Endometriosis

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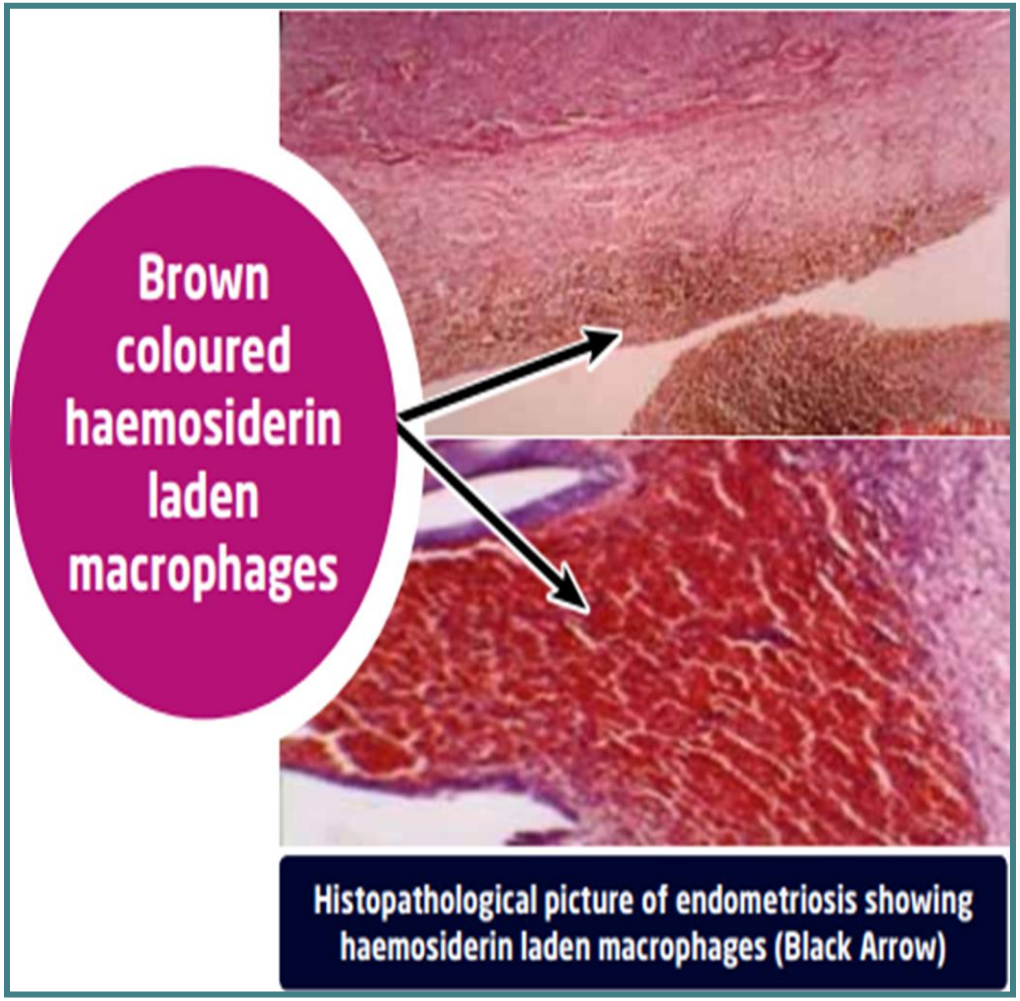
Definition

- Its an inflammatory disease associated with pelvic pain or infertility
- Its a proliferative, oestrogen-dependent disorder with growing evidence of progesterone resistance
- characterized by lesions of endometrial like tissue outside the uterus(endometrial glands and stroma).
- It is a chronic disease that requires a life long management plan.

Histopathology

- Microscopically:
  - the endometrial glands and stroma are seen with <u>hemosiderin-laden macrophages</u>



Aetiology

- underlying cause is uncertain

- it is likely to be multifactorial (genetic factors ,epigenetic influences, and perhaps promoted through environmental exposures).

- Theories Beyond

1. Genetic
2. Transplantation and implantation theory (Sampson's theory of retrograde menstruation).
3. Coelomic metaplasia theory of Meyer
4. The immune tolerance or immune defect theory.
5. Embolic transport (lymphatic or vascular dissemination)
6. Other potential sources of ectopic endometrial cells include mesothelium, stem cells, Müllerian rests (e.g. prepubertal endometriosis) , bone marrow stem cells , and embryonic) vestiges.

Factors influencing

Risk factor increase the risk

- Age
- increased peripheral body fat
- greater exposure to menstruation (short cycles, long duration of menses and reduced parity
- **environmental pollutant dioxin**
- **genetic predisposition**

Protective factors

- multiple births
- extended intervals of lactation
- Late menarche (after age 14 years)
- Smoking
- exercise
- oral contraceptive use (current and recent)
- Race (lower in black and Hispanic women compared with Caucasian and Asian women)

- Endometriosis is inherited as a complex genetic trait
- 6-9 times more common in the first-degree relatives of affected women than in controls
- The disease is frequently observed in monozygotic and dizygotic twins pairs
- Activation of k-RAS gene contributes to the genetic basis of endometriosis
- Stage 3–4 disease has a stronger genetic linkage than stage 1–2 disease
- The currently recognized nine endometriosis genetic loci explain only 3.5% of the heritability of endometriosis.

Prevalence

- highly variable
- estimated to be 8–10% in women in the reproductive years
- The prevalence of endometriosis ranged from 1 to 7%
- * Endometriosis has been reported in up to 40 % of adolescents with genital tract anomalies
- * Up to 50 % of women with infertility
- * Up to 70 %of women and adolescents with pelvic pain

Prevalence rates at laparoscopy for different indications

	Number of studies	Number of patients	Number with disease	Percent with disease (range)	Percent with stage I–II disease (range)
Pelvic pain	15	2 400	688	24.5 (4.5–62.1)	69.9 (61.0–100)
Infertility	32	14 971	2812	19.6 (2.1–78.0)	65.6 (16.3–95.0)
Sterilization	13	10 634	499	4.1 (0.7–43.0)	91.7 (20.0–100)

Source: Eskenazi & Warner [6]. Reproduced with permission of Elsevier.

Link to cancer

Endometriosis appears to be associated with some epithelial ovarian cancers (EOC).

- three times the risk of **clear cell EOC** and double the risk of **endometrioid** and **low-grade serous EOC** but **no** change in risk of high-grade serous or mucinous EOC.
- Activation of oncogenic *KRAS* and *PI3K* pathways and inactivation of tumor suppressor genes *PTEN* and *ARID1A* have been suggested as mechanisms for the transformation of endometriosis
- The risk of malignant transformation of endometriosis has been estimated at 1 percent for premenopausal women and 1 to 2.5 percent for postmenopausal women.
- While there appears to be an association between endometriosis and EOC, endometriosis is not considered a premalignant lesion, and screening is not recommended.
- There are no data indicating that prophylactic removal of endometriosis lesions reduces the risk of EOC. However, use of oral contraceptive pills decreases the risk of ovarian cancer in all users.
- Endometriosis-associated EOC appears to develop in younger women and has a better prognosis than most cases of EOC

Association of endometriosis with:

- Fibroids 26%
- Müllerian anomalies 20%
- Cancer
- ✓ Ovarian malignancy 1.3-1.9%
- ✓ breast cancers
- ✓ cutaneous melanoma
- ✓ decreased risk of cervical cancer
- asthma and some autoimmune atopic diseases
- Atherosclerosis and cardiovascular disease
- Endometriosis appears to negatively impact pregnancy outcome
- ✓ preterm delivery
- ✓ APH
- ✓ PE
- ✓ CS
- ✓ rare occurrences of intra-abdominal bleeding from endometriotic lesions requiring urgent surgery)

NATURAL HISTORY

- Disease progressed in 29 – 45 %of untreated women.
- Regressed in 22 - 29 %.
- Remained stable in 33 - 42 %.

Clinical manifestations

Symptoms

- The peak prevalence of endometriosis occurs in women 25 to 35 years of age.

1. pelvic pain (including dysmenorrhea and dyspareunia) = 80%.
2. Infertility =25%
3. An ovarian mass =20%.
4. incidentally
5. Others include bowel and bladder dysfunction, abnormal uterine bleeding, low back pain, or chronic fatigue, although these symptoms are less common.

- Symptoms can occur alone or in combination.
- Combination increase the likelihood of endometriosis.

Physical examination

- variable and depend upon the location and size of the implants.
- Findings suggestive of endometriosis include

1. tenderness on vaginal examination
2. nodules in the posterior fornix
3. adnexal masses
4. immobility or lateral placement of the cervix or uterus.
5. Rarely, an endometriosis lesion will be visualized on the cervix or vaginal mucosa.

Laboratory finding

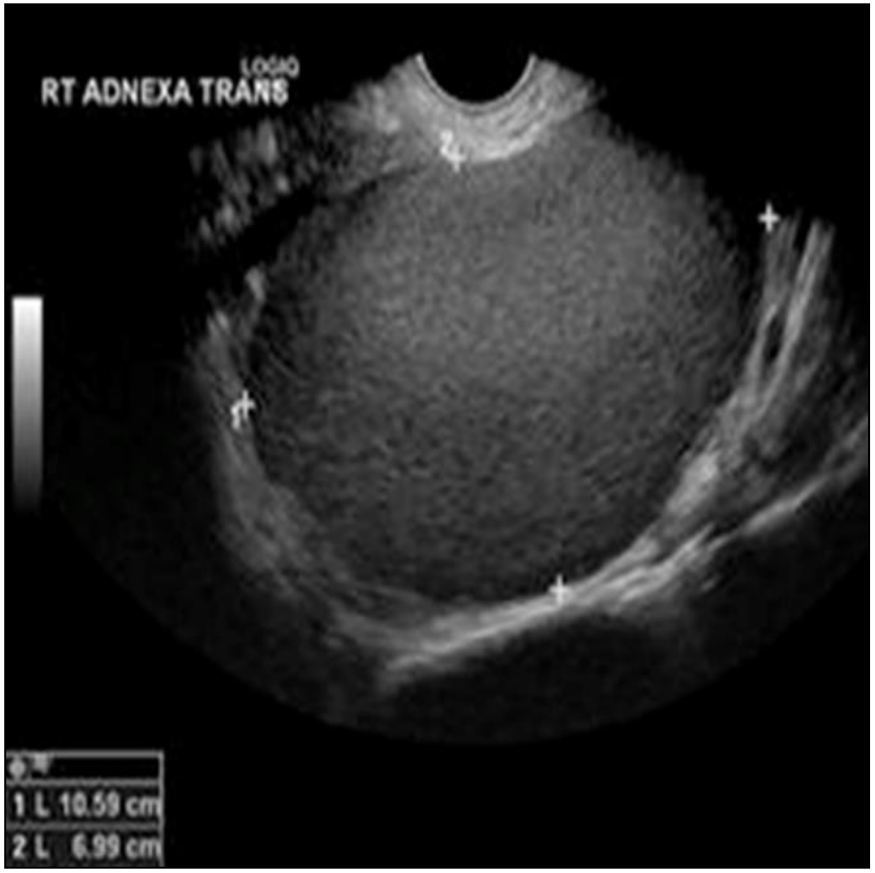
- There are no pathognomonic laboratory findings for endometriosis.
- (CA) 125 concentrations can be elevated (greater than 35 units/mL).
- serum CA 125 concentrations are not routinely ordered in women being evaluated or treated for endometriosis.
- The detection of endometrial nerve fiber antigens (protein gene product, PGP-9.5) showed promise as a replacement test in most studies but could not be reliably detected in all settings

Imaging - US

Ovarian cysts (Endometriomas)

- The GDG recommends that clinicians base the diagnosis of ovarian Endometrioma in premenopausal women on the following:
  1. ground glass echogenicity
  2. one to four compartments
  3. no papillary structures
  4. detectable blood flow
- Sonographic imaging of Endometrioma & hemorrhagic cyst overlap, hence, a follow up US can be done after 6-12 weeks.

