

Endometriosis Care:

Are we moving
forward?

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Objectives

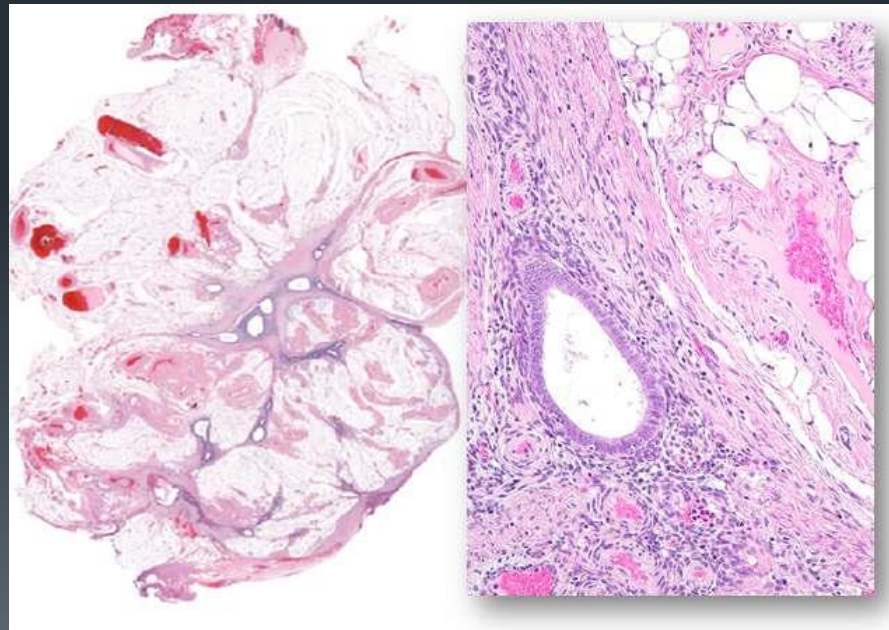
- Review typical and atypical clinical presentations of endometriosis
- Review current concepts of pathophysiologic basis of endometriosis
- Review available options/approaches for diagnosis and treatment of endometriosis
- Present ongoing research topics/future directions of diagnosis/treatment of endometriosis

Disclosures/Disclaimers

- Abbvie Speakers Bureau

Definition

- Estrogen-dependent, benign, inflammatory disease
 - Premenarcheal
 - Reproductive
 - Postmenopausal
- Endometrial-like glands and stroma outside the uterine cavity



Historical Perspective

- Classic Antiquity – animalistic uterus, “wandering womb”
- Hippocrates
 - Fumigation
 - Ground beetle
 - Male/bull urine
 - “Succession”
- Ancient Chinese
 - Pomegranate



Historical Perspective

- Plato - “strangulation or suffocation of the womb”
- Soranus of Ephesus – “inflammation of the uterus”
- Dioscorides – menstrual suppression
- Galen
 - Uterine contractions/inflamed ligaments
 - Association w/ mental illness
- Middle Ages: “lascivious” women, or “those who use drugs to prevent conception”



