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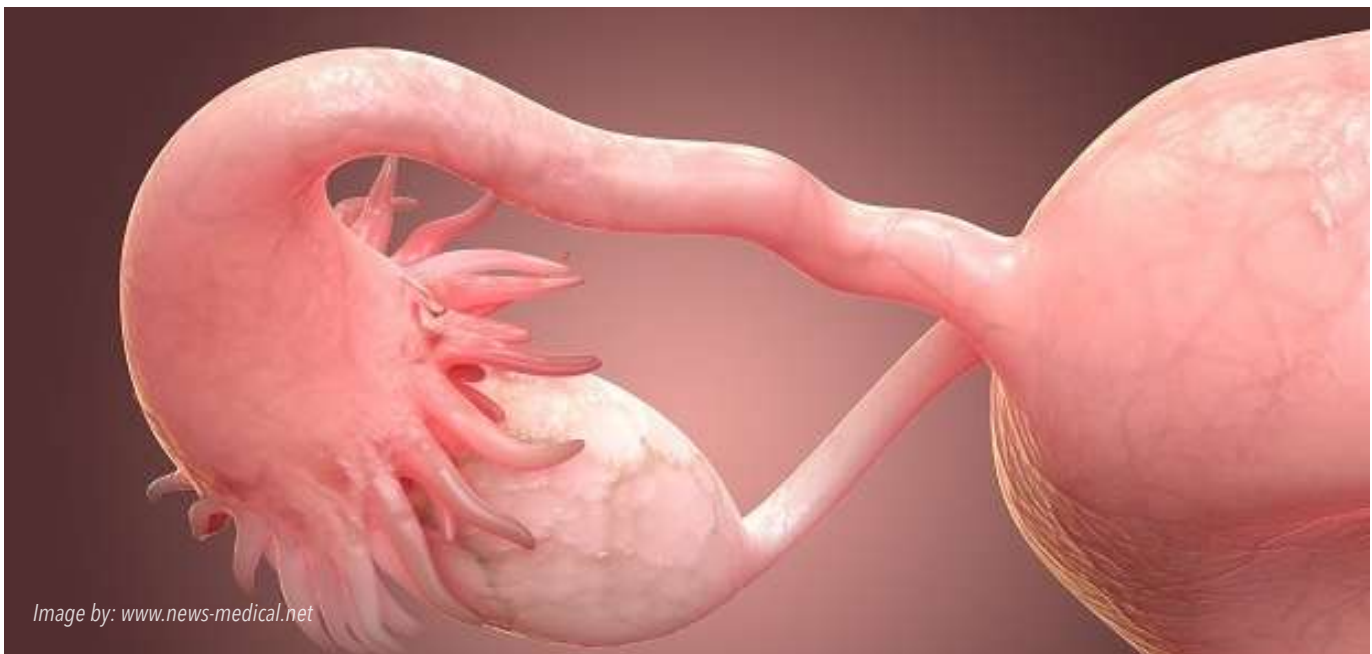
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Integrative Medicine Approach to Endometriosis

*(Article adapted from College of Integrative Medicine Module 28
Integrative Medicine Approach to Women's and Men's Health))*

Dr. Wayne Sodano DC, DABCI, DACBN, CFMP, BCTN



"Endometriosis is a common but enigmatic condition, affecting up to 50% of asymptomatic reproductive age women. Its diagnosis and management are hampered by poor correlation between the degree of symptoms and the extent of the disease."ⁱ "Endometriosis is defined as the presence of functional endometrial glands and stroma outside the uterine cavity. Women with endometriosis present with characteristic signs and symptoms: dysmenorrhea, dyspareunia, chronic pelvic pain or subfertility. The prevalence of endometriosis in women with pelvic pain and/or infertility is estimated to be between 20 and 90%."ⁱⁱ The incidence of endometriosis consists of: 4-10% of all women; 25-50% of women with infertility; 5-25% of women admitted with pelvic pain; and 7% of women with pelvic masses.ⁱⁱⁱ Increasing evidence suggests that endometriosis patients are at higher risk of several chronic diseases such as asthma, autoimmune, cutaneous melanoma, ovarian and breast cancer, cardiovascular disease and atopic disease.^{iv} Laparoscopy is considered the 'gold standard' for diagnosing endometriosis.