US

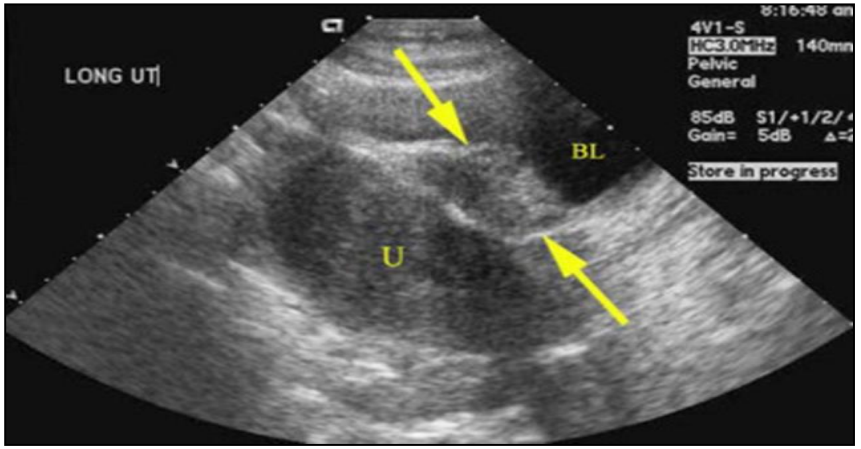


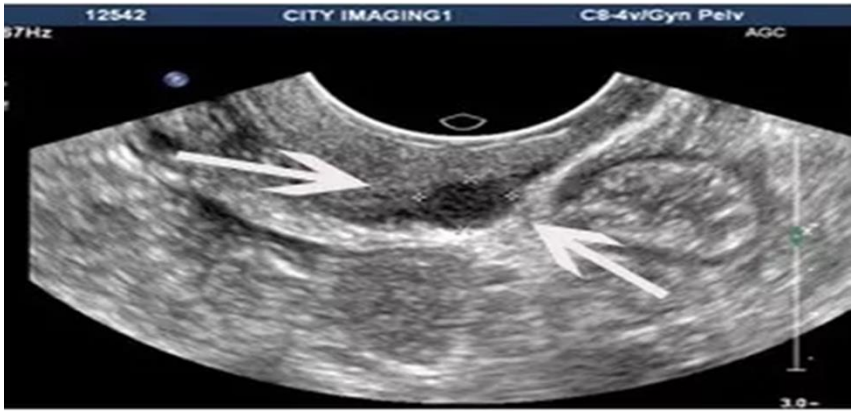
Imaging - US

Nodules of the rectovaginal septum, and bladder nodules

- These findings are typically seen with
  1. transvaginal ultrasound
  2. magnetic resonance imaging (MRI).

US



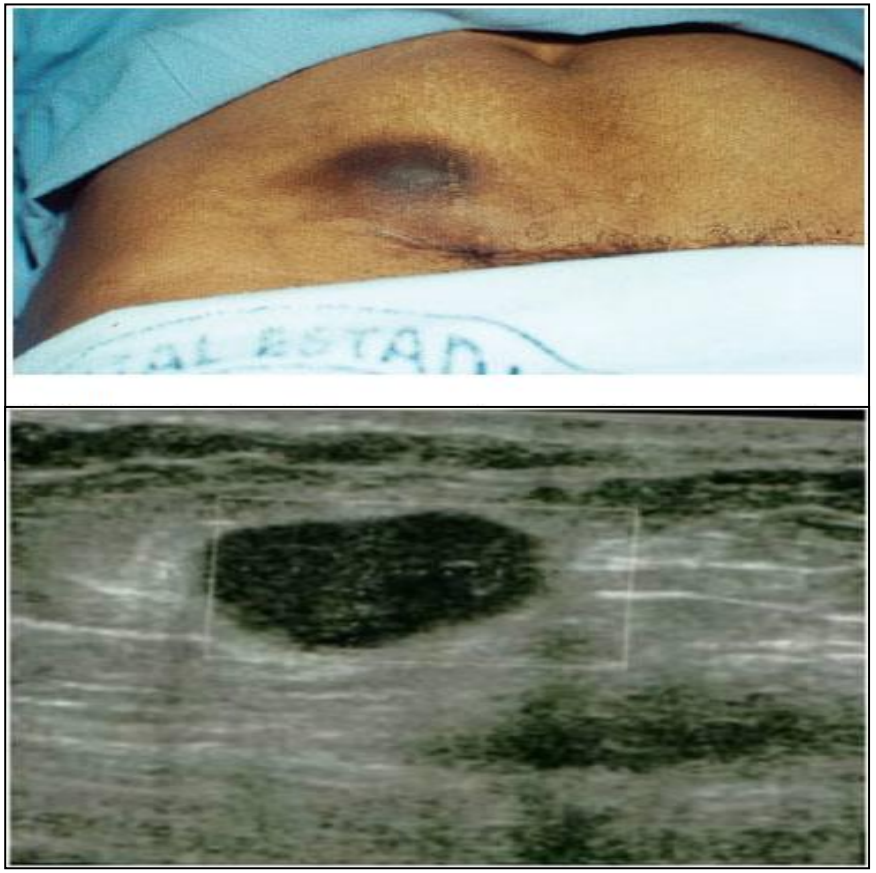


Imaging - US

Abdominal wall endometriosis

- appears as:
  - ✓ hypoechoic
  - ✓ Vascular
  - ✓ and/or solid mass
  - ✓ cystic changes
  - ✓ Margins are irregular, often speculated, and may appear to infiltrate adjacent tissues

Clinical & US

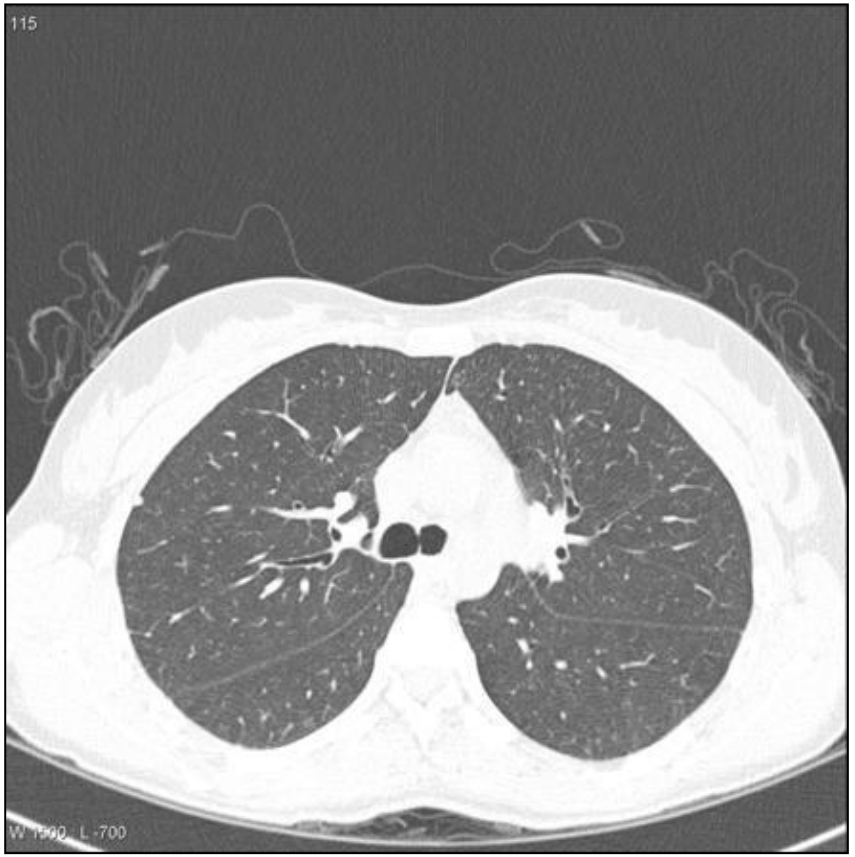


Imaging - CT

Thoracic endometriosis

- Thoracic endometriosis can be identified on computed tomography and MRI studies.
- MRI will accurately diagnose thoracic endometriosis in up to 95 percent of cases

CT

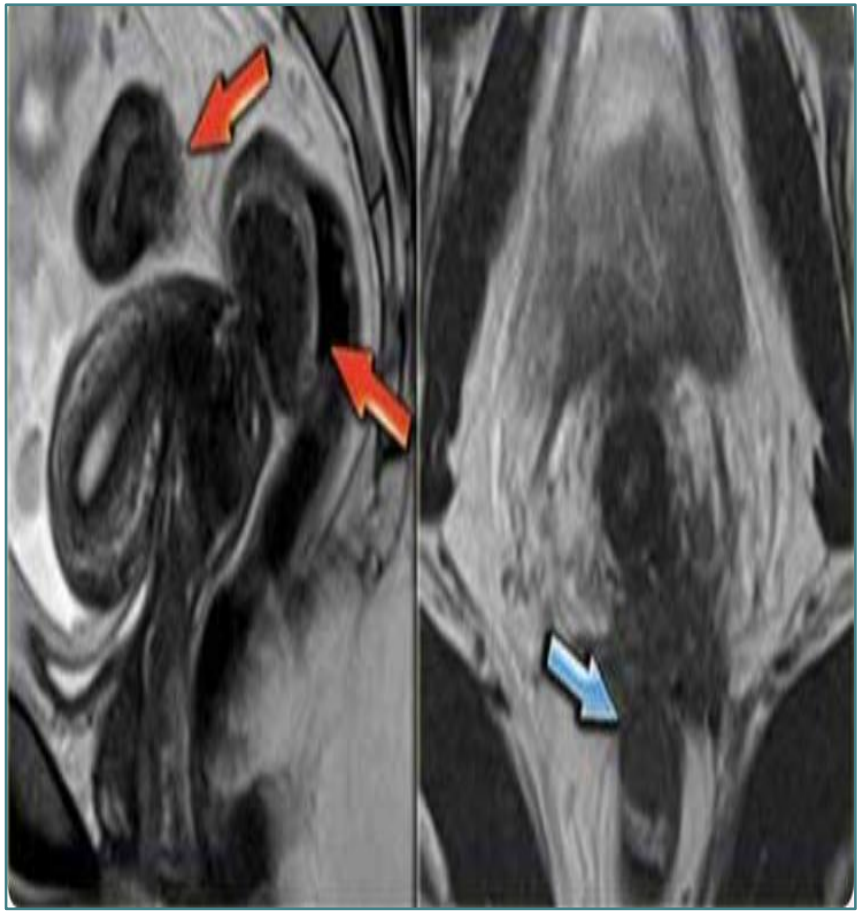


Imaging – MRI

MRI

- MRI can be helpful for detection and differentiation of ovarian Endometrioma form other cystic ovarian masses.
- MRI detects only 30-40% peritoneal lesions observed at surgery.
- It helps to differentiate between acute hemorrhage and blood clots.
- The blood clots in Endometrioma are homogenous and have high signal intensity on T1-weighted images and hypo intense on T2 weighted images.
- Acute hemorrhage has low intensity on both T1 and T2 weighted images.
- MRI is also helpful in assessing Endometriomas for enhancing mural nodules and for restricted diffusion in those suspected of undergoing malignant transformation

MRI



Diagnosis

- Endometriosis is definitively diagnosed by histologic evaluation of a lesion biopsied during surgery (typically laparoscopy).
- While visual confirmation of endometriosis without biopsy is considered diagnostic by some experts, visual confirmation alone is of limited value because the accuracy is impacted by the surgeon's expertise
- Definitive diagnosis of endometriosis is often delayed because the symptoms of endometriosis are

1. Vague
2. overlapped with a number of gynecological and gastrointestinal processes
3. surgical diagnosis entails risk.

Diagnosis

presumptive diagnosis (low-invasive diagnosis)

- Use combination of the low-invasive diagnostic tests including

1. clinical history
2. examination findings
3. imaging and/or
4. biomarkers

- The diagnostic test accuracy research to date suggests utility of the combination of

1) serum IL-6 with endometrial PGP9.5
2) TVU with serum CA-125 level (at cut-off >35IU/L)

- Other tests might have utility as triage tests:

1. high sensitivity which, if negative, rule out endometriosis (so-called SnOUT triage tests)
2. high specificity that, if positive, can raise the suspicion of, or rule in, endometriosis (so-called SpIN triage tests).

non-surgical diagnosis

- this approach is useful only for clinicians with significant skill in the examination, US , and cystoscopy.

