An Integrative Approach to Fibroids, Endometriosis, and Breast Cancer Prevention

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Summary

All integrative practitioners who care for women know firsthand about the need for a successful integrative approach to treating fibroids and endometriosis, as well as an effective strategy for breast cancer prevention. The purpose of this paper is to explain the common biologic pathways for these disorders and to provide therapeutic recommendations that are both science based and clinically effective.

What do fibroids, endometriosis, and breast cancer have in common? Estrogen. This hormone is a contributing factor in the growth of fibroid tumors, endometriosis lesions, and many breast carcinomas. In fact, estrogen-sensitive breast cancers are the most common type of breast cancer. Translated, this means that increases in estrogen production and decreases in estrogen elimination are potentially harmful for the body. Inflammation—a biologic process now implicated as fundamental in many systemic illnesses—also has a role, as do abnormal blood sugar metabolism (dysglycemia) and even emotional stress and spiritual uncertainty or discomfort. Therefore, the scientific basis for an integrative treatment plan involves 1) normalizing estrogen production, 2) enhancing estrogen elimination, 3) decreasing inflammation and dysglycemia, and 4) reducing as many life stressors as possible.

Fibroids

The technical term for fibroids is *leiomyoma*, a word describing benign smooth muscle tumors. Fibroids cause symptoms such as pelvic pain and abnormal uterine bleeding and are quite common, affecting 20% to 25% of women of reproductive age.[1] For unknown reasons, they occur more frequently in black women. In fact, by age 50, half of black women will have fibroids.[1]

Fibroids arise from the multiplication of a single cell and contain extracellular collagen and elastin. Based on this fact, a good treatment for patients is to take pancreatic enzyme formulations between meals. When enzymes are taken with meals, they digest the protein in the food. When enzymes are taken on an empty stomach, they are absorbed intact into the circulation[2,3] and have systemic anti-inflammatory and fibrinolytic effects.[4-7] Thus, pancreatic enzyme formulations are thought to degrade the fibroid proteins' collagen and elastin.

Fibroids are hormonally responsive and contain estrogen receptors in higher concentrations than the normal uterine smooth muscle that surrounds them. The hormonal sensitivity of fibroid tumors is supported by numerous observations. Specifically, fibroids are rare before puberty, enlarge during pregnancy, stop growing at menopause, and shrink with administration of medications that decrease estrogen levels.

When considering hormone factors in fibroid treatment, it is important to note that, while estrogens cause tumor growth by increasing the production of extracellular matrix, progesterone may also cause tumor growth by increasing the mitotic activity of myomas and may also allow for tumor enlargement by down regulating apoptosis in the tumor.[1] Hence, it is important that the foundation of an integrative approach ensures normalization of both estrogen and progesterone levels.

Endometriosis

Endometriosis is characterized by the presence of uterine tissue (endometrial glands and stroma) in areas other than the uterus, such as the pelvic floor or around the fallopian tubes and ovaries. The cause is believed to be reverse menstrual flow through the fallopian tubes into the pelvis, which enables glandular tissue that is supposed to leave the body through the vagina to implant and grow internally. This displaced endometrial tissue remains just as hormonally sensitive as it was in the uterus, responding to the influences of estrogen and progesterone. This explains the common endometriosis symptoms of pain and discomfort that occur immediately before and during menses. Such endometrial implants also stimulate the immune system and a local inflammatory response. These effects are thought to be the underlying mechanism for infertility that often accompanies endometriosis.

Breast Cancer

The most generally accepted interpretation of the documented risk factors for estrogen-sensitive breast cancer is that these risks result from increased exposure to estrogen. Early age of first menstruation, having no or few children, choosing not to breastfeed, later age of last menstruation, and taking hormone replacement therapy (HRT) all increase lifetime exposure of the breast to estrogen. In addition, controversy still exists in medical circles whether short term HRT given right at menopause increases breast cancer risk.

Current Medical Approaches

Conventional approaches to fibroids, endometriosis, and estrogen-sensitive breast cancers involve both prescription medications and surgical interventions. Integrative approaches involve natural, safe protocols that have the same desired end point as

conventional approaches but which can be used to reduce symptoms and avoid surgical interventions or help reduce recurrences after surgery. More specifics are given below.

