

EndoShare 2019: Personalizing Treatment Choices

Stephen Cohen, MD, FACOG
Andrea J. Singer, MD, FACP, CCD



Identified or perceived conflict of interest has been resolved
in accordance with ACCME guidelines.

1

Objectives

- Identify factors that delay an accurate and patient-centered diagnosis of endometriosis
- Describe validated, guidelines-recommended symptom assessment tools that can be used in clinical practice to initiate early intervention
- Employ approaches and tools for endometriosis care that invite patient preferences, goals, and values into clinical decision making
- Implement a personalized treatment plan for endometriosis-associated pain that consider individual clinical, biologic, and health-related quality of life measures as important outcomes
- Differentiate benefits and disadvantages of various therapies for managing endometriosis when developing a personalized care plan

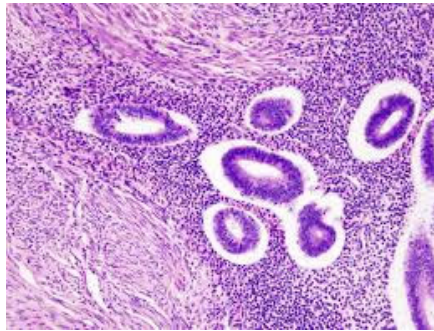


2

EndoShare 2019: Personalizing Treatment Choices

Definition of Endometriosis

- Endometrial glands and/or stroma beyond the endometrial cavity



https://radiopaedia.org/users/frank_gaillard

Women's Health



Annual Visit®



3

Endometriosis: Fast Facts and Impact

- It is estimated that **10%** of women have endometriosis¹
- Traditionally a diagnosis occurs in the 2nd and 3rd decades, but **1/3 experience first symptoms before age 15**²
- Annual healthcare cost estimate: \$2,801/patient
- Extrapolating these findings, the annual cost of endometriosis was **\$22 billion** in 2002
- Clinical studies show that endometriosis symptoms can disrupt work and home lives and contribute to physical and emotional suffering^{4,5,6}

1. Soliman AM, et al. Adv Ther. 2018;35:408.
2. Ballweg. Clin Obstet Gynecol, 2004; 18:201.
3. Simoens S et al. Hum Reprod Update. 2007;13:395-404.
4. Simoens S, et al. Hum Reprod. 2012;27(5):1292-1299.
5. Fourquet J, et al. Fertil Steril. 2010;93(7):2424-2438.
6. DeGraff AA, et al. Hum Reprod. 2013;28(10):2677-2685.

Women's Health



Annual Visit®



4

EndoShare 2019:
Personalizing Treatment Choices

Endometriosis: Symptoms

- Most Common Pain:
 - Dysmenorrhea (73%)
 - Non-menstrual pelvic pain - NMPP (57%)
 - Dyspareunia (43%)
- Infertility
 - GI: constipation, diarrhea, hematochezia, melena
 - GU: hematuria, dysuria, frequency, urgency

Fuldeore MJ. Gynecol Obstet Invest 2016;82(5):453-461.

Women's Health



Annual Visit[®]



5

Differential Diagnosis

Gastrointestinal Etiologies of NMPP

- IBS (irritable bowel syndrome)
- IBD (inflammatory bowel disease)
- Celiac disease
- Chronic constipation
- Diverticular disease
- Cancer (colon)

Urological Etiologies of NMPP

- Interstitial Cystitis (IC)
- Recurrent UTI
- Stone(s)
- Urethral Syndrome

Women's Health



Annual Visit[®]



6

EndoShare 2019:
Personalizing Treatment Choices

Obtaining Important Information: Chief Complaint, History of Present Illness and Physical Exam

- What is the pain like?
- Where is the pain?
- When did it start?
- What makes it worse?
- What makes it better?
- Is it cyclic?
- Effect of food, intercourse, bowel movements, urination
- Evaluate history of prior abuse
- Full review of symptoms: what else is associated with the pain?

Women's Health



Annual Visit®



7

ASRM Recommendation



ASRM recommends utilizing medical management before moving to multiple surgeries as key long-term treatment strategies.

[“Endometriosis is best viewed primarily as a medical disease with surgical back-up”](#)

Practice Committee of ASRM; Fertil Steril 2015;104(2):498.

Women's Health



Annual Visit®



8

EndoShare 2019:
Personalizing Treatment Choices

Opioids and Endometriosis

- Opioid pain medications and antidepressants are commonly prescribed to patients for chronic non-cancer pain
 - Little evidence exists for their effectiveness in most pain states, including chronic pelvic pain
- Guidelines do not discuss opioids for treating endometriosis pain
- A cross-sectional survey of opioid prescriptions by a national sample of ACOG Fellows found:
 - Respondents reported prescribing a median of 26 (5-80) pills per patient across all indications combined
 - 18% prescribed opioids for chronic pelvic pain of unknown cause

Steele A. Obstet Gynecol Clin North Am. 2014;41:491-501.
Madsen AM et al. Obstet Gynecol. 2018;131:150-157.

