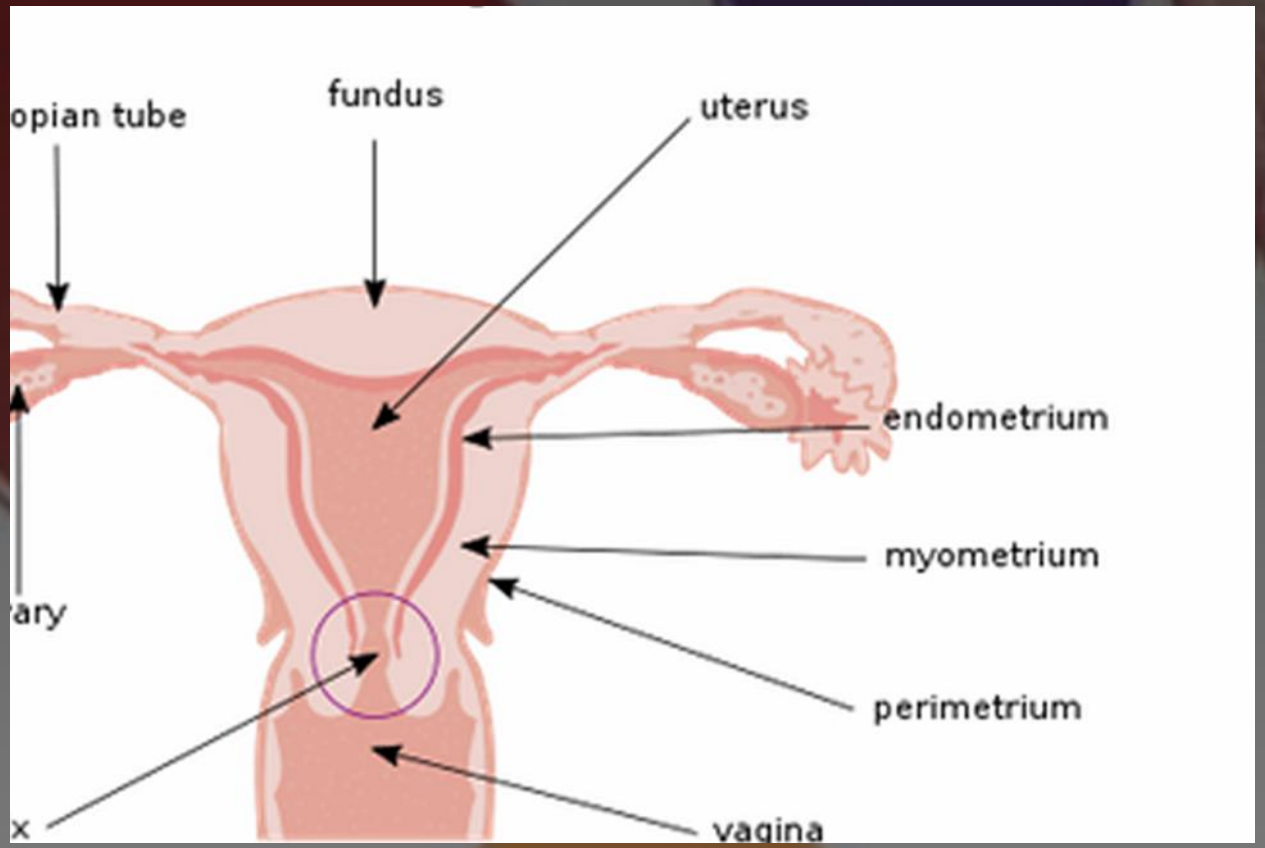
FEMALE GENITAL SYSTEM, LECTURE 3
Uterus and GTD



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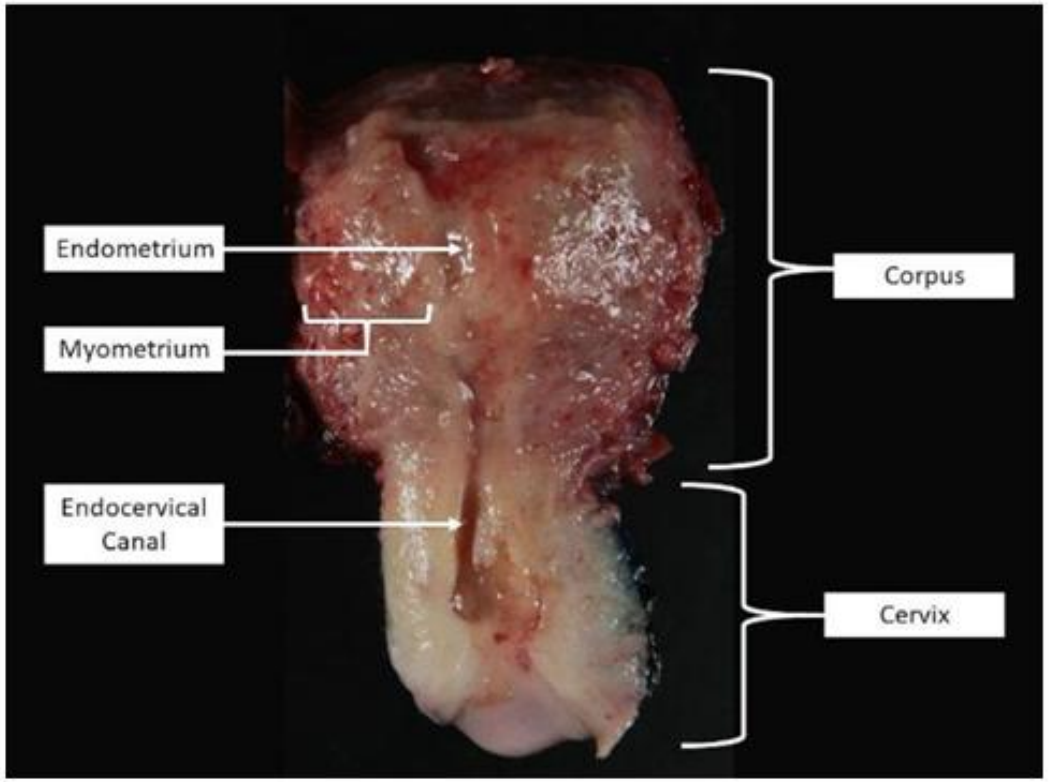
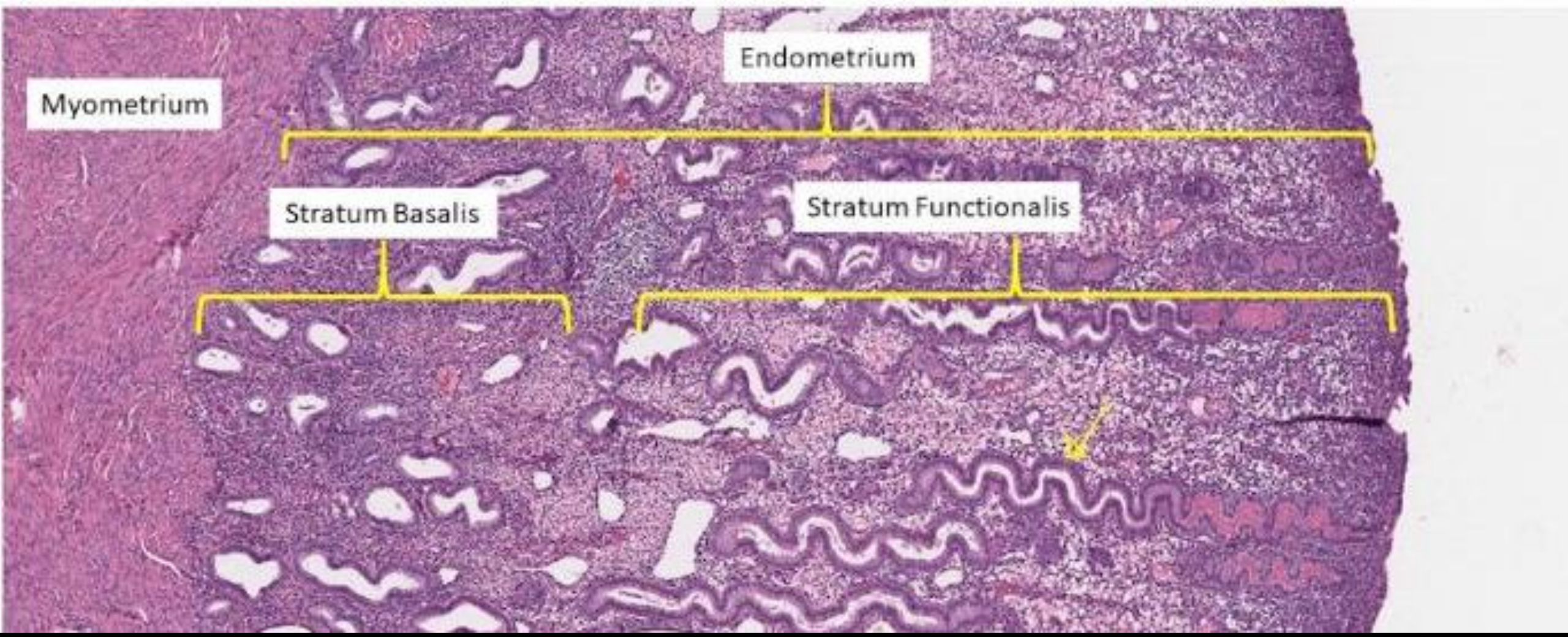
- **Department of Microbiology & Pathology**
- **Mutah University School of Medicine**
- **UGS lectures 2026**

