### Endometriosis

- Presence of endometrial tissues (superficial epithelium, glands and stroma) in places outside the uterine cavity. It is either:
  1. **External endometriosis**: Endometriotic tissues present outside the uterus (pelvis & other places).
  2. **Internal endometriosis (adenomyosis)**: The presence of endometriotic tissues inside the uterine wall within the myometrium.

### External Endometriosis:

**Prevalence:**
- Endometriosis is a common and important health problem of women.
- Its exact prevalence is unknown because surgery is required for diagnosis.
- Estimated to be present in 3-10% of women in the reproductive age group and 25-35% of infertile women.

**Pathogenesis:**

The cause of endometriosis is unknown. Many theories exist to explain the development of the disease but no single theory can explain all sites of the disease.

1. **Menstrual regurgitation and implantation**: It has been suggested that endometriosis resulted from retrograde menstrual regurgitation of viable endometrial glands and tissue within the menstrual fluid and subsequent implantation on the peritoneal surface. The prove for this theory is the presence of endometriosis in women with associated abnormalities of the genital tract, causing obstruction of the vaginal outflow of menstrual fluid.

2. **Coelomic epithelium transformation**: There is a common origin for the cells lining the mullerian duct, the peritoneal cells and the cells of the ovary. It has been suggested that these cells undergo de-differentiation back to their primitive origin and then transform into endometrial cells. This transformation into endometrial cells may be due to hormonal stimuli of ovarian origin.

3. **Vascular and lymphatic spread**: Vascular and lymphatic embolization of endometrial cells to distant organs has been demonstrated and explain the rare finding of endometriosis in sites outside the peritoneal cavity. This will explain foci in the kidneys, joints, skin and lung.

4. **Genetic and immunological factors**: It has been suggested that genetic and immunological factors may alter susceptibility of a woman and allow her to develop endometriosis. There appear to be an increased incidence in the 1st degree relatives of patients with the disorder. Also there is racial difference with increased incidence amongst oriental women and low prevalence in patients of Afro-Caribbean origin.

5. **The role of the immune system**: The activity of peritoneal natural killer and T-lymphocytes is suppressed in women with endometriosis, but whether these immunologic deviations are the cause or the result of endometriosis is still unclear. Endometriosis may occur when a deficiency in cellular immunity allows menstrual tissue to implant and grow on the peritoneum.

**Pathology:**

- The gross appearance of endometriosis is quite characteristic.
- The smallest and earliest implants are red, petechial lesions on the peritoneal surface.
- With further growth, menstrual-like detritus accumulates within the lesion giving it a cystic, dark brown, dark blue, or black appearance (burned drum-stick appearance).
- The surrounding peritoneal surface becomes thickened and scarred.
- These powder burn implants typically attain a size of 5-10 mm in diameter.
- With progression of the disease, number and size of the lesion increase and extensive adhesions develop.
- On the ovary, cysts enlarge to several centimeters in size and are called endometriomas or chocolate cysts.
The most common sites of the disease are:

1. The ovaries (approximately half of the cases) which of two types superficial small lesions and these lesions with time will go deep in the ovary and coalesces together forming single big cyst (deep lesion).
2. Then the uterine cul-de-sac (Pouch of Douglas).
3. Uterosacral ligaments.
4. The posterior surface of the uterus and broad ligaments.
5. The remaining pelvic peritoneum.

Other sites are:

1. Implants may occur over the bowel, bladder, and ureters. Rarely they may erode into underlying tissue and cause blood in stool or urine. Or the associated adhesions may result in stricture and obstruction of these organs.
2. Implants may occur on the cervix, posterior vaginal fornix.
3. Also within wounds contaminated by endometrial tissue e.g. scar of C/S or episiotomy.
4. Very rarely lesions may found in the lung, brain, and kidneys.