1. US finding of ovarian Endometrioma.
2. Visual inspection of the posterior vaginal fornix and biopsy of rectovaginal lesions.
3. Cystoscopy evaluation and biopsy of detrusor lesions.
4. Physical examination findings of rectovaginal endometriosis that are confirmed with imaging.

Can we start treatment ??????

- A clinical diagnosis can be sufficient to initiate therapy that is low risk and easily tolerated (eg, estrogen-progestin contraceptives).
- the presence or absence of a response to empiric treatment cannot be construed as definitive confirmation or exclusion of the diagnosis.
- Before treating with medications with a high risk of adverse effects (eg,danazole), a surgical diagnosis is advisable.

SURGICAL EXPLORATION

- Surgery, almost always laparoscopy, allows both definitive diagnosis and treatment

- A good quality laparoscopy should include systematic checking of:

1. The uterus and adnexa.
2. The peritoneum of ovarian fossae, vesico-uterine folds, Douglas and pararectal spaces.
3. The rectum and sigmoid (isolated sigmoid nodules),
4. The appendix and caecum and
5. The diaphragm.

- There should also be a speculum examination and palpation of the vagina and cervix under laparoscopic control, to check for 'buried' nodule.

Indications for surgical exploration include:

1. Diagnosis of persistent pelvic pain that does not respond to medical therapy.
2. Evaluation of severe symptoms that limit function.
3. Treatment of anatomic abnormalities, such as bladder lesions.
4. When fertility is an issue

Accuracy of laparoscopy VS. histology alone in DX of Endometriosis

- Sensitivity 98%
- Specificity 79%
- PPV 72%
- NPV 98%

Important considerations

- ✓ Women with classic endometriosis lesions at laparoscopy but negative histology are treated for endometriosis because negative biopsies can result from inadequate sampling.
- ✓ Laparoscopy that does not demonstrate visual or histologic disease is highly reliable for excluding endometriosis.
- ✓ Given that endometriosis lesions can regress in response to hormonal treatment, laparoscopy is not typically performed during or within three months of hormonal treatment to minimize the risk of under-diagnosis of disease
- ✓ **Ovoid 'low value care'** (meaning interventions with uncertain benefits and/or defined harms, or whose effectiveness is comparable with less expensive alternatives)
- ✓ **concept of 'diagnostic laparoscopy' should disappear, with laparoscopy being reserved for those women likely to benefit from laparoscopic removal of their endometriosis.**

Endometriosis phenotypes at laparoscopy

1. Superficial peritoneal lesions(typical)
2. Ovarian lesion (Endometrioma)
3. Deeply infiltrating endometriosis (DIE)

Anatomic sites

commonest site

- The ovaries
- anterior and posterior cul-de-sac
- posterior broad ligaments
- uterosacral ligaments
- uterus
- fallopian tubes
- sigmoid colon
- appendix
- round ligaments

less commonly

- Vagina
- Cervix
- rectovaginal septum
- cecum& ileum
- inguinal canals
- perineal scars
- urinary bladder
- ureters
- umbilicus

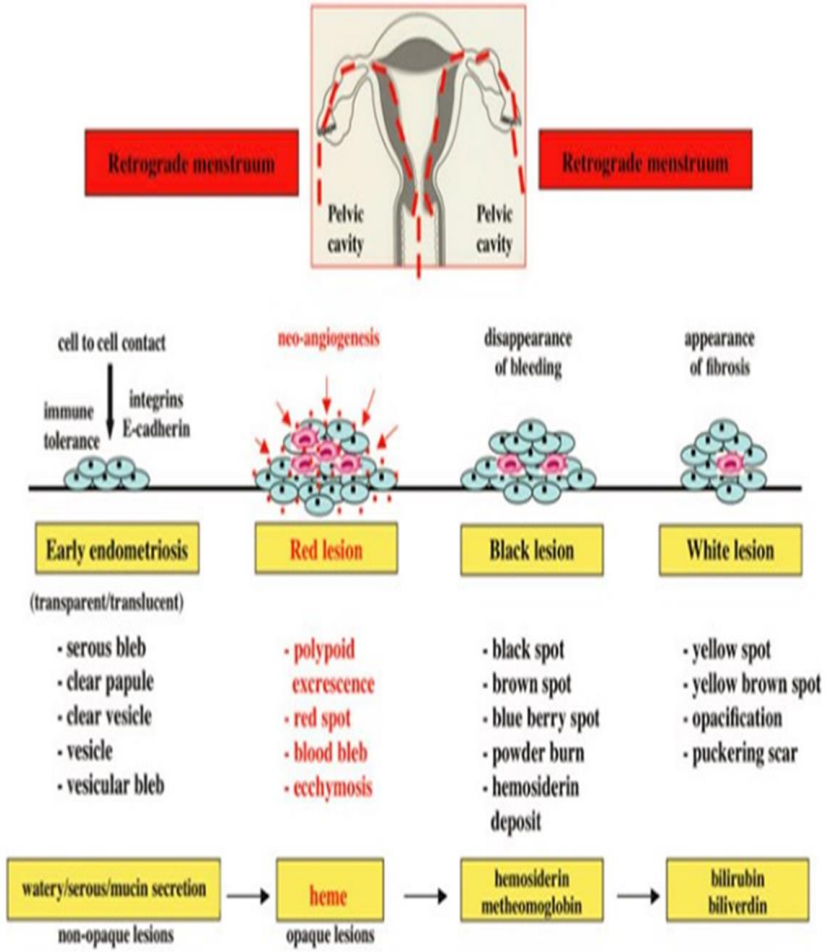


Fig. 3.1 Shows the diagrammatic representation of the natural course of visible peritoneal endometriosis in pelvic cavity. After initial attachment of refluxed endometrial cells with peritoneal cells producing early endometriotic lesions, the consequent events of mitosis, angiogenesis, metabolic degradation of heme, and appearances of fibrosis result in the generation of different morphological appearances of peritoneal endometriosis as shown in this figure

Type of lesion according to color

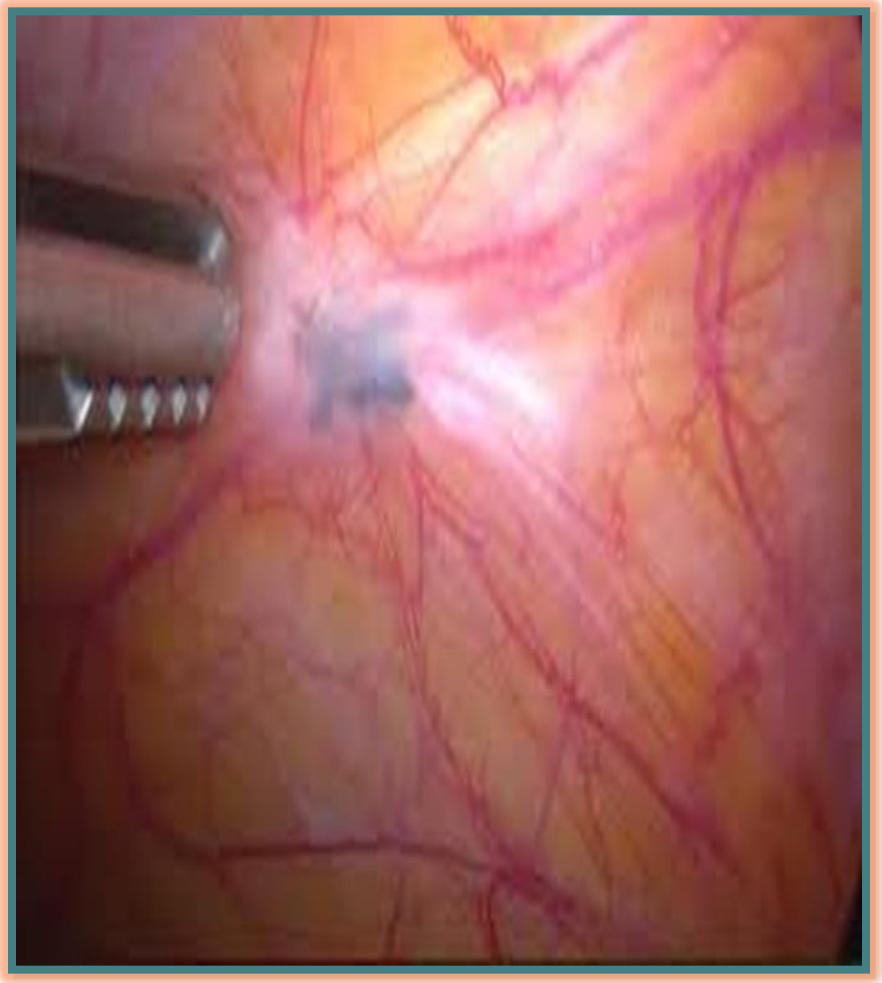
1. Red lesion = early endometriosis.
2. Black lesion = advanced endometriosis.
3. White lesion = healed or quiescent (latent) endometriosis

- R
- B
- W

Superficial peritoneal lesions(typical):

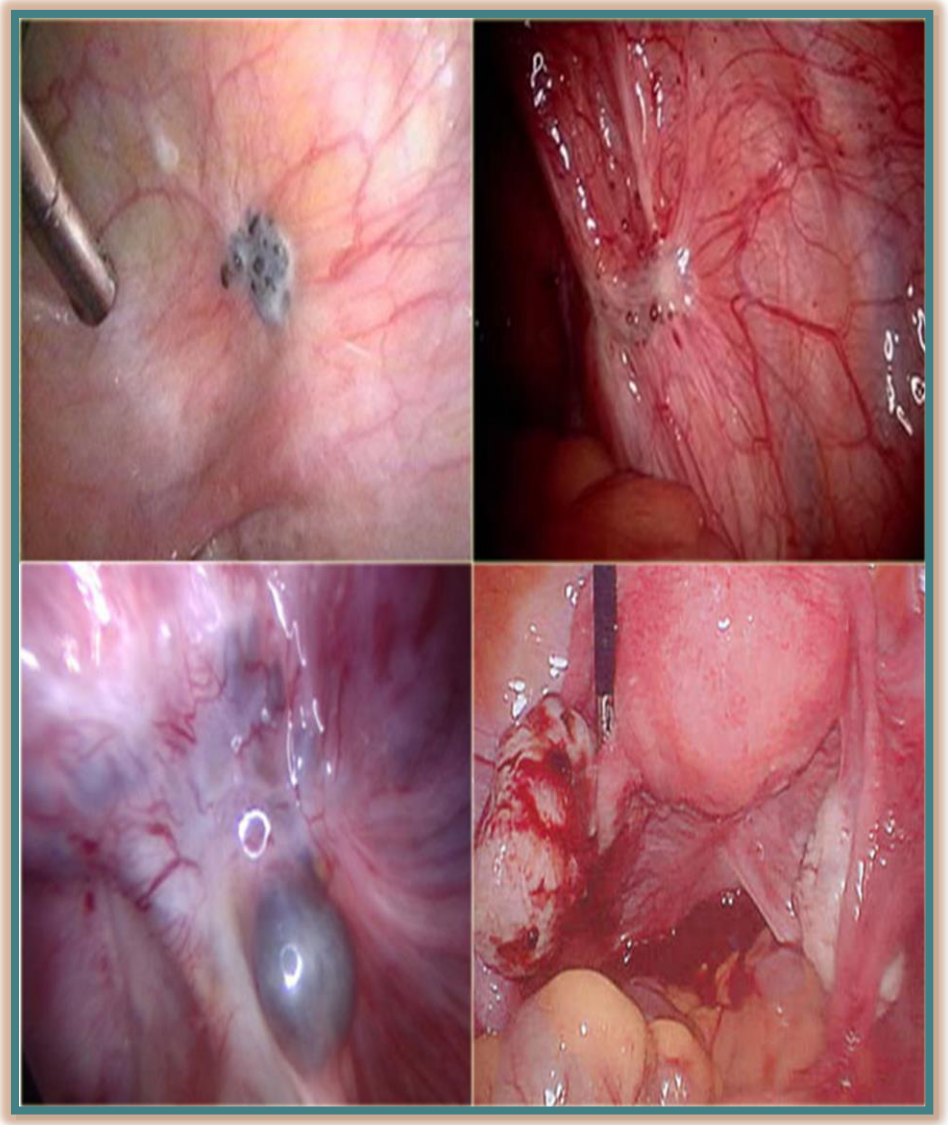
- Peritoneal endometriosis comprises superficial lesions scattered over the
- ✓ Peritoneal
- ✓ serosa
- ✓ ovarian surfaces.
- The appearance has been described as

'powder- burn' or 'gunshot' deposits.