Historical Perspective

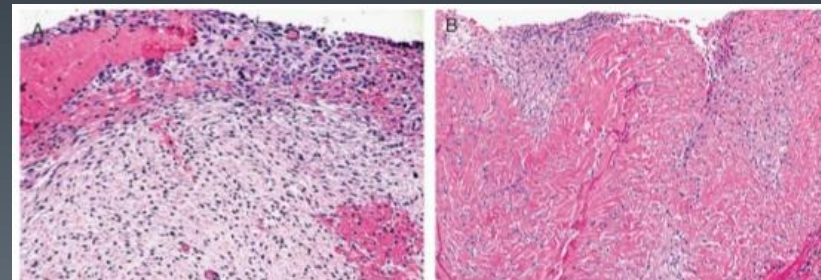
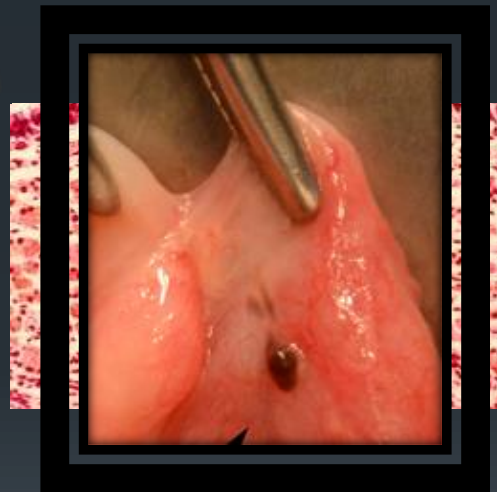
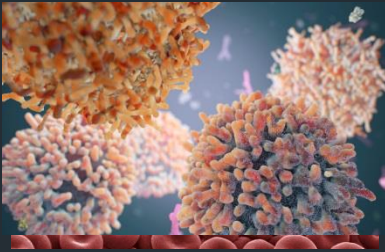
- Renaissance
 - Hysterical fits/Hysteria
 - Witchcraft
 - Nymphomania/Lovesickness/Furor Uterinus
 - Psychologic Disorders
 - Reflux Menses Theory
 - Schron and Ruysch
- 19th century
 - “Catamenial hematocoeles”
 - Karl von Rokitansky
 - Thomas Cullen
 - Diffuse adenomyomas
- 20th Century
 - John Sampson
 - “Endometriosis”



Pathophysiology

- Ectopic endometrial-like tissue and resultant inflammation
 - Dysmenorrhea
 - Dyspareunia
 - Chronic pain
 - Infertility