Fibroids that are found on routine exam (bimanual or ultrasound) are frequently asymptomatic, and the gynecologic standard of care is to do nothing until symptoms occur or the fibroids reach a particular size threshold. This is the ideal situation for an integrative approach, which is specifically designed to prevent the growth that would lead to development of symptoms. Once symptoms develop, the common surgical options are to remove the entire uterus (hysterectomy), remove the fibroid(s) only (myomectomy via laparotomy), or reduce the blood supply to the uterus in order to cut off blood supply to the fibroids (uterine artery embolization, which then precludes pregnancy). Conventional treatment may also involve inducing a medical menopause to reduce estrogen levels, which is not an effective long-term solution because the drug is approved only for 6 months of use and fibroids return within a year of stopping the drug. Conventional treatment for endometriosis is similar: surgical intervention to remove the implants (or hysterectomy, if the condition is severe) or medication to decrease estrogenic stimulation.

The foundation of today's conventional approach to breast cancer prevention involves early detection. ("Prevention" is actually a misnomer in this sense, as early detection is not prevention, but the terms are frequently used interchangeably in discussions of breast cancer prevention for high-risk patients.) Additional conventional approaches to breast cancer prevention include the prescription medications tamoxifen and raloxifene. Both can help reduce the incidence of breast cancer by 50% or more but carry with them the risk of serious side effects, such as uterine cancer and blood clots.[8]

Integrative Approach Part 1: Improving Estrogen Elimination

Because fibroids, endometriosis, and breast cancer prevention all involve estrogen, ensuring adequate estrogen elimination is fundamental to any integrative approach to managing them. Estrogen is eliminated through Phase I and II liver detoxification, a process by which estrogen is dissolved in bile and excreted into the gut to leave the body via stool. Thus, it should be clear that impaired detoxification (Phase I or II) or impaired elimination from the gut should be identified and corrected as part of any strategy to improve estrogen elimination.

Phase I and Phase II detoxification are both important in estrogen elimination but for different reasons. Phase I detoxification of estrogen involves the addition of a hydroxyl group to 1 of 3 carbons on the estrogen ring, at the 2, 4, or 16 position (a process known as hydroxylation). In terms of breast cancer risk, greater hydroxylation at the 2 position confers decreased breast cancer risk.[9] Although estrogen hydroxylation is partly genetically determined (dependent on a person's cytochrome P450 estrogen detoxification enzyme systems), the process is definitely modifiable through lifestyle factors and nutrition. Physical exercise, flax seed and other omega 3 essential fatty acid sources,[10] and cruciferous vegetables containing indole-3-carbinol[11] have all been shown to increase the 2 hydroxylation of estrogen and are important recommendations for patients who want to decrease their risk of breast cancer. Additionally, functional medicine laboratories offer simple urine or blood tests to assess both baseline and post-intervention estrogen metabolism profiles for high-risk patients.

Phase II detoxification of estrogen involves the attachment, or conjugation, of other compounds to enable the estrogen molecule to be excreted in bile. The most important conjugation reaction is glucuronidation, whereby a glucuronide molecule is bonded to estrogen to allow its excretion through the bile into the gut as the estrogen glucuronide. Impaired glucuronidation occurs most commonly when unhealthy gut flora secretes an enzyme called beta-glucuronidase. This enzyme cleaves the glucuronide molecule from estrogen and allows the estrogen that was supposed to be eliminated in stool to be reabsorbed systemically via enterohepatic recirculation.

Interventions that have been shown to improve glucuronidation include a low-animal-fat diet and supplementation with probiotics and calcium-D-glucarate.[12] And, as with other detoxification processes that are dependent upon excretion of compounds in stool, the importance of eliminating constipation and ensuring regular bowel movements cannot be overstated.

Optimizing other facets of detoxification is also important. Any detoxification abnormalities detected through laboratory testing should be corrected. General nutritional recommendations to improve detoxification include consumption of artichoke, broccoli, green tea, garlic, pomegranate, shallots, and watercress, as well as adequate protein intake.[13 (367)]

Integrative Approach Part 2: Assessing Estrogen Production

The basic metabolic principles of estrogen production serve as the scientific foundation for an integrative treatment plan to normalize production. These basic principles are as follows:

- All estrogen made in the body is produced by the enzyme aromatase.
- Aromatase is present and active in adipose tissue; therefore, adipose tissue produces estrogen.
- Certain pesticides (eg, atrazine) stimulate aromatase
- Insulin stimulates aromatase.
- Estrogen is transported throughout the body in an inactive form, bound to the carrier protein sex hormone binding globulin (SHBG).
- In order for estrogen to bind to its receptor and have an estrogenic effect, it must be free (unbound).
- Insulin decreases SHBG, leading to more unbound estrogen.

