ENDOMETRIOSIS

- The presence of a tissue similar to normal endometrium in structure and function outside the lining of the uterine cavity.
- Endom.interna → Adenomyosis

  Endom.externa → True endom.

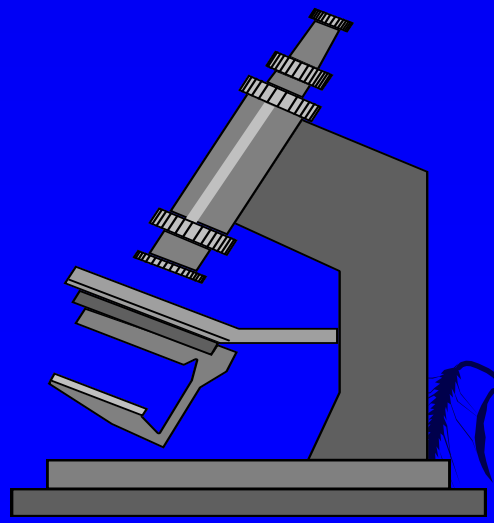
ADENOMYOSIS

- **Aetiology:**
  - **Repeated Pregnancies.**
  - **Vigorous Curettage.**
  - **Hormonal Imbalance.**

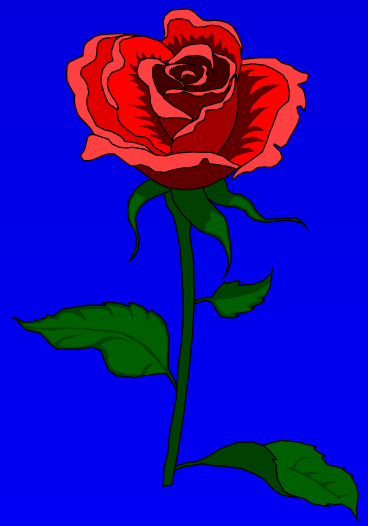
Adenomyosis---Pathology

- Symmetrical enlargement of uterus.
- Localized or diffuse.
- Histology:

-Glands +Stroma surrounded by muscle fibres.



Adenomyosis--Clinical features



- End of reproductive life.
- Multiparous.
- Asymptomatic.
- Menorrhagia:-Enlarg. of uterus.
  - ↑ Blood supply.
  -Impaired contractility.
  -Ass.endom.hyperplas.
- Dysmenorrhea &Dyspareunia.

Adenomyosis-----cont.

- Myoma vs Adenomyosis

  -Rarely enlarg.uterus >12-14wks.

  -Regular enlarg.of the uterus.

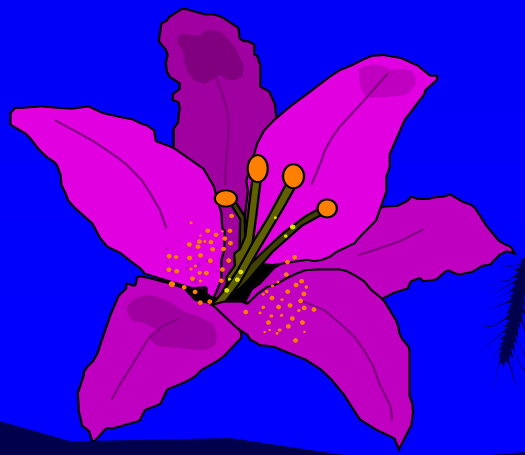
- Treatment TAH

ENDOMETRIOSIS

- Implantation Theory(sampson)
- Coelomic Metaplasia.
- Lymphatic&Vascular Dissemin.

Endometriosis--Predisp.factors

- Age → 4th decade.
- Reprod.history → delay 1st pregn.
- High Social class.
- Genetic → 7% of 1st degree relat.
  1% of unrelated control
- Auto-immune.



Endometriosis---Increase

- Better ability to recognise the disease.
- The growing number of laparoscopic procedure.
- Emergence of predisposing factors.
- Patients and physicians----more aware of the disease.

Endometriosis---Pathology

- **Macroscopic:**

  -Small black dots(powder burn)

  ↓

  Large cystic masses(choclate cysts)

- Others—black, dark brown, bluish puckered lesions, nodules.
- Atypical lesions:

  -Red implants(petechial, vesicular, polypoid, red flame like)

  - Serous or clear vesicles.

- White plaques and scaring.