Histopathophysiology

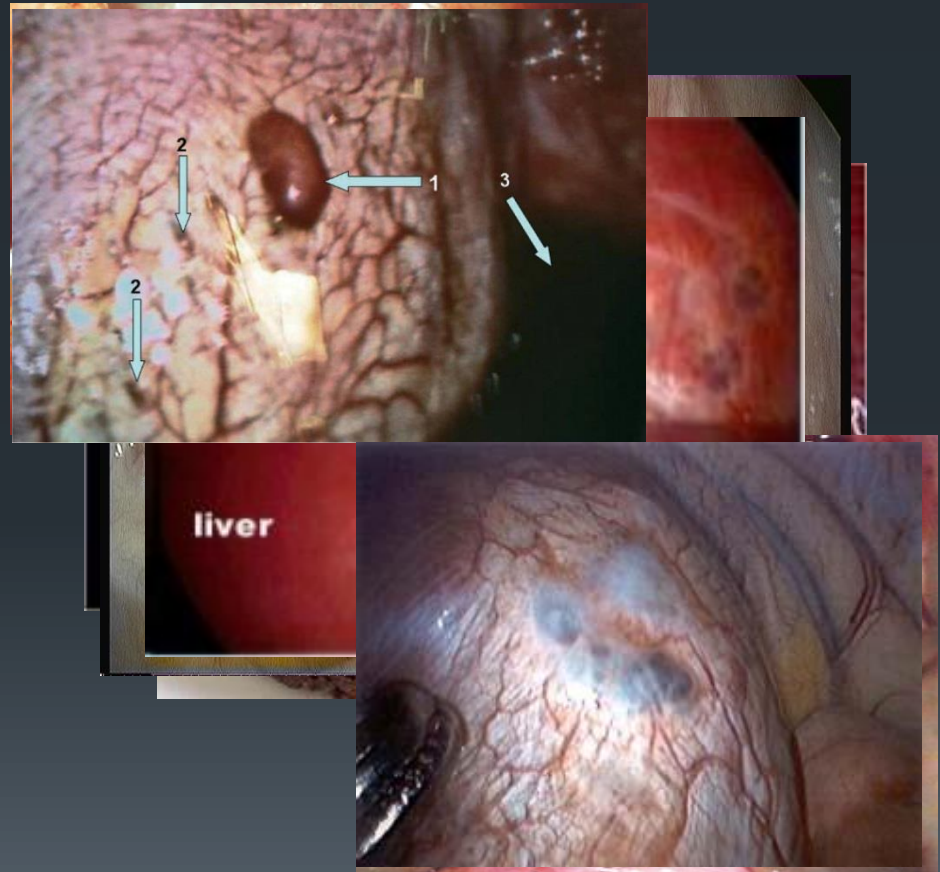


Multifactorial Nature of Etiology

- Ectopic endometrial tissue
- Altered immunity
- Imbalanced cell proliferation and apoptosis
 - TGF- β 1, VEGF, HIF-1 α increased
- Aberrant endocrine signaling
 - Estrogen - neuromodulator that selectively repulses the sympathetic axons while preserving sensory innervation
 - Aromatase activity in lesions → Estrogen
- Genetic factors
 - Heredity: At least six genomic regions associated with endometriosis
 - Mutations in the known cancer driver genes *ARID1A*, *PIK3CA*, *KRAS*, and *PPP2R1A*
 - Aggressive nature of deeply invasive lesions compared with superficial peritoneal lesions
- Epigenetic factors
- Neurologic dysfunction
 - Increase # of nerve fibers
 - Imbalance of sympathetic and sensory nerve fibers
 - Peripheral nerve sensitization

