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# A Novel Approach to Treating Endometriosis

## *A Report on Two Cases*

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**Jeffrey A. Morrison, M.D., and  
John Sullivan, M.D.**

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**E**ndometriosis is a condition that may cause a great deal of pain and suffering in affected woman. Symptoms include dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility. Current therapeutic regimens are directed at controlling symptoms by decreasing pain and reducing endometrial growth. This approach has not alleviated symptoms for all women and, in fact, has left some women dependent on narcotics without providing satisfactory relief. Recent theories on the pathogenesis of endometriosis have created the opportunity to tailor some very interesting alternative treatment options. This paper covers two case reports of women with infertility and laparoscopically diagnosed endometriosis who were unsuccessfully treated with current treatment protocols including oral contraceptive pills, medical menopause, and laparoscopic fulguration of chocolate cysts. When these women presented to our office, a novel treatment approach was used to treat this disabling condition as well as its associated complications, including infertility. We have found through the experience of our two patients that treating endometriosis as an allergic condition is a very effective nonsurgical, noninvasive alternative to alleviating all of the symptoms of endometriosis.

### **Endometriosis: Background**

Endometriosis is the presence of endometrial tissue in ectopic sites. Clinically, it is associated with complaints of dysmenorrhea, dyspareunia, chronic pelvic

pain, and infertility. Although the actual prevalence of the disorder is unknown, endometriosis is suspected to affect 2–15 percent of reproductive-age women. It is also believed to be the cause in 20–40 percent of infertile women.<sup>1</sup>

Despite extensive research, therapies for this condition continue to be ineffective for some women. However, one interesting and successful emerging treatment for endometriosis is therapy directed at immune abnormalities and related health problems found in women with endometriosis. According to data in the Endometriosis Association research registry, women with the disease had more yeast infections, hayfever, food sensitivities, eczema, and mononucleosis than a control group had.<sup>2</sup> In addition, women with endometriosis were frequently found to have imbalanced intestinal and vaginal microflora. Among the most thoroughly investigated of these microorganisms has been a ubiquitous one familiar to gynecology, *Candida* spp.<sup>2</sup>

In this paper we present the case histories of two patients with severe endometriosis and infertility who presented to our office after surgical and traditional medical management failed and who responded to therapy aimed at diet modification, food allergy neutralization, and eradication of systemic yeast infection.

### **Description of Cases**

#### *Case #1*

The first patient was a 33-year-old woman who presented to our office with chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility. She entered menarche at the age of 12 years, experiencing dysmenorrhea and heavy menstrual bleeding during menstruation. Her symp-

toms became intolerable by age 19 and laparoscopic examination at that time revealed endometriosis complicated by bowel and bladder adhesions. Treatment during the surgery included fulguration of chocolate cysts as well as lysis of adhesions. Afterwards she was placed on an oral contraceptive for 3 years, which controlled her symptoms temporarily.

Three years later a second laparoscopy was performed because of worsening symptoms, including abdominal pain, dysmenorrhea, menorrhagia, and dyspareunia. At that time more chocolate cysts were discovered and fulgurated. A similar pattern of initial symptom control following the procedure followed by progressive worsening led to a third laparoscopy.

In December 1996, treatment was begun with leuprolide injections and oral contraceptives. However, when her menstrual cycle resumed, her endometriosis symptoms returned. It was at this time in her therapy that she presented to our office.

Her past medical history is significant for thalassemia minor, Sjögren syndrome, chronic constipation, urinary frequency, and migraine headaches. She also suffered from multiple sinus infections requiring antibiotic treatment approximately four times a year for 13 years. These treatments resulted in chronic vaginal yeast infections.

At the time of examination the patient tested positive for *Candida albicans* serum immunoglobulin G antibody with an elevated titer of 145 units (nL 0–130 units). Only an initial laboratory value was obtained for the purpose of reinforcing our suspicion of *Candida* spp. overgrowth. She was also found to have multiple food allergies that were revealed via allergenic skin testing. These allergies included cane sugar, baker's yeast, wheat, barley malt, rye, and onions.