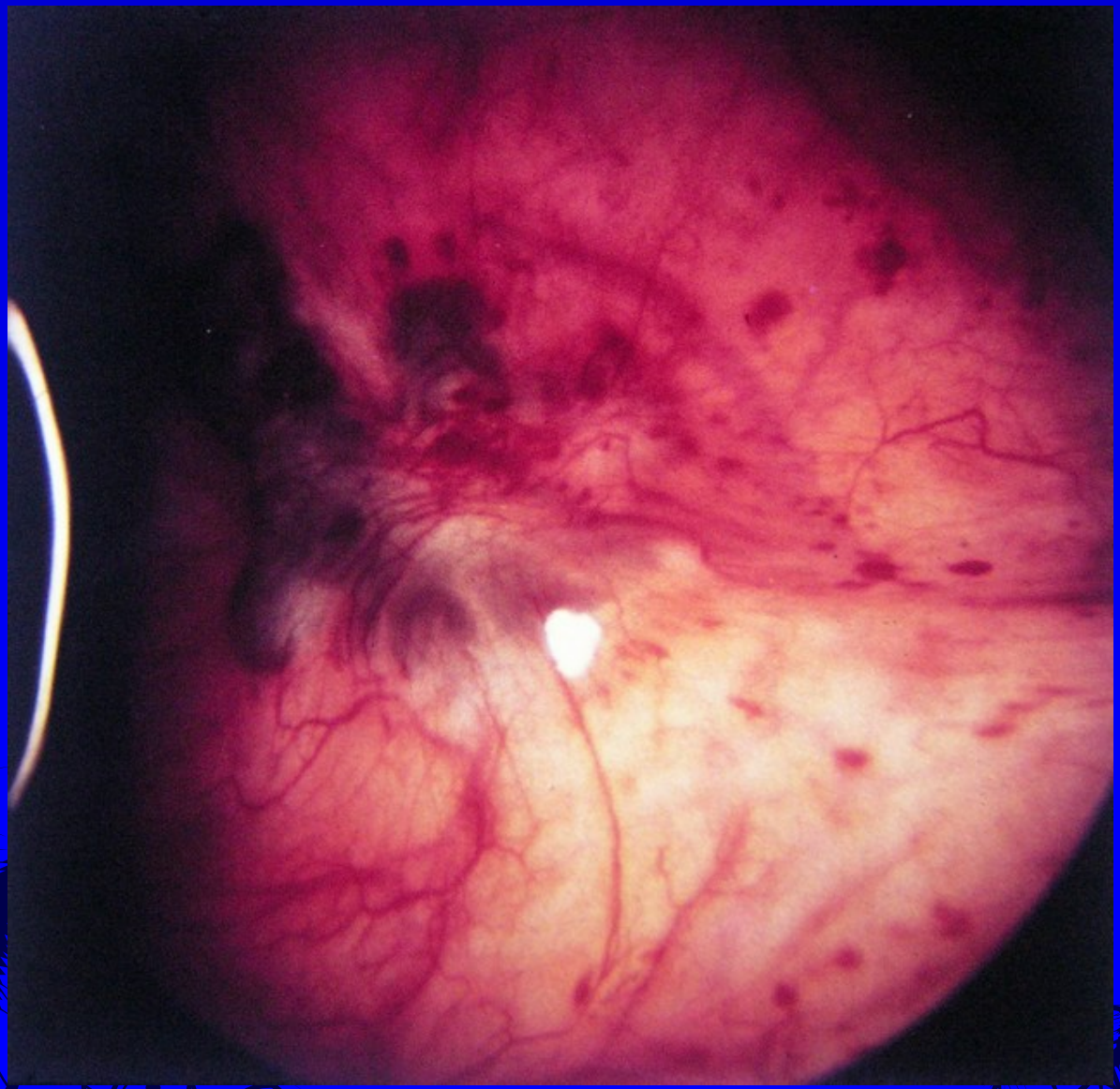
Endometriosis--Pathology

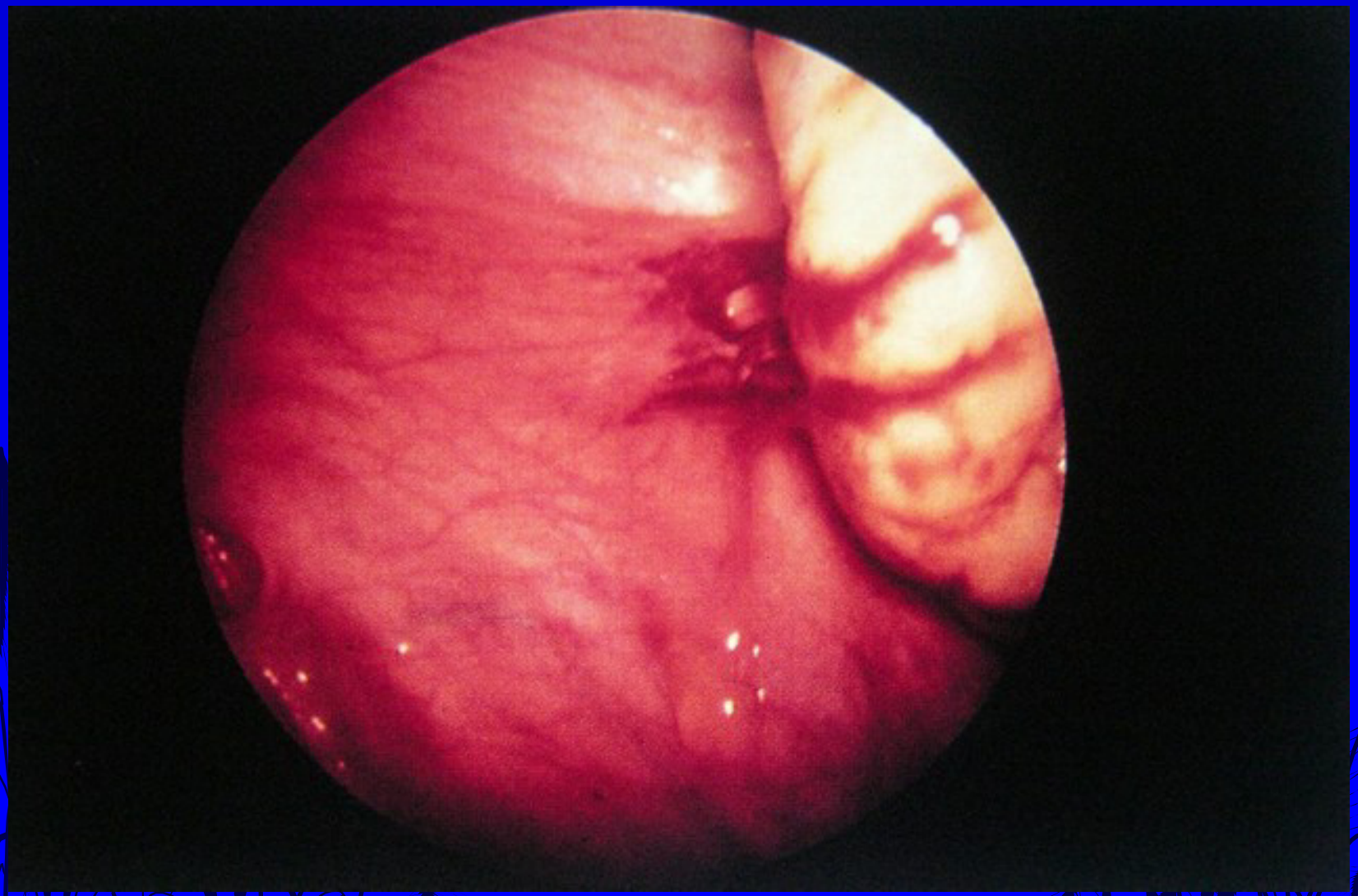