Women's Health



Annual Visit®



9

Endometriosis: Currently Available Medical Options

- NSAIDs
- COCs: continuous vs. cyclic
- Progestins: oral, injectable and intrauterine
- Danazol
- GnRH agonists
- GnRH antagonists

Women's Health



Annual Visit®



10

EndoShare 2019:
Personalizing Treatment Choices

GnRH Agonist Therapy

- Commonly reported side effects:
 - Breakthrough bleeding
 - Hot flushes and night sweats
 - Vaginal dryness
 - Mood alteration
 - Bone mineral density (BMD) loss
 - Diminished libido
- Minimizing side effects while maintaining effectiveness
 - Goal of add-back therapy

Women's Health



Annual Visit®



11

Treatment of Endometriosis-Associated Pain: Elagolix

- In July 2018, the FDA approved elagolix as the first oral GnRH antagonist specifically developed for the treatment of moderate to severe pain associated with endometriosis.

Women's Health



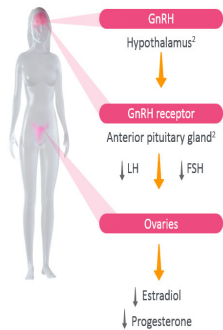
Annual Visit®



12

EndoShare 2019:
Personalizing Treatment Choices

Antagonist Effect: Elagolix Binds Competitively to the GnRH Receptor^{1,2}



FSH: follicle-stimulating hormone; GnRH: Gonadotropin-releasing hormone; LH: luteinizing hormone

1. Ng J, Chwalisz K, Carter DC, Klein DC, J Clin Endocrinol Metab. 2017;102(5):1683-1691.
2. Bulun SE, N Engl J Med. 2009;360(3):268-279.

Antagonist Effect^{1,2}



- Competes with endogenous GnRH for GnRH receptor occupancy in the anterior pituitary and blocks receptors upon binding, so fewer receptors are activated¹
- Suppresses LH and FSH in a dose-dependent manner¹
 - LH and FSH suppression begins within hours of administration* and is reversible upon discontinuation¹
- Leads to decreased serum levels of the ovarian sex hormones estradiol and progesterone¹

Women's Health



Annual Visit®



GnRH Agonists and Antagonists: *A Primer on their Mechanisms of Action*



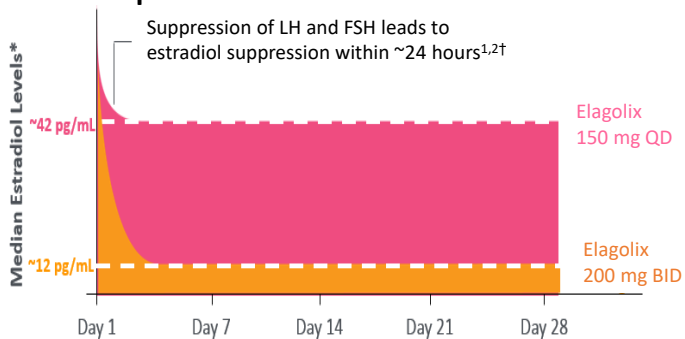
Women's Health



Annual Visit®



How Elagolix Works: Dose-Dependent LH and FSH Suppression^{1,2}



*Average 28-day cycle is for illustrative purposes only. Estradiol levels can vary throughout the cycle and individual responses may vary. Twenty-one-day results have been extrapolated to 28 days.

†Does not imply onset of efficacy during this time.

FSH: follicle-stimulating hormone
GnRH: Gonadotropin-releasing hormone
LH: luteinizing hormone

1. Ng J, Chwalisz K, Carter DC, Klein DC, J Clin Endocrinol Metab. 2017;102(5):1683-1691.
2. Bulun SE, N Engl J Med. 2009;360(3):268-279.

Women's Health



Annual Visit®



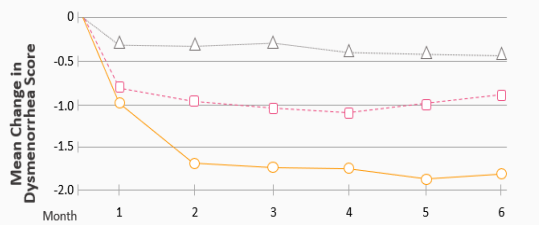
Dysmenorrhea Pain Scores

(Pain = 2.2)

MEAN CHANGE FROM BASELINE IN DYSMENORRHEA PAIN SCORES¹

Pain score = 2.2

Placebo-controlled ELARIS EM-1^{a,b}



	1	2	3	4	5	6
Placebo (n)	372	348	329	316	299	288
150 mg (n)	248	232	226	219	202	198
200 mg (n)	245	221	213	198	191	182

△ Placebo □ Elagolix 150 mg QD ○ Elagolix 200 mg BID

Adapted from: Taylor HS, et al. N Engl J Med. 2017;377:28-40.

