THE
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women's health
INSTITUTE

presents

Endometriosis: The Gut-Immune Link
Nutrition Strategies to Address Endometriosis

Dr. Jessica Drummond, DCN, CNS, PT

Objectives

- Systems not symptoms
- Endometriosis as Inflammatory and Autoimmune
- Intestinal Barrier Function and Optimization
- Nutrition as Root Cause Modulation in Endometriosis (There is no ONE "Endo Diet")
- Foods to Reduce & More importantly… Foods to ADD
- Interaction with Gut Microbiome
- Hormone disrupting chemicals
- Anti-inflammatory & Antioxidant supplements

> Don't chase symptoms.
>
> Optimize systems.
>
> DR. JESSICA DRUMMOND

Endometriosis as An Inflammatory and Autoimmune Disease

- In a retrospective study, data of 304 patients with endometriosis and 318 without endometriosis… The results obtained have shown that ***patients with endometriosis have a higher prevalence of allergies (p = 0.0003) and coexistence of both allergies and autoimmune diseases*** (p = 0.0274), compared to those without.
- **Correlation.**

Clin Exp Obstet Gynecol. 2016;43(3):354-7.
Endometriosis allergic or autoimmune disease: pathogenetic aspects--a case control study.
Caserta D, Mallozzi M, Pulcinelli FM, Mossa B, Moscarini M.

Endometriosis as An Inflammatory and Autoimmune Disease

- Mechanisms in cell mediated immunity
  - Diminished cell mediated response could facilitate ectopic implantation of the translocated endometrial cells (but T cell response has been shown to be inconsistent.)
  - Natural killer cells (NK) may play a role in the clearance of regurgitated endometrial cells from the peritoneal cavity of most women. In endometriosis there is a decrease in local NK-mediated cytotoxicity in the peripheral and peritoneal fluid to both autologous and heterologous endometrium.

Autoimmun Rev. 2012 Sep;11(11):806-14. doi: 10.1016/j.autrev.2012.01.005. Epub 2012 Feb 4. Is there an association between autoimmunity and endometriosis?
Eisenberg VH1, Zolti M, Soriano D.

Endometriosis as An Inflammatory and Autoimmune Disease

- Mechanisms in cell mediated immunity
  - Peritoneal macrophages are increased in total number, concentration, and activation status in women with endometriosis
  - Increased release of growth factors and cytokines, affecting the survival and growth of ectopic endometrial cells.
  - There are also several possible mechanisms under study that describe how endometriotic cells evade leukocyte recognition and immune surveillance.

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Endometriosis as An Inflammatory and Autoimmune Disease

- Several pro-inflammatory chemo-attractant cytokines for monocytes, macrophages and granulocytes have been identified in the peritoneal fluid of women with endometriosis.
- **Interleukin-1** (specifically IL-1β) may play a role in promoting angiogenesis in endometriotic lesions by inducing angiogenic factors

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Endometriosis as An Inflammatory and Autoimmune Disease

- **Interleukin-6** (IL-6) can inhibit the proliferation of human endometrial stromal cells.
- Peritoneal fluid levels of IL-6 were found to be well correlated with the severity of endometriosis.
- A high peritoneal fluid level of IL-6 in women with severe endometriosis is also accompanied by a decrease in IL-6 soluble receptor concentration, possibly accounting for the resistance of endometriotic implants to growth inhibition by IL-6.

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Endometriosis as An Inflammatory and Autoimmune Disease

- **Interleukin-8** (IL-8) is elevated in the peritoneal fluid of women with endometriosis and correlated with the severity of the disease, and may act as an autocrine growth factor in the endometrium.
- **Interleukin-12** (IL-12) levels are increased in the peritoneal fluid of women with endometriosis compared to those without endometriosis, possibly affecting NK cell activity.

Autoimmun Rev. 2012 Sep;11(11):806-14. doi: 10.1016/j.autrev.2012.01.005. Epub 2012 Feb 4. Is there an association between autoimmunity and endometriosis?
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Endometriosis as An Inflammatory and Autoimmune Disease

- **Monocyte chemotactic protein-1** (MCP-1) levels are is elevated in the peritoneal fluid of women with endometriosis compared to those without. MCP-1 level is correlated with disease severity and decreases with medical treatment.
- And many more…

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Endometriosis as An Inflammatory and Autoimmune Disease

- Changes in Humoral Immunity, include an increased incidence of autoantibodies in women with endometriosis:
  - These include antibodies to a variety of phospholipids, histones, polynucleotides and even lupus.
  - Some of these autoantibodies are organ-specific anti-endometrial and anti-ovarian antibodies

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The Coordination of The Immune Response

