamins when necessary.
Why Use a Multivitamin?
A balanced diet of grains, meat or alternative protein sources, legumes, dairy, fruits and vegetables, and some fats is considered adequate as a nutrition source in the majority of healthy adults. The risk of experiencing toxicities from high intake of any vitamin or mineral is nearly nonexistent with only dietary intake, because the body flushes out or stores what is not needed from the diet. However, multiple populations have inadequate and unbalanced diets or specialized nutrient needs that might require supplementation beyond food sources to avoid deficiencies of key nutrients.

Recommendations and consensus statements from the National Institutes of Health and the Institute of Medicine have identified almost no definitive long-term health benefits of multivitamin supplementation on the basis of research studies. The Institute of Medicine examined randomized clinical trials of individual vitamin effects on chronic health conditions such as cardiovascular disease and cancer. The results were frequently insignificant or inconclusive to support any benefits. Additionally, recent studies have discovered adverse health effects of some vitamins when used individually at doses much greater than 100 percent of the recommended daily allowance, often marketed as megadoses. Just as minimum recommended levels of essential vitamins and minerals have been determined, so have recommendations for safe upper limits of these nutrients. There is increasing evidence that vitamins taken in excess, particularly fat-soluble vitamins, are stored in the body’s liver and other tissues and can result in tissue damage, increased mortality, or chronic disease. For example, a 2005 study observed increased heart failure and all-cause mortality, rather than cardioprotection from antioxidant activity, in people with chronic diseases who received vitamin E 400 IU supplementation daily. In recent studies, vitamin D overdose in children using liquid formulations has been shown to cause fatigue, nausea, vomiting, dehydration and weakness from vitamin build-up. Hypervitaminosis D, such as is associated with ergocalciferol use, can lead to serious adverse reactions including soft tissue calcification (such as heart, blood vessels, lungs and renal tubules), renal insufficiency and abnormal growth in infants and children. Too little data from long-term evaluations are available to obtain conclusions about the safety of dietary supplement megadose vitamin or mineral levels.

Despite the supportive research of nutrition benefits obtained directly from the diet and despite reliable documentation about the lack of scientific evidence supporting multivitamin use for chronic disease treatment or prevention, the number of multivitamin users continues to increase. Higher prevalence of use is due to vitamin-consuming women who give a multivitamin to their children. The National Institutes of Health does not recommend the general use of a daily multivitamin in adults, nor does it discourage supplementation if the patient chooses. In expert opinion, such as Harvard Health, multivitamins can be used to balance an imperfect diet or buffer diet in patients with special dietary needs in order to maintain nutrition. However, available research has not been extended for long enough duration to determine the true effects of vitamins on chronic disease after decades of consistent use. Women in general present a nutritional challenge, because they have variable vitamin and mineral requirements across their life stages. Although all formulations of multivitamins contain essential vitamins and nutrients, women often require particular combinations or increased concentrations of certain nutrients. For example, multivitamin products formulated specifically for women in childhood, in childbearing years, and during menopause and beyond contain varying amounts of vitamin D and B12, folate, iron, and calcium to meet the changing requirements as the woman transitions in age and hormonal fluctuations. Pharmacists familiar with the variation between multivitamin formulations and female vitamin recommendations can help women select a suitable supplement from an overwhelming number of choices.

Special populations that require extra effort to avoid nutritional deficiencies include endurance athletes, vegans, smokers, pregnant women, dieters, and the elderly. Athletes commonly experience iron deficiency, because muscles under exertion use the body’s iron stores. Additionally, an imbalance of mineral electrolytes like sodium and potassium can occur secondary to water depletion; therefore replenishment becomes critical in maintaining
muscle, bone, and organ health. Vegans are at even greater risk of nutritional deficiencies—especially iron and vitamins D and B12, which are not obtained in their completely animal-free diets. Incorporating vitamin D–and iron-fortified grains and cereals contribute to a more balanced diet, but the lack of vitamin B12, which is found only in animal products, can lead to anemia in vegans without explicit vitamin supplementation. High-fiber or low-calorie diets may also justify vitamin supplementation. Diets high in fiber increase intestinal motility, which reduces vitamin and mineral absorption in the gut. Low-calorie diets, which are typically low in proper nutrients, may benefit from calcium, iron and zinc supplementation.

Smokers poorly absorb vitamins throughout the gastrointestinal tract and can require a general multivitamin. Patients with active alcoholism, or early in sobriety are often deficient in vitamin B1 (thiamine) and should supplement. Pregnant women carrying multiples require higher supplementation than that which is required for a single birth. In such cases, vitamins B6, folate, and iron are particularly beneficial in balancing the extra blood volume and growth burden, thereby protecting the mother’s body.

Vitamin needs for the elderly change perhaps more drastically than at any other age. As iron requirements decrease after menopause in women, calcium and vitamin D needs increase to counteract reduced bone density. Elderly have greater B12 requirements and a 15 percent increased risk of B12-deficiency anemia than the general adult population as a result of less-varied diets and poor vitamin B12 absorption by the gut. Evidence also indicates that maintenance of folate concentrations is beneficial for cognition and possibly for prevention of depression, dementia, and other chronic diseases of in the elderly. Minerals and antioxidative vitamins might benefit people at risk of age-related macular degeneration. The AREDS vitamin regimen in addition to a multivitamin appears to reduce the risk of this disease by 25 percent over six years in at-risk populations. Individual components of the AREDS regimens include 80 mg zinc oxide, 2 mg copper oxide, 15 mg beta carotene, 400 IU vitamin E, and 500 mg vitamin C, all of which can also be found in a combination product.

### Which Nutrient Sources Are Best?

Vitamins and minerals comprise water-soluble (such as B and C) and fat-soluble (such as A, D, E, and K) vitamins as well as trace elements, such as iron, copper, and zinc. These nutrients, required by our body to function, may be made within the body or obtained directly through the diet. Meeting the USDA’s recommended daily allowance for vitamins and minerals is suggested to maintain optimum health and can be achieved through a combination of naturally nutrient-rich foods and food products fortified with nutrients.

Before multivitamin supplementation, proper food selection is the first step to appropriate nutrition. Levels of thiamine, riboflavin, vitamin C, and vitamin A in vegetables are one third lower in canned products than in frozen or fresh vegetables, because canned foods leach their nutrients into the packed water, which is often discarded. Fruits and vegetables lose valuable nutrient content after refrigeration for more than one week, in part because the colder temperatures inhibit ripening to full nutritional content and in part because the natural oxidation process from exposure to air without the plant’s replenishing nutrients begins almost immediately after the food is picked. Vitamin C in particular begins to degrade quickly when fruits are sliced, because it works to counteract oxidative discoloration from air exposure. Heat has especially strong effects on vitamin concentrations of some foods; heavy heat degrades vegetable nutrients, particularly folate and B12, so much that fresh or frozen vegetables are most nutritious when cooked in a microwave or steamed gently. Longer durations of heat (such as slow cooking for two hours or more) can reduce folate, B6, and C levels at least 10 percent, and reheating leftover foods reduces folate and vitamin C by up to 30 percent. Riboflavin, though heat stable, is particularly sensitive to breakdown by ultraviolet light and requires opaque containers for foods fortified with the vitamin, such as milk, to prevent its loss. Stores of water-soluble B and C vitamins typically deplete from foods faster than those of fat-soluble vitamins, such as vitamin A.