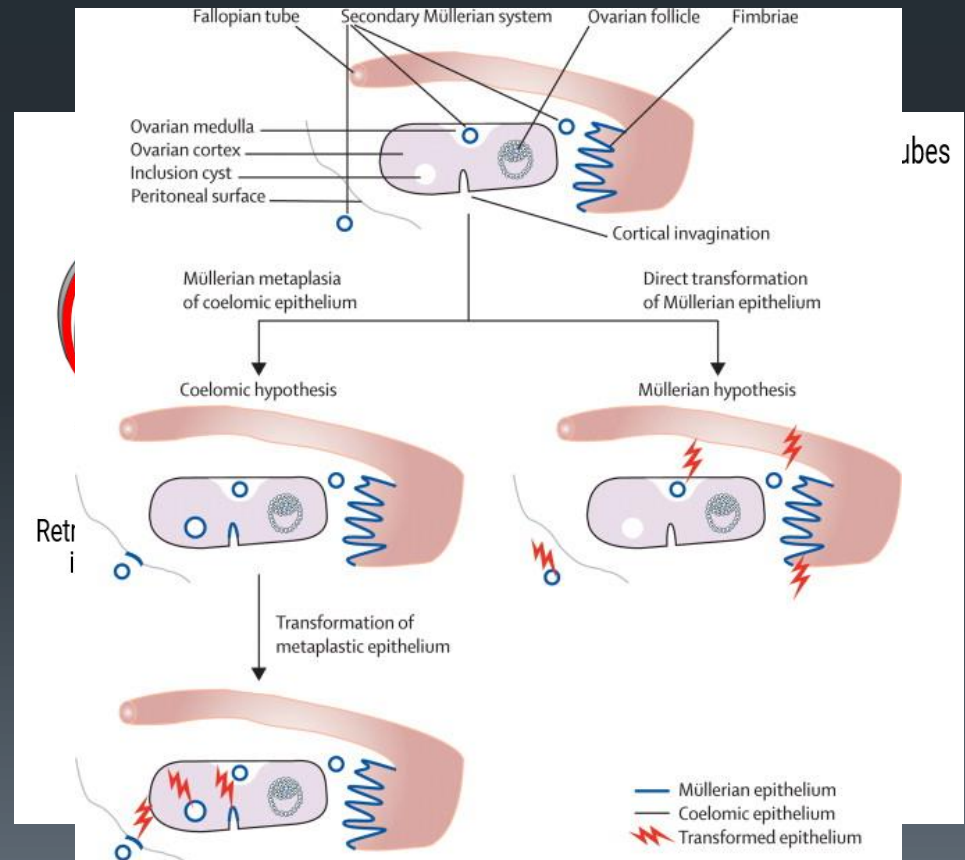
Location

- Gross appearance and size of implants are quite variable
- Pelvis
 - Superficial peritoneal
 - Ovarian (endometrioma, “chocolate cysts”)
 - Deep infiltrating (DIE)
- Extraneous site/organs
 - Bowel
 - Diaphragm
 - Pleural cavity
 - Mediastinum
 - Umbilicus
 - CNS
 - Men/Prepubertal girls



Origin/Spread

- Retrograde menstruation
 - Sampson's theory
- Müllerian embryonic rests/embryonic vestiges
- Coelomic metaplasia
- Lymphatic dissemination
- Vascular dissemination



Temporality

- Peak: 25 to 35 years of age
- 1-2 days before menses
- Persists throughout menses
- Several days afterward



Presentation

- Dysmenorrhea
- Dyspareunia
- Infertility
- Ovarian mass on imaging
- Bowel and bladder dysfunction
- Abnormal uterine bleeding
- Low back pain
- Chronic fatigue

Tissue Specific Presentation

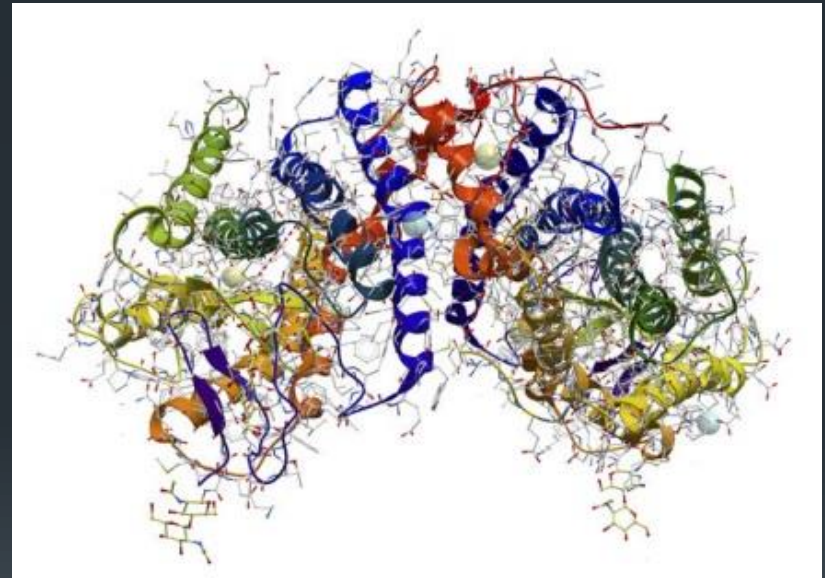
- Bladder
 - Frequency
 - Urgency
 - Dysuria
- Ureteral
 - Colicky flank pain
 - Gross hematuria
- Bowel
 - Diarrhea
 - Constipation
 - Dyschezia
 - Bowel cramping

Tissue Specific Presentation

- Deep infiltrating (DIE)
 - Dyspareunia
 - Painful defecation
- Abdominal wall/Umbilicus
 - Painful abdominal wall mass
 - Bleeding may also occur
- Thoracic
 - Chest pain
 - Pneumo/hemothorax
 - Hemoptysis
 - Scapular/cervical (neck) pain

Labs

- No pathognomonic lab study
- Cancer antigen (CA) 125
- *Update:*
 - Plasma urocortin 1
 - Zinc
 - Lead
 - Aromatase



Under Investigation

- Plasma urocortin 1
 - Severity
- Zinc
- Lead
- Aromatase
- ANTRX2

Imaging

- Modalities

- Transvaginal ultrasound
 - Rectovaginal lesions
- Magnetic resonance imaging (MRI)
 - Rectal lesions
 - Bladder lesions

