Changing the Dogma-
New Advances and Concepts in Endometriosis Management

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Relevant financial relationships in the past twelve months:

Consultant: Lumenis (Boston Scientific), Myovant
Outline

- What is and what causes endometriosis?
- Diagnosis
- Surgical Management
  - Excision vs. ablation
  - Deconstructing the posterior CDS
  - Role for hysterectomy or oophorectomy
- Advances in Medical Management
- Evidence-based Integrative Medicine
- Multidisciplinary Care Models
Implantation of endometrial tissue outside of the uterus
Diagnostic Delays


Diagnosis

- All age groups!
- Symptoms:
  - Dysmenorrhea/cyclic pain
  - Noncyclic abdominal, pelvic and/or back pain
  - Dyspareunia
  - Dyschezia or other bowel sxs
  - Dysuria or other bladder sxs
  - Infertility
  - Heavy menstrual bleeding
  - Chronic fatigue
Detection and Treatment

- **Gold standard = laparoscopy**
- Goals of surgery
  - Remove all visible endometriosis and adhesions
  - Restore normal anatomy
  - Improve fertility
  - Detect occult malignancy – rare
- Identification is subjective, inconsistent, and requires experience of surgeon to identify “atypical” and subtle lesions
- High rates of recurrence and pain 2/2 incomplete resection!

Classification

- 3 different entities
  1) **Peritoneal lesions** (superficial)
  2) **Endometriomas** (cysts w/in the ovary)
  3) **Deeply infiltrative endometriosis (DIE)** ≥ 5 mm
Laparoscopic Detection of Superficial Endometriosis

Role for Complete Surgical Excision
ICG for Detection of Endometriosis

- Identify areas of hypervascularity (neovascularization) on the surface of the peritoneum
- Lighted ureteral stents
- Near infrared camera system; With addition of ICG, it enhances visualization of vascular structures
Preoperative Detection of Deeply Infiltrative Endometriosis
Deeply Infiltrative Endometriosis (DIE)

Detection of DIE

*Imaging*

- Equal sensitivity/specificity for US and MRI
  - Largely institution specific!!
  - Better detection at referral/endometriosis centers
- European Society of Urogenital Radiology (ESUR) guidelines 2016 recommends:
  - Fasting, phased array coils, antiperistalsis glucagon, full bladder, abdominal strapping, IV gadolinium contrast for adnexal pathology +/- rectal and vaginal gel
  - More research on use of bowel preps, 1.5T vs. 3.0T, and clinical impact of MRI as a preop test
Surgical Management

Superficial Peritoneal Disease
Excision versus Ablation

- Advantages of excision
  - Tissue for diagnosis
  - Less chance of leaving unrecognized DIE

Excision versus Ablation

- Excision vs Ablation (fulguration/vaporization)
- Healy 2014 JMIG RCT 5 yr f/u – Improvement in dyspareunia w/ excision

**Advantages of excision**
- Tissue for diagnosis
- Less chance of leaving unrecognized DIE
- Decreased pain and less chance of recurrence
Surgical Management

Deeply Infiltrative Endometriosis

Deconstructing the Posterior Cul-de-Sac (pCDS)

Management of the Obliterated Cul-de-Sac

- Adhesive disease of pCDS involving uterus, rectosigmoid, ovaries
- ± DIE or rectovaginal nodule
- Approach

Step 1) Normalize anatomy by dissecting into rectovaginal septum

Step 2) Resect adherent surfaces

Step 3) Resect nodules
Surgical Management

Role of Hysterectomy and Oophorectomy

Postoperative Prevention of Recurrence

- Long term hormonal suppression (OCPs, mirena IUD)
- GnRH agonist for 6 months for advanced endometriosis or DIE
- Hysterectomy +/- Oophorectomy is not a cure!....but does increase pain free intervals
New Medical Options

Traditional Medical Treatment

- NSAIDs (decrease inflammation)
- Contraceptive hormones (prevent menstruation/oppose estrogen)
- Progestins (prevent menstruation/oppose estrogen)
- GnRH agonists (hypoestrogenic state; FDA approved)
- Danocrine (hyperandrogenic state; ~progestin-like activity on endometrium; FDA approved)
New Medical Options

- GnRH antagonist (hypoestrogenic state)
- Vaginal/rectal administration of danazol
- Aromatase inhibitors (inhibit synthesis of E2)
- Increased duration of use of GNRH agonists
- Other off label general pain medications, nerve blocks, botox, etc.