### Nutrient Food Sources and Properties

#### Iron

Iron provides oxygen to cells, stores oxygen in muscles, and contributes to hemoglobin and blood cell synthe-
sis and blood volume maintenance. Heme iron, found in meats and fish, is better absorbed than nonheme sources found in seeds, beans, apricots, prunes, and other plant products. As the essential mineral most commonly associated with anemia, iron needs increase during puberty and again during pregnancy. Conversely, they wane during and after menopause when iron levels are no longer regularly depleted, so vitamins marketed for women older than 50 years of age likely contain lower iron dosages. In supplements, 65 mg of elemental iron is frequently represented as 325 mg ferrous sulfate. Healthy adult women require 18 mg of iron; absorption can decrease with use of medications like quinolones, tetracyclines, H2-blockers, and proton pump inhibitors.

Calcium and Vitamin D
Calcium, obtained from dairy, eggs, almonds, white beans, tofu, salmon, and cabbage; and vitamin D, from dairy and egg products or fortified replacement sources, are inextricably linked for proper bone health but also benefit muscle and circulatory functions. Although the recommended intake of these nutrients for women is similar to that recommended for men during teenage and young adulthood, both calcium and vitamin D needs increase during pregnancy - as infant bone and teeth develop - and especially during elderly and postmenopausal years in women at risk of osteoporosis or bone fractures. Most vitamins for adult women of any age contain at least 200 mg calcium; approximately 80 percent of adult vitamin D needs are met through sunlight and ultraviolet light exposure. Vitamin D supplementation should be evaluated for those who limit their ultraviolet light exposure whether due to limited time in sunlight or diligent use of sunblock. Vitamins aimed at women older than 50 years of age might contain greater amounts of vitamin D, though, to improve calcium absorption.

Folate and Other B Vitamins
B vitamin needs fluctuate across the decades in women. These water-soluble vitamins play a role in myriad body functions and tissue development, yet they are not stored in the body as surplus. Folate plays an important role in early and late stages of life. In early life, it prevents newborn neural tube defects. Folate affects later stages of life by reducing homocysteine, a promoter of chronic vascular diseases like thromboembolism and peripheral artery disease; DNA changes that can increase the risk of cervical, colorectal, or breast cancers; and cognition impairment potentially related to Alzheimer’s disease—all conditions that occur more frequently in the elderly. The recommended daily allowance of folate for women older than 51 years is 400 mcg from diet and supplementation, and the upper intake of supplementation is 1,000 mcg. Folate in the diet can be found in leafy greens, orange juice, strawberries, legumes, asparagus, and fortified cereals and grains. The synthetic formulation, folic acid, is absorbed twice as well as natural folate, and approximately 85 percent of a folic acid product is absorbed when taken with food. Deficient folate levels can result from use of methotrexate, an antifolate; similarly, alcohol, phenytoin, and sulfasalazine reduce folate levels by preventing folate metabolism or absorption. Several medical conditions, such as liver disease or kidneys dialysis, may also result in increased loss of folic acid.

Deficiencies of most B complex vitamins are rare, because these vitamins are easily obtained from food sources. For example, thiamine is common in yeast, cereals, and nuts; niacin is most likely found in legumes, meats, and fish; and riboflavin is present in dark green vegetables, dairy and egg products, and meat. Vitamin B12, however, is found only in animal products, and B12 deficiency is a frequent cause of anemia in special populations. Although B12 is often included at higher doses in multivitamins marketed as energy boosting or better for active individuals, it is unlikely to increase energy in people who are not experiencing deficiency-related anemia.

Does Formulation Matter?
Unfortunately, knowing which nutrients are required from diet or supplementation is not always enough. Vitamin selection and administration timing impact product absorption, tolerability, and usefulness. Standardization of multivitamins is historically poor, and reports of product compositions and absorptions can be inadequate and unreliable. Beyond age and dietary replacement factors, the quality of multivitamin products is poorly understood by health
professionals and consumers alike. In addition, consumer awareness about what constitutes a multivitamin appears lacking.

When consumer watch organizations have compared numerous multivitamins in spot-check market evaluations, major brand names and store generic brands have been found typically reliable in their vitamin and mineral content within an expected dosage range. Conversely, discount vitamin products did not always contain their stated ingredients or dosages. Even the US Pharmacopoeia (USP), which oversees quality standards for over-the-counter and prescription medications in the United States, has also evaluated multivitamin supplements in an attempt to increase consumer confidence about multivitamin product consistency.

Because so little is known about traditional absorption patterns and actual blood concentrations of individual vitamins and minerals in a multivitamin product, the USP sought to identify concentrations of representative vitamins and minerals to determine standard benchmarks of a well-absorbed vitamin product and as a reflection of bioavailability of each nutrient. Bioavailability or the proportion of the product digested, absorbed, and metabolized to be used in the body, is just as important as the quantity of the ingredients. Multivitamins, unlike medications, have no clear dose-response curves or dissolution rates. In addition, bioavailability is altered drastically by user parameters, excipients, chemical or synthetic formulations, and combinations used.

The USP identified likely disintegration rates of common nutrients to determine the true nutrient absorption and use in the body. USP disintegration results were based on index vitamins and minerals that could represent the absorption patterns of all other related vitamins and minerals. Folate was evaluated individually as a uniquely essential vitamin, and minerals were measured in order of importance to nutrition (such as iron, calcium, zinc, and magnesium). Riboflavin (vitamin B2), the least-soluble of the water-soluble vitamins, was considered the index vitamin to evaluate the absorption of water-soluble vitamins, particularly B6, C, and niacin. Bioavailability of the vitamins and minerals was measured for multivitamin tablets in whole or crushed forms and for vitamins taken with or without food. Absorption levels and concentrations for riboflavin, folate, vitamin C, and vitamin B12 were greater after any multivitamin use, whether as a whole or crushed tablet, than they were after only ingesting a meal, implying that multivitamin use effectively improves nutrient concentrations in the body regardless of initial disintegration rates. Conversely, iron serum levels were better absorbed when whole tablets, rather than crushed ones, were ingested. Despite supplementation, all mineral levels remained low (that is, at maintenance body levels instead of exhibiting surplus peak concentrations) and the body’s mineral levels decreased severely when only a meal was ingested; it appears that mineral supplementation is required to maintain healthy levels.

Finally, although liquid stability was not standardized or evaluated, water-soluble B and C vitamins appear more vulnerable to product changes, so liquids could provide less adequate nutritive impact. However, even liquid formulations provide some level of nutrition and were considered likely better than using no vitamin at all.

The USP, along with individual researchers, have concluded that vitamins and minerals in a single compressed multivitamin tablet are dissolved, absorbed, and metabolized in the body with such variability that traditional dosage standards are unlikely achievable. Newer formulations, such as capsules, liquid gels, and chewable products, are usually marketed to consumers according to their ease of use, rather than because enough evidence exists that their components are better absorbed in these formulations. Future research must confirm or dispute this belief.

Does Timing Matter?