- ***Microscopic***

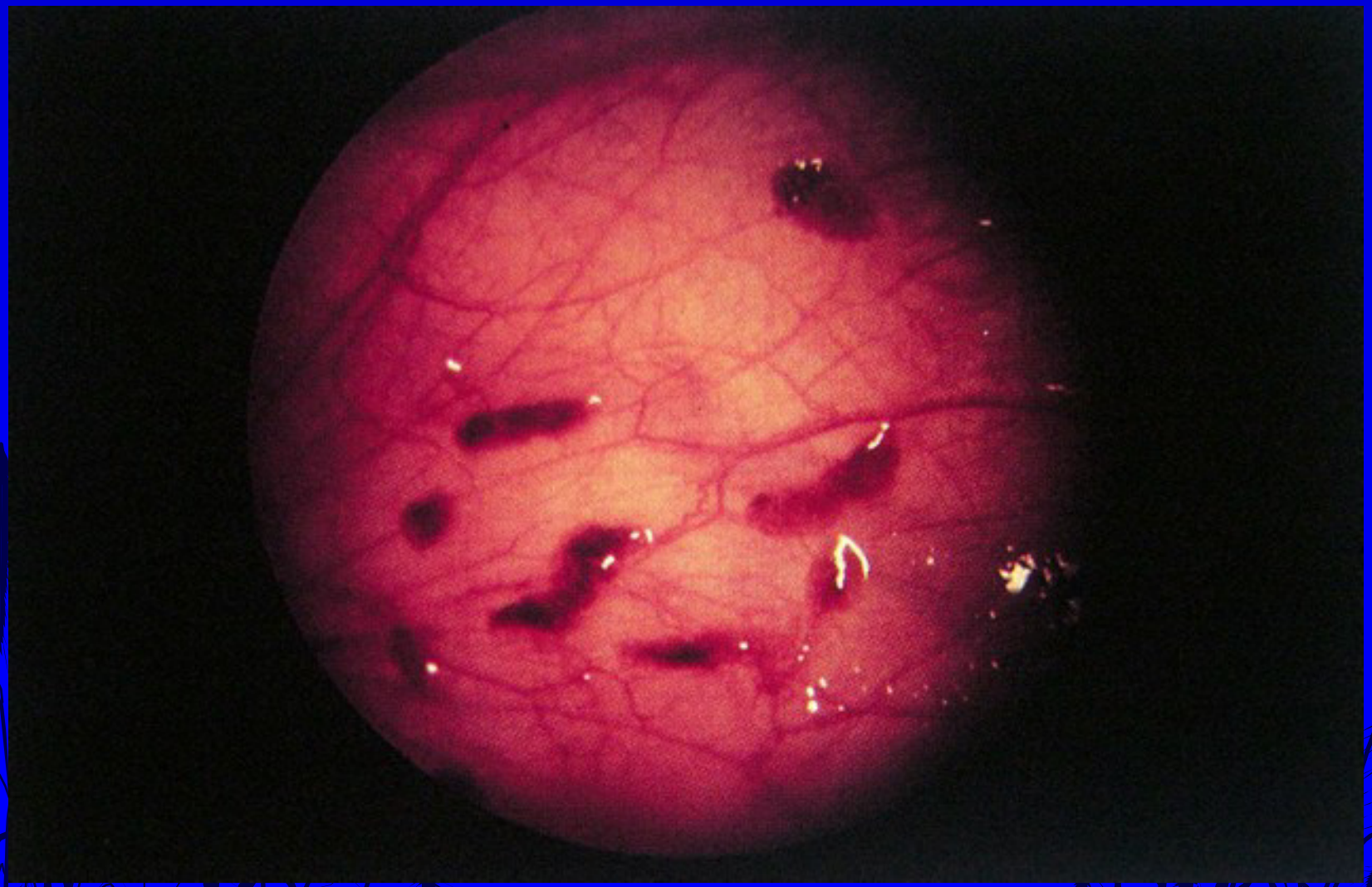
  -Endometrial glands.