Gross anatomy




Endometrium
Myometrium
Stratum Basalis
Stratum Functionalis

Histology

Uterine pathology

- ➢ Non-neoplastic:
  - •Endometritis.
  - •Adenomyosis.
  - •Endometriosis.
  - •Hyperplasia without atypia.

➢Neoplastic: •Hyperplasia.
- •Malignant tumors.

1. Endometritis

- Inflammation of the endometrium.
- Risk factors:

  Pelvic inflammatory disease (PID).

  Retained products of conception.

  Intrauterine device (IUCD).

- Clinically: fever, abdominal pain, menstrual abnormalities, infertility & ectopic pregnancy

due to damage to the fallopian tubes.

- Management: Correct the cause, antibiotics.

2. Adenomyosis

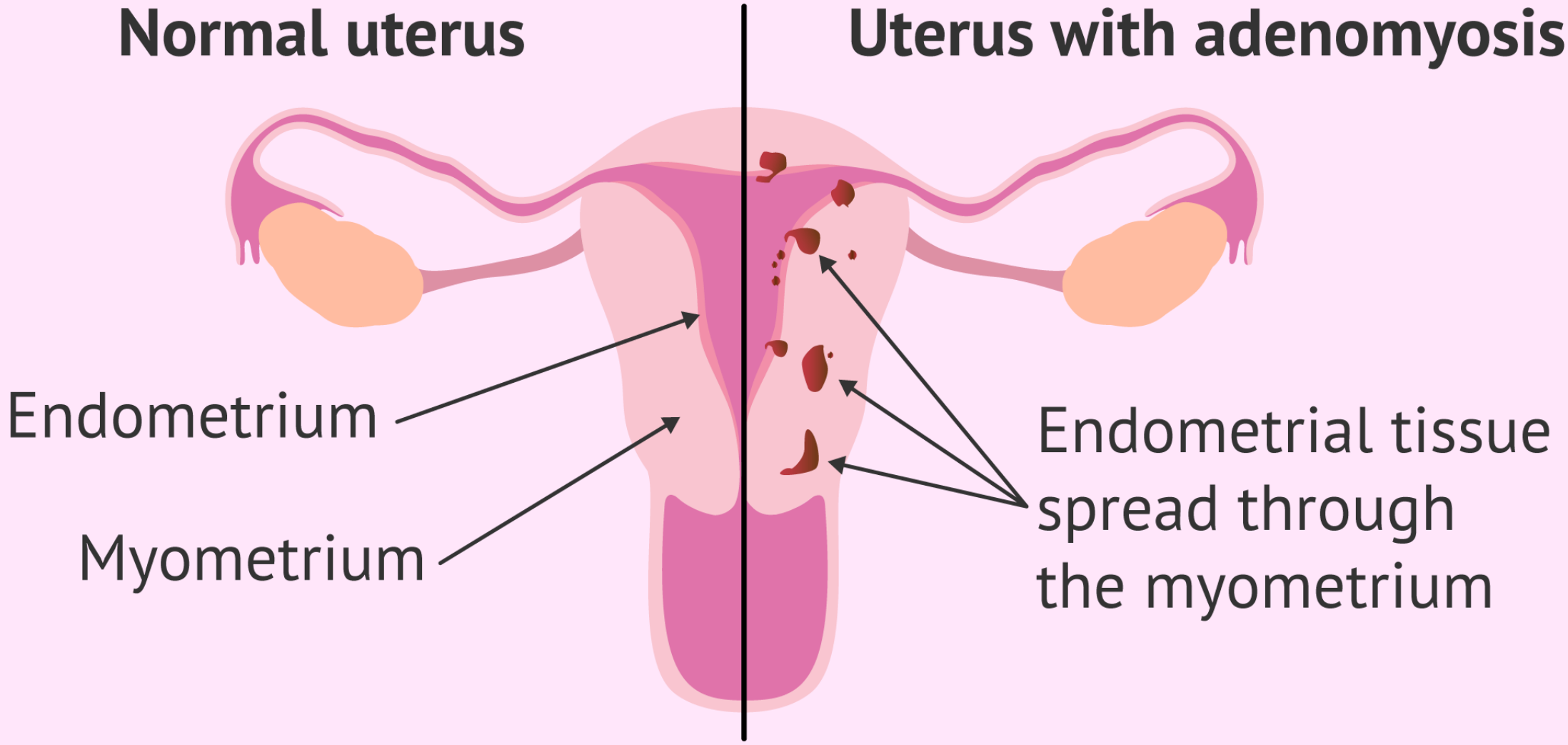
- The presence of endometrial tissue (stroma, glands, or both)in myometrium, between muscle bundles.

- Result in thickened uterine wall & enlarged uterus due to reactive muscle hypertrophy.

- Presentation: menorrhagia, dysmenorrhea.

- Usually Coexist with endometriosis.

Microscopic features



3. Endometriosis

The presence of estrogen-dependent endometrial tissue outside the uterine cavity.

Affecting women in the reproductive years.

Usually it’s a multifocal process involving:

❖ pelvic structures: ovaries, uterine ligaments, rectovaginal septum, cul de sac

❖OR involves distant areas of peritoneal cavity or periumbilical tissues.