- *Update:*

- Radiographic parameters to distinguish between cancer and endometriosis
- Transvaginal ultrasound with a bowel preparation

Link to cancer

- Epithelial ovarian cancers
 - Activation of oncogenic *KRAS* and *PI3K* pathways?
 - Inactivation of tumor suppressor genes *PTEN* and *ARID1A*?
- *Update:*
 - Association with overall future cancer, ovarian and breast cancer
- Not considered premalignant lesion
 - Screening is NOT recommended

Atherosclerosis and Cardiovascular disease

- Systemic chronic inflammation
 - + Increased oxidative stress
 - Elevated risk of atherosclerosis
 - Coronary heart disease
- *Update:*
 - Studies report proatherogenic profile and increased subclinical atherosclerosis in women with endometriosis
 - More data needed on risk and benefits screening

Other links

- Chronic pelvic pain
- Painful bladder syndrome
- IBS
- Sleep disorders
- Mood disorders

Medical Treatment

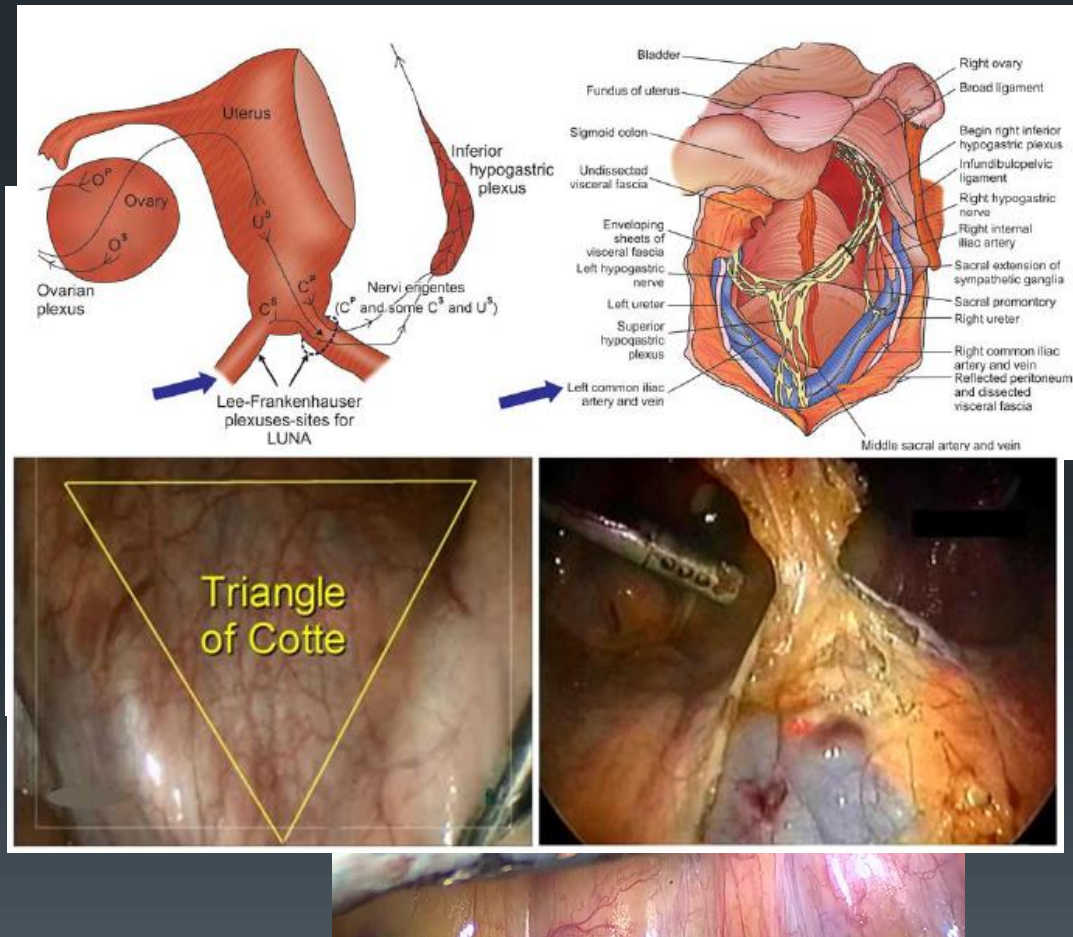
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- Estrogen-progestin contraceptives
- Progestins
 - - Alternate progestin treatment options
- Gonadotropin-releasing hormone (GnRH) agonists
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- Danazol
- Aromatase inhibitors
- Neuropathic pain treatments

