ENDOMETRIOSIS

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

■ Pain
■ Infertility
Etiology

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

Coelomic Metaplasia
- Peritoneal mesothelium → metaplastic transformation

Stem Cells from Bone Marrow
- Progenitor cells

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.

Menstrual Irregularities
- Premenstrual spotting 15-20%
- Heavy menstrual bleeding
- GI involvement 5%
- 70% Rectum/sigmoid

Bladder involvement

Diagnosis

- **Exam**
  - Uterosacral ligament nodularity
  - Ovarian enlargement
  - Fixed uterus
- **Serum markers in development**
  - CA-125 nonspecific, not recommended
- **Pelvis ultrasound**
  - Endometrioma
  - Homogenous hypoechoic
- **MRI**
  - 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

- Add medical therapy postoperatively for add’t 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. Reduced egg supply & quality
B. Scarred 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. Scarred tube may prevent embryo from progressing to the uterus
F. Systemic inflammation may produce an interferon from implanting in the uterine wall
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 GnRH adjuvant therapy

Pregnancy Outcomes

- Higher incidence
  - Preterm delivery
  - Preeclampsia
  - Antepartum bleeding
  - Placental complications
  - C-section
Fertility Factors:
- Age
- Duration
- Pain
- Stage

Questions?
hcottrell@ivf-mi.com

Thank you!