Women's Health



Annual Visit®



Medical Therapies Under Investigation

- Aromatase inhibitors (*need for add-back given vasomotor symptoms/bone loss; concern for thrombosis with currently available agents*)
- Selective progesterone receptor modulators
- Immunomodulators
- Angiogenesis inhibition
- Metalloproteinase inhibition
- Estrogen receptor inhibition
- Additional unapproved GnRH antagonists:
(*OBE2019; Relugolix; ASP1707*)

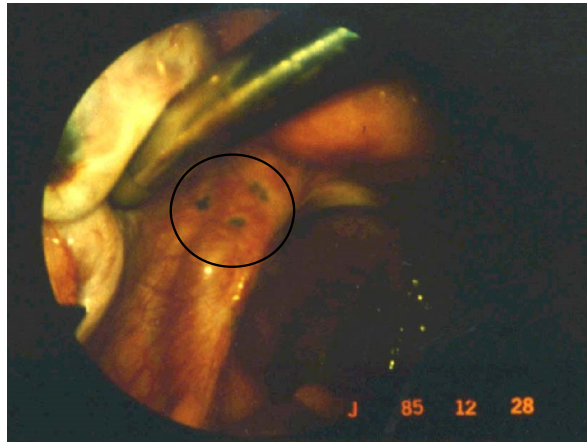
Women's Health



Annual Visit[®]



17



Classic powder burn lesion, ovarian disease and thickening of the uterosacral ligament

Women's Health



Annual Visit[®]



18

EndoShare 2019:
Personalizing Treatment Choices

Visualization for Diagnosing Endometriosis

- 70% of women with pelvic pain¹
- 25% of biopsies of normal peritoneum³
- 7% of women with no symptoms²
- PPV of visualization 43-45%^{4,5}

1. Koninckx et al, Fertil Steril 1991;55:759-65.
2. Rawson JM, J Reprod Med 1991;38:545-547.
3. Murphy et al, Fertil Steril 1986;46:522-4.
4. Walter et al, Am J Obstet Gynecol 2001.
5. Stratton et al, Fertil Steril 2002; 78:461-7.

Women's Health



Annual Visit[®]



19

How Can We Work Together with Our Endometriosis Patients?

**Optimizing Care for Women with Endometriosis:
Shared Decision Making and Patient-Centered Care**

Women's Health



Annual Visit[®]



20

EndoShare 2019:
Personalizing Treatment Choices

Evaluation of a Woman with CPP

“Be quiet and listen to the patient. She is trying to tell you what is wrong”

Sir William Osler



Women's Health



Annual Visit[®]



21

Potential Benefits of Effective Risk Communication and Shared Decision Making

- Patients have better understanding of:
 - Disease consequences
 - Benefits of therapy
 - Potential harms of therapy
- Reduced mistrust and fear
- Better collaboration between provider and patient; improved patient experience
- Improved adherence with therapy
- Improved health outcomes and quality of life
- Possible reduced costs



EndoSHARE

www.endoshare.net

Stacey Det. al. Cochrane Database Syst Rev. 2014; 1:CD001431.
O'Connor A.M. et al. Health Aff (Millwood). 2004;Suppl Variation:VAR63-72.
Wilson S.R. et al. AM J Respir Crit Care Med. 2010;181:566-577.
Naik A.D. et al. Circulation. 2008;117:1361-1368.
Clever S.L. et al. Med Care. 2006;44(5):398-405.

Women's Health



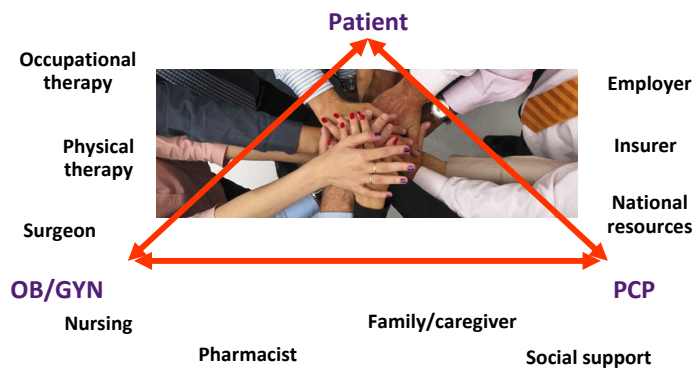
Annual Visit[®]



22

EndoShare 2019:
Personalizing Treatment Choices

Endometriosis Management: A Team Approach



Women's Health



Annual Visit®