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Theories of Pathogenesis of Endometriosis ^v

| NAME | THEORY | SUPPORTING EVIDENCE |
|--------------------------------|---|--|
| RETROGRADE MENSTRUATION | Implantation of endometrial cells onto peritoneum due to retrograde flow of menses through the fallopian tubes. | Increased incidence of endometriosis in women with congenital obstruction of the reproductive tract. |
| COELOMIC METAPLASIA | Transformation of multipotential peritoneal cells into endometrial glands. | Development of endometriosis in women with uterine agenesis. |
| COELOMIC METAPLASIA | Transport of endometrial glands through the vascular and lymphatic systems. | Presence of endometriosis in sites outside the abdominal cavity. |

Multiple mechanisms have been implicated in the etiology and progression of this disease. The most outstanding appears to be the involvement of immunological factors." The immune response has been suggested as one of the factors that is involved with the attachment or clearance of refluxed endometrial tissue fragments. Alteration in the immune response may prevent satisfactory disposal of menstrual debris, possibly increasing the chance of endometriosis development."^{iv}

Alteration of both the cell-mediated and humoral immune response has been implicated in this disorder. The following immune dysregulations have been reported with endometriosis:

| | |
|--|---|
| Decreased NK (natural killer) cells | <ul style="list-style-type: none"> Turkey tail mushroom, curcumin, green tea |
| Humoral-mediated immunity | <ul style="list-style-type: none"> Resveratrol from grape seeds, boswellia, curcumin, aloe vera, lycopene |
| Increased cytokine production | <ul style="list-style-type: none"> Green tea, curcumin, flavonoids, mistletoe (Viscum alba) |
| Peritoneal fluid | <ul style="list-style-type: none"> Turkey tail mushroom, ginkgo biloba, soy, green tea, curcumin |
| Oxidants are proposed to stimulate endometrial cell growth | |
| Autoimmunity | <ul style="list-style-type: none"> Association with polyclonal B-cell activation, immunological abnormalities in T-cell and B-cell function, increased apoptosis, tissue damage, multi-organ involvement, familial occurrence involvement of environmental factors, female preponderance and association with other autoimmune disease |

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Laboratory Test Considerations

| | |
|-------------------------------------|---|
| Celiac Profile | <ul style="list-style-type: none">• A potential link between endometriosis and celiac disease has been hypothesized since these disorders share some similarities, specifically concerning a potential role of oxidative stress, inflammation, and immunological dysfunctions. There appears to be an increased prevalence of celiac disease among patients with endometriosis.^{vii} |
| Adrenal Hormone Profile | <ul style="list-style-type: none">• Assess cortisol and DHEA levels |
| Female Hormone Profile | <ul style="list-style-type: none">• Assess estrogens and estrogen metabolites |
| Estrogen Metabolism Genomic Testing | <ul style="list-style-type: none">• Assessing estrogen clearance efficiency (Phase I and phase II detoxification capacity - methylation [MTHFR, COMT], cytochrome P450 enzymes) |
| Stool analysis | <ul style="list-style-type: none">• Assess GI function |
| Food Allergy /Sensitivity Profile | <ul style="list-style-type: none">• IgG and IgE. Remove reactive foods contributing to digestive dysfunction and immune systems dysregulation |
| CA125 | <ul style="list-style-type: none">• Low levels are common in endometriosis; elevated levels warrant investigation; the most important clinical use has been monitoring the course of ovarian cancer in response to treatment |
| Serum placental Protein 14 (PP14) | <ul style="list-style-type: none">• Serum PP14, which varies during the menstrual cycle and originates almost exclusively in human secretory endometrium, has been shown to be greatest with advanced endometriosis, but its utility as a diagnostic test warrants further investigation because of a low sensitivity.^{viii} |
| Interleukin 6 (IL-6) | <ul style="list-style-type: none">• IL-6 is a regulator of inflammation and immunity, which may be a physiologic link between the endocrine and the immune systems.^{ix} |
| CRP | <ul style="list-style-type: none">• CRP is produced in the liver in response to IL-6 |
| Serum anti-endometrial antibodies | <ul style="list-style-type: none">• Although this marker has limitation, it was proposed not only as a screening marker but also as a follow-up marker of treatment results and recurrence.^x |