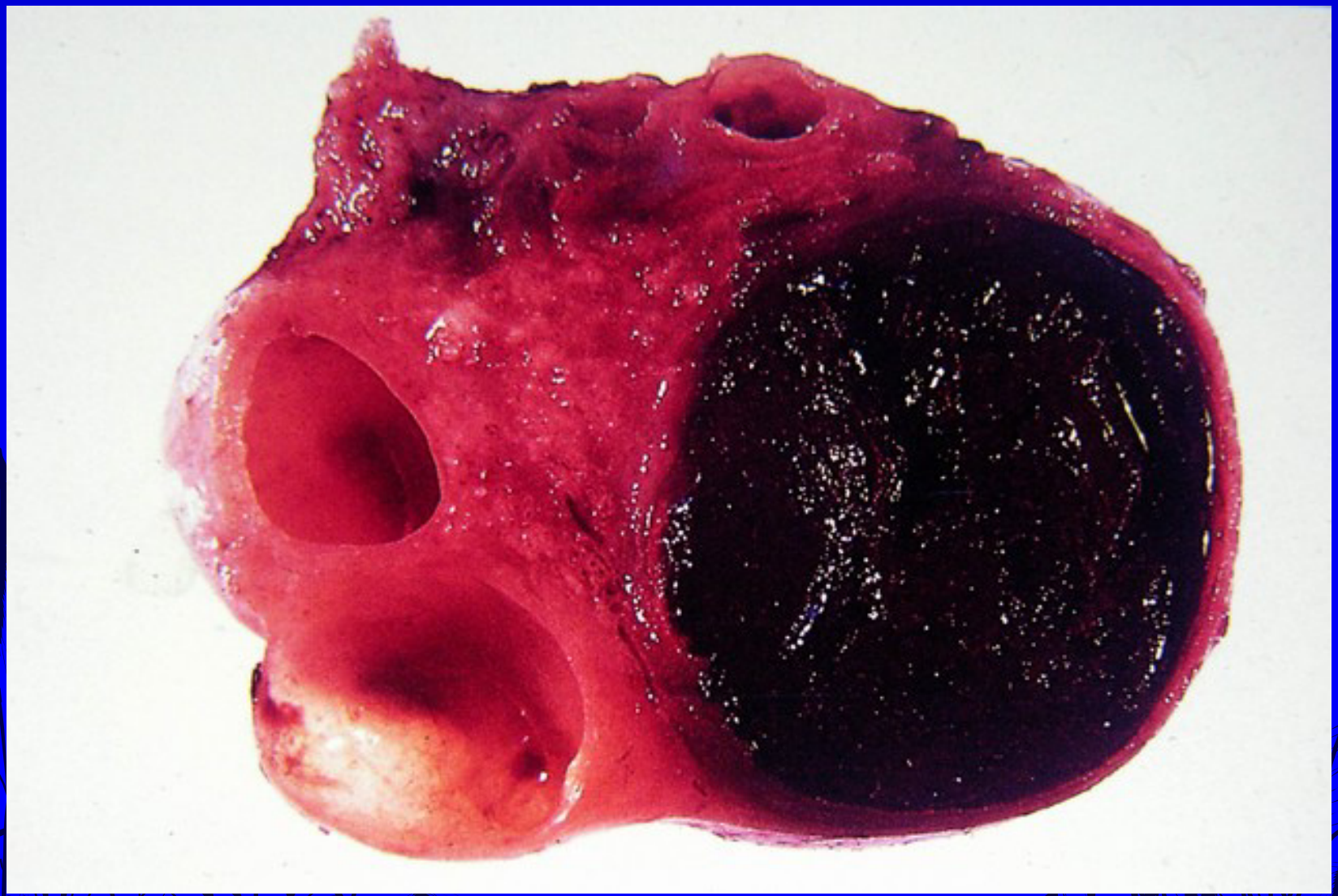
  - Stroma.

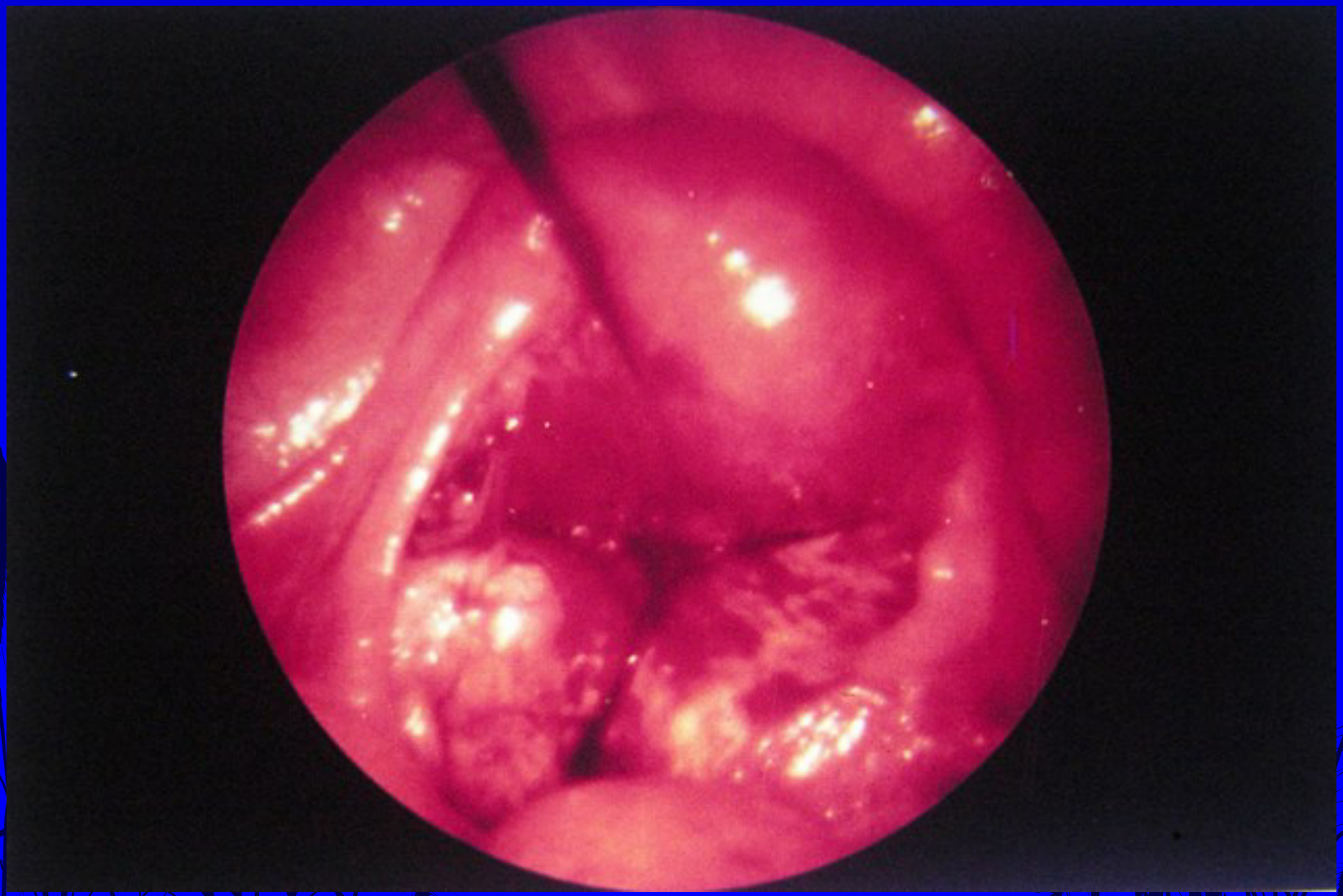
  - Evidence of bleeding.