Endometriosis - Pathogenesis

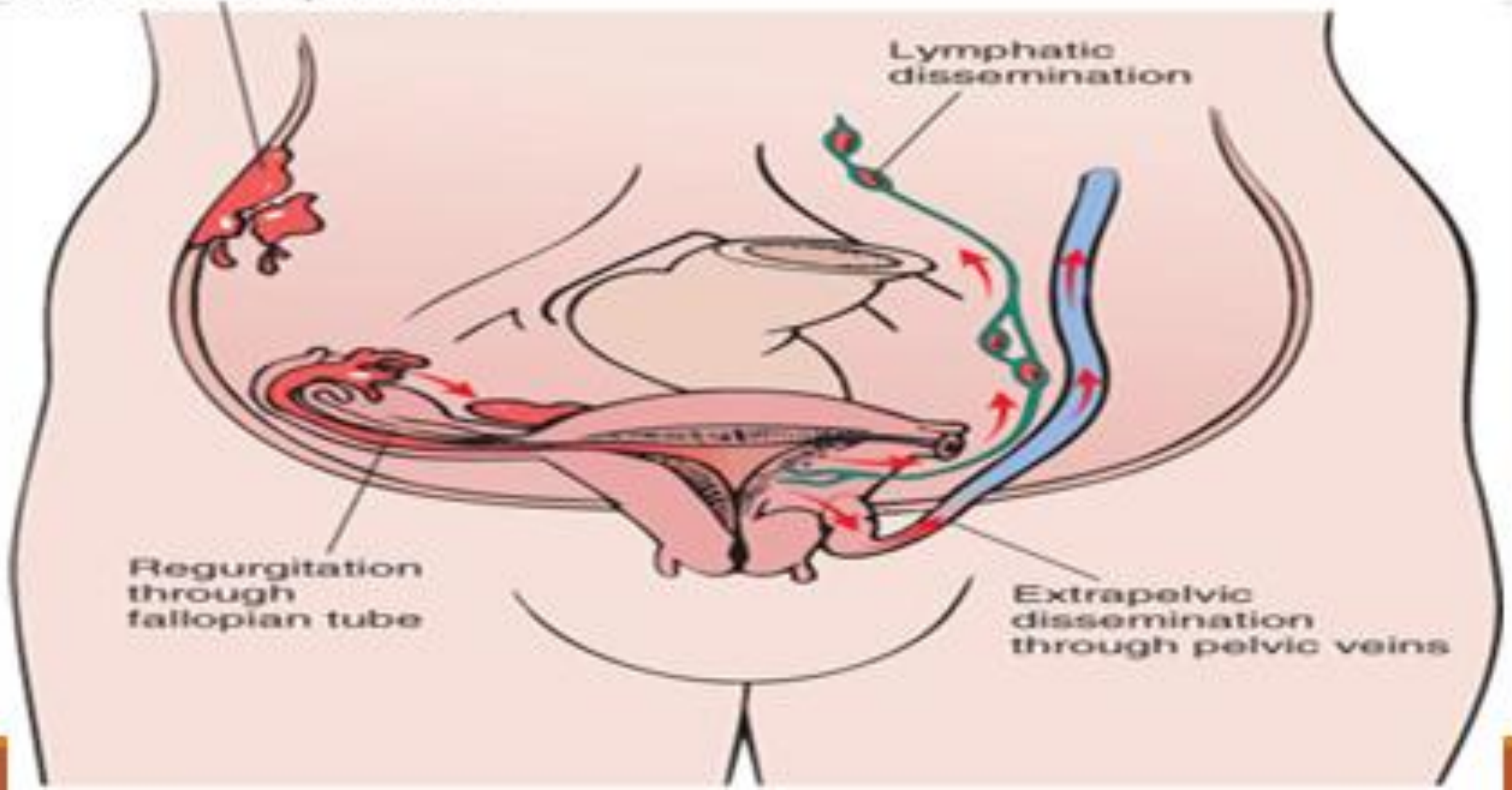
Four hypotheses:
1-Regurgitation theory, favored, → menstrual backflow through the tubes → implantation.

2-Benign vascular and lymphatic dissemination.

3-Metaplastic theory, endometrial differentiation of coelomic epithelium.

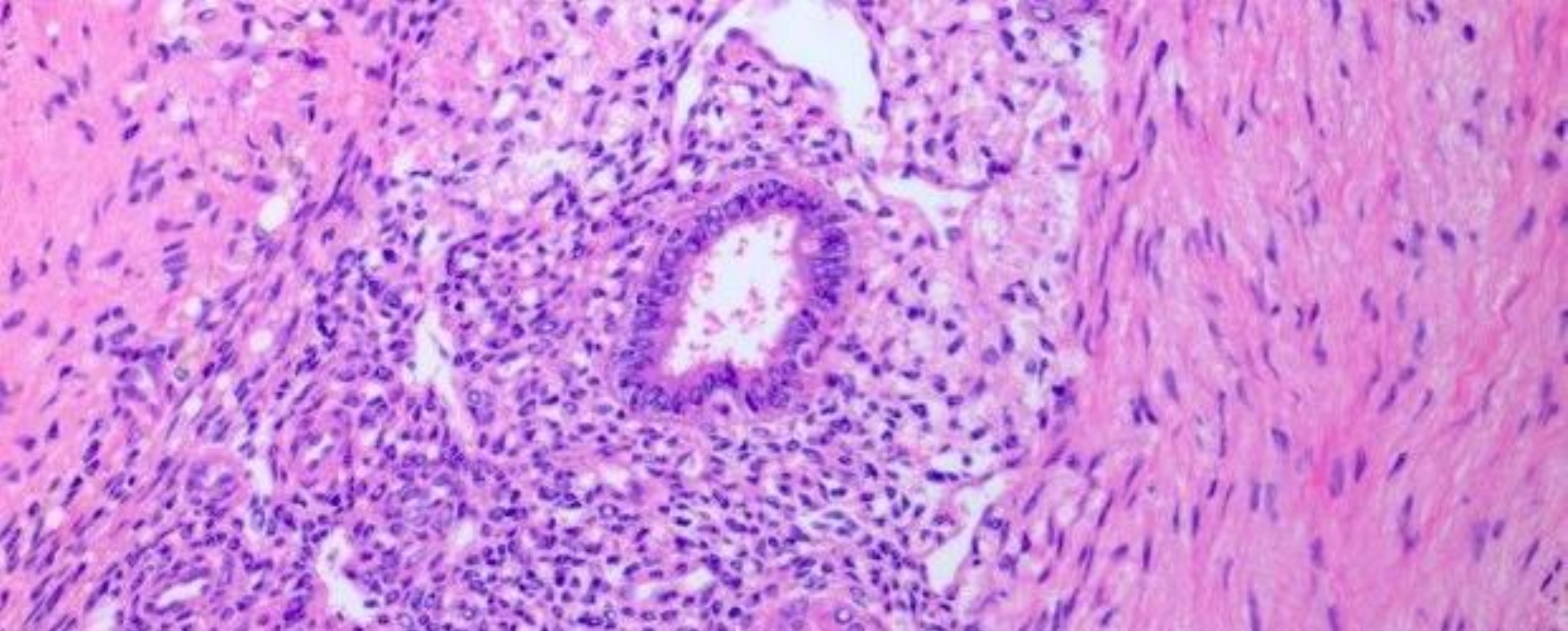
4-The extrauterine stem/progenitor cell theory.

