

# Endometriosis Update Atlantic Society, Sept 2007

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# Based on BMJ Review

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- RCT and review articles studied in Cochrane as well as Medline- no nonrandomized trials studied by C. Farquhar

# Clinical Presentation

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- Variable- some asymptomatic, some with crippling pelvic pain
- Prevalence in women without symptoms is 2-50% depending on diagnostic criteria and population studied
- Incidence is 40-60% in those with dysmenorrhea, 20-30% with subfertility

# Probability of Diagnosis

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- Severity of symptoms and probability of diagnosis increase with age
- Most common age of diagnosis is 40 in a study from a family planning clinic
- Symptoms and laparoscopic appearance do not always correlate
- ASRM has published a classification of severity based on laparoscopic findings related to infertility prognosis

# What are the Causes of Endometriosis?

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- Retrograde menstruation- still the dominant theory although not the sole explanation since it is almost universal
- Quantity and quality of endometrial cells, failure of immunological mechanisms, angiogenesis and production of antibodies against endometrial cells may have a role
- Embryonic cells may give rise to distant sites such as the umbilicus, pleural cavity, even brain

# What are Risk Factors for Endo?

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- Risk factors relate to exposure to menstruation
- Early menarche, and late menopause increase the risk
- Use of OC reduces risk

# What is the Natural History?

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- Difficult study due to the need for repeat laparoscopy
- Two studies with repeat laparoscopy after treatment in women given placebo reported that over 6-12 months, endometrial deposits resolved spontaneously in up to 1/3 of women, deteriorated in nearly half and were unchanged in the remainder
- Ref: F&S 2003:80 p 305, HR 2005;20:1993

# What Features of Hx and Px are Important for Diagnosis?

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- Recurrent dysmenorrhoea, or pelvic pain in reproductive age warrants full hx of reproduction and pelvic exam
- Cyclic nature of pain and relation to menstruation points to endo
- Often have painful voiding, defecation and dyspareunia

# Differential

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- Pelvic infection
- Problems in early pregnancy
- Ectopic
- Ovarian cyst torsion
- Appendicitis

# During Exam-May Indicate Endo

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- Tenderness in the posterior fornix or adnexa
- Nodules in the posterior fornix
- Adnexal masses
- Adolescents presenting with dysmenorrhoea do not require a pelvic exam as disease is uncommon (BMJ 2007 Feb)

# How is Endo Diagnosed?

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- TVUS can reliably detect endometrioma (cysts of endometriosis)

but failure to reveal cystic structures does not exclude the diagnosis of endometriosis

MRI is increasingly used to identify subperitoneal deposits although retroversion, endometrioma and bowel structures may mask small nodules

# Diagnosis-CA125 and Endo

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- Concentrations of CA125 are slightly raised in some women with endometriosis, the test neither excludes nor diagnoses endo and is not considered useful in establishing the diagnosis
- Threshold for surgery is unlikely to be influenced by the CA125 concentration
- Guidelines from the Royal College of O&G described CA 125 as having only limited value as screen or diagnostic test.

# Diagnosis

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- Laparoscopy is the only test that can reliably rule out endometriosis
- It is also accurate in detecting endometriosis and is considered the standard investigation

# After Diagnosis

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- Appropriate therapy may involve a multidisciplinary approach with pain clinic and counselling
- Important to involve the woman in all decisions, be flexible in diagnostic and therapeutic thinking
- Maintain a good relationship with the woman
- Seek advice where appropriate from more experienced colleagues

# What are the Indications for Laparoscopy?

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- Many young women experience dysmenorrhoea (60-70%)
- Unless there are other features to indicate endometriosis laparoscopy is not recommended
- Some women need further investigation to guide management

# Indications for Scope

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- Recommended dysmenorrhoea management in adolescents remains NSAIDs and OC
- Lack of measurable pain relief with these drugs is an indication for scope. Also
- Severe pain over several months
- Pain requiring systemic therapy
- Pain resulting in days off work or school
- Pain requiring admission to hospital

# What are Effective Medical Treatments for Endo Pain?

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- OC, Progestogens, Androgenic Agents, GnRH analogues.
- All suppress ovarian activity and menses and atrophy of endometrial implants, although extent varies
- Few RCT of treatment vs placebo but many trials compared different types of Rx
- All medical treatments are similarly effective in relieving pain during treatment

# Side Effects and Cost

## Decide Choice of Treatment

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- Progestogens-associated with irregular bleeding, wt gain, mood swings and decreased libido
- Danazol can induce skin changes, wt gain and occasionally voice deepening- infrequent use now
- GnRH analogues dramatically reduce estrogen concentrations cause menopausal symptoms and loss of bone density(reversible)
- In RCT Depo MPA vs GnRH agonist bone loss was less with progestin

# After Medical Treatment

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- Recurrence of painful symptoms after 6 mo of medical therapy may be as high as 50% in the 12-24 mos after stop treatment
- Recurrence may be due to large lesions responding poorly to medical therapy
- Generally accepted: endometriomas do not respond to medical therapy- temporary clinical relief may be achieved

# Mirena

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- Can be used in dysmenorrhoea and endometriosis as well as heavy menstrual bleeding
- One study: only 10% of women with Mirena after surgery for endometriosis had moderate or severe dysmenorrhoea compared with 45% of women who had surgery only
- Ref: FS 2003;80:305