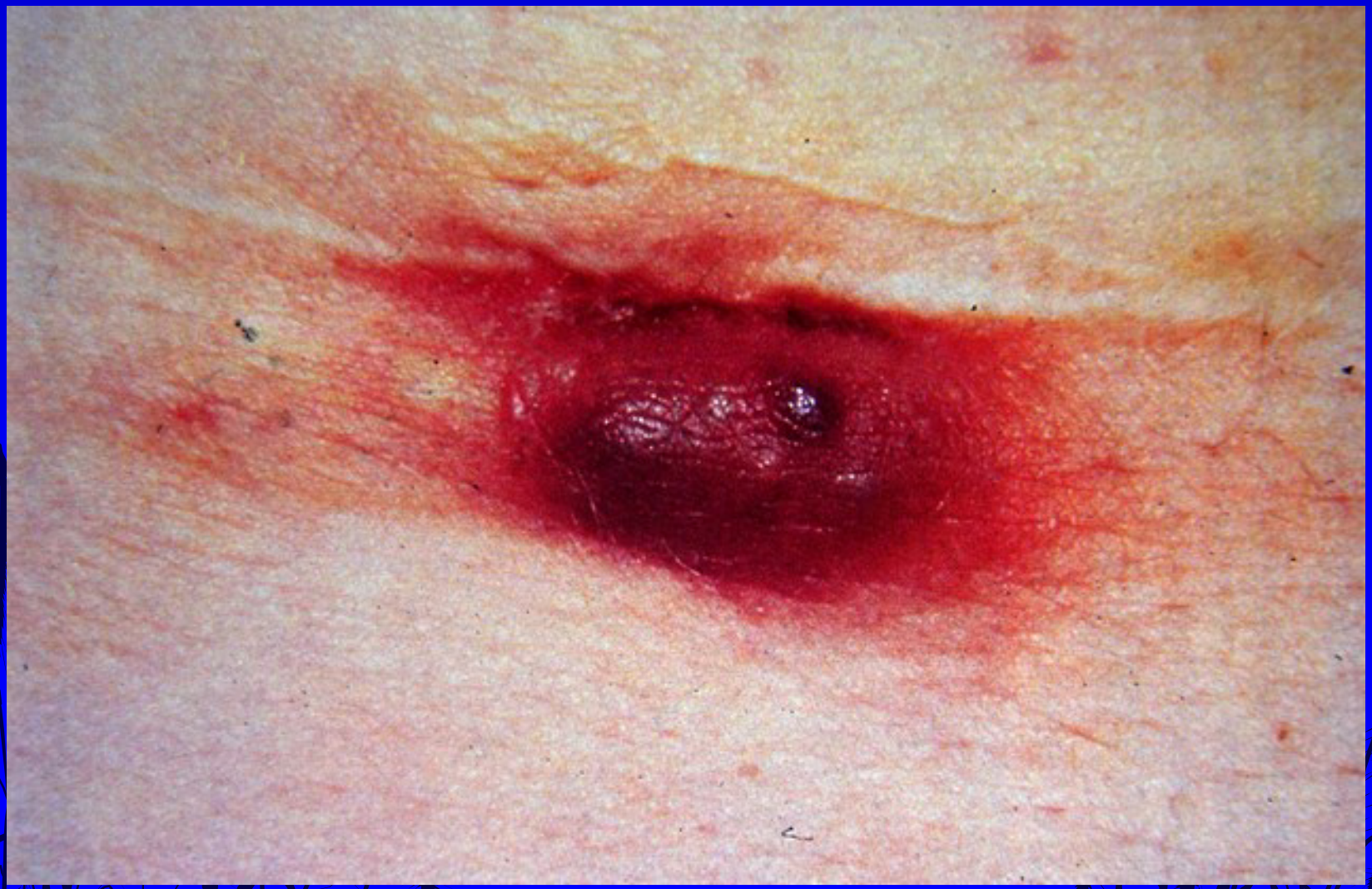


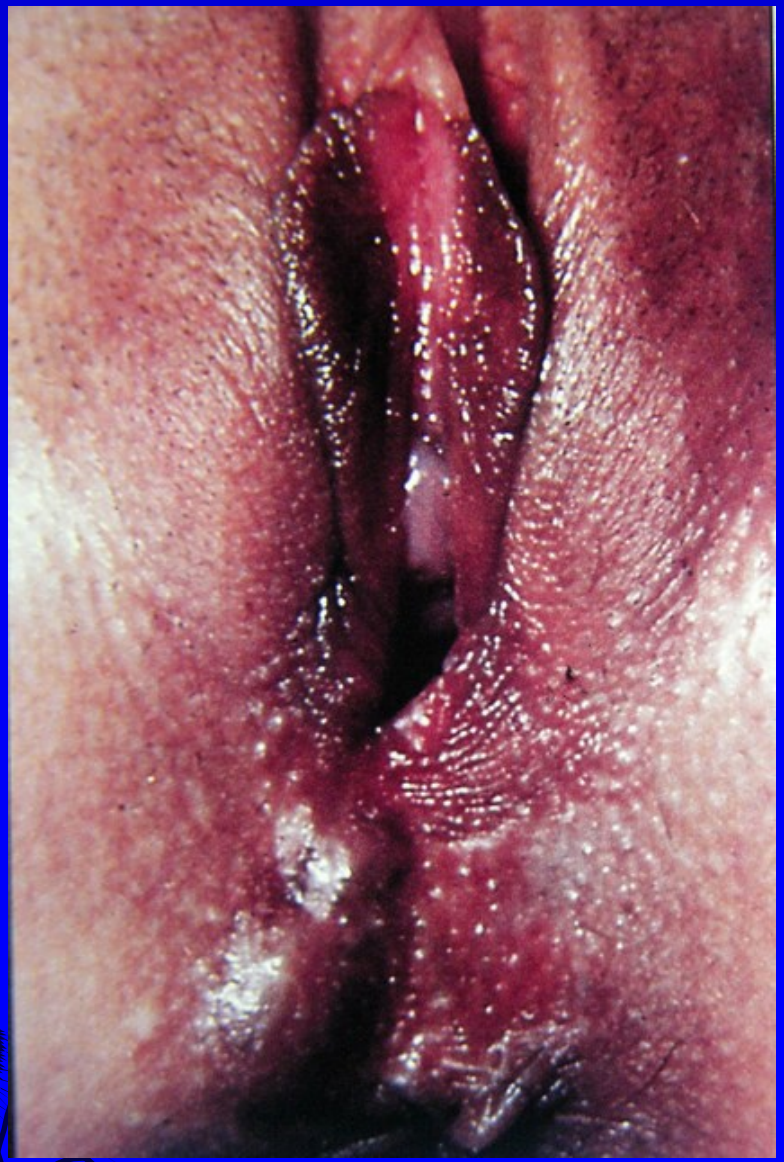


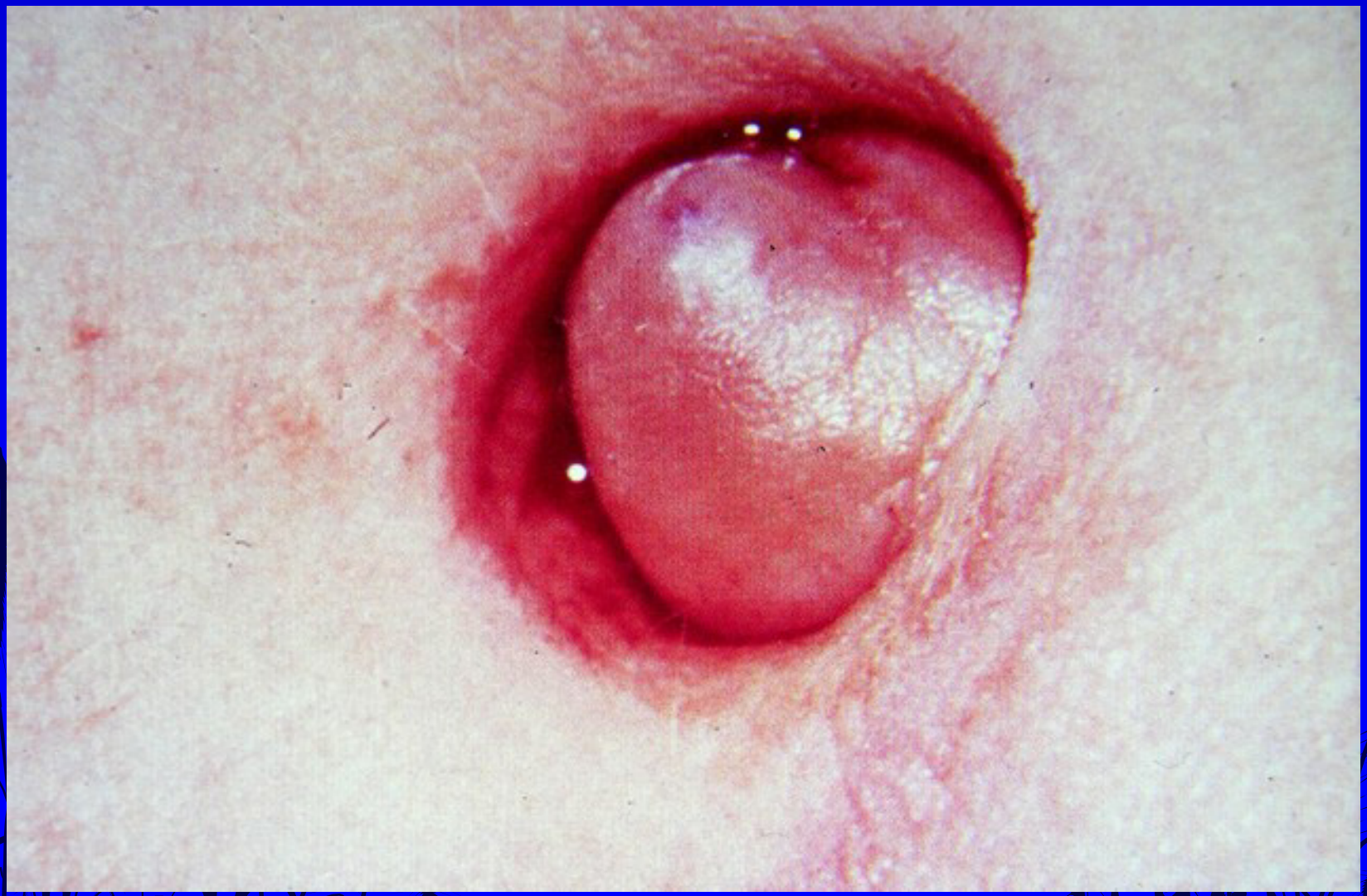






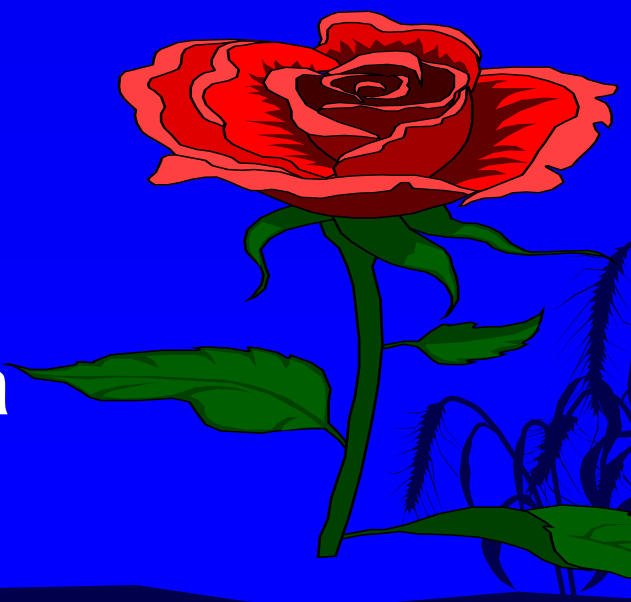






Endom.---Clinical presentation

- Asymptomatic → 25%
- Pain → -The commonest
  -Pelvic pain,Dysm,Dysp.
- Menorrhagia
- Infertility
- Acute abdomen
- Intermittent pyrexia



Endometriosis--presentation

- **Suggestive of endom:**
  - Pelvic tenderness
  - Fixed retroverted uterus.
  - Tender uterosacral ligament.
  - Enlarged ovaries.
- Deeply infiltrating nodules---most reliably detected when clinical exam performed during menstruation.