As a result of dissimilar bioavailability among vitamins and minerals and because of product standardization difficulties, the method of multivitamin administration is likely more useful than the product formulation itself to provide benefits for most people. Consumer choices about food and the timing of food and supplements can be more important to obtaining adequate nutrition than the product itself. In addition to cooking heat, oxidation, and related factors, vitamin-mineral and multivitamin-food interactions all affect nutrient concentrations in the body.

Multivitamins as a whole and individually are suscep-
Food components and processes that can prevent adequate nutrition:

- **Phylates**: Found in grains, legumes, and seeds, can lower iron, calcium, magnesium, and zinc absorption.
- **Oxalates**: Found in chocolate, fiber, spinach, and beets, lower calcium absorption.
- **Cooking heat**, especially prolonged low heat, causes up to 30 percent breakdown of water-soluble vitamins.
- **Oxidation of fruits and vegetables** through air exposure and meal preparation reduce vitamin C content.
- **Ultraviolet light** induces breakdown of riboflavin, most commonly in milk found in translucent containers.

**PRENATAL NUTRITIONAL SUPPLEMENTATION**

**When to Start**

Prenatal nutrition needs differ from those at other life stages. It is important to ensure adequate nutrition from the very beginning of the pregnancy, even before conception is known. Though multivitamins may not be necessary in a healthy adult woman, diet alone is not usually enough of a nutrient source during pregnancy, when the burden of certain nutritional needs increases dramatically. Even women who have safely maintained healthy vitamin choices in early adulthood can quickly develop nutrient deficiencies during pregnancy. Further, even moderate morning sickness during the first trimester can inhibit nutrition obtained from a well-rounded diet, and more severe hyperemesis can counteract any benefits from dietary nutrients. Therefore, commitment to a tolerable multivitamin becomes even more essential. In addition to well-known folate requirements for all pregnant women, basic increased nutrient needs include iron and supportive trace elements, vitamin C, and vitamin D to support greater calcium needs. In recent years, supplementation with DHA and EPA, two healthful, essential long-chain omega-3 fatty acids, has become more aggressive as awareness of their wide-ranging benefits increases and depletion during pregnancy has been discovered.

**Minimum Nutrient Requirements**

Basic prenatal multivitamin use as a supplement to a balanced diet has been linked to potentially reduced risk of low birth weight in newborns. According to the American Pregnancy Association and the Cleveland Clinic Foundation, prenatal vitamin formulations should contain a minimum of the following essential nutrients: folate 400 mcg, vitamin D 400 IU, calcium 200 to 300 mg, vitamin C 70 mg, thiamine 3 mg, riboflavin 2 mg, niacin 20 mg, B12 6 mcg, vitamin E 10 mg, zinc 15 mg, and iron 27 mg. These quantities support infant growth during each trimester without depleting nutrients from the mother’s body unnecessarily.
Folate
Folate requirements increase immediately to prevent early neural tube defects. In addition to food intake, folic acid supplementation of at least 400 mcg daily is recommended by the American Pregnancy Association for women of childbearing age. Supplementation should be started at least one month before becoming pregnant to reduce the risk of spinal cord exposure and neural tube defects that can develop within the first 28 days of conception and cause paralysis or severe mental impairment.

Iron
Iron requirements increase during pregnancy because of the increased blood volume of pregnant women; nearly all prenatal vitamins meet or exceed the increased minimum recommended intake of 27 mg daily for pregnancy. The Centers for Disease Control and Prevention recommend 30 mg of daily routine iron use beginning at the first prenatal visit, because of the difficulty of maintaining iron stores as pregnancy continues. Because iron is considered safe in pregnancy, increased supplementation can be considered with health professional guidance. Iron 60 to 120 mg daily is warranted if hemoglobin and hematocrit lab parameters are low at two separate measurements. Higher dosages should be continued for four weeks and reassessed. To minimize the severity of iron's most common side effects—stomach upset and constipation—iron products should be taken by themselves during afternoon or evening hours to avoid compounding morning sickness.

Related trace minerals have increased amounts in prenatal vitamins as well. Greater amounts of zinc and copper in prenatal supplements used during pregnancy promote better iron absorption in an effort to prevent anemia.

Vitamin C
Vitamin C needs are traditionally well provided by dietary sources, so the recommended intake is not officially increased during pregnancy. However, a focus on habitually selecting good food can ensure that vitamin C needs are met to maintain adequate fluid balance, promote tooth and bone development, and assist with wound healing. Vitamin C levels can be maintained at 185 mg daily from citrus fruits, melons, potatoes, and peppers, but supplements may be preferable for women experiencing taste or smell aversions or heartburn worsened by citric foods.

Calcium and Vitamin D
Extra supplementation of calcium and vitamin D during pregnancy should be considered if dietary sources are regularly low. Calcium needs increase in pregnancy, because infant bone and teeth development needs draw calcium from the mother's bones. Vitamin D is obtained primarily from sunlight, so women who live at more northern latitudes or who otherwise avoid sunlight (such as by staying indoors or using strong sunblock) can be deficient, especially during the third trimester during the final stages of infant development.

Vitamin A
Vitamin A requirements do not increase during pregnancy, primarily to avoid the potential for undue toxicity to the growing baby. Vitamin A can cause malformations in epithelial tissue and can impair retinal development in embryos. As a fat-soluble essential vitamin, vitamin A is important to adults and to fetal development, because it helps cells differentiate and develops vision, helps keep mucous membranes and sinuses, and also maintains wound healing and immune function.

Vitamin A comprises retinoids from animal products, such as beef, chicken, eggs, fish oil, and dairy, and carotenoids, such as beta carotene, from plant sources like leafy greens and orange vegetables and fruits. Although all forms are absorbed and used in the body, carotenoids require conversion to active vitamin A after absorption and are less likely to build up and cause toxicities. Vitamin A deficiency is unusual, and toxicities primarily occur from use of prescription retinoid products rather than diet or vitamin supplements. Symptoms include headache, fatigue, itchy skin and dry eyes, nausea, weight loss, and hair loss; toxicity is more likely when multiple vitamin A products that promote immune wellness or eye health are used together.

Omega-3s: Vital Fatty Acids
Non-multivitamin supplements have become essential to
a healthy pregnancy as well. Unlike short-chain fatty acids from flaxseed, omega-3 fatty acids, found almost exclusively in cold-water fish (such as salmon, tuna, and sardines), are traditionally depleted in all adults in the United States. Omega-3 fatty acids can be particularly low in pregnant women who avoid fish due to concerns about increased mercury intake and its health risks. Mercury is absorbed into muscles and tissues of fish, especially large fish like mackerel, shark, or swordfish, and cooking does not alter mercury content. Possible toxicities of mercury to the fetus include brain damage, learning disabilities, and hearing loss. The FDA recommends that women include 8–12 ounces of seafood in their weekly diet during pregnancy and suggest low-mercury options like shrimp, crab, salmon, cod, and tilapia, as well as a maximum of 6 ounces of canned tuna in a week.