Image by: freepek

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Treatment Considerations

Allopathic approach to endometriosis generally comprises hormonal therapy, anti-inflammatory medication, and surgery. Naturopathic/Nutritional medicine approach includes the following:^{xi}

1. Improvement of hormone cascades and receptor responsiveness
2. Avoidance of compounding estrogen interferences
3. Avoidance of environmental toxins and support of elimination
4. Support of hepatobiliary function to support toxin clearance, lipid metabolism, hormone synthesis and metabolism
5. Antioxidant supplementation
6. Immune modulation
7. Microflora recolonization
7. Improvement to digestive function
9. Improvement of lymphatic and circulatory function
10. Lifestyle and dietary changes
11. Symptomatic support - decrease inflammation, reduce pain, reduce endometrial displacement

Comprehensive treatment protocol for endometriosis consists of the following^{xii} (Additional recommendations were added):

1. Diet: increase omega-3; decrease omega-6 (low saturated fats diet); soy isoflavones most days; reduce inflammatory foods
2. Multivitamin/mineral (assess the need for iron via blood tests)
3. Circuminoids: e.g. 750 mg of BCM-95 Curcumin - yielding a minimum of 500 mg curcuminoids per capsule; 1 capsule twice a day
4. Pine bark: e.g. pycnogenol 100 mg/day
5. Vitamin D: 2000 IU/day
6. N-acetylcysteine: 600 mg tid
7. Melatonin: 10 mg before bedtime
8. EPA/DHA: e.g. EPA 1200mg/DHA 900 mg with 1.5 mg mixed tocopherols
9. Consider: oral micronized progesterone 200 mg before bedtime; days 15 - 26 in those with a regular monthly menstrual cycle
10. Antioxidant formula - (e.g. Pure Encapsulation)



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AntiOxidant Formula

Each vegetarian capsula contains

- Vitamin A (as beta carotene) 10.000 iu
- Vitamin E (as d-alpha tocopherol succinate) 100 iu
- Riboflavin (vitamin B₂) 25 mg
- Zinc (as zinc picolinate) 5 mg
- Selenium (as selenomethionine) 100 mcg
- n - acetyl - l - cysteine (NAC) (free - form) 100 mg
- Milk thistle (Silybum marianum) extract (seed) 100 mg
(Standardized to contain 80% silymarin)
- Mixed carotenoids (from lutein, lycopene and zeaxanthin) 500 mcg

**Other Ingredients: Ascorbyl palmitate, vegetarian capsule (Cellulose, water)
1 - 2 capsules daily, in divided doses, with meals.**



Botanical Medicines^{xiii}

| CLASS | | HERBAL ACTION | |
|-------|---------------------|--|--|
| ✓ | • Analgesic | <i>Symptomatic pain relief</i> | <ul style="list-style-type: none"> • Pasque flower • Chamomile • Willow bark |
| ✓ | • Antispasmodic | <i>Symptomatic pain relief</i> | <ul style="list-style-type: none"> • Dioscorea villosa (Wild Yam) • Viburnum opulus (Cramp Bark) • Viburnum prunifolium (Black Haw) |
| ✓ | • Anti-inflammatory | <i>Symptomatic pain relief, reduction in oxidation</i> | <ul style="list-style-type: none"> • Rehmannia glutinosa (Rehmannia) |
| ✓ | • Immunomodulator | <i>Modulate immune response</i> | <ul style="list-style-type: none"> • Echinacea root • Withania • Siberian ginseng • Korean ginseng • Ashwagandha |