In the context of endometriosis and fibroids, research has shown that both tissue types have high levels of aromatase activity, which is stimulated by prostaglandin E2 (PGE2). Breast cancer cells also have higher levels of aromatase than surrounding normal breast tissue. This is the rationale for using pharmacologic aromatase inhibitors as part of the current medical approach to these disorders. Thus, the next steps in the integrative treatment plan involve decreasing aromatase activity, adipose tissue, and insulin levels while increasing SHBG. However, some fine points

warrant further discussion: Although all fat cells (adipocytes) contain aromatase and produce estrogen, we will now discuss the additional qualities of adipocytes that support the growth of fibroids, endometriosis, and breast cancer.

The first is the amount of lipid (fat) in the cytoplasm of the adipocyte. If the adipocyte is too full of fat (yes, a fat cell can be too full of fat), it will produce less of the hormone adiponectin. This leads to decreased insulin sensitivity and higher circulating insulin levels because adiponectin causes insulin sensitivity. As stated previously, insulin decreases SHBG and, therefore, increases free estrogen. Thus, a body filled with full adipocytes leads to even higher free estrogen levels.

Second, in addition to secreting adiponectin, adipocytes secrete pro-inflammatory cytokines (such as PGE2 and others), making obesity a pro-inflammatory state. Inflammation is important to our discussion of estrogen-related disorders because PGE2 stimulates aromatase, causing increased production of estrogen. Interestingly, estrogen itself stimulates the pro-inflammatory enzyme cyclooxygenase (COX 1 and COX 2), causing the production of PGE2, which in turn stimulates aromatase to make more estrogen in a kind of "feed forward" cycle.

Third, it is important to note that not all adipocytes are equally metabolically active. The adipocytes surrounding the internal organs of the abdomen and pelvis (visceral adipocyte) are the most metabolically active, and some forward-thinking endocrinologists even view the visceral adipose tissue (VAT) as its own metabolic endocrine organ. Therefore, a trip to the plastic surgeon for liposuction will do nothing to improve the pro-inflammatory, estrogenic effects of the "apple" phenotype because liposuction does not remove the visceral adipose tissue. The only solution is weight loss and exercise. (This is not such a concern for the "pear" phenotype that has weight [fat] around the hips, which is not a metabolically active fat.)

To review,

- visceral fat increases estrogen (increases aromatase),
- estrogen causes inflammation (stimulates COX 1 and 2),
- inflammation increases estrogen (stimulates aromatase),
- visceral fat also increases inflammation (produces pro-inflammatory cytokines), and
- insulin increases total and free estrogen (lowers SHBG).

Integrative Approach Part 3: Normalizing Estrogen Production

So after taking the steps discussed above both to improve estrogen elimination and assess estrogen production, the next step in addressing estrogen-related disorders (fibroids, endometriosis, and breast cancer) is to normalize estrogen production. This is done by reducing visceral adipose tissue, inflammation, and insulin levels and increasing SHBG. Specifics on how to achieve these well-known objectives of functional medicine are beyond the scope of this article but can be referenced in *The Textbook of Functional Medicine* chapters on inflammation and dysglycemia.[14-16] As a recap of the chapters, patients can achieve these health goals in the following ways:

- Maintain a healthy weight (through proper eating and exercise and, if necessary, weight loss).
- Decrease inflammation (through eating a pescatarian diet and supplementing with omega 3 essential fatty acids [EFAs], bromelain, curcumin, and quercetin).
- Normalize insulin and glucose dynamics (through eating a low-glycemic-index diet and supplementing with micronutrients such as alpha lipoic acid, cinnamon, chromium, and vanadium).
- Increase SHBG (through lowering insulin levels and supplementing with flax or other EFAs).

There are also other ways to decrease the amount of estrogen in the body. The first is to be aware of and reduce the amount of estrogens entering the body through environmental and nutritional sources. Pesticides and plastics have long been known to have estrogenic effects, and now there are additional concerns that municipal sewage treatment plants are not able to remove all the estrogens and estrogen-like chemicals from the water supply. In addition, estrogens are routinely added during the farming of conventional chicken, beef, and dairy cows to enhance productivity, taste, and consistency.