Clinical features:

- Clinical findings vary greatly depending on the number, size and extent of the lesion.
- The main presenting symptoms are:
  - Infertility.
  - Dysmenorrhea usually congestive type.
  - Dyspareunia (usually deep Dyspareunia).
  - Most patients complain of constant pelvic pain or a low sacral backache that occur premenstrually. There may cycle abnormalities like menorrhagia or polymenorrhea
  - Lesions on or near the external surface of the cervix, vagina, vulva urethra and rectum may cause pain or bleeding with defecation, urination or coitus at any time in the menstrual cycle
  - Other symptoms are related to the site of the lesion.
    - Lesions in the urinary tract cause cyclical dysuria and haematuria.
    - In Gastrointestinal tract cause dyschezia, cyclical rectal bleeding and obstruction.
    - In the Lung cause cyclical haemoptysis and haemopneumothorax.
    - In the umbilicus and surgical scars: cyclical pain and bleeding.
- The occurrence of abnormal cyclical bleeding at the time of menstruation from the rectum, bladder or umbilicus is pathognomonic of the disease.
- The physical examination classically reveals:
  - Tender nodules in the posterior vaginal fornix.
  - Pain upon uterine motion.
  - The uterus may be fixed and retroverted due to cul-de-sac adhesions.
  - Tender adnexial masses may be felt due to the presence of endometriomas.
  - Careful inspection may reveals implants in healed wounds especially episiotomy and caesarian section incisions, in the vaginal fornix or on the cervix.
  - Many patients are asymptomatic and have no abnormal findings on examination.

Diagnosis

- The diagnosis of endometriosis can be suggested by the clinical findings mentioned above.
- However a specific diagnosis requires visualization and in uncertain cases, biopsy of lesions, either at laparoscopy or laparotomy.
Laparoscopy:

- Laparoscopy remain the gold standard means of diagnosing this condition. It provide:
  - Direct visualization of endometriotic lesions.
  - To take biopsy from suspected areas.
  - Allows staging of the disease depending on extent of adhesions and the number and size of lesions.
  - Also allows concurrent therapy in the form of cautery or laser treatment in selected cases.
- Ultrasound, CT-scan and MRI have little value in the diagnosis of endometriosis.

Staging of the disease:

- Endometriosis is classified into mild, moderate, sever and extensive using the American Fertility Society’s scoring system which depend on the
  1. Extent of the lesions (number and size).
  2. Associated adhesions in the peritoneum.

<table>
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Endometriosis and infertility:

- It is estimated that 30-40% of patients with endometriosis have difficulty in conceiving.
- In the severe disease there is usually anatomical distortion with peri-adnexial adhesions and destruction of ovarian tissues when endometriomas develop.
- But with mild disease it is still unclear why it cause infertility.
  - Numerous mechanisms have been proposed, including abnormal folliculogenesis, anovulation, luteal insufficiency, luteinized unruptured follicle syndrome, recurrent miscarriage, decreased sperm survival, altered immunity, intraperitoneal inflammation and endometrial dysfunction.
  - However, all these functional disturbances can occur in subfertile women without endometriosis, which suggests that finding disease during investigation for subfertility may be coincidental.
Treatment:

_Treatment options are dictated by_

- The patient’s symptoms.
- Her age.
- The stage of her disease.
- Her desire for future fertility.

_The aim of the treatment are:_

- To relieve pain.
- Allows satisfactory coitus.
- Improves the patient’s fertility if possible.

_Treatment modalities available:_

Medical treatment:

1. NSAID.
2. Oral contraceptive pills.
3. Progestational agents.
4. Danazol and Gestrinone.
5. LHRH- analogue (GnRH agonist).

Surgical treatment:

1. Conservative (by laparoscopy or laparotomy)
2. Radical surgery.

**Medical treatment:**

1. **Analgesic therapy:**
   - Non-steroidal anti-inflammatory drugs are potent analgesics.
   - They are helpful in reducing the severity of dysmenorrhoea.
   - It has no effect on the disease and its progression.
   - So their use is as adjunctive treatment only.

2. **Hormonal Therapy:**

   The aim of treatment with hormonal therapy is to interrupt the cycles of stimulation and bleeding of endometriotic tissue by giving drugs that suppress the ovarian cycle. This can be achieved with various agents.