Metaplastic differentiation of coelomic epithelium



Clinical presentation

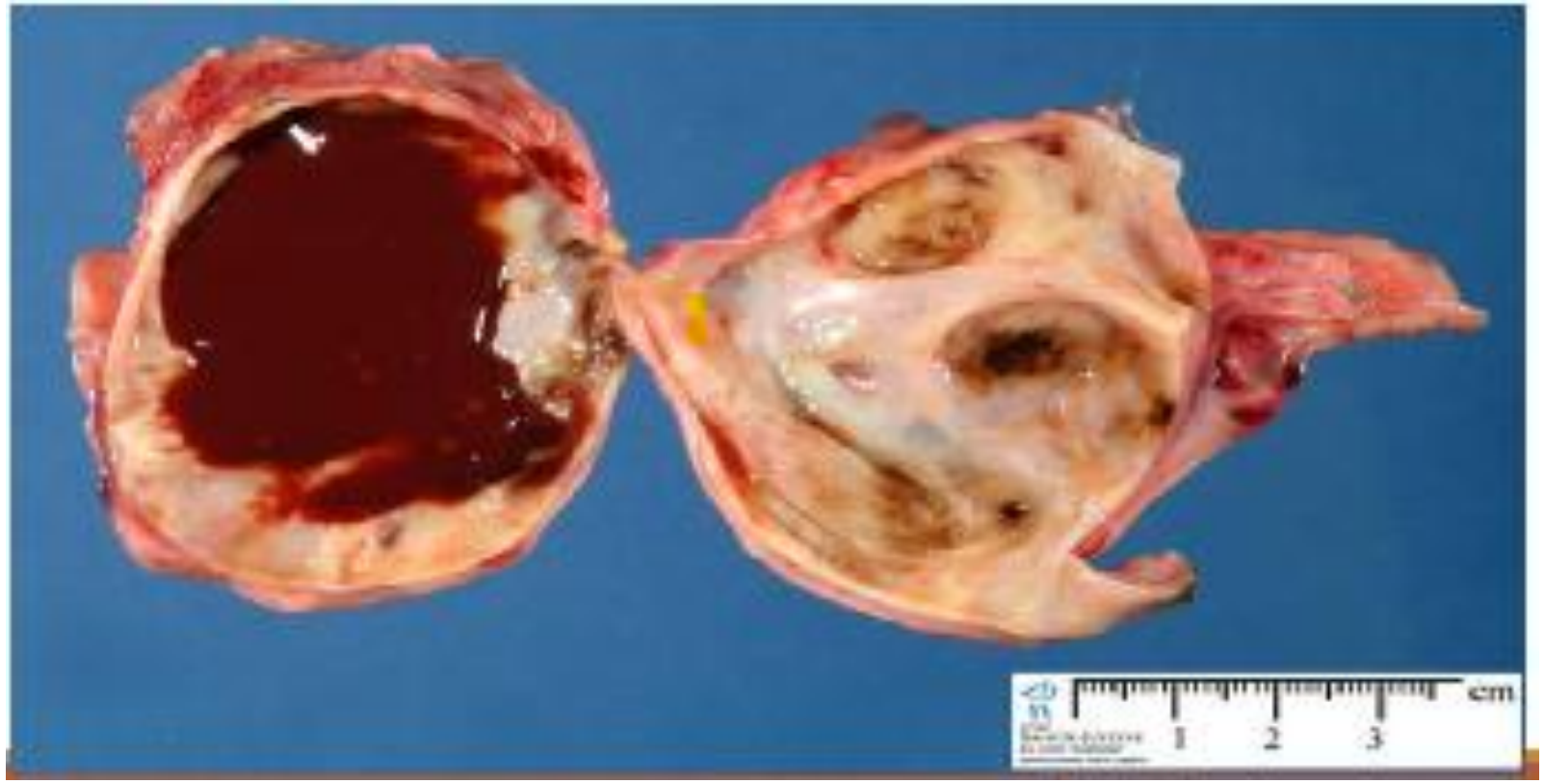
- Clinically presented with pain and infertility.
- Dysmenorrhea.
- pain on defecation.
- dyspareunia
- dysuria

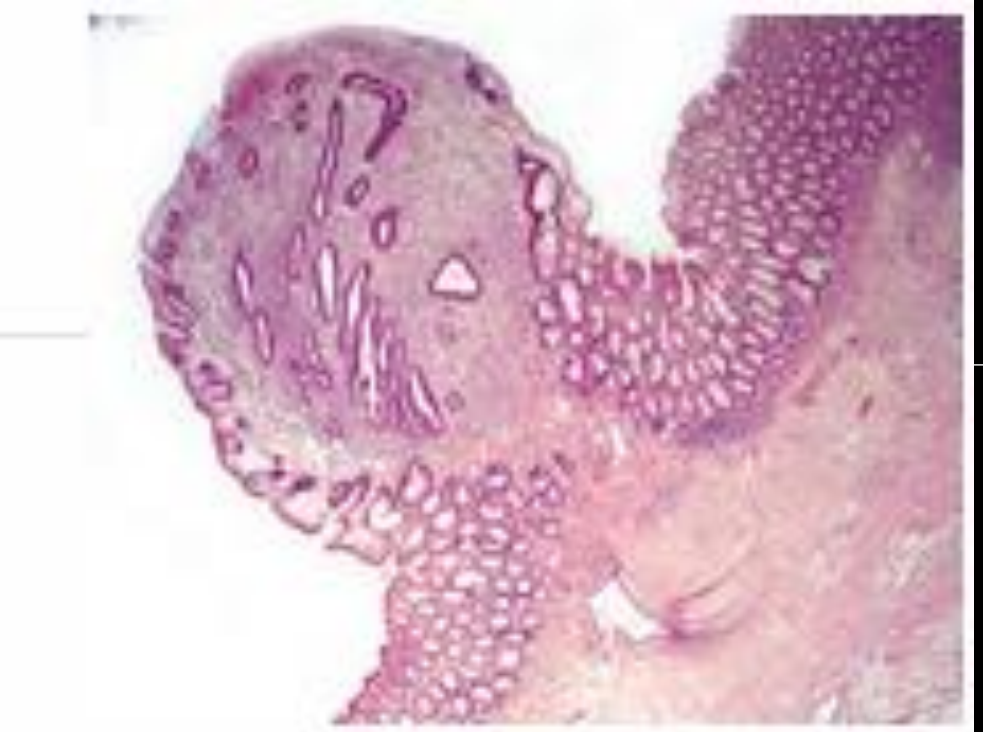


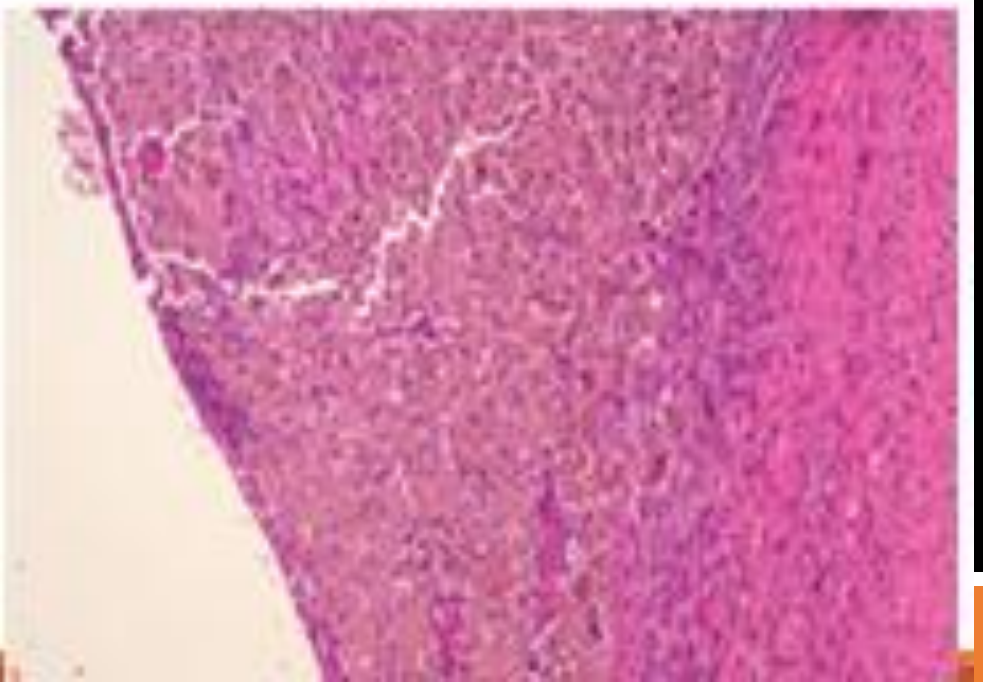
Endometriotic foci

▪Consists of functioning endometrium → undergoes cyclic bleeding → organization of blood → widespread fibrosis →adhesions among pelvic structures.