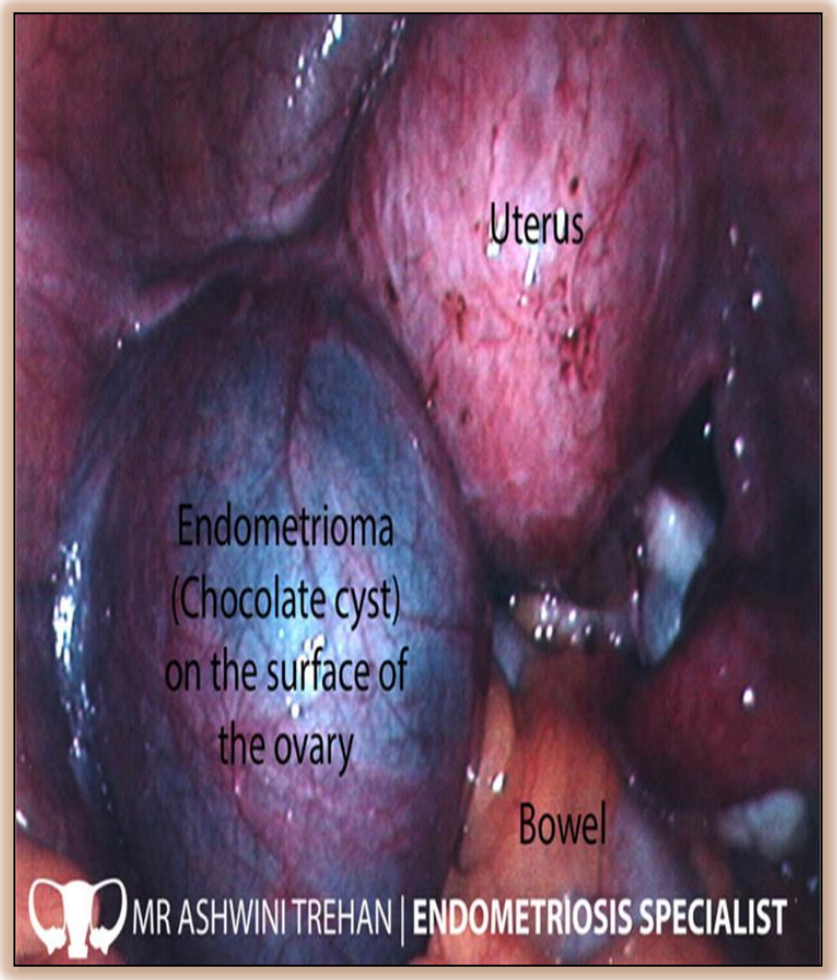
What we see during laparoscopy

- During laparoscopy, areas of peritoneal endometriosis appear as
- ✓ raised flame-like patches
- ✓ whitish opacifications
- ✓ yellow-brown discolorations
- ✓ translucent blebs
- ✓ reddish or reddish-blue irregularly-shaped islands.
- The appearance of some blue/brown lesions has been described as "powder burns."
- The peritoneal surface can be scarred or puckered, have defects (Allen-Masters syndrome), or
- give rise to nodules or cysts.
- Rarely, endometriosis appears as a polyploid mass, which may mimic the appearance of malignant tumor.
- Dense fibrous adhesions signify severe disease.



Ovarian lesion (Endometrioma)

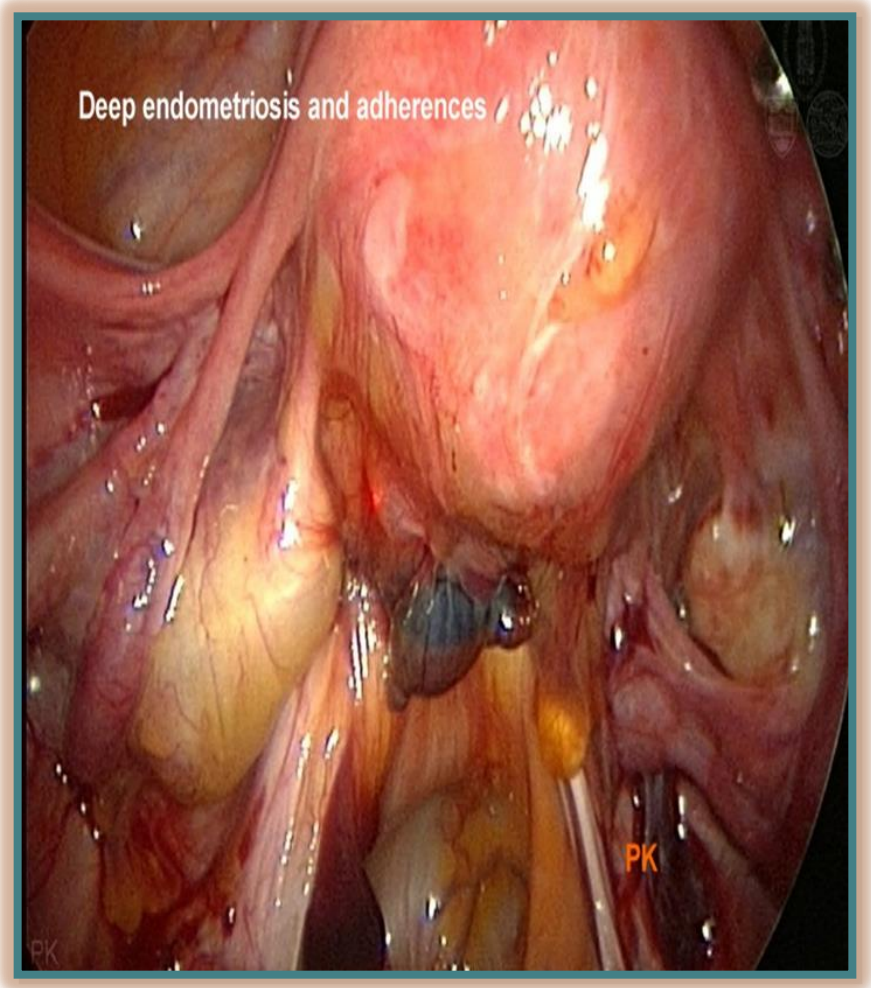
- is formed when ectopic endometrial tissue within the ovary bleeds and results in a hematoma surrounded by duplicated ovarian parenchyma



Deeply infiltrating endometriosis (DIE)

- is defined as a solid endometriosis mass situated more than 5 mm deep to the peritoneum
- +/ or DIE found in the

✓ retrovaginal septum
(rectocervical septum)
✓ Rectum
✓ retrosigmoid colon
✓ Bladder
✓ ureter
✓ uterine ligaments
✓ vagina



Surgical staging of disease
Classification systems

- **The World Endometriosis Society consensus identified three classification systems of value:**

- There is an argument that all women with endometriosis undergoing surgery should have a **Revised American Society of Reproductive Medicine (r-ASRM)** score and stage completed
- women with deep endometriosis should have an **Enzian classification** completed
- women for whom fertility is a future concern should have an **Endometriosis Fertility Index (EFI)** completed and documented in the medical/surgical records

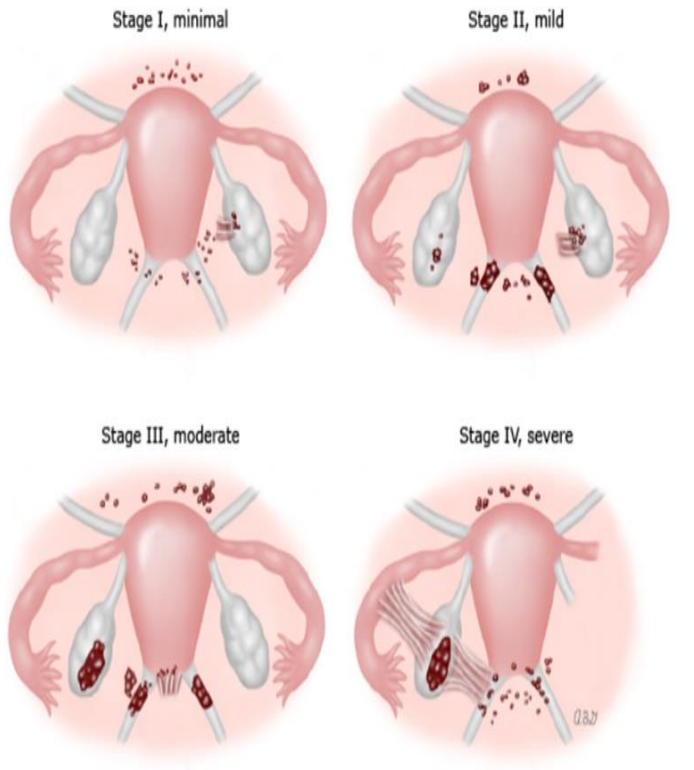
Revised American Society of Reproductive Medicine (r-ASRM)

- The most widely used classification
- Stages I and II consist mainly of superficial lesions, and stages III and IV of Endometriomas
- If the r-ASRM classification is to be used, the Enzian classification system should be employed when deep endometriosis is also present to give a complete description of the operative findings
- Classification include 4 stages:

1. Stage I: Minimal disease
2. Stage II: Mild endometriosis
3. Stage III: Moderate disease
4. Stage IV: Severe disease

Revised American Society of Reproductive Medicine (r-ASRM)

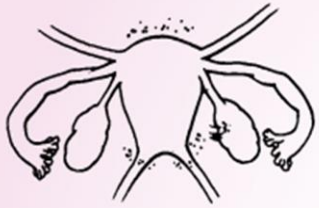
Examples of the classification of endometriosis



Original figure modified for this publication. Revised American Society for Reproductive Medicine classification of endometriosis: 1996. Fertil Steril 1997; 67:817. Illustration used with the permission of Elsevier Inc. All rights reserved.