- **Inappropriate inflammation is a prerequisite for the development of immunologic autoreactivity.**
- Autoantibodies are a serologic characteristic in autoimmune diseases, but also may occur in other conditions, such as cancer, massive tissue damage.
- **It is not yet clear whether autoantibody formation in endometriosis is simply a natural response to chronic local tissue destruction, or a pathologic response leading to more generalized autoimmune dysfunction.**

Autoimmun Rev. 2012 Sep;11(11):806-14. doi: 10.1016/j.autrev.2012.01.005. Epub 2012 Feb 4. Is there an association between autoimmunity and endometriosis?
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How Can Nutrition and Supplementation Support Digestive, Immune, and Pain Modulation in Endometriosis?

- Optimize digestive function and lining of intestines (interface between digestive and immune systems - like “inner skin.”)
- Anti-inflammatory nutrition
- Antioxidant nutrition
- Hormone Balance supportive nutrition
- Pain modulating nutrition

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Digestive Function

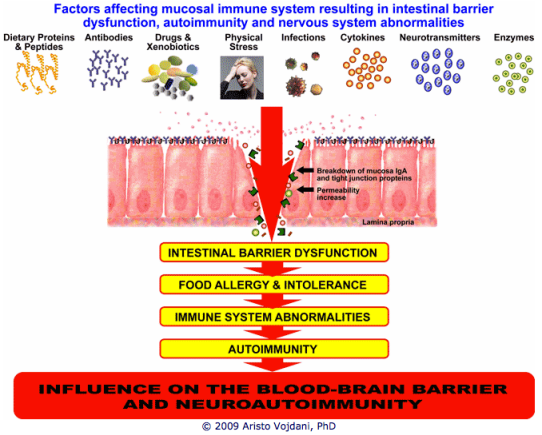
1. Adequate stomach acid?
2. Adequate digestive enzymes?
3. Eating mindfully?
4. Chewing?
5. Intact intestinal lining?
6. Healthy gut microbiome?
7. Good gut motility?
8. Healthy colonocytes
9. Healthy pelvic floor function and toileting position for defecation?

For example: Digestive Enzyme Stimulation with Nutrition or Supplements

- Spices can increase secretion of bile and digestive enzymes.
- For example, curcumin stimulated lipase activity by 80%, and a single dose of mint led to a 43% increase in lipase activity.
- The dietary intake of whole spices - ginger, ajowan, fennel, coriander, garlic, and onion - significantly enhanced trypsin activity. Ginger by 133%.
- An increase in intestinal lipase activity was observed in animals given single oral doses of mint, garlic, onion, ajowan, ginger, fennel, piperine, fenugreek and curcumin (between 20% and 461% depending on the spice.)
- Consider supplements, especially if energy is low (highly ATP dependent.)

Indian J Med Res. 2004 May;119(5):167-79.
Digestive stimulant action of spices: a myth or reality?
Platel K1, Srinivasan K.

Gut Permeability



History to Determine Increased Intestinal Permeability

- Potential Signs: food sensitivities, allergies, nutrient deficiencies, chronic inflammation
- Potential Causes: NSAIDS, antibiotics, lack of chewing, weak digestive enzymes (common after age 35 and with chronic stress/ pain/ illness), physical stress, emotional stress, inflammatory cytokines, infections, toxins, intense exercise + dehydration, etc.

Testing to Determine Increased Intestinal Permeability

- What is the intestinal barrier? It includes the physical barrier, support from the gut microbiota, and the functional barrier of the immune system.
- Read: Bischoff et al. (2014) Intestinal Permeability-a new target for disease prevention and therapy. BMC Gastroenterology 14:189
- The most commonly used functional test to determine the integrity of the intestinal barrier in the small intestine where most nutrients are absorbed: Mannitol-Lactulose test

Jones, DS (2010) Textbook of Functional Medicine, Institute for Functional Medicine, Gig Harbor, MA.

Leaky Gut and Autoimmunity

- ***"...the autoimmune process can be arrested if the interplay between genes and environmental triggers is prevented by re-establishing intestinal barrier function."***

http://www.direct-ms.org/pdf/LeakyGutMS/Fasano%20intestinal%20barrier%20autoimmunity.pdf

Normalizing The Intestinal Barrier Function

- The Pelvic Pain Elimination Diet - as an assessment tool!
- Zinc, Glutamine, Demulcent Herbs
- Berberine
- Probiotics
- Get to the "Why?" - stress, poor stomach acid/ digestive enzyme function, inflammatory diet, exposure to chemicals in the diet, dehydration, etc.