Omega-3 fatty acids are polyunsaturated long-chain fatty acids that are considered especially supportive of neurologic, cardiac, and immune system health in all populations; omega-3s specifically contribute to proper brain development and immune response in growing children, both during gestation and after birth. DHA and EPA are the two omega 3 fatty acids identified as most healthful individually, thus combined into a single formulation; DHA promotes brain, eye, and overall nervous system health, and EPA promotes cardiac health as well as appropriate inflammatory and immune responses through regulation of prostaglandin activity. Adult women require a minimum of 220 mg of each product, and children up to 15 pounds require 32 mg/lb of the combined fatty acids. Clinical trials continue to identify the added benefits of DHA and EPA during pregnancy for mothers and children. According to current recommendations, pregnant women require a minimum of 300 mg DHA daily, because omega-3 fatty acids become even more depleted by the growing baby’s needs during pregnancy. Omega-3 fatty acids contribute to milk development for nursing, so women experience continued depletion during nursing as well. Because of the generally poor fatty acid intake by U.S. women, omega-3 fatty acid depletion is compounded with each pregnancy and is unlikely to be fully replenished between pregnancies. This continued deficiency leads to potentially worsened health concerns during subsequent pregnancies and may impact women’s health for years after deliveries. For example, recent research has linked insufficient omega-3 concentrations in new mothers to an increased risk of postpartum depression and to prolonged depressive symptoms compared with women who obtain recommended amounts of these essential fatty acids.

The primary reliable non-fish sources of omega-3 fatty acids are soft-gel fish oil capsules containing DHA and EPA. They are generally well tolerated, with diarrhea as one of the most common side effects. Combination capsules, however, can be large and difficult for pregnant women to swallow. Some manufacturers provide fish oil liquid supplements that often are marketed toward children, but could be recommended for adult patients who have trouble swallowing large pills. Only purified fish oil supplements, whether as liquid or a capsule, should be ingested. Brand-name and store generic products are well-documented by manufacturers and consumer research labs as safe, pure (free of contaminants from pollution), and of good quality, with low mercury parts that meet U.S. food regulation standards for maximum mercury content of seafood products. Any fish oil supplements with a rancid or fishy odor should be avoided because of the possibility of impurities or improper handling and processing of the source fish.

Aversions and Adherence: Formulation Possibilities

Women experience complicating symptoms of nausea, constipation, and sensory aversions during pregnancy that adversely impact their diet and adherence to multivitamin use. Compounding these symptoms are the side effects of multivitamins themselves, especially those containing high amounts of iron, which cause additional nausea and constipation. With any formulation, timing and behavioral efforts can minimize some symptoms. For example, nausea may lessen when prenatal vitamins are taken with a meal, if tolerated; are taken at night to avoid compounding morning sickness symptoms; are followed by traditional or sugar-free hard candy (particularly sour-flavored candies) to minimize any aftertaste that can trigger nausea; or are taken at night to allow women to sleep through the side effects. Some research also supports the use of an additional vitamin B6.
supplement (30 mg total) to prevent morning sickness–related nausea and subsequently improve vitamin adherence. Minor dietary changes, such as increased water intake and high-fiber foods or fiber supplementation ingested separately from vitamins to avoid nutrient loss from restored intestinal motility, can improve mild constipation common to pregnancy in all trimesters.

More severe constipation, defined as a lack of bowel movements for three or more days or by the development of hemorrhoids, which result from heavier iron and calcium intake combined with the excessive physical pressure on the intestinal tract, may necessitate stool-softening medications such as docusate. Docusate is recommended for up to one week, taken once daily at bedtime to avoid side effects of cramps and nausea. When these attempts are not enough to resolve discomfort, or when aversions to formulations become too strong and too difficult to manage, women require assistance to determine better formulation options.

Adherence to prenatal vitamins becomes a greater challenge for many pregnant women, because of the product formulations. The primary marketed form of prenatal multivitamins is a compressed tablet. Prenatal tablets are traditionally large, distasteful, heavily coated, and flavored to prevent early breakdown and mask the mineral taste. They often cannot be cut into more manageable sizes because of their coatings. Liquid products and chewable tablets avoid the coating and size concerns but remain poorly flavored and have metallic aftertastes. These unwelcoming formulations and aversions make traditional prenatal multivitamins unacceptable treatment options for pregnancy wellness in many women who seek alternatives from their doctors and pharmacists to maintain adequate nutrition during pregnancy.

Prenatal vitamin supplementation options have expanded to accommodate these particular pregnancy concerns. Formulations to avoid side effects and aversions allow women to adapt to prenatal nutrition maintenance more easily. Chewable formulations may have more palatable flavorings, such as chocolate or fruit flavors, and liquid vitamins may be flavored successfully in some compounding pharmacies to mask the common metallic aftertastes. Newly marketed products such as Belly Bars and NataChew soft chews provide nutrient supplementation in unusual forms to increase adherence. If no formulations succeed at increasing adherence to prenatal vitamins, one alternative is to guide supplementation individually with smaller, non-prenatal multivitamins or with individually required vitamin or mineral products. For example, some obstetricians recommend taking double the child dose, often two chewable tablets depending on the formulation, of children’s chewable multivitamins in place of a single large, coated tablet prenatal vitamin for women with extreme compliance difficulties. For example, using most national children’s chewable multivitamin complete formulations children’s vitamins on this regimen provide 800 mcg of folate and 36 mg of iron to meet the greater requirement and does not exceed recommended vitamin A intake. Multiple medical and pharmacy associations caution against using numerous individual supplements during pregnancy to achieve nutritional needs because the risk of overdose of nutrients found in multiple overlapping products is higher than with use of a single supplement. Careful health professional guidance and supervision to replenish specific deficiencies in this manner for women with protracted aversions is necessary. By adding single vitamin or mineral supplements to correct particular depletions that occur during pregnancy, women may avoid adverse effects of large, unpalatable multivitamins while providing themselves and their babies with the building blocks required for healthy development. During pregnancy, when nausea, aversions, and side effects of multivitamins impair a woman’s ability to maintain her own and her growing child’s health, the “some is better than none” approach might be necessary to maintain critical nutrients, specifically folic acid, calcium, vitamin D, iron, and omega-3 fatty acids.

MANAGING DISORDERS OF THE PELVIC FLOOR AND BLADDER

Women’s health and disease management become multifaceted with the development of pelvic or urinary tract disorders that occur as a result of age, pregnancy, childbirth, and hormonal changes. Structural, hormonal and age-related factors, including pregnancy and menopause, cause disproportionate occurrences of pelvic or bladder disorders in women compared with men. These
changes do not necessarily occur only after pregnancy or menopause, nor do they occur in a vacuum. Rather, the symptoms and often entire diseases overlap and confound diagnosis and treatment. From postpartum pelvic floor prolapse conditions to recurrent UTIs, incontinence, or bladder dysfunction, symptoms of frequency, urge, pain, and discomfort manifest as true disorders, not a natural postpartum or menopausal state. Women must be encouraged to discuss pelvic discomfort frankly and become proactive at identifying symptoms and taking control of disease management. Localized differential diagnoses for chronic bladder conditions include interstitial cystitis, prolapse, incontinence, and infection. Each of these disorders has varied and overlapping manifestations (such as urge and frequency), but are also indicative of the individual disease when viewed in combination. So too do treatment modalities overlap, but become selective according to the needs of the disease. Viewing collective symptoms is essential for accurate diagnosis and leads directly to accurate treatment options according to experienced symptoms.