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A modified diet was initiated to avoid allergy-provoking foods along with nystatin powder to reduce the *Candida* spp. load in the gastrointestinal tract (see Treatment Methods, below). After 1 month, the patient reported feeling 80 percent improved with fewer episodes of migraine headache, dyspareunia, abdominal pain, bloating, constipation, and urinary frequency. Oral itraconazole, 100 mg twice a day, was added to the diet and nystatin therapy for 7 days to improve the systemic coverage of *Candida* spp. One month later she continued to experience improvement, with no cramps, irritability, or premenstrual symptoms during menstruation as well having an overall feeling of increased energy. Three months later, the oral contraceptive pill was discontinued and the patient, at

age 33 years, and for the first time, became pregnant.

### Case #2

The second patient was a 25-year-old woman who was interested in alternative approaches to treating endometriosis. She began having severe abdominal, rectal, vaginal, and lower-back pain during menstruation at the age of 18. She underwent her first laparoscopy at that time, which revealed multiple chocolate cysts confirming the diagnosis of endometriosis. Laser ablation was employed to treat the cysts, which helped her symptoms temporarily. Recurrence of symptoms led to four more laparoscopic laser ablations over the next 2½ years.

Treatment to control symptoms between laser ablations included the use of oral contraceptives, leuprolide, and narcotics

for breakthrough pain during menses, which typically lasted from 5 to 15 days. On a scale of 1–10, the patient reported her pain as being at least 5 in between her periods and 10 during menses. She would typically have such severe dyspareunia that she would be incapacitated with pain for an entire day after coitus. Despite these symptoms she became pregnant and delivered a healthy male infant after 37 weeks of gestation.

Her other medical problems included asthma and multiple ear and throat infections requiring treatment with antibiotics 2–12 times per year from the age of 12 years until she had a tonsillectomy at the age of 17. She also suffered from multiple yeast and bladder infections during that time. This patient was noted to have had reactions to multiple narcotics, nonsteroidal anti-inflammatory drugs (NSAIDs), and

**Table 1. Symptoms, Findings, and Treatment in Cases #1 and #2**

	Symptoms Before Treatment	Surgical/Laboratory Findings	Three-Phase Treatment
Patient #1	Dysmenorrhea Dyspareunia Chronic abdominal and pelvic pain Infertility Menorrhagia Migraine headaches Bloating Constipation Irritability Lack of energy	Laparoscopy × 3 revealed adhesions and chocolate cysts. Laboratory tests revealed elevated <i>Candida</i> IgG and multiple food allergies.	I. <i>Diet Modification</i> —avoidance of allergy-provoking foods and avoidance of sugar II. <i>Allergy Neutralization</i> III. <i>Antifungal therapy</i> —Nystatin powder, 400,000 units PO BID for 9 months, and itraconazole, 100mg, PO BID for 7 days
Patient #2	Dysmenorrhea Severe dyspareunia Chronic abdominal and pelvic pain Irritability	Laparoscopy × 5 revealed chocolate cysts. Laboratory tests revealed elevated <i>Candida</i> IgG and multiple food allergies.	I. <i>Diet Modification</i> —avoidance of allergy-provoking foods and avoidance of sugar II. <i>Allergy Neutralization</i> III. <i>Antifungal therapy</i> —Nystatin powder, 400,000 units PO BID for 9 months, and itraconazole, 100mg PO BID for 7 days

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prednisone, all of which she had tried for endometriosis pain control.

On examination a serum *Candida* antibody level was found to be positive 559 units (nL 0–130 units). Allergenic skin testing showed that she was sensitive to the following foods: cane sugar; corn; baker's yeast; eggs; milk; peanuts; potatoes; and tomatoes.

This patient was started on a modified diet with avoidance of allergy-provoking foods and nystatin powder orally twice per day to treat *Candida* spp. in the digestive tract (see Treatment Methods). After 2 months, she felt that her endometriosis pain was down to a 2 between menses and 7 during menstruation. Three months later, she began neutralization therapy for her food allergies (see Treatment Methods) and, after this therapy, she reported her pain to be a 0 in between periods and 4 during periods. Additional treatment was begun at that time with itraconazole, 100 mg twice per day for 1 month, in order to decrease the systemic load of *Candida* spp. The patient became pregnant several months later.

### Treatment Methods

Before the treatment program begins, a thorough allergy history is obtained with an emphasis on determining any past history of asthma, frequent antibiotic usage, family history of allergies, and chronic or recurring bacterial and yeast infections. Symptoms such as eczema, intestinal bloating and flatus, and rectal and vaginal pruritis are also important to ascertain. Standard allergy skin testing then identifies whether a patient is sensitive to foods, environmental allergens, endogenous hormones, or *Candida* spp. Additionally, *Candida* serum antibody levels are drawn at

the outset to reconfirm suspicions of *Candida* overgrowth.