The Pelvic Pain Elimination Diet
Eliminate

- Processed meats (except for low nitrate lunch meats as a short cut)
- Canned beans (except for Eden Foods brand)
- Animal protein that is not organic/ grass-fed/ pastured/ wild caught
- Fish that are heavy in toxins
- Sugar or other natural or artificial sweeteners
- Wheat or any other gluten containing grains (sometimes all grains)
- Corn
- Caffeine/ Alcohol
- Trans fats or partially hydrogenated oils
- Processed foods/ Fast foods
- Dairy (a bit of conflicting literature)
- Soy (rare, organic, fermented)
- Eggs

The Pelvic Pain Elimination Diet
Eliminate

- Don't skip the re-challenge phase to personalize and optimize the individual's food plan.

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The Pelvic Pain NOURISH Diet
ADD

- 8-10 servings of vegetables daily (increase slowly, cooked first)
- Poultry: Chicken or turkey (preferably organic and pasture raised with no added sugars or other fillers)
- Fish (preferably wild caught)
- Beef, veal, or liver (preferably grass fed and organic)
- Wild game
- Protein Powder: Rice, pea, hemp, collagen (from grass fed beef), or hydrolyzed beef
- 1-2 servings of fruit (low glycemic/ colorful - berries, stone fruits, apples, cantaloupe, coconut, avocado)
  - Be mindful of dried fruits
  - Avoid citrus fruits if comorbid bladder pain

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The Pelvic Pain NOURISH Diet
ADD

- Soaked and slow cooked beans
- Gluten and corn free grains as tolerated (test after initial assessment phase)
- Nuts and nut butters: Almonds, cashews, pecans, and more • All seeds (be mindful of estrogenic effects of flax seeds & chia seeds)
- Nut and Seed milks - minimize preservatives
- Oils: Coconut, olive, and avocado
- Wide variety of herbs and spices
- Bone and vegetarian broths

A few sample recipes:
http://integrativewomenshealthinstitute.com/masterclass-endometriosis/

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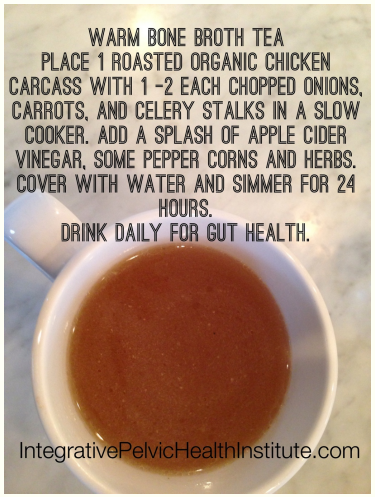

The Gut Microbiome: Is It Related to the Cause of Endometriosis?

- In experimental and clinical studies have shown that **changes of the gut microbiota contribute to the development and progression of various diseases**… including inflammatory bowel diseases, arthritis, psoriasis, and cancer.
- The literature ascribes this interaction between the gut microbiome health and disease to the potent immunoregulatory capacity of gut bacteria, which markedly affects systemic inflammatory cell responses.

The gut microbiota: a puppet master in the pathogenesis of endometriosis?
Laschke, Matthias W. et al.
American Journal of Obstetrics & Gynecology , Volume 215 , Issue 1 , 68.e1 - 68.e4

Normalizing The Intestinal Barrier Function: Probiotic Strains

- To keep up to date on the research, and to read through the studies to assess quality and study population, consider a subscription to Probiotic Advisor (www.probioticadvisor.com)
- In a mouse endometriosis model, Lactobacillus gasseri OLL2809 suppressed the development of endometriosis by activation of natural killer (NK) cells
- Lactobacillus gasseri OLL2809 + a progestin medication also reduced endometriosis lesions in a mouse model.

Masayuki UCHIDA & Orie KOBAYASHI (2014) Effects of Lactobacillus gasseri OLL2809 on the Induced Endometriosis in Rats, Bioscience, Biotechnology, and Biochemistry, 77:9, 1879-1881, DOI: 10.1271/bbb.130319

The Estogen-Gut Microbiome Axis

- The gut microbiota is involved in the regulation of estrogen cycling.
- Gut dysbiosis increases the levels of circulating estrogen.