Pelvic Organ Prolapse
Pelvic organ prolapse, the descent of any pelvic organ into the vaginal area, has multiple risk factors, including reduced muscle mass with increased age, changes in elastic fiber, and physical stressors such as obesity or pregnancy. Prolapse is possible as a result of pelvic procedures as well, particularly hysterectomies because of the reduced muscle tone and nerve sensitivity after even minimally invasive surgery. Prolapse appears to occur more frequently in women with a family history and may be genetically linked. Genetic alterations similar to those seen with connective tissue diseases are slowly being identified as potential markers for risk.

In many women with existing risk factors who develop prolapse, pregnancy is the first structural stressor to trigger the condition. Although pelvic damage most often is associated with first pregnancies, when the tissues and muscles are first stressed, initial pelvic organ prolapse is possible with second and subsequent pregnancies as well. Cesarean section rates appear to approach those of vaginal deliveries.

Pelvic organ prolapse should not be accepted as a normal, untreatable condition. Rather, physical therapy and surgical options can drastically improve quality of life and strengthen the pelvic floor at any age once the condition is identified. The role of medications for prolapse treatment is minimal and primarily addresses symptom relief, such as pain relief. Diagnosis can be complicated by the non-descript symptoms of pelvic organ prolapse, especially when they are mild to moderate. Pelvic organ prolapse symptoms include pelvic pain, pressure and heaviness, difficulty urinating, and incontinence. Symptoms overlap with those of bladder conditions treated with medications (such as overactive bladder or interstitial cystitis), so any women experiencing pelvic symptoms should work with health professionals to identify the true cause—whether structural or pathologic—to identify appropriate pharmacologic treatments.

Incontinence Syndromes
Urinary incontinence, the involuntary leaking or gushing of urine from the bladder, occurs in 40–50 percent of women of all ages in the United States. The incidence increases in populations of increasing age. Incontinence occurs two times more frequently in women than in men, primarily because of pregnancy, childbirth, urinary tract infections, and related changes to the pelvis. In fact, urinary incontinence rates during pregnancy alone approach 50 percent, and 9–13 percent of women continue to experience symptoms postpartum. However, despite commonly held patient beliefs, incontinence is not inevitable and is a treatable condition. Although incontinence is usually uncomplicated, different types have been identified according to causes and mechanisms.

Urge incontinence is characterized by the sudden sensation of a need to empty the bladder followed directly by uncontrolled urine loss. The likely causes are an involuntary and inappropriate contraction of bladder muscles before the bladder is full and weak constriction of the sphincter that holds back urine through voluntary nerve reflexes. Additional nerve miscommunication may play a role, so that urge incontinence may be elicited by sensory factors: water heard, touched, or sipped can trigger urine release. In addition, urge incontinence has a distinct as-
sociation with urine loss during sleep, rather than simply nocturia (waking at night to void).

Stress incontinence, unlike urge incontinence, occurs as a result of purely structural assaults or weaknesses, such as pregnancy, childbirth, and menopause. Incontinence occurs due to weakened pelvic floor muscles and the bladder-contracting muscles rather than resulting from nerve miscommunication. Urine loss from stress incontinence is associated with fewer sudden urges than the loss from urge incontinence, primarily occurring after physical activities that stress the bladder, such as running, coughing, or intercourse. Stress incontinence worsens the week prior to menstruation and permanently after menopause as a result of lowered estrogen levels, because estrogen affects urogenital muscle tone.

Numerous women experience an overlap of stress and urge incontinence called mixed incontinence. Mixed incontinence is more difficult to identify, but can be correctly diagnosed through documentation of symptom triggers from both urge and stress etiologies. Awareness of the incontinence type can support lifestyle changes to avoid structural or sensory stressors. Although incontinence can spontaneously resolve, especially when it is caused by a temporary physical assault on the bladder, prescription medications also reduce symptoms, improve quality of life, and hasten disease resolution. For example, first-line treatments for overactive bladder also can improve symptoms of stress urinary incontinence in 40 percent of patients.

Overactive Bladder

Overactive bladder is very similar to urge incontinence in its association with urge and spontaneous urine loss. However, it is a more complex condition than pure incontinence disorder. Twelve percent of all adults have overactive bladder and experience urge incontinence, in addition to symptoms of greatly increased frequency and discomfort. The disease mechanisms are multimodal. Healthy adult women relieve their bladders an average of seven times daily, and nocturia is uncommon. In overactive bladder, frequency increases to eight or more times daily on a regular basis and potentially twice nightly in addition to daytime voids. Etiologies of overactive bladder are not clearly elucidated, but part of the disease mechanism appears related to abnormal nerve signals: bladder muscles squeeze unnecessarily before the bladder is full enough to trigger the contraction signals normally. Classic symptoms of an overactive bladder are sudden urge, increased frequency, nocturia, and urge incontinence as leaks or gushes.

Overactive bladder without a primary physical cause is unlikely to resolve on its own. Unlike incontinence, overactive bladder is a chronic disease that worsens without lifestyle and pharmacologic therapies. Guidelines for medication treatment include structured attempts with one of four drug classes: antimuscarinics, tricyclic antidepressants, estrogens, or botulinum toxin. Clinical selection relies on the symptomatic experiences, drug tolerabilities, and potential drug or disease interactions. An understanding of each drug class’s treatment mechanisms and goals is vital to select appropriate therapy. Pharmacists can play a valuable role reassuring and counseling women who may be apprehensive about discussing their bladder condition or about using any of these medications, particularly the hormonal or psychologic treatments.

Antimuscarinics are the traditional first-line medications for overactive bladder. They work directly on the bladder muscle activity to relax smooth muscle and decrease bladder muscle contractibility, thereby minimizing urgency, frequency, and incontinence within two weeks of medication onset. However, muscarinic receptors, designated M1 through M5, are found throughout the body. Although M2 receptors are more prevalent in the bladder, muscle relaxation occurs more often at the bladder’s M3 receptors. Side effects of antimuscarinic agents relate to the receptor activity of individual drugs. For example, side effects at M2 receptors in the intestinal tract reduce motility and increase constipation, whereas M3 blockade reduces urine and saliva. Antimuscarinic effects in cardiac muscle M2 receptors can cause QT prolongation. Conversely, M4 and M5 receptors in the brain appear related to decreased cognition, memory, and coordination, as well as increased confusion in some people. Dilated pupils and blurred vision occur as a result of anticholinergic effects at unspecified muscarinic receptors.

The antimuscarinic drug class contains the most
widely marketed agents approved for overactive bladder and continues to be a key avenue of research and development. Antimuscarinics are available as immediate- or long-acting oral tablets, liquids, topical gels, and topically absorbed systemic patches. Nearly all are metabolized in the liver. Pharmacologic activity is characterized as selective or nonselective and according to receptor activity at any combination of the M1 through M5 receptors.

Oxybutynin (Ditropan, Ditropan XL, Gelnique, Oxytrol) and tolterodine (Detrol, Detrol LA), two related and nonselective muscarinic antagonists, are available as immediate- or extended-release products. Oxybutynin was the first agent approved for overactive bladder in 1975. Both drugs increase quality of life and are considered equally effective at reducing urge and incontinence symptoms. Oxybutynin can reduce frequency as well, but has greater incidence of adverse effects, particularly of dry mouth. Oxybutynin and tolterodine are the least tolerated in its drug class because of their widespread antimuscarinic activity throughout the body.