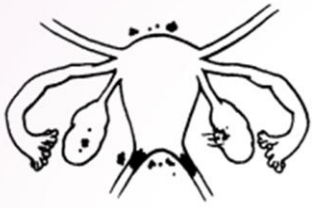
EXAMPLES & GUIDELINES

STAGE I (MINIMAL)



PERITONEUM		
Superficial Endo	1-3cm	· 2
R. OVARY		
Superficial Endo	< 1cm	· 1
Filmy Adhesions	< 1/3	· 1
TOTAL POINTS		4

STAGE II (MILD)

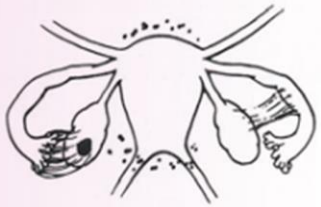


PERITONEUM		
Deep Endo	> 3cm	· 6
R. OVARY		
Superficial Endo	< 1cm	· 1
Filmy Adhesions	< 1/3	· 1
L. OVARY		
Superficial Endo	< 1cm	· 1
TOTAL POINTS		9

STAGE III (MODERATE)

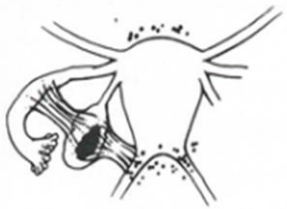
PERITONEUM		
Deep Endo	> 3cm	· 6
CULDESAC		
Partial Obliteration		· 4
L. OVARY		
Deep Endo	1-3cm	· 16
TOTAL POINTS		26

STAGE III (MODERATE)



PERITONEUM		
Superficial Endo	> 3cm	-4
R. TUBE		
Filmy Adhesions	< 1/3	· 1
R. OVARY		
Filmy Adhesions	< 1/3	· 1
L. TUBE		
Dense Adhesions	< 1/3	· 16*
L. OVARY		
Deep Endo	< 1 cm	-4
Dense Adhesions	< 1/3	-4
TOTAL POINTS		30

STAGE IV (SEVERE)



PERITONEUM		
Superficial Endo	> 3cm	-4
L. OVARY		
Deep Endo	1-3cm	· 32**
Dense Adhesions	< 1/3	· 8**
L. TUBE		
Dense Adhesions	< 1/3	-8**
TOTAL POINTS		52

*Point assignment changed to 16
**Point assignment doubled

STAGE IV (SEVERE)

PERITONEUM		
Deep Endo	> 3cm	· 6
CULDESAC		
Complete Obliteration		· 40
R. OVARY		
Deep Endo	1-3cm	· 16
Dense Adhesions	< 1/3	· 4
L. TUBE		
Dense Adhesions	> 2/3	· 16
L. OVARY		
Deep Endo	1-3cm	· 16
Dense Adhesions	> 2/3	· 16
TOTAL POINTS		114

Revised American Society of Reproductive Medicine (r-ASRM)

Revised American society for reproductive medicine classification (Am Soc Reprod Med 1997; 5:817-21)

Patient's Name _____ Date _____

Stage I (Minimal) - 1-5
Stage II (Mild) - 6-15
Stage III (Moderate) - 16-40
Stage IV (Severe) - >40
Total _____

Laparoscopy _____ Laparotomy _____ Photography _____
Recommended Treatment _____
_____
Prognosis _____

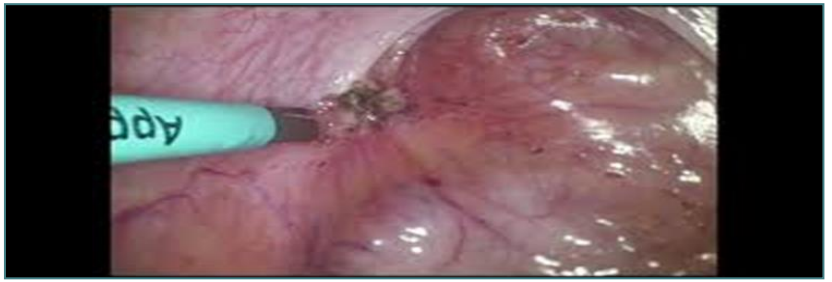
PERITONEUM	ENDOMETRIOSIS	<1cm	1-3cm	>3cm
	Superficial	1	2	4
	Deep	2	4	6
OVARY	R Superficial	1	2	4
	Deep	4	16	20
	L Superficial	1	2	4
	Deep	4	16	20
	POSTERIOR CULDESAC OBLITERATION	Partial	Complete	
		4	40	
OVARY	ADHESIONS	<1/3 Enclosure	1/3-2/3 Enclosure	>2/3 Enclosure
	R Filmy	1	2	4
	Dense	4	8	16
	L Filmy	1	2	4
	Dense	4	8	16
TUBE	R Filmy	1	2	4
	Dense	4*	8*	16
	L Filmy	1	2	4
	Dense	4*	8*	16

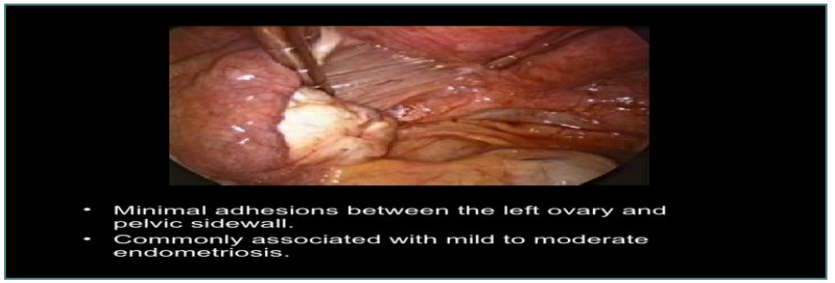
*If the fimbriated end of the fallopian tube is completely enclosed, change the point assignment to 16.

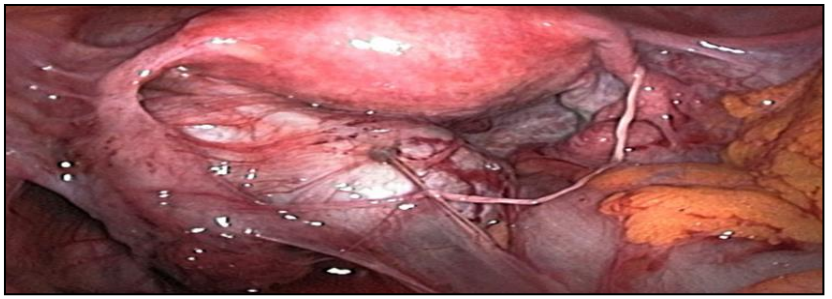
Denote appearance of superficial implant types as red [(R), red, red-pink, flamelike, vesicular blobs, clear vesicles], white [(W), opacifications, peritoneal defects, yellow-brown], or black [(B) black, hemosiderin deposits, blue]. Denote percent of total described as R____%, W____% and B____%. Total should equal 100%.

r-ASRM

1. **Stage I: Minimal disease** is characterized by isolated implants and no significant adhesions.
2. **Stage II: Mild** consists of superficial implants that are less than 5 mm in aggregate and are scattered on the peritoneum and ovaries. No significant adhesions are present.
3. **Stage III: Moderate** exhibits multiple implants, both superficial and deeply invasive. Peritubal and periovarian adhesions may be evident.
4. **Stage IV: Severe disease** is characterized by multiple superficial and deep implants, including large ovarian Endometriomas. Filmy and dense adhesions are usually present.







r- ASRM Pros - Cons

The main forces that perpetuate the r-ASRM classification system are :

1) its longevity
2) its widespread clinical use
3) its prevalence in the literature describing the operative appearance of endometriosis, and
4) its incorporation into other classification systems of potentially greater value.

The limitations of the r- ASRM classification system are that :

1) it does not describe deep endometriosis adequately.
2) has poor correlation with fertility outcomes
3) very poor correlation with pain symptoms and quality of life
4) gives poor prognostic information
5) has poor predictive accuracy with respect to treatment outcomes

Enzian classification

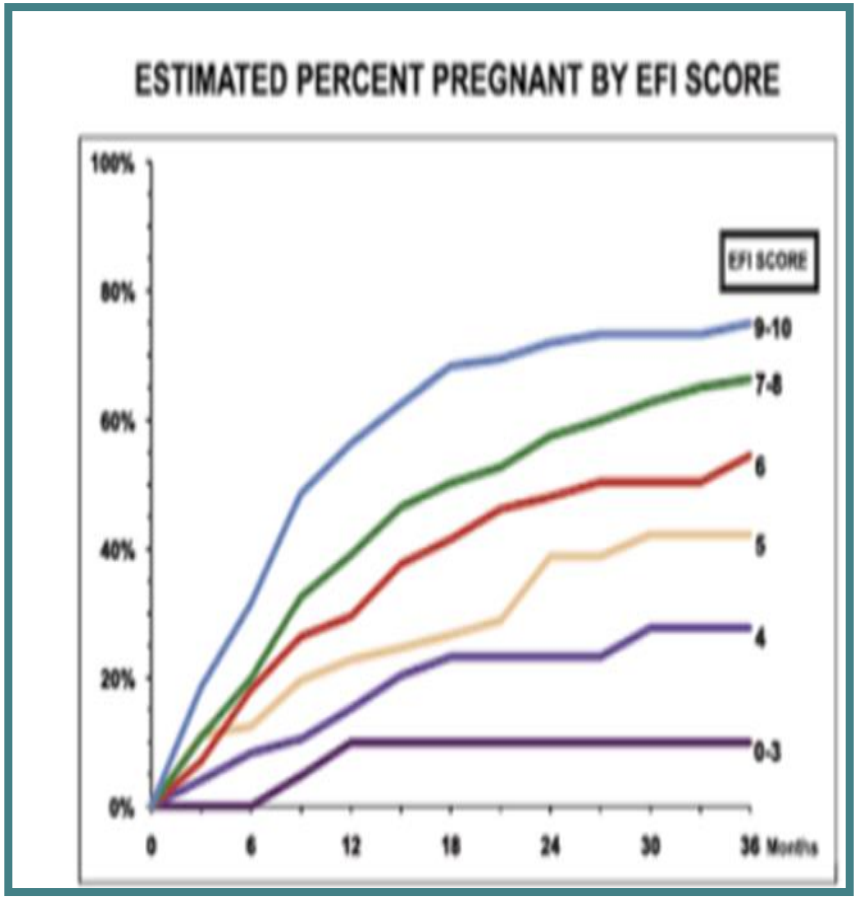
- Usually combined with r-ASRM classification in deep endometriosis
- Enzian may also be used preoperatively based on findings on clinical examination, transvaginal ultrasound and MRI in order to assist planning of surgery by predicting the extent of deep endometriosis and the time required for surgery.
- the Enzian classification also has poor correlation with symptoms and infertility, and limited prognostic value for the course of symptoms, quality of life and infertility, with an uncertain capacity to detect a woman's likely response to treatment for pain and/or infertility

Endometriosis Fertility index (EFI)

- The endometriosis fertility index (EFI) is used to predict fecundity after endometriosis surgery.
- In addition to providing a detailed score to the appendix (fallopian tubes, fimbriae of fallopian tubes, ovaries) by calculating the least-function scores, the EFI also combines conception-related factors such as age, duration of infertility, and gravidity history.
- EFI is a simple, robust and validated clinical tool that predicts fertility outcome for women following surgical staging of endometriosis and it may have considerable utility in developing treatment plans for infertile women with endometriosis, now with extensive external validation .
-

Endometriosis Fertility index (EFI)

- The EFI score ranges from 0-10
- 0-poorest prognosis
- 10- best prognosis)



Endometriosis Fertility index (EFI)

ENDOMETRIOSIS FERTILITY INDEX (EFI) SURGERY FORM

LEAST FUNCTION (LF) SCORE AT CONCLUSION OF SURGERY

Score		Description
4	=	Normal
3	=	Mild Dysfunction
2	=	Moderate Dysfunction
1	=	Severe Dysfunction
0	=	Absent or Nonfunctional

To calculate the LF score, add together the lowest score for the left side and the lowest score for the right side. If an ovary is absent on one side, the LF score is obtained by doubling the lowest score on the side with the ovary.