After allergy testing the treatment program is initiated. It consists of dietary modifications, neutralization to allergens, and antifungal treatment. Treatment begins with phase I, which involves working with a diet and with antifungal drug therapy. The modified diet restricts the consumption of raw sugar as well as foods that provoke the allergy symptoms. The women in these case reports were found to be sensitive to sugar, which was not surprising.<sup>3</sup> At least three studies have found that the ingestion of yeast foods, wine and beer, and simple and complex sugars were correlated with recurrent *Candida* vulvovaginitis.<sup>4,5</sup> In Phase II, allergy desensitization is achieved by using neutralizing-dose immunotherapy. This is a well-documented and effective therapy that uses dilute doses, in oral drops or injections, of the allergenic substance, to reduce or eliminate the allergic response.<sup>5–12</sup>

The third part of the treatment program, phase III, consists of antifungal drug therapy directed at *Candida* spp. overgrowth if it exists. A systemic antifungal, itraconazole, 100 mg twice per day for a 1-week pulse dose, is initiated to eliminate *Candida* from the bladder, vagina, and nasopharynx. Following the systemic antifungal, oral nystatin powder, 1/8 tsp powder, 400,000 units) in 1/2 glass of seltzer water, orally twice per day with food, is used for at least nine months to clear the digestive tract of *Candida*. Because of its high sugar content the oral suspension of nystatin is not used.

### Discussion

This article has presented two case reports of women with laparoscopically diagnosed endometriosis for whom con-

ventional treatment failed and whom responded well to this new treatment approach. After an extensive review of the medical literature, we were unable to find any reports of women treated for endometriosis using the paradigm of allergic sensitization as the primary culprit. Typically, symptoms of dysmenorrhea and menometrorrhagia have been treated with oral contraceptive pills and occasionally leuprolide to induce "medical menopause." Chronic pelvic pain and dyspareunia symptoms have been treated with NSAIDs and narcotics, which proved to provide inadequate symptom control for our patients. And some patients have also been given hysterectomies. Additionally, infertility, which has been associated with endometriosis,<sup>13</sup> has been a challenge to manage.

After piecing together many different research findings and coupling that information with the reports from our patients, we have come to a conclusion that certain women are prone to develop sensitivities to *Candida* spp. and endogenous hormones or foods, which may manifest itself as endometriosis pain. Women with endometriosis and infertility have increased peritoneal macrophages and increased concentrations of immune-system modulators including interleukin (IL)-1, tumor necrosis factor (TNF), and IL-6.<sup>14–20</sup> Additionally, changes in T cells have been noted, including an increase in the ratio of T-helper to T-suppressor cells in peritoneal-fluid samples from women with endometriosis and a decrease in T-suppressor cell activity in peripheral blood.<sup>2</sup> These studies suggest that the immune system plays an important role in the pathogenesis of this disabling disease. In studies based on the Endometriosis Association research registry, women with

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endometriosis were found to experience yeast infections, hayfever, food sensitivities, and eczema more frequently than a control group.<sup>2</sup>

Interestingly, *Candida* spp. has potent immunomodulating effects, including inducing production of IL-1, TNF, and IL-6.<sup>21–28</sup> Furthermore, *Candida* spp. induces macrophage prostaglandin (PG)E2 production that, in turn, simulates *Candida* germ tube formation.<sup>29–32</sup> These changes are consistent with the abovementioned findings of peritoneal-fluid changes in women with endometriosis. Additionally, studies show a cell-mediated immune deficiency in women with chronic yeast infections.<sup>33–35</sup> Thus, in chronic *Candida* infections, there is an overproduction of PGE2 in response to *Candida*<sup>35</sup> that, in turn, inhibits the cell-mediated immune response of mononuclear cells needed to limit *Candida* proliferation.<sup>36</sup>

A weakened immune system may allow a person to become sensitized to typically nonallergenic compounds, such as endogenous hormones or foods. Some women with endometriosis tend to have increased symptoms up to 14 days prior to menstruation coinciding with the luteinizing hormone and follicle-stimulating hormone surge and the increased progesterone in the second half of the menstrual cycle. This also helps to explain why, in certain women, medical menopause, which effectively stabilizes hormone release, can diminish symptoms. Additionally, this may help to illustrate why prednisone, which is an immunomodulator, helps to alleviate symptoms as well.