For the above reasons it is important to consume organic produce; spring or filtered water; organic beef and chicken (better yet, free-range and pasture-fed animals because the standard feedlot diet introduces other problems that go beyond the scope of this article*); organic eggs; and organic, fat-free dairy products. As an added note, the best milk is that which is obtained from cows that are not pregnant, which is the industry standard since keeping cows pregnant means they produce more milk. But the problem is that milk from pregnant cows contains more estrogen. In addition to these dietary recommendations, it is also good to add wild, cold-water fish to the diet for the EFAs.

Additionally, the impact of stress and emotional and spiritual health on estrogen-related disorders cannot be minimized. Stress is known to cause an increase in pro-inflammatory cytokines, so stress reduction is an important component of an integrative treatment plan. Recently, studies have shown that even eating the flesh of animals raised and slaughtered under stressful conditions transmits the animals' stress hormones (and their effects) to the person eating the animal.[19]

Finally, I have witnessed in my own clinical practice the direct impact that emotional and spiritual issues—such as childbearing conflicts, lack of creative self-expression, sexual issues, unresolved anger, and severe self-criticism—have on these illnesses in my patients.

Conclusion

The solutions of conventional medicine discussed earlier,

*On the hypotheses that consumption of wild ruminant fat represented the primary lipid source for preagricultural humans, researchers at the Department of Health and Exercise Sciences, Colorado State University, Fort Collins, set out to discover if the lipid composition of these animals' tissues might provide insight into dietary requirements that could offer protection from chronic disease in modern humans. The research showed that tissue lipids of North American and African ruminants were similar to those of pasture-fed but not grain-fed cattle,[17] and a later study concluded that "the evolutionary collision of our ancient genome with the nutritional qualities of recently introduced foods [eg, feedlot beef] may underlie many of the chronic diseases of Western civilization."[18]

Summary of Ways to Reduce Patient Estrogenic Influences

Advise patients to

1. **Consider testing**
   - Examine functional detoxification testing
   - Examine simple urine or blood tests to assess both baseline and post-intervention estrogen metabolism profiles for high-risk patients
2. **Improve estrogen elimination**
   - Exercise[10]
   - Eat foods that enhance detoxification (artichoke, broccoli, green tea, garlic, pomegranate, shallots, and watercress, as well as adequate protein intake)[13]
   - Take supplements (flax seed and other omega 3 essential fatty acid sources,[10] cruciferous vegetables containing indole-3-carbinol,[11] probiotics,[12] and calcium-D-glucarate[12])
3. **Decrease estrogen intake**
   - Eat meat/dairy and poultry/eggs from organic, hormone-free, pasture-fed animals
   - Avoid hormone replacement therapy (HRT)
4. **Avoid environmental and food-related toxins that are carcinogenic**
   - Eat organic
   - Drink spring or filtered water
   - Use an organic shopping list to find out about the most important produce to buy organic (See http://www.foodnews.org/pdf/EWG_pesticide.pdf)
5. **Improve gut health to decrease estrogen levels**
   - Decrease beta-glucuronidase by eating a plant-based diet and taking appropriate supplements (eg, probiotics and calcium-D-glucarate[12])
   - Eliminate constipation and ensure regular bowel movements by consuming flax (it also decreases estrogen levels)[20]
6. **Maintain proper body weight**
   - Reduce visceral adipose tissue (via diet and exercise, not liposuction)
7. **Maintain proper blood sugar and insulin levels**[16]
   - Eat a low-glycemic-index diet
8. **Reduce inflammation**[14-16]
   - Eat a highly pescatarian diet
   - Maintain ideal body weight
   - Improve oral health
   - Treat nagging injuries
   - Normalize highly sensitive C-reactive protein levels with fish oil and other anti-inflammatory supplements, if necessary (eg, bromelain, curcumin, quercetin)[14]
   - Do not eat animals raised or slaughtered under stressful conditions
   - Reduce stress and resolve as many conflicts as possible (they are pro-inflammatory.)

with their surgeries and side effects, drive many women to seek safer and more natural approaches to fibroids, endometriosis, and breast cancer prevention. We have discussed how these disorders can all be addressed by a holistic treatment plan that focuses on normalizing estrogen production and then optimally metabolizing it, reducing inflammation, and optimizing blood sugar metabolism and body composition. In addition, the importance of reducing stress, resolving conflicts, and addressing spiritual issues should not be underestimated. It is only when practitioners are able to transcend the rushed atmosphere of the 15-minute office visit and stay centered in order to connect with the part of themselves that is the intuitive healer that the magic happens: The causality between physical problems and emotional and spiritual issues will unfold, and the healing can truly begin.

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