Gross features Ovarian endometriosis: chocolate cyst.







Microscopically:
At least 2 of the following 3 features:

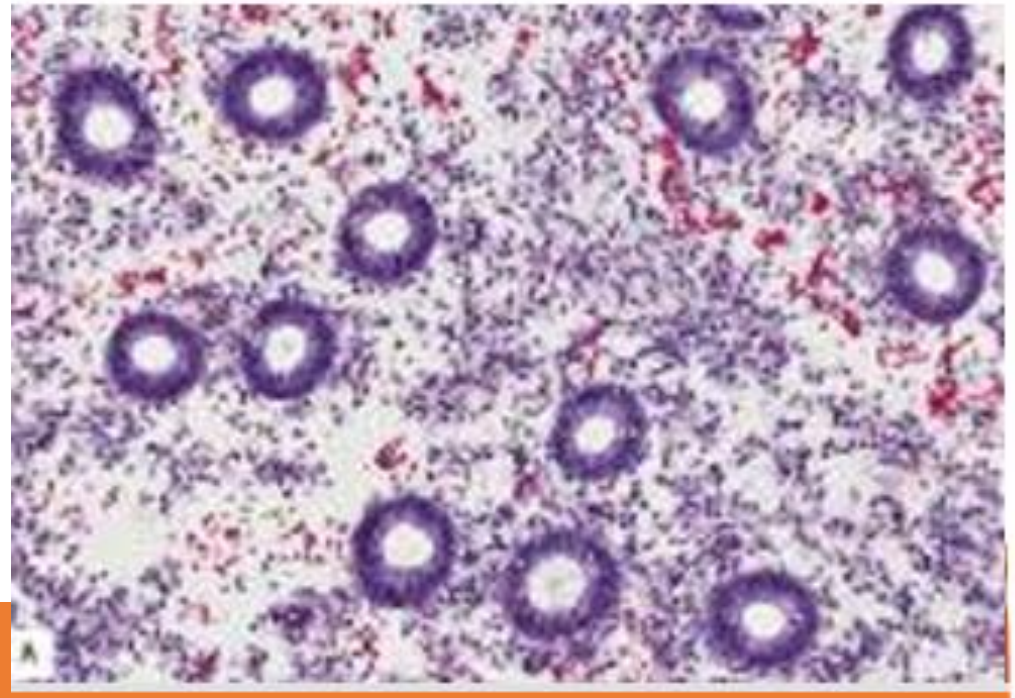
- endometrial glands.
- endometrial stroma.
- hemosiderin pigment.

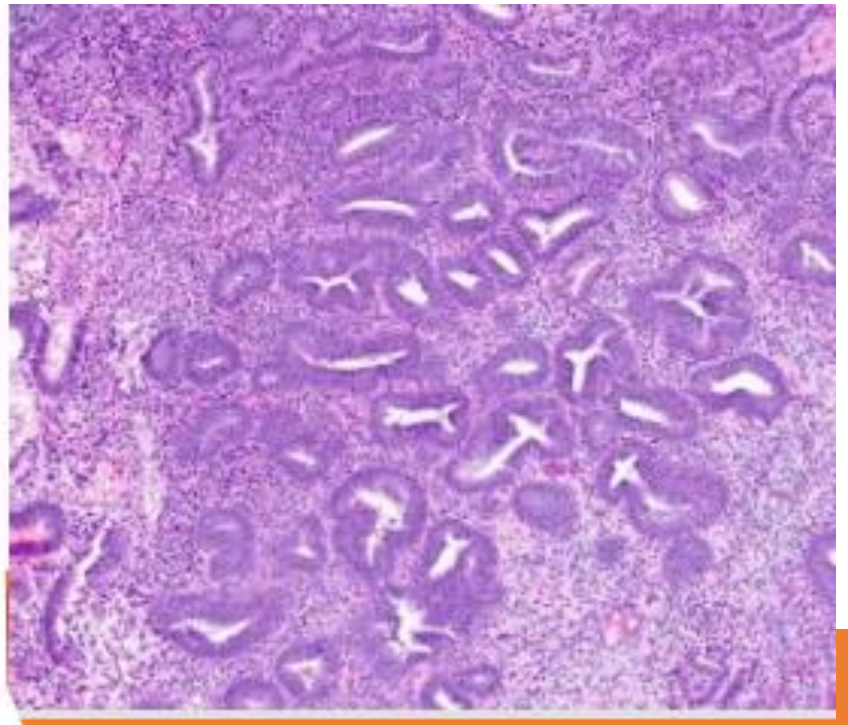
4. Endometrial Hyperplasia:

➢Proliferation of endometrial glands with a resulting increase in gland to stroma ratio.

➢Increased endogenous or exogenous estrogen, unopposed by progesterone .

➢Chronic estrogenic stimulation without progesterone affects glands to a greater extent → glandular overgrowth (hyperplasia)