Trospium (Sanctura, Sanctura XR), a unique antimuscarinic medication for the treatment of overactive bladder, is a fully nonselective cholinergic antagonist at M1 through M5 receptors. It is metabolized renally and undergoes minimal hepatic transformation. Dose reduction guidelines are available for use in the elderly. Both trospium immediate- and extended-release products do not cross the blood brain barrier, so the drug is a treatment option for patients with hepatic disease or for patients who may not tolerate central nervous system–related side effects, such as poor coordination, confusion, or memory problems, particularly in elderly patients. However, its non-selective mechanism results in undesirable side effects of severe blurred vision and excessively dry mouth, trospium is not a first-line agent for most patients.

Tolerability and adherence difficulties with oxybutynin, tolterodine, and trospium can be avoided with newer, bladder-selective agents that work primarily at M3 receptors in the bladder wall. Solifenacin (Vesicare) once-daily tablet reduces all symptoms of overactive bladder, especially when compared against tolterodine, and has not been associated with cardiac side effects of QT prolongation from M2 receptor activity. Darifenacin (Enablex), similarly, is an M3-selective, once-daily tablet with related treatment benefits. Although dry mouth and constipation occur as a result of M3 antagonism in the intestines and mucosa, cardiac and nervous system toxicities are unlikely because of the lack of M1 and M2 activity.

Fesoterodine (Toviaz) is a moderately selective muscarinic antagonist. Its disease activity results from blockade at M2 and M3 receptors in the bladder, but fesoterodine also acts at M1 and M5 receptors. Fesoterodine is less likely to impair cognition than oxybutynin, but is more likely to do so than the M3-selective agents. Despite its M2 receptor activity, no QT alterations have been identified with fesoterodine in clinical trials so far.

Any antimuscarinic agent should be prescribed for at least a two-week trial to allow time for symptom improvement and tolerability adaptations. Refractory disease is defined as nonresponding disease after treatment with maximum tolerable doses for four weeks. If nonselective and selective antimuscarinic agents are unable to adequately improve disease symptoms, combination therapy may be warranted. Tricyclic antidepressants (TCAs), specifically imipramine (Tofranil) and amitriptyline (Elavil), are not FDA approved for overactive bladder, but can be added off-label to the existing antimuscarinic therapy to obtain additive effects. TCAs block serotonin and norepinephrine reuptake to increase the amounts of these neurochemicals in the central nervous system. They also inhibit cholinergic activity to reduce bladder wall contractility and reduce incontinence. The anticholinergic effects of TCAs compound the adverse effects of antimuscarinic drugs. Without careful counseling and disease management, the effects can be intolerable enough in some patients to reduce adherence.

For patients with disease that remains refractory to all possible oral medications after four to six weeks, use of botulinum toxin injections to block bladder activity, in otherwise healthy adults, or other procedural treatments can be attempted. Botulinum toxin injections, which have recently been approved by the FDA to treat bladder hyperactivity resulting from neurologic disorders (such as multiple sclerosis or spinal cord injury), are successful at symptom reduction in 40–80 percent of patients.
treatments are invasive and repetitious (every six to nine months), making them less useful as long-term treatment options in healthy adults.

The natural postmenopausal reduction of estrogen levels is considered possibly linked to risk of overactive bladder. Vaginal administration of estrogen products appears to reverse tissue atrophy and significantly relieve urinary urgency symptoms. However, dosages are not clearly indicated and estrogens are not approved by the FDA specifically for the treatment of overactive bladder.

Because of the variety of product types, adverse effects, and bladder selectivity, pharmacist-led selection of proper anticholinergic and alternative choices can be the difference between successful treatment and inadequate care. Antimuscarinic agents should be changed as necessary according to side effect development. All treatment selection should be guided by patient side effects and symptom improvement to ensure maximal treatment benefit with continued adherence.

**Interstitial Cystitis**

Despite recognition in 1914 as “painful bladder,” interstitial cystitis in the 21st century remains poorly characterized, poorly diagnosed, and poorly treated. Interstitial cystitis affects up to 865 per 100,000 adults and occurs 10 times more often in women than in men. Up to 700,000 people have been diagnosed in the United States, and 10 percent of these have severe, ulcerative, disease. Misdiagnosis as overactive bladder, recurrent urinary tract infection, or incontinence is common. The classic triad symptom set of the disease has remained consistent since its earliest descriptions and comprises bladder and pelvic area pain or discomfort for up to six weeks whether holding or voiding urine; extreme frequency; and continual urges. Without treatment, interstitial cystitis continually progresses and can cause blood vessel breakage and severe ulcerations in the bladder wall as a result of continued irritation. Known as Hunner’s ulcers, these eventually scar without treatment, inhibit the stretch of the bladder wall, and further reduce the bladder’s ability to function. In 2010, the first-ever comprehensive diagnosis and treatment guidelines were developed by the American Urological Association. These guidelines were presented to direct health care professionals who treat and care for patients with interstitial cystitis in efforts to control the disease and improve quality of life.

Diagnosis of interstitial cystitis has become less complicated as knowledge about the disease expands. Urgency and frequency are two of the three characteristic symptoms, but pain is the lynchpin symptom needed for proper diagnosis. Prolonged pain or discomfort in and around the bladder separates interstitial cystitis from other bladder disorders, such as overactive bladder or incontinence syndromes, and symptoms are not relieved by traditional antimuscarinic agents used to treat overactive bladder. Because pain is notable, many women with interstitial cystitis actually receive antibiotic therapy for inappropriately diagnosed recurrent urinary tract infections. When a urine culture rules out infective bacteria but pain remains, interstitial cystitis may be suspected. Throughout the 1980s and 1990s, interstitial cystitis diagnosis was made by direct exam of the bladder, through cytoscopic identification of ulcers in the bladder and through purposely provoked bladder irritation with potassium instillation. However, the recent guidelines do not recommend invasive procedures for diagnosis except for complicated occurrences (such as overlapping infection and cystitis or overactive bladder and cystitis) or for patients who are diagnosed at later stages after ulceration and bladder wall scarring have occurred to identify the extent of damage.

Causes of interstitial cystitis are still poorly understood as well. Diagnoses are most often made in women during their fourth decade of life. However, teenage women with early signs of interstitial cystitis are being identified more often as awareness increases. Although
no genetic link has been documented, interstitial cystitis appears to occur more often in women with a family history. An autoimmune component has not been ruled out, as women with interstitial cystitis seem to experience symptoms of other chronic pain syndromes as well (such as fibromyalgia). Allergic and nervous systems likely are involved in the symptom reactions, and treatments aimed at histamine-1 receptors and nerve endings in the bladder wall are common. Acidic foods and drinks appear to be primary triggers of these allergic and nerve reactions; as acidic substances in the urine contact the bladder wall, mast cells are activated to release histamine, and wall nerve endings transmit signals of pain throughout the region and the central nervous system.

Treatments directed solely at halting interstitial cystitis progression are rare. First-line treatment recommendations do not, in fact, address the disease mechanisms as much as they provide coping strategies for symptom control and prevention. Like other chronic and possibly autoimmune disorders, the greatest burden is on the patient for maintaining a good quality of life, despite an interstitial cystitis diagnosis.