	Left	Right
Fallopian Tube		
Fimbria		
Ovary		

Lowest Score: Left [ ] + Right [ ] = LF Score [ ]

ENDOMETRIOSIS FERTILITY INDEX (EFI)

Historical Factors

Factor	Description	Points
Age		
	If age is ≤ 35 years	2
	If age is 36 to 39 years	1
	If age is ≥ 40 years	0
Years Infertile		
	If years infertile is ≤ 3	2
	If years infertile is > 3	0
Prior Pregnancy		
	If there is a history of a prior pregnancy	1
	If there is no history of prior pregnancy	0
Total Historical Factors		

Surgical Factors

Factor	Description	Points
LF Score		
	If LF Score = 7 to 8 (high score)	3
	If LF Score = 4 to 6 (moderate score)	2
	If LF Score = 1 to 3 (low score)	0
AFS Endometriosis Score		
	If AFS Endometriosis Lesion Score is < 16	1
	If AFS Endometriosis Lesion Score is ≥ 16	0
AFS Total Score		
	If AFS total score is < 71	1
	If AFS total score is ≥ 71	0
Total Surgical Factors		

EFI = TOTAL HISTORICAL FACTORS + TOTAL SURGICAL FACTORS: Historical [ ] + Surgical [ ] = EFI Score [ ]

Endometriosis Fertility index (EFI)

Descriptions of least function terms

Structure	Dysfunction	Description
Tube	Mild	Slight injury to serosa of the fallopian tube
	Moderate	Moderate injury to serosa or muscularis of the fallopian tube; moderate limitation in mobility
	Severe	Fallopian tube fibrosis or mild/moderate sapingitis isthmica nodosa; severe limitation in mobility
	Nonfunctional	Complete tubal obstruction, extensive fibrosis or salpingitis isthmica nodosa
Fimbria	Mild	Slight injury to fimbria with minimal scarring
	Moderate	Moderate injury to fimbria, with moderate scarring, moderate loss of fimbrial architecture and minimal intrafimbrial fibrosis
	Severe	Severe injury fimbria, with severe scarring, severe loss of fimbrial architecture and moderate intrafimbrial fibrosis
	Nonfunctional	Severe injury to fimbria, with extensive scarring, complete loss of fimbrial architecture, complete tubal occlusion or hydrosalpinx
Ovary	Mild	Normal or almost normal ovarian size; minimal or mild injury to ovarian serosa.
	Moderate	Ovarian size reduced by one-third or more; moderate injury to ovarian surface
	Severe	Ovarian size reduced by two-thirds or more; severe injury to ovarian surface
	Nonfunctional	Ovary absent or completely encased in adhesions

Adamson G D, Pasta DJ. Fertil Steril 2010;94;1609-15

Treatment

- **GENERAL PRINCIPLES**

- Treatment decisions are individualized and consider

1. clinical presentation (eg, pain, infertility, mass)
2. symptom severity
3. disease extent and location
4. reproductive desires
5. patient age
6. medication side effects
7. surgical complication rates,
8. cost.

- the ASRM Practice Committee statement that
  - "endometriosis should be viewed as a chronic disease that requires a lifelong management plan with the goal of maximizing the use of medical treatment and avoiding repeated surgical procedures".

Treatment of pelvic pain

- **Aim** to manage the patient's pain with medical therapy for as long as possible and thus limit the number of surgical interventions

Mild to moderate pain

Line of medical Rx

- **NSAIDs** & **continuous hormonal contraceptives** as the **first line of treatment** because these therapies are low-risk, have few side effects, and provide relief of symptoms for many women
- no superiority of one NSAID or hormonal contraceptive over another.
- Selection is based on patient preference, availability, and cost.

1. combined estrogen-progestin contraceptives (pill, patch, or vaginal ring) combined with an NSAID
2. For women who cannot or choose not to use estrogen therapy, we prescribe progestin-only contraceptive pills (ie, norethindrone 0.35 mg taken once daily) with an NSAID

Follow –up

- We reassess the woman's symptoms after three to four months of combined treatment

1. Women with adequate symptom improvement are continued on the hormonal therapy/NSAID regimen **until pregnancy is desired or the average age of menopause is reached.**
2. 2. Women whose symptoms **do not** improve continue NSAID treatment and are offered a different hormonal combination (eg, other estrogen-progestin contraceptive, oral norethindrone acetate 5 mg taken once daily, gestrinone 2.5 mg orally twice weekly) or depot medroxyprogesterone acetate 150 mg intramuscularly every three months.

severe pain

Indications

1. regularly missing school or work because of pain
2. symptoms that do not respond to the above therapies
3. recurrent symptoms are offered

Rx

1. GnRH agonist with add-back hormonal therapy. Endometriosis society recommended starting the GnRH therapy and the add-back simultaneously
2. aromatase inhibitors are reserved for women who continue to have refractory symptoms
3. laparoscopy for diagnosis and treatment:

1.conservative (retain uterus and ovarian tissue) or

2.definitive (removal of the uterus and possibly the ovaries After surgery, hormonal suppression is started to prevent recurrence of symptoms.

3. Nerve transection — laparoscopic uterosacral nerve ablation (LUNA) and presacral neurectomy (PSN) ???

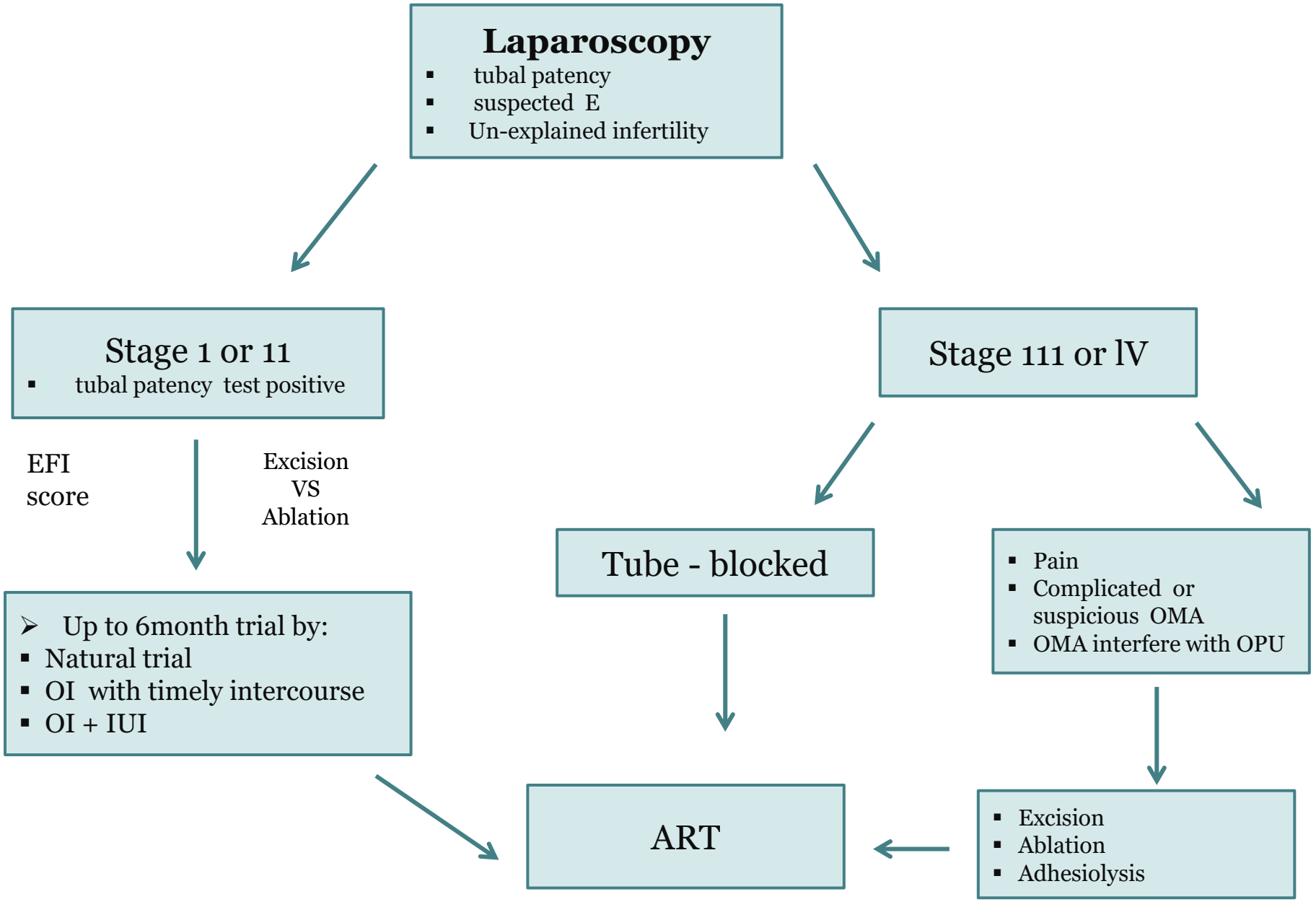
Endometriosis& infertility

Causes

- The mechanisms of infertility associated with endometriosis remain controversial and include in addition to Distorted pelvic anatomy

1. abnormal folliculogenesis
2. elevated oxidative stress
3. altered immune function, and hormonal milieu in the follicular and peritoneal environments
4. and reduced endometrial receptivity.

- These factors lead to poor oocyte quality, impaired fertilization, and implantation


Laparoscopy
tubal patency
suspected E
Un-explained infertility
Stage 1 or 11
tubal patency test positive
EFI score
Excision VS Ablation
Stage 111 or lV
Tube - blocked
Pain
Complicated or suspicious OMA
OMA interfere with OPU
Up to 6month trial by:
Natural trial
OI with timely intercourse
OI + IUI
ART
Excision
Ablation
Adhesiolysis

Role of surgery - laparoscopy

Stage of Endometriosis	Outcome
1. **Minimal & mild**	➢ The clinical pregnancy rate was significantly improved following laparoscopic removal of endometriosis compared with diagnostic laparoscopy
2. Moderate & sever	➢ No RCTs have yet assessed whether surgery improves fertility in women with stage III and IV endometriosis and those with deep endometriosis. ➢ The functional appearance of the fallopian tubes and ovaries at the end of the laparoscopic procedure, gauged by the EFI, gives prognostic information that is helpful in counseling women postoperatively ➢ Laparoscopic surgery for deep endometriosis is usually considered a second-line treatment option after failed IVF (unless IVF is not feasible or the patient has severe pain symptoms
3. Endometrioma	➢ Laparoscopic excision (cystectomy) whenever possible for Endometriomas greater than 4 cm in diameter improves fertility more than ablation comprising drainage and coagulation

Medically Assisted Reproduction (OI+IUI)

Stage of Endometriosis	Outcome
1. **Minimal & mild**	➢ clinicians may perform IUI with COS , instead of expectant management, as it increases live birth rates (Dunselman GA et al. ESHRE guideline: 2014) ➢ The live birth rate was found to be 5.6 times higher compared with expectant management ➢ (IUI) with gonadotrophins in minimal to mild endometriosis is not recommended (RCOG guideline) ➢ Endometriosis and infertility have has decreased per cycle conception rate compared with male factor and unexplained infertility. ➢ Repetitive superovulation with IUI (3-4 cycles) may have a plateau effect over time, so timely decision for IVF to be considered.
2. Moderate 3. **Sever** **3. Endometrioma**	**depend on patency of fallopian tube**

Medically Assisted Reproduction (OI+IUI)

OI – drugs

1. **CC**
2. **Letrozole**
3. **Gn**

Outcome

- CC & IUI is an effective treatment option resulting in a higher clinical pregnancy rate compared to Natural Contact and timed intercourse
- Third generation aromatase inhibitors produce a thicker endometrium, no downstream effect on cervical mucus, comparable pregnancy rate but fewer follicles in comparison to CC.
- Treatment with gonadotrophins and IUI results in a higher clinical pregnancy rate compared to CC and IUI
- (5.1 time higher)

When do you move these patients to IVF?