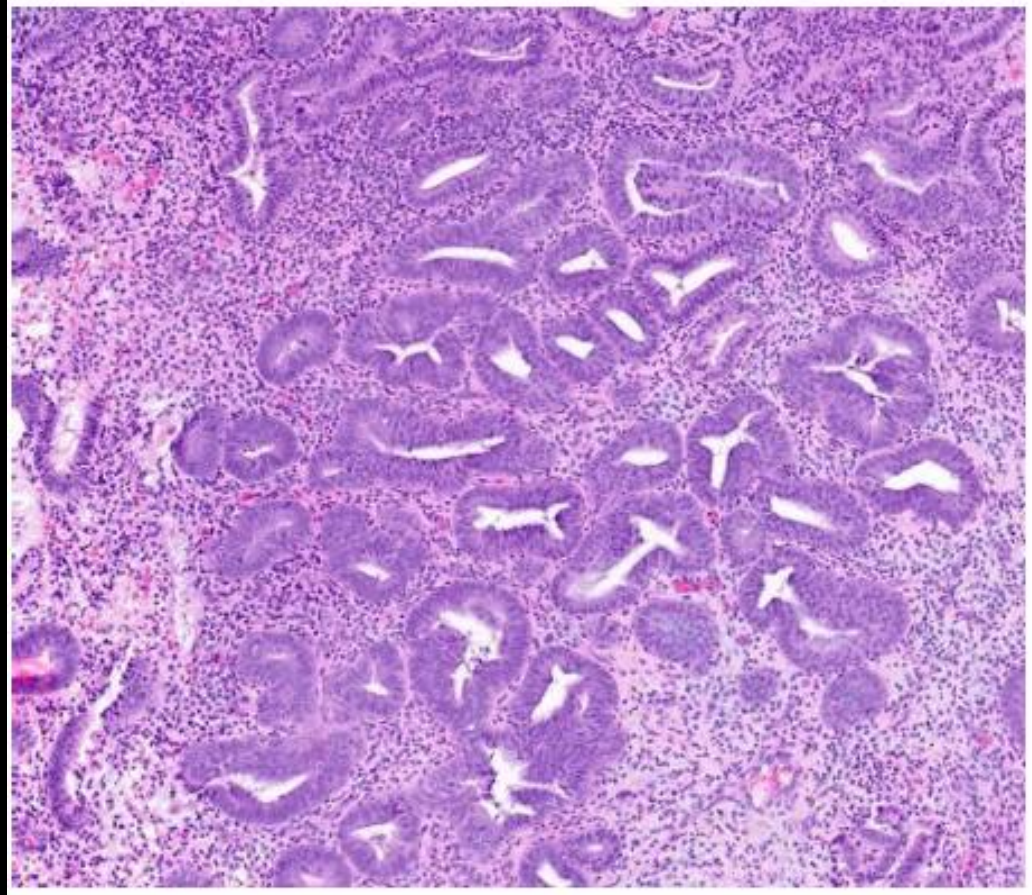




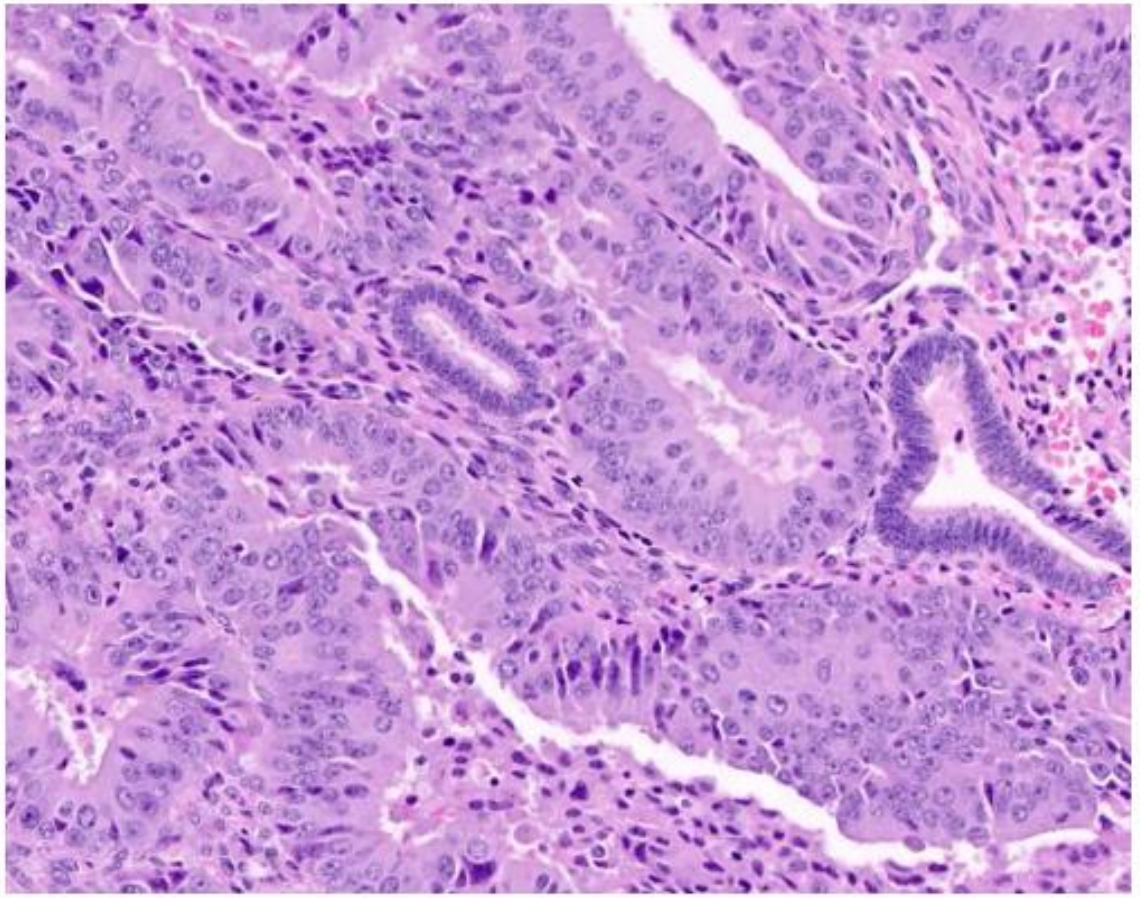
Two categories based on the presence of cytologic atypia:

Two categories based on the presence of cytologic atypia:

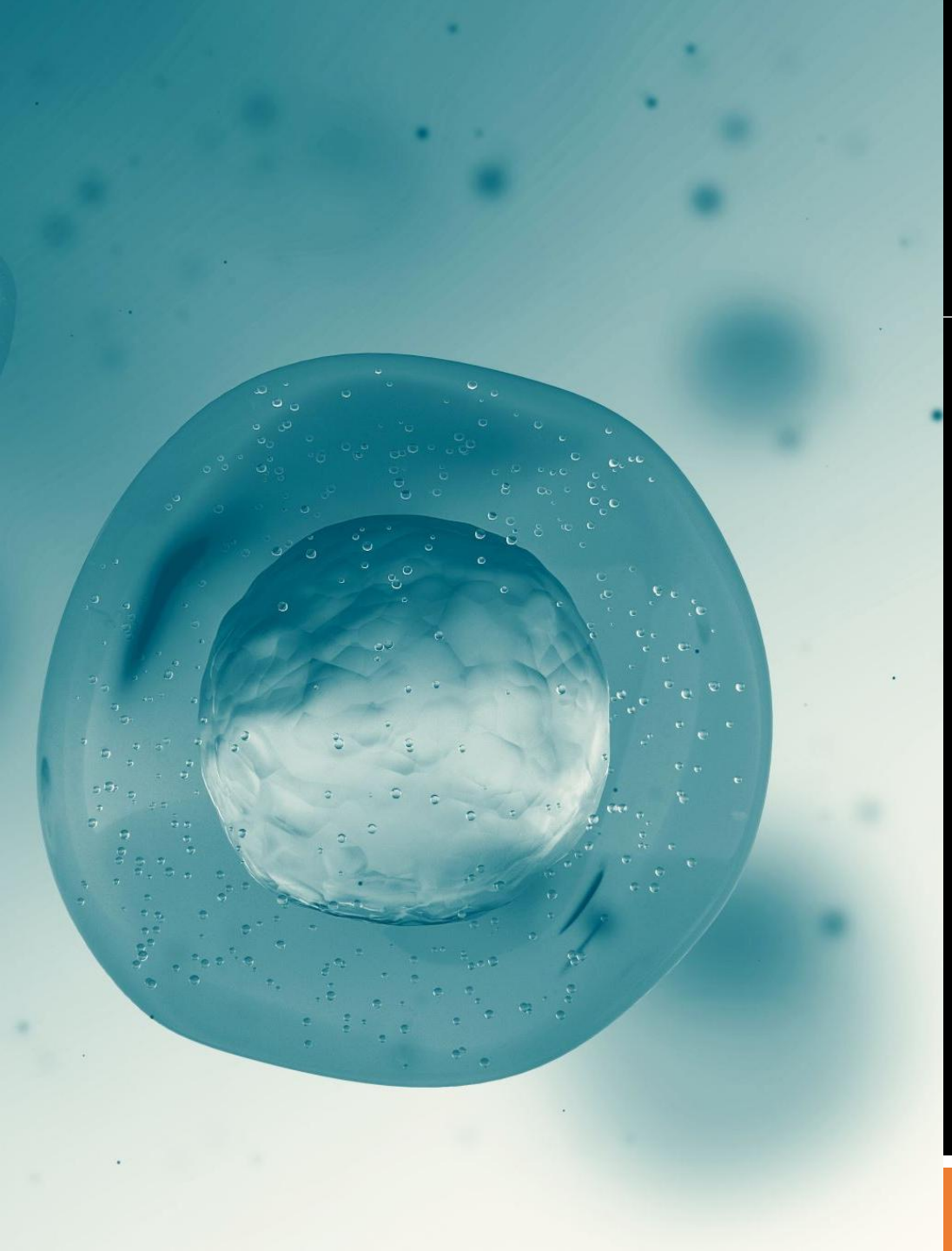
- Hyperplasia without atypia; low risk for progression to endometrial Ca.
- Hyperplasia with atypia(endometrial intraepithelial neoplasia (EIN) higher risk for progression to endometrial Ca. → 20%.