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| CLASS | | HERBAL ACTION | |
|-------|--|---|--|
| ✓ | <ul style="list-style-type: none"> Hormonal modulator | <p style="text-align: center;"><i>Stabilize hormonal cascades and regulate hormonal secretion; improve estrogen metabolism, regulate estrogen-to-progesterone ratio</i></p> <ul style="list-style-type: none"> Vitex agnus-castus (Chaste Tree Berry) | |
| ✓ | <ul style="list-style-type: none"> Uterine tonic | <p style="text-align: center;"><i>Reduce endometrial tissue size and impact, improve uterine health</i></p> | <ul style="list-style-type: none"> Anemone pulsatilla (Pasque Flower) Chamalerium (False Unicorn Root) |
| ✓ | <ul style="list-style-type: none"> Hepatic, cholagogue | <p style="text-align: center;"><i>Support hepatic clearance of estrogen metabolites and hormonal synthesis, support clearance of environmental toxins</i></p> <ul style="list-style-type: none"> Silybum marianum (St Mary's Thistle) | |
| ✓ | <ul style="list-style-type: none"> Bitter | <p style="text-align: center;"><i>Encourage and support GI tract microecology</i></p> | <ul style="list-style-type: none"> Gentian |
| ✓ | <ul style="list-style-type: none"> Lymphatic | <p style="text-align: center;"><i>Improve pelvic circulation and immunological function</i></p> | <ul style="list-style-type: none"> Cinnamomum spp. (Cinnamon) Rehmannia glutinosa (Rehmannia) |
| ✓ | <ul style="list-style-type: none"> Adaptogen; thymoleptic | <p style="text-align: center;"><i>Support patient emotionally and reduce impact of excessive cortisol production both on immune irregularities, HPA negative impact and inflammation</i></p> <ul style="list-style-type: none"> Siberian ginseng Lavender Lemon balm | |

- ⁱ Cole MM. Endometriosis. In: Maizes V, Low Dog T. Integrative Women's Health. Oxford: Oxford University Press; 2010. p. 284.
- ⁱⁱ Hechtman L. The Female Reproductive System. In: Hechtman L. Clinical Naturopathic Medicine. Australia: Elsevier; 2012. p. 807.
- ⁱⁱⁱ Ibid.
- ^{iv} Kvaskoff M, Mu F, Terry KL, Harris HR, Poole EM, Farland L, Missmer SA. Endometriosis: a high-risk population for major chronic disease? Hum Reprod Update. 2015 Jul-Aug; 21(4): 500-16.
- ^v Cole MM. Endometriosis. In: Maizes V, Low Dog T. Integrative Women's Health. Oxford: Oxford University Press; 2010. p. 285.
- ^{vi} Hechtman L. The Female Reproductive System. In: Hechtman L. Clinical Naturopathic Medicine. Australia: Elsevier; 2012. p. 809.
- ^{vii} Santoro L, Campo S, D'Onofrio F, Gallo A, Covino M, Campo V, et al. Looking for Celiac disease in Italian Women with Endometriosis: A Case Control Study. Biomed Res Int. 2014; 2014: 236821.
- ^{viii} Bedaiwy MA, Falcone T. Laboratory testing for endometriosis. Clinica Chimica Acta. 2004; 340: 41-56.
- ^{ix} Ibid.
- ^x Ibid.
- ^{xi} Hechtman L. The Female Reproductive System. In: Hechtman L. Clinical Naturopathic Medicine. Australia: Elsevier; 2012. p. 820.
- ^{xii} Hudson T. Women's Health Update: Women's Health Treatment Protocols That I Count On. Townsend Letter. February/March 2016; 391/392: 107- 109.
- ^{xiii} Hechtman L. The Female Reproductive System. In: Hechtman L. Clinical Naturopathic Medicine. Australia: Elsevier; 2012. p. 826.