Endometriosis

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Endometriosis: Challenges and Hope

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Disclosures

Advisory Board: Abbvie, Allergan

Endometriosis

Presence of endometrial glands and stroma outside the uterus

Features:
- Estrogen-dependent
- Inflammation
- Angiogenesis
- Cellular proliferation

Bulan S.E. NEJM 2009

COMMON LOCATIONS

NOT SAME AS NORMAL ENDOMETRIUM
Multifactorial Etiology

- Retrograde menstruation
- Coelomic mtaplasia
- Lymphatic and/or vascular metastasis
- Transformation of embryonic rests
- Altered cellular immunity
- Genetic
- Hormonal
- Environmental

Endometriosis

- Affects 10% of reproductive age women (higher prevalence in women with infertility or pain)
- Chronic, relapsing disorder, though not always progressive
- Great economic impact (1.8 Billion/yr Canada, 18-22 billion/yr US)
- Pelvic pain is the most common presenting symptom and has the most important clinical burden:

  Requires long-term plan for management

Fraser IS. J Hum Reprod Sci 2008
Gao et al., Fertil Steril 2006
Simoens et al. Hum Reprod Update 2007
Management of Pain Associated With Suspected Endometriosis

Suspected endometriosis

CHCs (preferably administered continuously) Or progestins

Laparoscopy for diagnosis and treatment

Failure of surgical or medical therapy (after 3-6 month trial)

1. Reconsider diagnosis: additional testing ± non-gynecologic referrals
2. Chronic pain management and multidisciplinary support

Recurrence rates after surgery

Source, year  No. of patients
Redwine, 1991  359
Crosignani et al., 1996  149
Busacca et al., 1999  141
Abbott et al., 2003  176
Jones & Sutton et al., 2003  73
Vignali et al., 2005  115
Vercellini et al., 2006  425
Wykes et al., 2006  62
Ferrero et al., 2007  68
Cheong et al., 2008  486
Shakiba et al., 2008  107

Vercellini et al, Hum Reprod Update 2009
Medical Treatment of Endometriosis Pain

• Available hormonal suppressive treatments are equally effective but have different costs and side-effects (CHC, progestins, danazol, GnRH ag)
• Post-operative hormonal suppression decreases recurrence of dysmenorrhea (CHC, LgIUS) and endometriomas (CHC)
• Ideal treatment would target inflammatory, angiogenic and neuropathic process while allowing ovulation/pregnancy

Prentice et al Cochrane Database Syst Rev 2000
Davis et al Cochrane Database Syst Rev 2007
Vercellini et al Hum Reprod 2011

Endometriosis-Associated Pelvic Pain: A Clinical Puzzle

• Pain does not occur in all patients with endometriosis
• Pain pattern can vary in individual patient and between patients
• Pain not related to disease burden/ stage
• Treatments targeted to endometriosis are not always successful at eliminating pain
• Some women develop chronic pelvic pain
Integrated approach to endometriosis associated persistent pain

- **Endometriosis**
  - Menstrual suppression
  - Surgery

- **Central Sensitivity**
  - Pain education
  - Mindfulness/CBT
  - Physiotherapy (PT)
  - Sleep restoration
  - Mood treatment
  - Neuromodulators

- **IBS**
  - Diet
  - PT
  - Medications

- **PBS**
  - Diet
  - PT
  - Medications

- **Myofascial**
  - Trigger point injections
  - PT

Allaire C. et al. JEPPD 2017
Patient and Provider Driven Research Priorities

1. Can a cure be developed for endometriosis?
2. What causes endometriosis?
3. What are the most effective ways of educating healthcare professionals throughout the healthcare system resulting in reduced time to diagnosis and improved treatment and care of women with endometriosis?
4. Is it possible to develop a noninvasive screening tool to aid the diagnosis of endometriosis?
5. What are the most effective ways of maximising and/or maintaining fertility in women with confirmed or suspected endometriosis?

6. How can the diagnosis of endometriosis be improved?
7. What is the most effective way of managing the emotional and/or psychological and/or fatigue impact of living with endometriosis (including medical, nonmedical, and self-management methods)?
8. What are the outcomes and/or success rates for surgical or medical treatments that aim to cure or treat endometriosis, rather than manage it?
9. What is the most effective way of stopping endometriosis progressing and/or spreading to other organs (e.g., after surgery)?
10. What are the most effective nonsurgical ways of managing endometriosis-related pain and/or symptoms (medical/non medical)?

Horne Andrew W et al. The Lancet, 2017

The purpose of EPHect is to enable large-scale, cross-centre, epidemiologically robust research into the causes of endometriosis, novel diagnostic methods, and better treatments, through the development of an international consensus on:

- Standardized detailed clinical and personal phenotyping (phenome) data to be collected from women with endometriosis and controls, to improve patient and disease characterization

- Standard Operating Procedures (SOPs) for banking of biological samples from women with endometriosis and controls, with respect to collection, transport, processing, and long-term storage

Fertil Steril 2014; 102(S)
Hope from Big Data: 18 Centers in 11 Countries

Oral abstract:

Sukhbir Singh, MD
“Primary efficacy and safety results from two double-blind, randomized, placebo-controlled studies of elagolix, an oral gonadotropin-releasing hormone antagonist, in women with endometriosis-associated pain”

Katy Vincent, MD
“Associated pain: why should we consider the CNS?”

Robert Taylor, MD, PhD
“Endometrial nerves, cytokines and endometriosis-associated pain”

Stacy Missmer, ScD
“Epidemiology of endometriosis and pelvic pain”