Addressing the role of endometriosis in infertility is another perplexing endeavor. However, if we believe that the immune system plays a significant role in the

pathogenesis of endometriosis, we may be able to explain why 20–40 percent of women with endometriosis are infertile.<sup>1</sup> We suggest that when a woman is afflicted with endometriosis her immune system is at a heightened state of arousal, which provides a hostile and unfavorable environment for fertilization. It is also possible that a woman's immune system may also mistake the ovum to be an antigen.

### Conclusion

There is no question that endometriosis is poorly understood and that current treatment options are inadequate for many women. Our patients felt that their endometriosis symptoms were controlled inadequately with conventional treatments. For this reason, we attempted an unconventional treatment directed at what we feel are potential instigators of endometriosis: systemic allergies and yeast. Accordingly, our therapies were directed at eliminating yeast from the digestive tract via the phase I diet and the phase III antifungal therapies. Additionally, we attempted to modify their immune response through allergy desensitization. The combination of these two approaches produced dramatic results.

We realize there are limitations to our case reports, which have made interpreting the results difficult. The cases were poorly controlled, they were not tested against placebos, there was no standardization of therapy protocols and follow-up was random. Additionally, we are unsure whether the elimination diet, neutralization therapy, or the antifungal treatment was more effective, or whether a combination of the three treatment strategies was best. It is entirely possible that the patients may have improved

without any antifungal therapy. Additionally, these patients may have only been suffering from yeast allergy and not yeast overgrowth. There is really no way to know from these case reports what treatment strategy is truly the best. However, our intuition suggests that the allergy component plays a very important role. Therefore, despite our dramatic results, we feel that further investigation into these three therapy modalities will help to clarify which combination of therapies will produce the best results.

Because endometriosis is poorly understood, as such, it is important that we do not fail to explore any option that may help us to arrive at an answer elucidating its pathogenesis, treatment, and possible cure. Furthermore, we do not feel that we have even begun to account for all of the intricacies of this disease. We hope that, as a result of this report about our two cases, more physicians will be willing to attempt a broader approach to the treatment of endometriosis in an effort to decrease suffering in thousands of patients with poorly controlled endometriosis. We recommend further investigation into these treatment modalities to help women overcome this disabling disease. □

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- Jeffrey A. Morrison, M.D.**, is a family practice resident, Harrisburg Family Practice Residency, in Harrisburg, Pennsylvania. **John Sullivan, M.D.**, is in private practice in Harrisburg.
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Treatment for endometriosis usually involves medication or surgery. The approach you and your doctor choose will depend on how severe your signs and symptoms are and whether you hope to become pregnant. Doctors typically recommend trying conservative treatment approaches first, opting for surgery if initial treatment fails. Pain medication. Your doctor may recommend that you take an over-the-counter pain reliever, such as the nonsteroidal anti-inflammatory drugs (NSAIDs) ibuprofen (Advil, Motrin IB, others) or naproxen sodium (Aleve) to help ease painful menstrual cramps. We report an uncommon case of deep infiltrating endometriosis of the colon presenting as iron deficiency anemia nine years after hysterectomy with bilateral salpingo-oophorectomy. The endometrial implant was found at the hepatic flexure, an exceedingly rare location for endometriosis invasion with no cases distinctly reported in the literature. Instead of surgery, we prescribed a novel medical therapeutic approach using conjugated estrogen-basedoxifene to antagonize the proliferative effects of estrogen on endometrial tissue. Her history was significant for endometriosis in early reproductive years and uterine fibroids treated by hysterectomy with bilateral salpingo-oophorectomy nine years before her current presentation. Treatments for pain or infertility from endometriosis may include pain medicines, hormone treatments, or surgery. Learn more. Surgical treatments. Hormone Therapy. Because hormones cause endometriosis patches to go through a cycle similar to the menstrual cycle, hormones also can be effective in treating endometriosis symptoms. Additionally, different hormones may alter our perception of pain. Hormone therapy is used to treat endometriosis-associated pain. Hormones come in the form of a pill, a shot or injection, or a nasal spray. Hormone treatments stop the ovaries from producing hormones, including estrogen, and usually prevent ovulation. This may help slow the growth and local activity of both the endometrium and