# Mirena vs GnRH Analogues

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- Trial of 82 women with endometriosis the LNG system had similar effectiveness to GnRH analogues
- Potential for long term use of this system if the woman doesn't want to conceive
- Has been used in deep rectovaginal disease

# New Therapy

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- Aromatase inhibitors may have a therapeutic role in endometriosis
- Inhibit estrogen production selectively in endometriotic lesions without affecting ovarian function

# Surgery vs Medical Treatment Efficacy

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- No RCT compared medical vs surgical treatment for management of endometriosis
- Decision about medical or surgical treatment at time of diagnosis depends
  - On patient's choice
- Availability of laparoscopic surgery
- Desire for fertility
- Concerns about long term therapy

# What are the Effective Surgical Strategies?

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- Can be performed laparoscopically or open
- Requires excision or ablation by laser or diathermy or (both) of the endometriotic tissue with or without adhesiolysis

# Laparoscopic Surgery

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- Few trials of laparoscopic treatment
- Surgical excision of endo results in improved pain relief and improved quality of life after 6 mo compared to diagnostic laparoscopy only
- In one trial of laparoscopic treatment with LUNA more than 50% of women had pain improvement persisting up to 5 years
- About 20% of women do not report any improvement after surgery

# Surgical Modalities

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- No RCT's compare laser vs electrosurgical removal of endo
- Only 1 small trial with inconclusive results compared excision vs ablation

# How Often Does Endo Recur After Surgery?

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- Recurrence of endo is common after surgery
- Even with experienced laparoscopic surgeons cumulative rate of recurrence after 5 years is nearly 20%
- Another study reported recurrence of dysmenorrhoea in almost 1/3 of women within a year of laparoscopic surgery in women who received no other treatment

# What is the Role of Uterine Nerve Ablation at Scope?

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- RCT of laparoscopic uterine nerve ablation at the time of scope excision of endo compared with laparoscopic excision only showed **no evidence** of benefit although there was limited evidence of benefit with presacral neurectomy
- Ref: Cochrane Database Rev 2005; (4):CD004992

# What is the Evidence for Surgery in Women with Endometrioma?

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- RCT comparing excision vs drainage and ablation for endometrioma >3cm reported that recurrences were reduced and subsequent spontaneous pregnancy increased in the women who underwent excision Ref Cochrane Database Rev 2005(3):CD004992
- Although excisional surgery of the capsule leads to removal of normal ovarian tissue and could result in decreased ovarian reserve
- Recurrence of symptomatic

# Best Approach with Rectovaginal Disease?

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- Challenges surgically with difficult access and possibility of injury to bowel
- Long term outcomes encouraging with laparoscopic techniques- few prospective trials and no RCT

# RV Disease

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- Small 1yr Mirena study in RV endo: improvement in dysmenorrhea, pelvic pain and dyspareunia
- E&P combination vs low dose Norethindrone Acetate in 90 women with RV disease: substantial reductions at 12 mos in all types of pain without major differences. 2/3 satisfied

# Should Women have Hormonal Treatment Before Surgery?

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- Only 1 study
- No evidence of a difference in difficulty of surgery in women who had received preop hormonal treatment

# Should Women have Hormonal Treatment after Conservative Surgery?

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- No evidence of improved pain relief with postop hormonal treatment (including danazol, GnRH analogues, OC, and MPA) up to 24 months after surgery
- Studies are small and there is insufficient followup to rule out a benefit

# What are the Effects of Hormonal Treatment after Oophorectomy with or without Hysterectomy

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- No evidence of increased rates of recurrence in women who had both ovaries removed and who were given 4 years of combined hormone therapy but the study was underpowered to detect clinically important differences

# What is the Impact of Endometriosis on Fertility?

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- Although pain management may be more immediate issue, long term fertility outcome should not be overlooked
- Systematic review of medical treatment for women with infertility and endometriosis did not find evidence of benefit and it is not recommended for women trying to conceive

# Endo and Fertility

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- Systematic review of laparoscopic treatment of mild/minimal endometriosis in sub fertility suggested an improvement in pregnancy rate in 9-12 mos after surgery
- 2nd systematic review of laparoscopic excision compared to ablation of endometriomas reported a 5x increase in pregnancy rate. Still ovarian reserve concerns.

# Endometriomas and ART

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- Impact of endometriomas on ART
- ESHRE recommends surgery if endometriomas are  $\geq 4$  cm

# GnRH Agonist and IVF

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- Downregulation with GnRH agonists for 3-6 mo before starting IVF quadruples the odds of clinical pregnancy
- Early referrals to centres of excellence and early treatment of infertility should always be considered in these patients

# Conclude

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- Endo should be suspected in any women of reproductive age who presents with dysmenorrhea or chronic pelvic pain
- Only laparoscopy can reliably identify endo
- If endo is diagnosed at the time of laparoscopy, laparoscopic surgery should be the first choice of treatment especially in young women of reproductive age with an endometrioma

# Conclude

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- In women with endometrioma, consider stripping cyst wall..
- No evidence of benefit of post op medical treatment but LNG IUS has potential for longterm use
- In women who wish to conceive surgical rather than medical treatment should be offered.

# Best References

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