- **AVOID STARTING OPIOIDS!!!!**

Elagolix (Orilissa)

- Oral GnRH antagonist
- RCTs were 6 months in length
- 150 mg daily, 200 mg BID, placebo
- Significant dose-dependent improvement in cyclic and non-cyclic pain vs placebo
  - Only higher dose had significant decrease in rescue analgesic use and dyspareunia
Elagolix (Orilissa)

- SEs: hot flushes, headache, insomnia, mood swings, night sweats, arthralgia
- AEs: increased chol & triglycerides, decreased bone mineral density
- 8 pregnancies in the treatment group
- Take home: oral alternative to leuprolide acetate that may allow for dose titration
- Cost?
Treatment –
Complementary and Alternative Medicine

- Yoga*
- Acupuncture*
- Dietary Changes
- Physical Therapy
- Massage
- Biofeedback
- TENS
- Psychological counseling to treat significant stress and anxiety associated with chronic pelvic pain
- Anti-inflammatory diets and supplements

From: Multi-disciplinary centres/networks of excellence for endometriosis management and research: a proposal
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UCSF Endometriosis Center Goals

- Enhance collaboration in clinical care and research
- Serve as a portal for patients to reach correct providers
- Improve patient satisfaction by promoting earlier diagnosis, comprehensive treatment plans, and improved education
- Provide community and social media outreach
- Train medical students, residents, health care providers and support staff
- Holistic care

This is a learning process to determine how to improve our patients’ experience
A Collaborative Effort

Management from several different services including:

- Patient Navigator
- Gynecology
- Psychologist
- Reproductive Endocrinology & Infertility
- Pain Service
- Pelvic Floor Physical Therapy
- Integrative Medicine/Osher Center
- Sexual Health
- Urogynecology
- Radiology
- Pathology
- Researchers
- Patient Advisory Board

Colorectal Surgery
Urology
Thoracic Surgery

Endometriosis Care at UCSF

- Multidisciplinary team
- Interdisciplinary case conference & journal clubs
- Complete surgical excision
  - Superficial disease
  - DIE, obliterated pCDS
- Standard and innovative medical/integrative Rx options
  - Mind Body Course
  - Yoga for pelvic pain
  - Acupuncture
  - Support groups
  - Educational resources
- Research
- Education
Conclusions

- Endometriosis management requires an interdisciplinary holistic care model including surgical, medical, and integrative medicine options
- Early diagnosis and treatment is important
- Complete surgical excision matters
  - Atypical endometriosis can be hard to diagnose and requires experience
  - The first surgery is the most important predictor in recurrence!!!
- Consider newer options
An anti-inflammatory diet is recommended for those who live with chronic illness and pain, including those with endometriosis. Eating a whole foods, plant-based diet is the simplest way to adopt an anti-inflammatory approach and may reduce rates of inflammation associated with endometriosis. Plus, a diet filled with fresh, real food is delicious!

Work toward these dietary goals:
Eat foods in as whole a form as possible. Choose whole or steel-cut oats over instant oats, fresh fruit over juice or jam, brown rice over white. Minimize your consumption of processed, packaged and fast foods.

Have 2-3 servings of fruit and 6-7 servings of vegetables each day, fresh or frozen. Have fruit with breakfast- whole fruit or cut-up fruit on oatmeal. Fruit is also good in salads. Eat dark green leafy vegetables every day (spinach, chard, collards, kale, arugula, lettuces, broccoli). Have a green salad or steamed greens with your vegetable-rich lunch and dinner daily. Choose fruits and vegetables for snacking.