1. Primarily IVF would be suggested if during laparoscopy severe endometriosis is found compromising tubal function
2. Secondly after cystectomy if no conception even after superovulation and IUI for 3-4 cycles
3. Early referral for IVF in case of reduced ovarian reserve, Tubal factor and Male factor

ART

- similar in tem of implantation & clinical PR
- agonist produce more M11 & embryo

Long – agonist protocol
- **Good ovarian reserve**
- **Concomitant adenomyosis**

VS.

Extra -Long protocol
- **Long acting 3.75mg s.c. of Triptorelin/Leuprolide acetate**
- **3.6 mg Goserelin**

Down regulation for 3–6 months with GnRHa in women with endometriosis increases the odds of clinical pregnancy by more than 4-fold.
(Dunselman GA et al. ESHRE guideline: 2014)

Stimulation & OPU- ET

Antagonist protocol
- **Poor ovarian reserve**

Fresh embryo transfer
- **E2 < 2500**
- **P< 1.2ng/ml**
- **Number & quality of embryo is poor**

Fresh ET

freeze all
- **High E2**
- **Risk of OHSS**
- **Endometrium – embryo asynchrony**
- **P > 1.4 ng/ml**

2-3 m long GnRH analogs

FET

Precautions during ovum pickup with Endometrioma:

1. In women with Endometrioma, clinicians may use antibiotic prophylaxis at the time of oocyte retrieval to reduce the risk of ovarian abscess.
2. vaginal douching prior to (OPU) with povidone-iodine decreases the risk of PID.
3. The use of povidone-iodine followed by saline solution is more effective procedure than saline douching alone to prevent OPU-pelvic infection, without spoiling the oocyte quality.
4. the use of strict asepsis in the surgical field, avoiding successive punctures of the vaginal wall and ovarian capsule and avoiding puncture and aspiration of the Endometrioma

Fertility Preservation(FP):

- FP should be offered in:

1. patients suffering from mild endometriosis with reduced ovarian reserve and at older reproductive age.
2. It should also be considered before an extensive or bilateral pelvic surgery for endometriosis
3. in those cases if a woman is not planning immediate conception after surgery.

Endometrioma

TREATMENT GOALS :

1. Relieve symptoms (eg, pain or mass).
2. Prevent complications related to the adnexal mass (eg, rupture or torsion).
3. Exclude malignancy.
4. Improve subfertility.
5. Preserve ovarian function.
6. Size of OMA ≥ 4cm

Endometrioma (Deep Endometriosis)

< 3-4cm

Assess risk factors

Characteristics	Favors surgery	Favors ART
Previous intervention	None	≥ 1
Ovarian reserve	Good	Poor
Pain	Present	Absent
Growth	Rapid	Stable
Bilaterally	Unilateral	Bilateral
Malignancy risk	Present	Absent

Type of surgery

1. Cystectomy
2. Ablation (CO_2 laser)
3. Coagulation
   - Bipolar
   - Unipolar
4. Fenestration - ovoid it

≥ 3-4cm

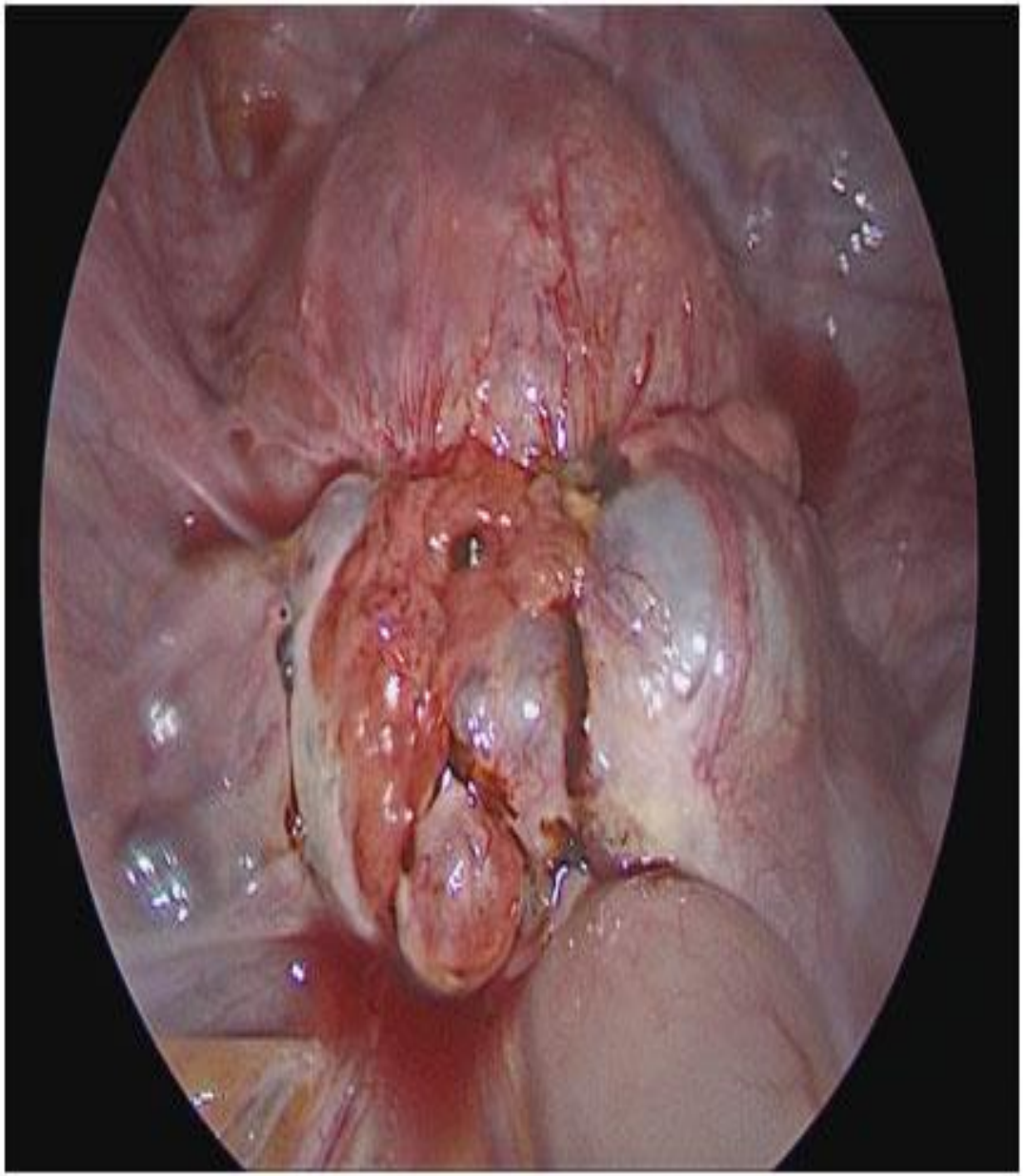
Assess fertility factors

Characteristics	IUI	ART
Tubes	Patent	blocked
Pelvic adhesions	Absent	Present
SFA	Normal	Abnormal

Surgery

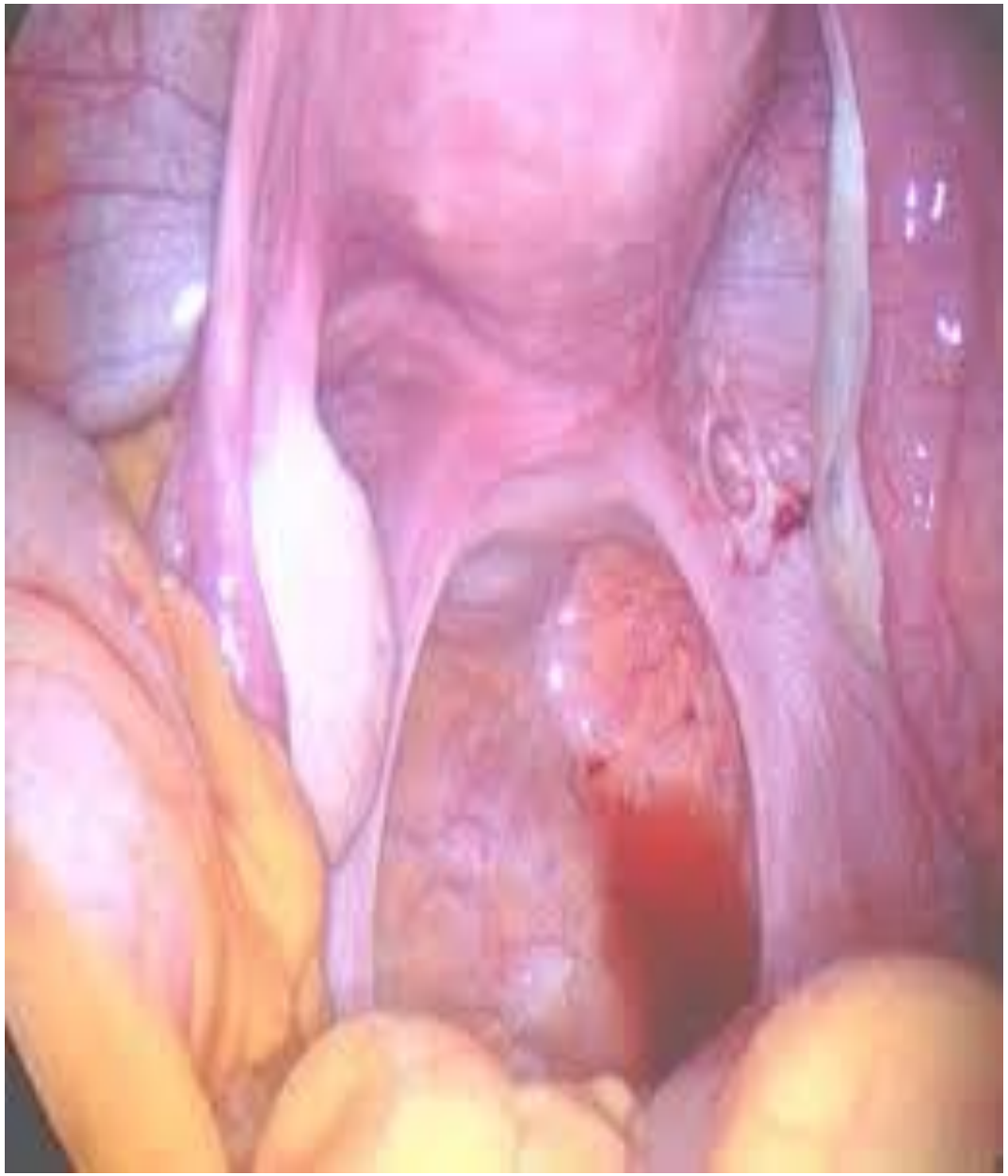
- Excision of Endometriomas improves pregnancy rates in subfertile women.
- Excision of the Endometrioma increased spontaneous pregnancy rate compared with women who had cyst wall ablation only
- Endometrioma resection has not been shown to improve IVF/ICSI outcomes.
- Women undergoing IVF/ICSI should consider Endometrioma resection only if they are having symptoms (eg, pain or mass) or to exclude malignancy.
- ovarian surgery to remove the Endometrioma reduce ovarian reserve(bilateral?)
- **Recommendation cautioned against repeat surgical intervention for Endometriomas**