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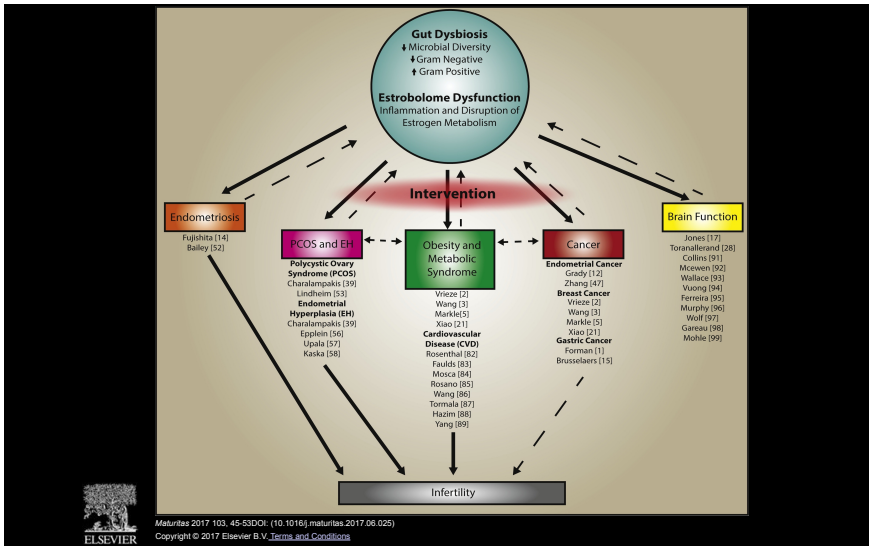

The Impact of Hormone Disrupting Chemicals

- Developmental exposure of mice to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) leads to a progesterone-resistant phenotype in adult animals that can persist for several generations.
- To reduce exposure to industrial dioxins - eat organic meat and diary (or eliminate dairy), trim the fat.

Bruner-Tran, K. L., Ding, T., & Osteen, K. G. (2010). Dioxin and Endometrial Progesterone Resistance. Seminars in Reproductive Medicine, 28(1), 59–68. http://doi.org/10.1055/s-0029-1242995

http://www.who.int/mediacentre/factsheets/fs225/en/

Anti-Inflammatory & Antioxidant Supplements

- Curcumin
- Bromelain,
- N-Acetyl Cysteine
- Alpha-Lipoic Acid
- Quercetin (anti-histamine)
- Ginger root
- Boswellia
- Fish oil
- Resveratrol
- Pine Bark/ Pycnogenol
- Green Tea
- Selenium, Zinc, C & E
- Melatonin

Curcumin: Many possible mechanisms (*need clinical trials!)

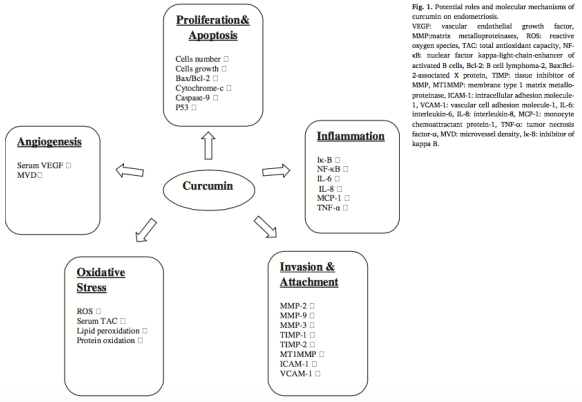

Fig. 1. Potential roles and molecular mechanisms of curcumin on endometriosis.
VEGF: vascular endothelial growth factor, MMP:matrix metalloproteinases, ROS: reactive oxygen species, TAC: total antioxidant capacity, NF-κB: nuclear factor kappa-light-chain-enhancer of activated B cells, Bcl-2: B cell lymphoma-2, Bax:Bcl-2-associated X protein, TIMP: tissue inhibitor of MMP, MT1MMP: membrane type 1 matrix metalloproteinase, ICAM-1: intracellular adhesion molecule-1, VCAM-1: vascular cell adhesion molecule-1, IL-6: interleukin-6, IL-8: interleukin-8, MCP-1: monocyte chemoattractant protein-1, TNF-α: tumor necrosis factor-α, MVD: microvessel density, Ik-B: inhibitor of kappa B.

Biomed Pharmacother. 2018 Jan;97:91-97. doi: 10.1016/j.biopha. 2017.10.119. Epub 2017 Nov 6.
Curcumin and endometriosis: Review on potential roles and molecular mechanisms. Arablou T1, Kolahdouz-Mohammadi R2.

Protocols

- As always, there is no “one-size-fits-all” protocol for women with endometriosis.

- Consider each client…
- Start with food, and digestive function… Is she on an antiinflammatory, nutrient dense food plan? Can she absorb the nutrients?
- Digestive support supplements
- Nutrient support for deficiencies - selenium, zinc, C, E, D, omega-3 fatty acids
- Add antioxidant/ antiinflammatory/ estrogen metabolism supplements - curcumin, NAC, ALA, resveratrol, green tea, pycnogenol, proteolytic enzymes (bromelain), etc.