Under Investigation

- Immunomodulatory therapy for autoimmune disease
- Microbiome changes

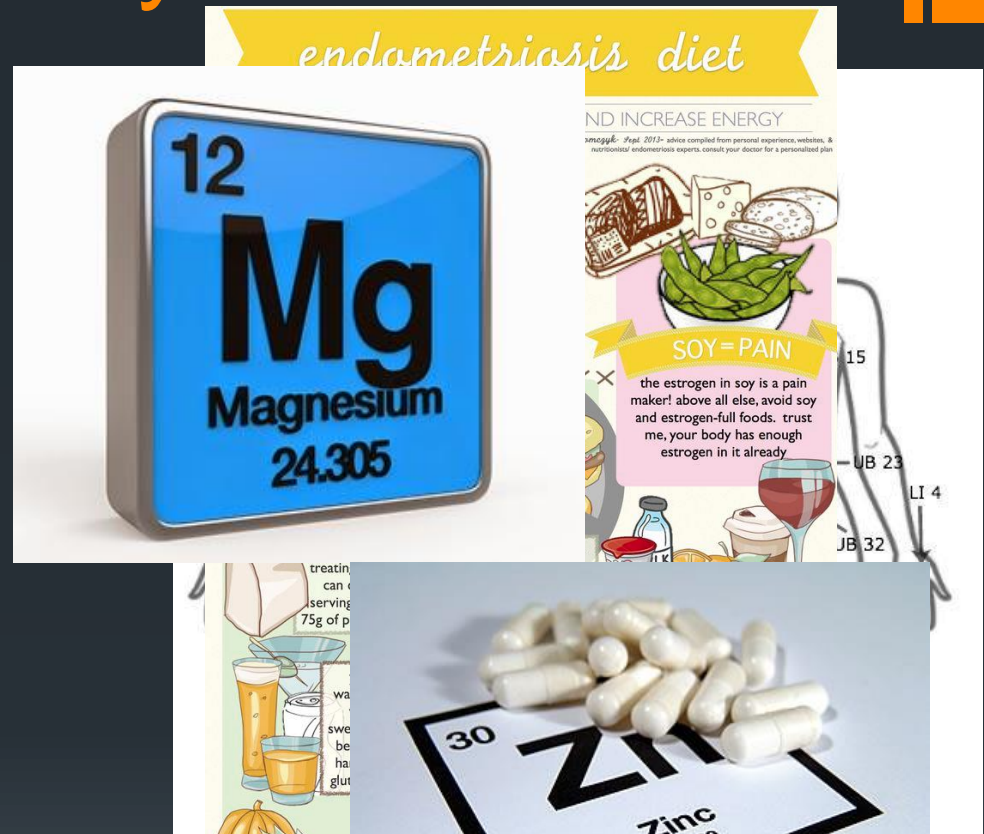
Surgical Treatment

- Resection
- Destruction
 - Electrocautery
 - Laser
 - Plasma
- Nerve transection
 - LUNA
 - PSN



Complementary Treatment

- Acupuncture/Acupressure
- Diet
 - Probiotics
- Supplementation
 - Magnesium
 - Zinc
- Manual therapy



Thank You

Wow uterus. Sorry for not getting you pregnant. No need to throw a temper tantrum.



som^{ee}cards
user card