Endometriosis slide exam



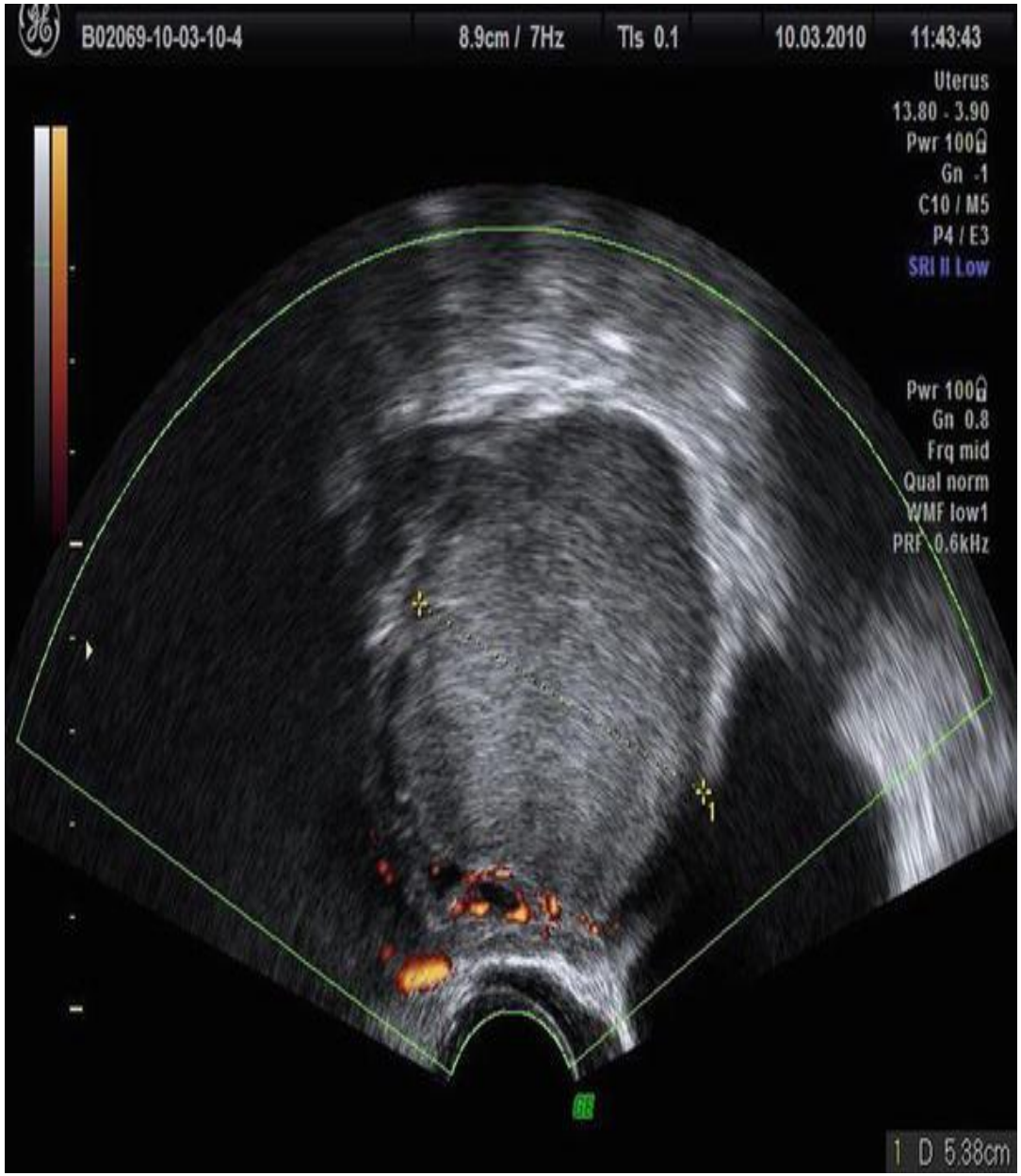
Slide no 1

- According to r-ASRM classification , stage this disease
- What is the optimum treatment for her ?
- If fertility was an issue – what is your plane for her next to surgery ?



Slide no 2

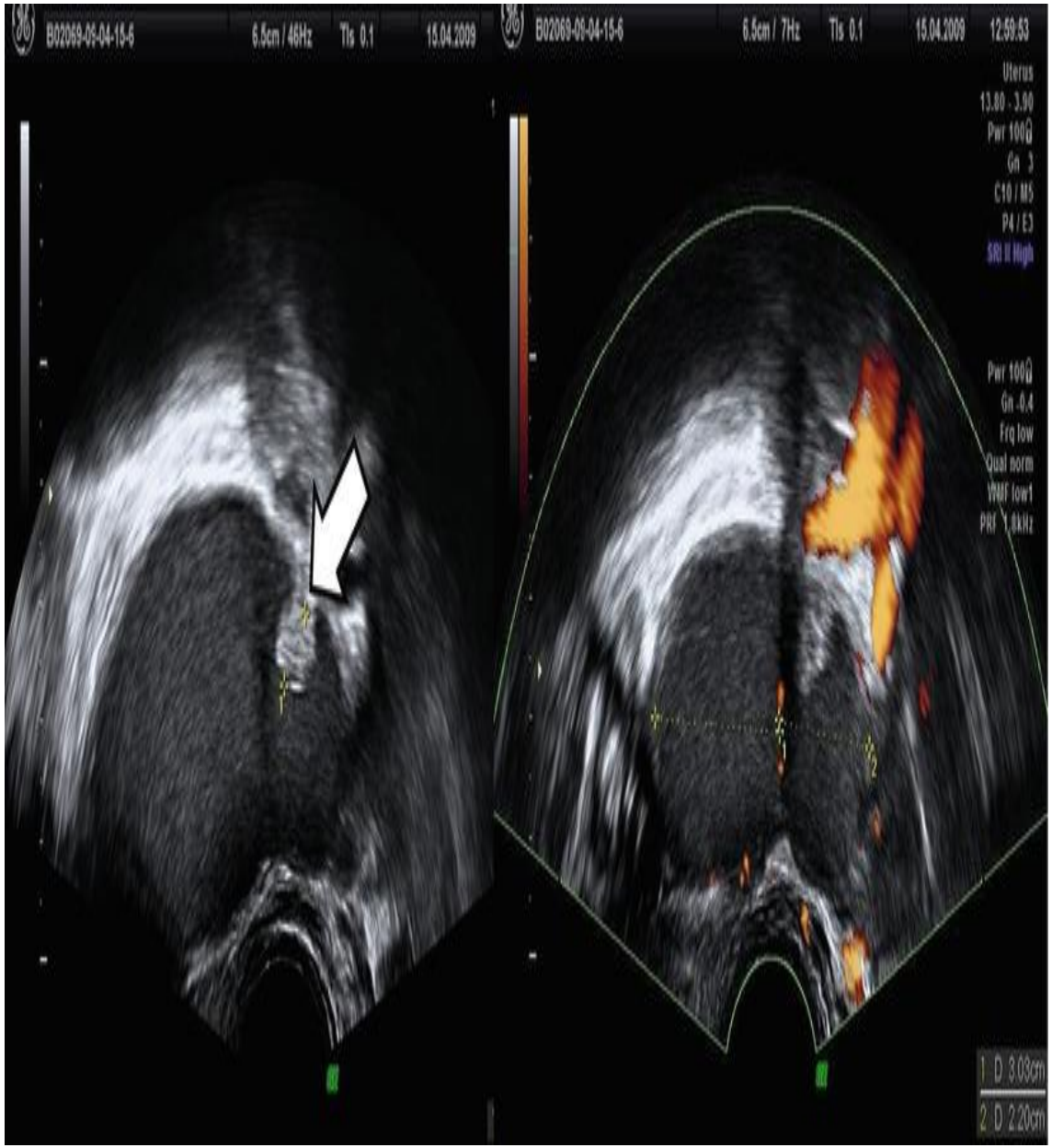
- According to r-ASRM classification , stage this disease
- What is the optimum treatment for her ?
- If fertility was an issue – what is your plane for her next to surgery ?



Slide no 3

- 28 years old woman presented to infertility clinic with history of primary infertility of 2 years duration
- Her partner SFA normal
- HSG shows patent tube
- Ultrasound reveal this persistent ovarian cyst of 1 year duration

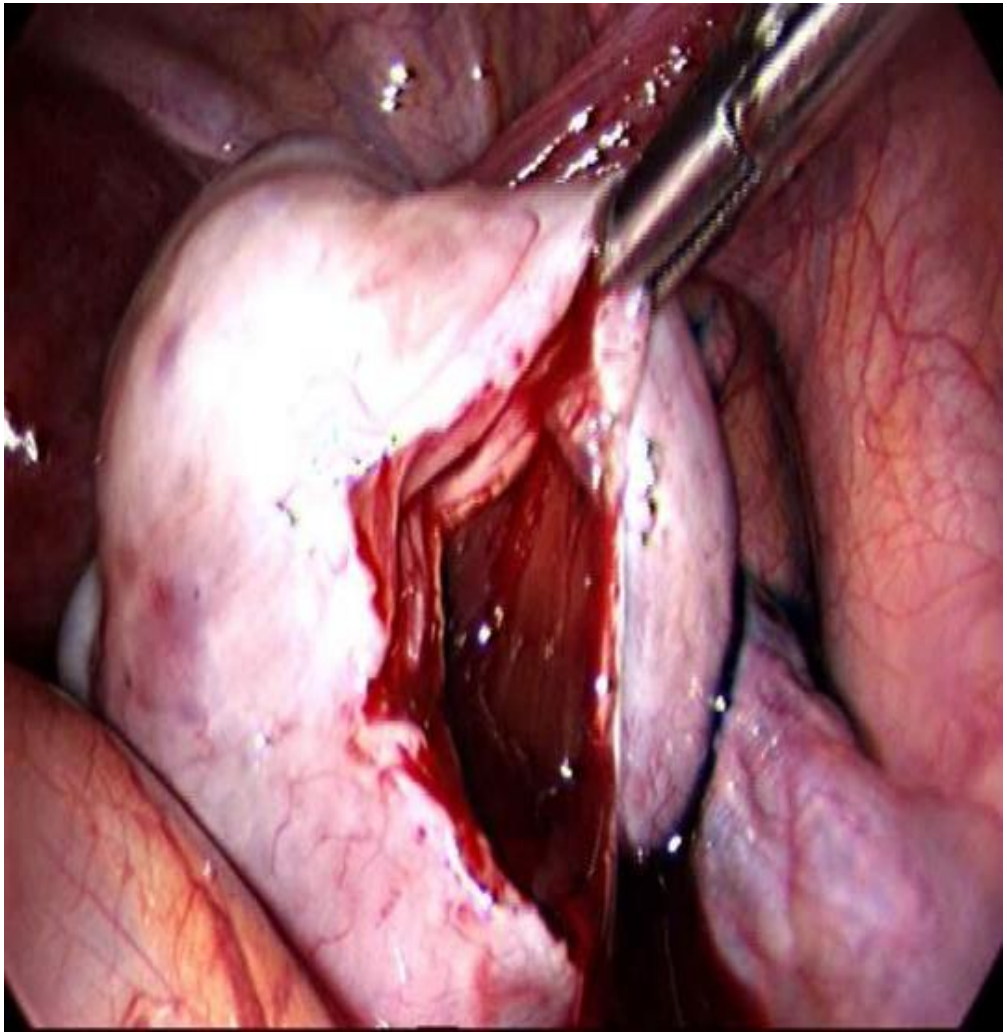
- What dose this US picture show?
- What's your provisional diagnosis ?
- What's your plan of treatment of her infertility ?



Slide no 4

- This is Endometrioma seen by TVUS With Doppler

1. What is the abnormality seen ?
2. What is its significance ?
3. Is there any role for risk of ovarian malignancy algorithm (ROMA) in this scenario , how?



Slide no 5

- What dose this slide show?
- What is the name of this procedure?
- What are the steps of this surgical procedure?

Answer of slide no 5

A. **Laparoscopic ovarian cystectomy /** Laparoscopic cyst fenestration followed by capsule ablation

A. **Cystectomy, Drainage , stripping &/or bipolar fulguration, ablation of internal surface of chocolate cyst.**


Thank
You