# REI REVIEW

## PART 2: ENDOMETRIOSIS

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### Definition
- Functional endometrial glands and stroma outside uterine cavity
- Chronic
  - Pain
  - Infertility
- Multifactorial inheritance

### Prevalence
- 10% reproductive age women
- 25-35% infertile women
- 70% chronic pelvic pain
- Peak 40 years of age

### Etiology

**Transplantation Theory**
- Retrograde menstruation (Sampson)
  - Higher incidence
  - Outflow obstruction
  - Earlier menarche
  - Shorter cycles
  - Menorrhagia
  - Delayed child bearing

**Stem Cells from Bone Marrow**
- Progenitor cells

**Coelomic Metaplasia**
- Peritoneal mesothelium → metaplastic transformation
Etiology

Immunologic Theory
- Alterations in cell-mediated immunity
  - NK
  - Macrophages
  - T-cells
  - B-cells

Hematogenous or Lymphatic Transport
- Distant sites

Environment
- Dioxin

Embryologic
- Aberrant migration of Mullerian tissue

Inflammatory Altered State

- Prostaglandin overproduction
- Increase COX-2
- Increase estradiol by aromatase
- Progesterone resistance
- Inflammatory cytokines
- Tumor necrosis factor alpha
- IL 1, 6, 8
- Growth factors

Clinical Presentation

- Pain
  - Dysmenorrhea
  - Dyspareunia
  - Chronic pelvic pain
- Asymptomatic
- Infertility
  - Mild, moderate, severe

Multiple studies have noted that severity of symptoms do not correlate with the extent of disease
Diagnosis

- Exam
  - Uterosacral ligament nodularity
  - Ovarian enlargement
  - Fixed uterus
- Serum markers in development
  - CA 125 nonspecific, not recommended
- Pelvis ultrasound
  - Endometrioma
- MRI
  - Homogenous hypoechoic
  - Endometriomas
  - Deep infiltrative disease
- Laparoscopy – gold standard
  - Definitive diagnosis by histology
  - Variable lesions
    - Ovary, posterior cul-de-sac, broad ligament, uterosacral ligaments, rectosigmoid colon, bladder
    - Left ovary > right ovary
    - Blue-black “powder burns”
    - Red, white, yellow, clear

Histology
- Glands and stroma
- Fibrosis
- Hemosiderin laden macrophages

ASRM Classification

- Limitations
  - Does not correlate to symptoms
  - Not a good predictor of pregnancy
Treatment Goals

- Pain control
- Prevention of disease recurrence
- Fertility preservation
- Reduction of operative interventions

Medical Treatment

- NSAIDs
  - Inhibit COX-1 and COX-2 → decrease prostaglandins
- Combined oral contraceptives – First-line mgmt
  - Decidualization and atrophy of endometrial tissue
  - Continuous vs. cyclic
  - 60-90% effective
  - Comparable efficacy as GnRHa, 6 month treatment

Medical Treatment

- Progestins
  - Decidualization
  - Norethindrone acetate 5mg/d
  - MPA 20-30mg/d
  - Depot MPA
  - Levonorgesterol-IUD
GnRH Agonist

- 75-90% effective
- 6-12 month treatment
- "Menopause-like" side effects
- Add-back therapy
  - For vasomotor symptoms and bone preservation
  - Initiate with GnRH-a
    - Norethindrone acetate 5mg/d
    - Estradiol 25ug transdermal patch/wk
    - Conjugated equine estrogen 0.625 mg/d

Other Medical Options

- Aromatase Inhibitor
  - Letrozole 2.5mg/d
  - Anastrozole 1mg/d
  - Ovarian cysts, bone loss, off label use
- Danazol
  - Hyperandrogenic side effects
- Non Peptide GnRH antagonist (Orlissa)
  - 150mg/d up to 24mo
  - 200mg BID up to 6mo

Conservative Surgical Management

- Indication
  - Need for definitive diagnosis
  - Medical therapy failed
  - Persistent adnexal mass
  - Pelvic organ dysfunction: bladder, bowel
- Remove via excision/ablation
Endometriomas

- Drainage and cauterization vs. Cystectomy
  - Both more effective than simple drainage
  - Drainage and cauterization
    - Higher recurrence rate
  - Cystectomy
    - Less recurrence
    - Reduction of ovarian reserve

Other Considerations

- Laparoscopic Uterosacral Nerve Ablation LUNA
  - Disrupt the efferent nerve fibers
  - Does not appear to offer additional benefits
- Presacral Neurectomy
  - Interrupt the sympathetic innervation to the uterus
    - Level of the superior hypogastric plexus
    - Treatment for midline pain
    - Technically challenging

Other Considerations

- Robotics
  - DIE
    - Bowel
    - Bladder, ureter
Other Considerations

- Add medical therapy postoperatively for add’l benefit
- Definitive surgery
  - Refractory to medical and conservative surgery
  - Hysterectomy +/- BSO + remove endometriosis
  - HRT with estrogen is not contraindicated after
    - Estrogen + Progestin for possible residual disease

ENDOMETRIOSIS AND INFERTILITY

Clinical Presentation

- Pain
  - Dysmenorrhea
  - Dyspareunia
  - Chronic pelvic pain
- Infertility
- Menstrual Irregularities
- GI involvement

Where Endometriosis Impacts Fertility

- A. Systemic inflammation may prevent embryos from implanting in the uterine wall
- B. Scared fallopian tubes may not pick up egg after ovulation
- C. Sperm damaged by an inflamed reproductive tract
- D. Scarring in tube may prevent sperm and egg from meeting
- E. Scarring in tube may prevent embryos from progressing to the uterus

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Fertility Treatment

- Medical
  - No evidence improves fertility
  - Ovulation suppression will decrease fertility
- Surgery
  - Minimal/Mild, Stage I-II
  - Moderate/Severe, Stage III-IV

Surgery for Stage I-II

- Two RCTs
- NNT if endometriosis
  - 12 surgeries for 1 live birth
- 30% of asymptomatic patients will have endometriosis
- Overall NNT
  - 40 surgeries for 1 live birth

Surgery for Stage III-IV

- No RCTs
- Case series estimating success to 25% after 36 months
- Complications
  - Surgical
    - Damage to ovarian reserve
- Endometriomas
  - Removal does not improve ART outcomes
  - Consider operating for symptom relief, large >4cm or for ovarian access

Canadian Trial 1997
Superovulation IUI

- Clomiphene or Gonadotropin
  - Low success, NNT 14
- Gonadotropin
  - Increased risk of high order multiples

ART

- IVF overcomes most detrimental effects
- High success >45% if <age 35
  - May be lower compared to other fertility factors
- Role of GnRHa adjuvant therapy

Pregnancy Outcomes

- Higher incidence
  - Preterm delivery
  - Preeclampsia
  - Antepartum bleeding
  - Placental complications
  - C-section
QUESTIONS?
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