Endometriosis--Diagnosis

- Symptomatology.
- Defenitive Diagnosis:
  - **Laparoscopy**
  - **Histology**

Endometriosis--Diagnosis

- ***Laparoscopy:***

  -Gold standard investigation.

  - Specific time in the menstrual cycle

  ----Insufficient evidence.

  - Classification systems----subjective & correlate poorly with pain symptoms

Endometriosis---Histology

- Is it necessary----controversial.
- Positive histology-----confirm.
- Negative histology----doesn't exclude.
- Histological confirmation of at least one lesion is ideal.
- Endometriomas > 3 cm and deep infiltrating disease----Histology.

CA 125

- May be elevated.
- Compared with laparoscopy----has no value as a diagnostic tool.

Endometriosis &Infertility

- 15% of infertile women → Endom.
- 40-60% of endom. → Infertility
- Mechanisms:

-Adhesions -Dyspareunia

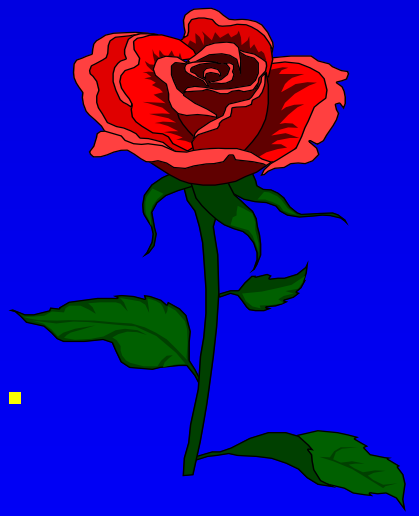
- ↑ prostaglandins -Tubal motility

-Folliculogen.

-C.L function

- ↑ Macrophages -LUF - ↑ prolactine

Endometriosis--Treatment



- Depends on:
  - Severity of symp. -Prev.Rx.
  - Age -Fertility expectation.
- Types:
  - Expectant -Surgical -Medical

Endometriosis---Medical Rx

- Endom.goes into remission during pregnancy → Pseudopregnancy
- Endom.invariably disappears after menopause → Pseudomenopause
- Androgen causes regression of endometriosis → Androgen

Endometriosis--Medical Rx

- Combined pills.
- Progestogen.
- Testosterone.
- Danazol.
- Gestrinone.
- GnRh agonists
- Aromatase inhibitors

DANAZOL

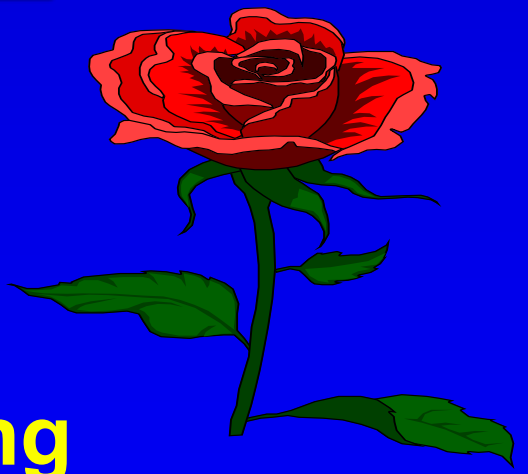
- Isoxazole derivative of 17-alpha-ethinyltestosterone.
- Action:
  - -Bind to SHBG → ↑ Free testost.
  - - ↓Synthesis of SHBG by the liver
  - -Prevent medcyclic surge of FSH,LH
  - -Inhibits several enzym. processes involved in ovarian steroidogenesis

↓Estrogen & ↑Androgen

Danazol---Side Effects

- Weight gain.
- Fluid retention.
- ↓ Breast size.
- Growth of facial hair.
- Emotion.lability
- Fatigue.
- Oily skin
- Atrophic vagin.
- Muscle cramps.
- Irrever.deepen. of voice.
- ↑ Choles. ↓ HDL
- Insuline resist.

DANAZOL----cont.



- Rx for 6-9 months.
- Dose 200mg twice daily.
- Contraindications:

  -Pregnancy -Breast feeding

  -Severe hepatic,cardiac,renal dis.

  -Thromboembolism -Porphyria

  -Androgen dependent tumours

Medical Rx----cont.

- **Gesrinone:(Trienic-19-Norsteroid)**

  -Inhibits midcyclic surge of FSH,LH

  -Same side effects as danazol.

  -Long 1/2 life(2.5-5mg twice weekly)

- **GnRh agonists:**

  -Menopausal symptoms.

  -Breakthrough bleeding.

  -Loss of bone Ca.