   _A. Oral contraceptive pills:_
   - This is prescribed as 1 pill a day for 6-12 months.
   - The continuous exposure to combined oral contraceptive pills results in decidual changes in the endometrial glands.
   - Rate of pregnancy following discontinuation of therapy can be as high as 50%.
   - The patient may have break through bleeding, weight gain, headache, nausea, mood changes.
B. Progestational agents:

- These agents cause decidualization in the endometriotic tissue.
- Oral medroxyprogesterone acetate can be prescribed as a 10-30mg daily.
- Depot medroxyprogesterone acetate 150mg i.m can be given as a single dose every 3 months.
- Side effects: Irritability, depression, breakthrough bleeding, and bloating.

C. Danazol:

- Danazol is a weak androgen.
- Danazol acts via several mechanisms to treat endometriosis by causing amenorrhea and atrophy.
- The dosage of Danazol is 400-800mg/day in divided doses for 6 months.
- Side effects:
  - Acne.
  - Oily skin.
  - Deepening of the voice.
  - Weight gain.
  - Edema.
  - Adverse plasma lipoprotein changes.
  - Most changes are reversible upon cessation of therapy.
- Gestrinone inhibit LH & FSH secretion in a dose of 2.5mg twice weekly with similar side effects of Danazol.

D. Gonadotropin-releasing hormone agonists (GnRH agonist)

- These agents are analogues of GnRH.
- When given continuously cause suppression of gonadotropin secretion.
- So suppress ovarian cycle and endometrial implants.
- GnRH agonists can be administered
  - Intramuscularly e.g. leuprolide acetate 3.75mg once a month.
  - Intranasaly as nafarelin 200mg twice daily.
  - Subcutaneously as goserlin 3.75mg once a month.
- These agents are used for 6 months because of their side effects related to the hypo-estrogenic state including:
  - Loss of bone mineral density (the most important one causing osteoporosis).
  - Vasomotor symptoms.
  - Vaginal dryness.
  - Mood changes.
- Now a days they start to add low dose estrogen e.g. 0.625 mg of conjugated equine estrogen to relieve the side effects of these drugs especially the bone lose.
Surgical treatment:

Conservative surgical treatment:

- This is indicated for women with infertility, who have severe disease and symptoms with adhesions.
- By surgery we should:
  - Excise or destroy all endometriotic tissues
  - Remove all adhesions (adhesolysis).
  - Restore pelvic anatomy to the best possible condition.
  - Tubal surgery.
  - Pre-sacral neurectomy or Uterosacral ligaments ablation to relieve pain.
  - Uterine suspension also done if required.
- All these procedures can be performed by laparoscopy or laparotomy.
- For women with infertility who failed all other therapy can undergo assisted reproduction (IVF).

Definitive surgery:

- For patient with severe disease or symptoms, who does not desire further pregnancy
- This includes total abdominal hysterectomy and bilateral salpingo-oophorectomy with excision of the remaining adhesions or implants.
- Post-operative medical therapy may be indicated in some patients to get rid of all remaining implants.
- Women who undergo definitive surgery can be given hormone replacement therapy with out reactivation of endometriotic tissues.

Adenomyosis

- Means the presence of endometrial glands and stroma deep within the myometrium.
  - It has a different etiology than endometriosis.
  - The exact etiology is unknown but it has been suggested to be related to weakness of the myometrial smooth muscle from repeated pregnancies, or trauma induced by surgery.
  - The incidence of this condition is more in:
    1. Multiparous women in their late thirties or early forties of age.
    2. Women who has previous curettage or induced abortion.
    3. More common in women having endometrial hyperplasia and fibroids.
- Clinically the patient presented with increasingly severe secondary dysmenorrhoea and menorrhagia.
- The uterus is bulky and tender particularly if examined perimenstrually.

Diagnosis:

- Clinical features are non-specific.
- Transvaginal ultrasound may show alteration of echogenicity within the myometrium from the localized distended endometrial glands. Sometimes the appearance may resemble uterine fibroid.
- MRI may be more specific than ultrasound in the diagnosis.
- However specific diagnosis for suspected cases is only obtained by pathological examination of the hysterectomy specimen performed for symptomatic reasons.

Treatment:

- Drugs that induce amenorrhoea are helpful since they relieve pain and excessive bleeding (Danazol, Gestrinone and GnRH agonist can be used).
- However on stopping the treatment symptoms return rapidly in the majority of patients.
- So hysterectomy is the only definitive treatment available.