After a preliminary interstitial cystitis diagnosis, all patients should undergo behavior modification therapy, supported by a health professional team, to track symptoms and to identify dietary triggers to avoid. Typical components of behavior modification therapy include a voiding diary to consciously reduce the number of voids per day resulting from unnecessary urge; disease education to explain what interstitial cystitis is not (infection, overactive bladder, cancer) and what treatments are not likely to be safe or beneficial (long-term corticosteroids or antibiotics for swelling or infection, respectively); and fluid intake monitoring to reduce the number of voids. Supportive care efforts should be encouraged from the start, to include local hot and cold packs for pain and stress reduction techniques. Localized physical therapy to the pelvic and lower back areas are better at reducing symptoms than traditional Kegel exercises, which are performed solely to strengthen muscles that are not related to interstitial cystitis symptoms.

Because acidity tends to irritate the bladder wall in a similar manner to its effect on the esophagus in patients with gastroesophageal reflux disease, over-the-counter alkalinizing agents can be taken with food to minimize irritation. Dietary supplements marketed for bladder symptom relief contain calcium glycerophosphate (Prelief) to bind to low-pH components of some foods. Alkalinizing agents are not a replacement for food avoidance, simply a means of expanding dietary options to maintain quality of life.

According to the newly released treatment guidelines, five additional lines of therapy are available to supplement the first-line behavioral directives. Initial medical treatment revolves around pain control. Simple OTC nonsteroidal anti-inflammatory drugs (NSAIDs), like ibuprofen or naproxen, are the recommended starting points for early or mild disease. Prescription NSAID options may be considered in patients with more moderate pain symptoms.

When pain management is not enough to maintain symptom control, second-line medication options involve treatments of varying mechanisms and modalities. Pentosan polysulfate (PPS) is the only oral agent approved distinctly for the treatment of interstitial cystitis. PPS is similar to low molecular weight heparins and acts to prevent wall inflammation and scarring through unclear mechanisms. PPS may mimic the bladder wall’s own lining to protect it from assault and to repair existing damage. Doses of 100 mg three times daily without food should be attempted for six months, if well tolerated. Pain reduction typically occurs after two to four months, but frequency does not resolve until at least six months of treatment. Side effects most commonly include stomach pain, heartburn, and dizziness. Pentosan can also cause excessive bleeding and bruising as a result of its heparin-like nature, making it a poor treatment choice in patients with clotting disorders or taking medications that affect blood clotting (such as warfarin). Pentosan has been widely studied in populations of interstitial cystitis, but its efficacy in clinical trials is mixed and does not support use as a gold-standard treatment.

Other oral treatment options include histamine blockers and antidepressants, specifically the tricyclic antidepressant amitriptyline. This antidepressant prohibits nerve transmissions of pain sensations from the bladder and increases muscle relaxation. Amitriptyline also provides
mild analgesic, sedative, and histamine1-blocking activity to ease pain, frequency, and urge. Although there is good evidence to support amitriptyline use in any patient with interstitial cystitis, only one trial currently confirms these observed benefits.

Mast cell receptors in the bladder epithelial wall contain histamine-1 receptors similar to those found in mucous membranes of the sinus passages. The allergic response to substances that irritate the bladder wall could play a key role in progressive disease and the development of wall ulcerations. Although preventing the histamine-related immune response can minimize immediate symptoms of interstitial cystitis and possibly slow long-term damage to the bladder wall, the full effects of mast cell activity in the bladder is unknown and may only partially contribute to the damage. OTC and prescription antihistamine options include diphenhydramine, cimetidine, hydroxyzine, and fexofenadine. Hydroxyzine, in particular, has supportive evidence for use in patients with interstitial cystitis, though all symptoms are not relieved with its sole use. Second-line medications are administered directly to the bladder, intravesically. The difficulty of cytoscopic administration by the provider, and its invasive manifestations physically, mentally, and logistically on the patient makes them less preferable to oral agents. Dimethyl sulfoxide (DMSO), heparin, and lidocaine have all been used alone or in combination within the bladder. DMSO acts as an anti-inflammatory and relaxant agent at the bladder wall and is the only FDA approved intravesical treatment. Lidocaine is used as a numbing agent in combination or as monotherapy, while DMSO is most often used in combination. Intravesical heparin can be used daily and can be administered by the patient at home via self catheterization. Although symptom relief is likely after intravesical therapy, it is of short duration (such as one week) and requires repeat administration, possibly indefinitely. In addition, catheterization can increase pain and discomfort during and immediately after the procedure before symptoms improve.

Unfortunately, with disease that is already progressed in severity or is not responding to the behavioral and first- or second-line medication options, treatments are still lacking. Third-line treatments focus on procedures, such as cytoscopic distension and ulcer fulguration (electrocautery or laser to destroy local nerves or remove stiffened scar tissue). Nerve stimulation techniques with external or implanted devices increase muscle strength and blood flow and are feasible for protracted disease. Recalcitrant disease has speculative fourth-line options, including highly toxic cyclosporine and investigational botulinum toxin.

Last-line treatment of interstitial cystitis is reserved for the most severe disease and includes surgical re-routing of urine or removal of the bladder. Even these operations cannot guarantee complete symptom relief because the complex disease mechanisms can cause continued pelvic pain through unclear mechanisms. Supportive care continuation is important to maintain quality of life.

Investigational agents to halt disease progression are underway. Agents in the pipeline include IPD1151T, or suplatast tosilate, a T-helper cell antagonist that reduces markers of inflammatory response; interleukins 4 and 5; and tumor necrosis factor. Suplatast inhibits histamine actions through non–mast cell activity, leading to its potential use in combination therapy. Treatment options will continue to increase as research about interstitial cystitis expands.

CONCLUSION
Pharmacists well positioned to reach out to women who might appear healthy, but may have hidden health concerns or poor nutrition strategies. Addressing wellness through nutrition and symptom identification in youth, childbearing years, midlife, and beyond can improve quality of life and prevent long-term disease, as well as instill a sense of partnership between women and their pharmacy healthcare providers.

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CASE 1

D.G., a 45-year-old, non-menopausal adult woman who is married without children, wants advice on a new multivitamin to try that has “the most important nutrients.” She currently takes one children’s chewable vitamin daily and is not vegetarian or vegan. Her pertinent physical and medical history includes one low BMD test result, followed by one that was within normal limits; regular exercise routine that includes long-distance running or swimming for one hour each day; moderate joint pain in fingers without a diagnosis of osteoarthritis; and both parents deceased secondary to complications of Alzheimer’s disease. Her other medications and supplements include one chewable calcium tablet daily with her breakfast cereal and acetaminophen, as needed for finger pain. What vitamin(s) do you suggest for D.G. and why? How should she take these supplements for maximum benefit, and what improvements or side effects should she note?

Response

D.G. needs an adult (chewable or tablet) vitamin, or possibly two children’s vitamins, daily to meet her nutritional needs. She likely does not need a special formulation for energy or for eye health, and her vitamin D requirements are probably met by her outdoor exercise. However, you suggest that D.G. take her vitamin and her calcium chews separately from each other and from her morning dairy intake to obtain maximum calcium absorption. In addition, D.G. should ensure that her vitamin provides iron, because she is still at risk of iron-deficiency anemia as a result of continued menstruation and her long-distance running. Any symptoms of deficiency, including fatigue, should be discussed with her physician to address possible extra supplementation needs.