Eat a rainbow of brightly colored fruits and vegetables. This ensures diversity of vitamins and minerals in your diet. Berries and tomatoes (red); sweet potato, winter squash, carrots, oranges, cantaloupe, peaches, apricots, persimmons and mango (orange/yellow); dark leafy greens and other green vegetables- asparagus, broccoli, brussels sprouts (green); eggplant, blueberries (blue/purple); onion, garlic, mushrooms, cauliflower (white).

Include more plant proteins in your diet Eat beans, lentils and/or split peas several times a week. Once or twice a week make a pot of soup with beans and vegetables, make extra and freeze some for later. Examples: lentil soup, split pea soup, minestrone with beans and vegetables, black bean soup, chickpea soup.

Eat whole grains several times each day Learn to cook brown rice, quinoa, buckwheat, amaranth, millet, oats, polenta. Other whole grain foods include sprouted whole grain bread, whole grain pasta, 9-or 12- grain cereal. Try hot cereals in the morning such as whole oats, amaranth or millet with real maple syrup, yogurt and fruit.

Eat healthy fats Add nuts and seeds to your daily diet-walnuts, almonds, pumpkin seeds, flax seeds, chia seeds and many others. They're good for snacking, on salads, in desserts. Try anchovies, halibut, herring, sardines, mackerel, trout, wild salmon (fresh, frozen or tinned/canned). Other sources of healthy fats are omega-3 fortified eggs, avocados, olives, seaweed. Use extra virgin olive oil for cooking.
Fluids Drink about 2 quarts of water daily. Get a reusable quart bottle (preferably BPA and BPS free) and carry it with you everywhere you go. Never leave the house without it. Drink every two hours or more. Limit fruit juices and soda, they are high in sugar and low in fiber and cause dramatic blood sugar changes.

Eating plenty of fruits and vegetables and drinking lots of water keeps your bowels moving regularly.

Snack on healthy foods
Suggestions:
- dinner leftovers
- fruit- sliced apple with nut butter; fruit in season (berries, melon and stone fruits in spring/summer; apples, pears, grapes and persimmon in fall; citrus in winter)
- plain yogurt with nuts, dried fruit, fresh fruit or frozen fruit
- cut up veggies- carrots, red bell peppers, celery, snap peas, jicama- with hummus or other bean dips, nut butters, guacamole, salsa
- nuts and seeds of any kind (try honey-roasted or tamari-roasted nuts or trail mixes), roasted chickpeas, soy nuts
- whole grain crackers with bean dips, nut butters, guacamole, salsa
- hard-boiled eggs
- smoothies made with fresh fruit and yogurt
- corn tortillas with mashed beans, avocado, salsa
- air-popped popcorn

Eat organic foods to decrease your exposure to pesticides and xenoestrogens
Become familiar with Environmental Working Group's "Dirty Dozen" and "Clean Fifteen"- an annually updated list of produce that is most ("dirty") and least ("clean") likely to carry pesticide residues and shop accordingly. www.ewg.org . If you’re able, choose organic animal products.

Develop a collection of 7-10 recipes that you love that have lots of vegetables, beans, or non-gluten whole grains. Commit them to memory and use them over and over again.

The best way to ensure that you are eating healthfully is to prepare your own food.

Inflammatory foods to avoid:
Processed foods, red meat, soy, refined sugars, fried foods, soda, refined carbohydrates, saturated and trans fats, caffeine, alcohol.

If you eat sweets, make it a real treat Try to keep it to once or twice a week if you can. Choose sweets that contain some nutritional value- for example, an oatmeal cookie has grains; a peanut butter cookie has protein; ice cream has calcium and protein, or eat something containing fruit and nuts. Avoid the blood sugar roller coaster- don't eat sweets on an empty stomach. Don't allow sweets to crowd out healthy foods. Eat
sweets after meals or eat something healthy before you eat the sweet.

Choose eggs, fish, or poultry over red meat (pork, beef, lamb).

For patients with gastrointestinal discomfort related to endometriosis, including nausea, bloating, gas and indigestion, a trial of removing gluten and dairy from the diet may be helpful.

Our integrative nutritionist at the UCSF Osher Center is available to all Osher patients for ongoing nutritional support. (415) 353-7700