Medical Treatment---cont

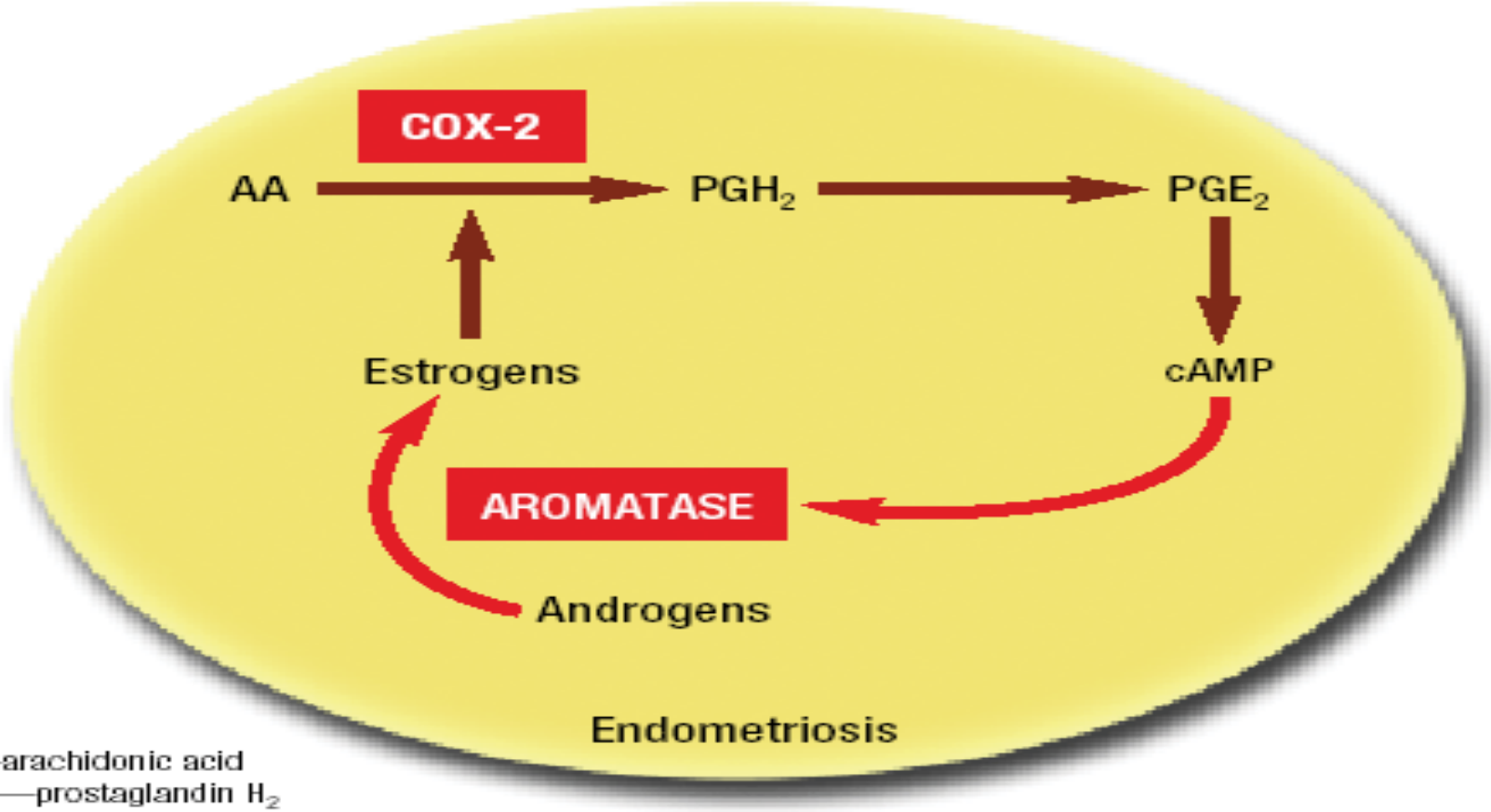
- **Aromatase Inhibitors:(anastrozole,letrozole)**

-Aromatase— **enzyme that catalyzes the final and the key step of estrogen production.**

- Decrease both peripheral and local estradiol production.
- May be better at suppressing local estrogen formation in endometriotic tissues than GnRH

  -----**More effective.**
- Combined with ovarian suppression.

FIGURE 2. Mechanism of local estrogen and prostaglandin biosynthesis in endometriosis



AA—arachidonic acid
PGH_2—prostaglandin H_2
PGE_2—prostaglandin E_2
cAMP—cyclic adenosine monophosphate

In endometriotic tissue, COX-2 regulates a key step in PGE_2 formation. It catalyzes the conversion of arachidonic acid (AA) to PGH_2, which is then converted to PGE_2. PGE_2 is the most potent known inducer of aromatase activity via a cAMP-mediated pathway. Aromatase catalyzes the conversion of androgens to estrogens, and estrogen, in turn, induces COX-2 production in uterine endothelial cells. Thus, a positive feedback cycle favors continuous production of PGE_2 and estrogens in endometriosis.

Endometriosis--Surgical Rx

- **Radical:**

  TAH+Removal of as much endom. tissue as possible+Bilat.oophorect.

- **Conservative:**

  -Division of adhesions,Tuboplasty---

  -Presacral neuroectomy

  -Laser uterine nerve ablation

Medical treatment of endom associated pain.

- **Empirical treatment without definitive diagnosis----Appropriate.**
  - **-Adequate analgesia.**
  - **- Progestogens**
  - **- Combined oral contraceptives.**

Medical RX---cont

- Effectiveness of NSAIDS----inconclusive evidence.
- Suppression of ovarian function for 6 months----reduce pain.
- Symptom recurrence is common following medical treatment.
- Aromatase inhibitor---may be effective.
- LNG-IUS-----reduce pain

Surgical Rx of Endom-associated pain

- Ideal practice –diagnose and remove surgically.
- Ablation----reduce pain.
- LUNA-----Doesn't reduce pain.
- Can be reduced by removing the entire lesions in severe and deeply infiltrating disease.
- Preop & postop hormonal rx----insuficient evidence of benefit.

Treatment of Endom-associated Infertility

- Medical treatment:

  -Minimal-mild disease----Not effective and shouldn't be offered.

  -More severe disease---No evidence of effectiveness.

- Ablation & adhesiolysis----effective in minimal-mild disease.
- The role of surgery in improving pregnancy rate for moderate-severe disease is uncertain.
- Postop hormonal rx ---no beneficial effect.

Assisted Reproduction in Endometriosis

- IUI in minimal- mild---- Improves fertility.
- IVF is appropriate treatment:
  - -Tubal function is compromised
  - - Male factor
  - - Other treatment have failed
- GnRH agonists for 3-6 months before IVF--- increase rate of clinical pregnancy

Thank you