CASE 2

A regular customer, 35-year-old H.H., approaches your counseling center to ask about a dietary supplement for bladder discomfort, which her registered nurse recommended at the end of her recent doctor’s visit. She is filling an antibiotic prescription, a pain-relief prescription (Vicodin), and a prescription for an antimuscarinic agent typically used for overactive bladder (trospium). She has recently finished nursing her second child and is not taking any other prescription medications from your pharmacy. She has just stopped taking her prenatal vitamin. Because of her healthy but complex history, you would like to discuss her new medications to ensure accurate diagnosis, disease management, and treatment. Although stress or mixed incontinence and a secondary urinary tract infection are possible, she may need counseling about chronic, progressive bladder disorders, such as overactive bladder or interstitial cystitis. You are aware of the latest interstitial cystitis and overactive bladder treatment guidelines and algorithms. How do you counsel this patient? How can you potentially help her and her physician with long-term disease identification and control?

Response

Before meeting H.H. or filling her prescriptions, you call her physician and verify that she does have a bladder infection identified by positive urine culture. You learn that he is concerned about possible bladder
diseases, because of H.H.’s frequent voids and pelvic discomfort. You discuss his antimuscarinic drug choice and offer to change the prescription to a more selective agent. He declines your recommendation, so you prepare counseling notes for trospium. Upon meeting H.H. at the counseling window, you find that she did not receive a tentative diagnosis of any condition yet and that she is experiencing some stress, not urge, incontinence similar to what she experienced while pregnant. You counsel H.H. to take all of her antibiotic and caution her about common antimuscarinic side effects to monitor during her two-week trial of trospium. In addition, you suggest that H.H. works with you and her physician to track the response to the prescribed medications. She should also track her number of voids per day and her pain flare-ups in relation to foods through a food diary. You provide her with some websites that discuss overactive bladder and interstitial cystitis, and you explain why the dietary supplement recommended by the RN might improve her pelvic pain and discomfort associated with eating.

In addition, you recommend a new multivitamin for women, because her iron and folate needs are lower than what a prenatal vitamin provides. You also suggest that H.H. start taking a fish oil supplement to maintain healthful levels of omega-3 fatty acids, particularly during her first postpartum year.

CONTINUING EDUCATION QUIZ
Select the correct answer.

1. At least what percent of adults use a multivitamin daily?
   a. Fifty percent
   b. Forty percent
   c. Thirty percent
   d. Twenty percent

2. Medical experts recommend a daily multivitamin because
   a. Government guidelines mandate multivitamin nutrients for all adults.
   b. Adequate nutrition cannot be obtained through diet alone.
   c. Most adults have insufficient vitamin C.
   d. It is a likely safe nutritional buffer for people who may not always eat balanced diets.

3. Postmenopausal women benefit from supplementation of which nutrients?
   a. Vitamin D
   b. Zinc
   c. Vitamin B12
   d. A and C above
   e. None of the above

4. Combined nutrients that can worsen existing constipation as a side effect include which of the following?
   a. Zinc plus iron
   b. Vitamin B12 plus folate
   c. Calcium plus iron
   d. All of the above

5. Which nutrient requirement is commonly increased during pregnancy?
   a. Vitamin A
   b. Vitamin D
   c. Vitamin B12
   d. Vitamin C
6. Folate prevents birth defects that occur when?
   a. Any time during the first trimester
   b. In the first month after the pregnancy is confirmed by the physician
   c. In the first month after conception, when the spinal cord is exposed and susceptible to damage
   d. None of the above

7. Which of the following is a known toxicity of Vitamin D?
   a. Vitamin D has no known toxicities or safety concerns
   b. Vascular calcification
   c. Scotoma
   d. Epistaxis

8. Which of the following lists types of vitamin A in order from most to least teratogenic?
   a. Meat-based retinoids, prescription retinols, plant carotenoids
   b. Prescription retinols, beta carotene, meat-based retinoids
   c. Meat-based retinoids, beta carotene, prescription retinols
   d. Prescription retinols, meat-based retinoids, beta carotene

9. Safe coping strategies for pregnancy-related constipation include
   a. Increasing fluids
   b. Increasing fiber at the same time as iron supplementation to prevent iron-induced constipation
   c. Using a stool softener plus stimulant to moisten stool and move bowels
   d. All of the above

10. Use of fish oil capsules should be continued during the postpartum period
    a. Because they are required for infants to successfully breastfeed
    b. Because they might prevent or lessen postpartum depression
    c. Because infant stores are greatly reduced between pregnancies
    d. Two of the above

11. Which statement correctly differentiates urge and stress incontinence triggers?
    a. Fluid sensations trigger stress but not urge incontinence.
    b. Fluid sensations trigger both stress and urge incontinence.
    c. Physical activity triggers both stress and urge incontinence.
    d. Physical activity triggers stress but not urge incontinence.

12. Treatment recommendations for urge incontinence include which of the following?
    a. Atropine
    b. Antimuscarinic medications approved for overactive bladder
    c. Tricyclic antidepressants
    d. None of the above

13. Overactive bladder symptoms include which of the following?
    a. Involuntary night voiding
    b. Increased voiding frequency
    c. Reduced urge after meals
    d. Two of the above

14. Antimuscarinic drugs selective for M3 receptors retain which side effects?
    a. Constipation
    b. QT prolongation
    c. Memory loss
    d. Tremor

15. What is a first-line antimuscarinic drug choice for a patient with hepatic disease?
    a. Oxybutynin
    b. Fesoterodine
    c. Tropsium
    d. Two of the above
16. Maximum-tolerated dosages of overactive bladder antimuscarinic treatment should be attempted for at least how many weeks before adding tricyclic antidepressants to the regimen?
   a. Two weeks
   b. Four weeks
   c. Six weeks
   d. Eight weeks

17. Overactive bladder is differentiated from interstitial cystitis by which of the following?
   a. Recurrent infection with interstitial cystitis and not overactive bladder
   b. Frequency and urge with overactive bladder and not with interstitial cystitis
   c. Pain in the bladder area only for interstitial cystitis but not for overactive bladder
   d. Multifactorial pain with interstitial cystitis but not with overactive bladder

18. Supportive treatment for interstitial cystitis includes which of these?
   a. Voiding more frequently to avoid pain associated with a filled bladder
   b. Dietary supplements for bladder symptom relief taken after pain starts
   c. Dietary supplements for bladder symptom relief taken before or with a meal
   d. Two of the above

19. When NSAIDs do not provide adequate symptom relief, which of the following oral medications may treat interstitial cystitis symptoms?
   a. Amitriptyline
   b. Pentosan polysulfate
   c. Hydroxyzine
   d. All of the above

20. Tricyclic antidepressants work to reduce bladder symptoms by
   a. Reducing the number of pain receptors
   b. Reducing bladder wall scarring
   c. Reducing pain sensations
   d. Increasing histamine release

26. Is this program used to meet your mandatory C.E. requirements?
   a. yes  b. no

27. Type of pharmacist:  a. owner  b. manager  c. employee

28. Age group:  a. 21–30  b. 31–40  c. 41–50  d. 51–60  e. Over 60

29. Did this article achieve its stated objectives?
   a. yes  b. no

30. How much of this program can you apply in practice?
   a. all  b. some  c. very little  d. none

How long did it take you to complete both the reading and the quiz? ______ minutes