Hyperplasia without atypia



Hyperplasia with atypia

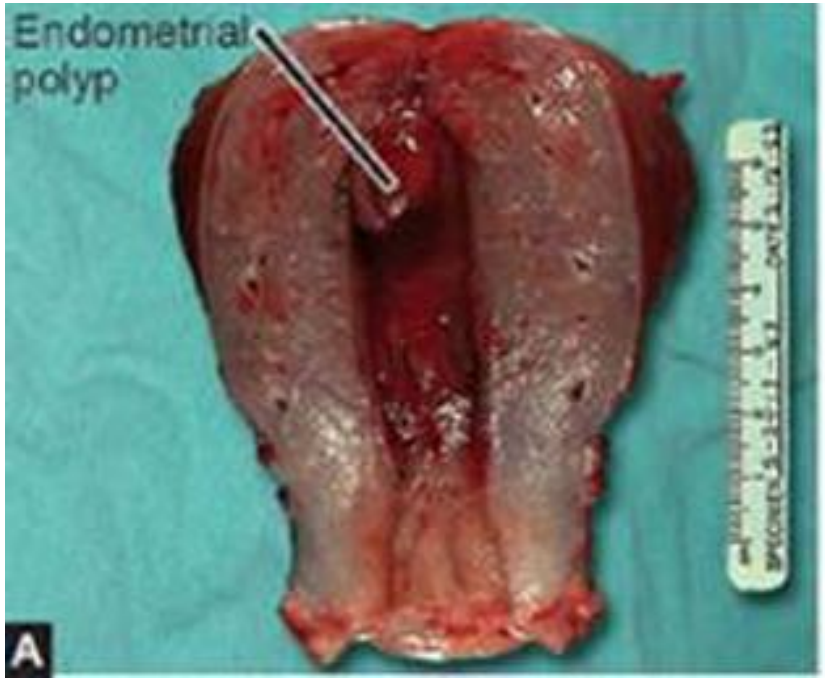


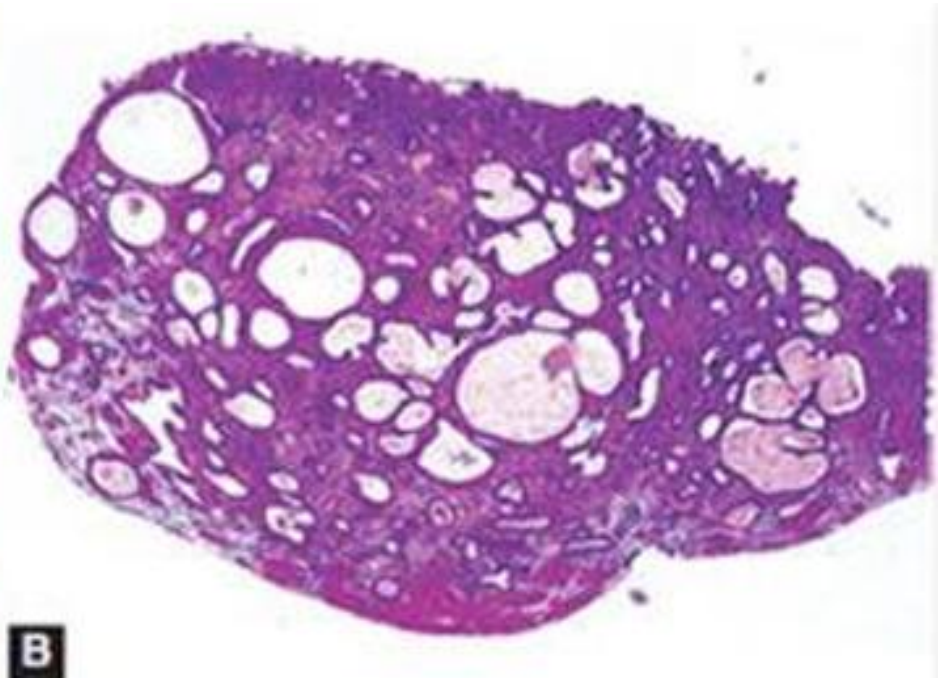
Tumors:

- Endometrial tumors.
- Myometrial tumors.

1. Endometrial Polyps:

- Exophytic masses of variable size that project into the endometrial cavity.
- Endometrial dilated (cystically) glands, with small muscular arteries and fibrotic stroma.
- Present with abnormal uterine bleeding.





2. Endometrial Carcinoma

- The most frequent cancer occurring in the female genital tract.
- Affecting female between 50s & 60s.
- Presentation: irregular or postmenopausal bleeding. With progression, the uterus enlarges.

- Two histological subtypes:

1. Endometrioid carcinomas.
2. Serous carcinoma.

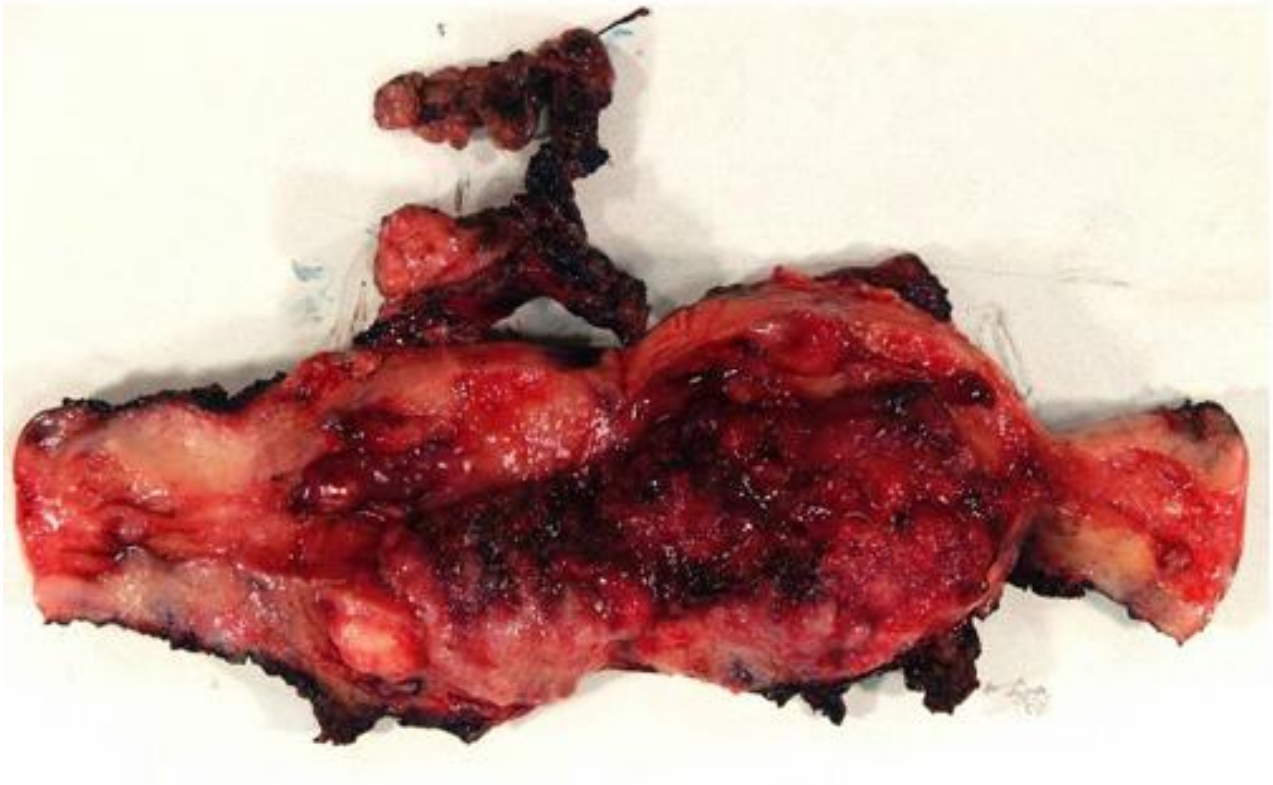
1. **Endometrioid carcinomas:**

- 80% of cases of endometrial carcinomas.
- Designated Endometrioid because of their histologic similarity to normal endometrial glands.
- Genetic: Mutations in mismatch repair genes & PTEN tumor suppressor gene.
- Risk factors:

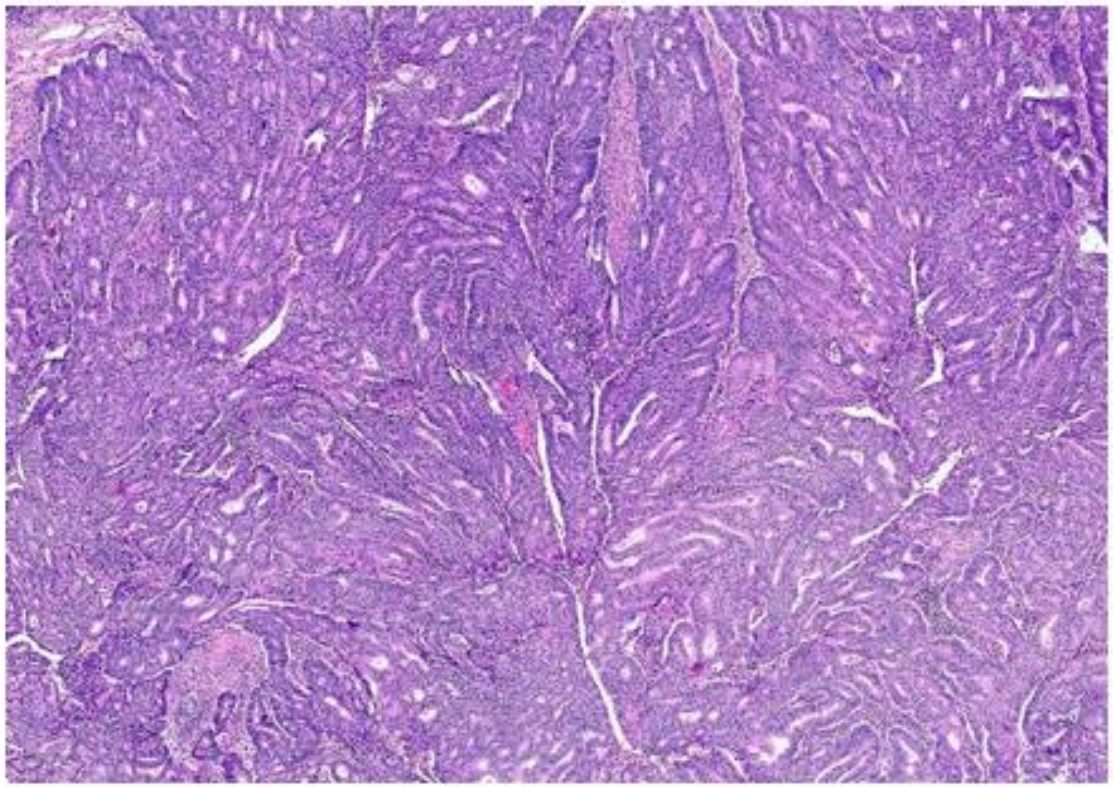
(1) obesity.
(2) diabetes.
(3) hypertension.
(4)infertility.
(5) exposure to unopposed estrogen.

- Prognosis: slow to metastasize, but if untreated, eventually disseminates to regional nodes & distant sites.

Gross and microscopic features



#Friable, hemorrhagic mass occupying the endometrial cavity

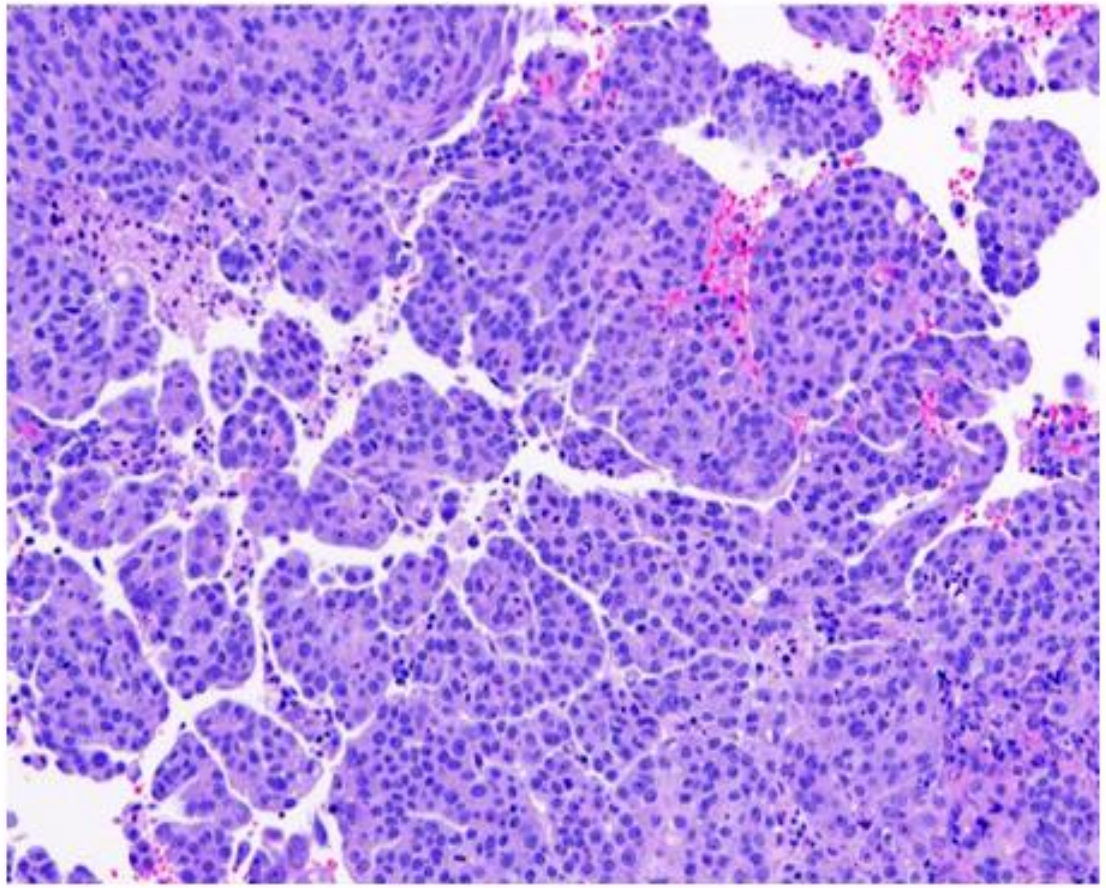


#back to back glands lacking intervening stroma.
#nuclear atypia.

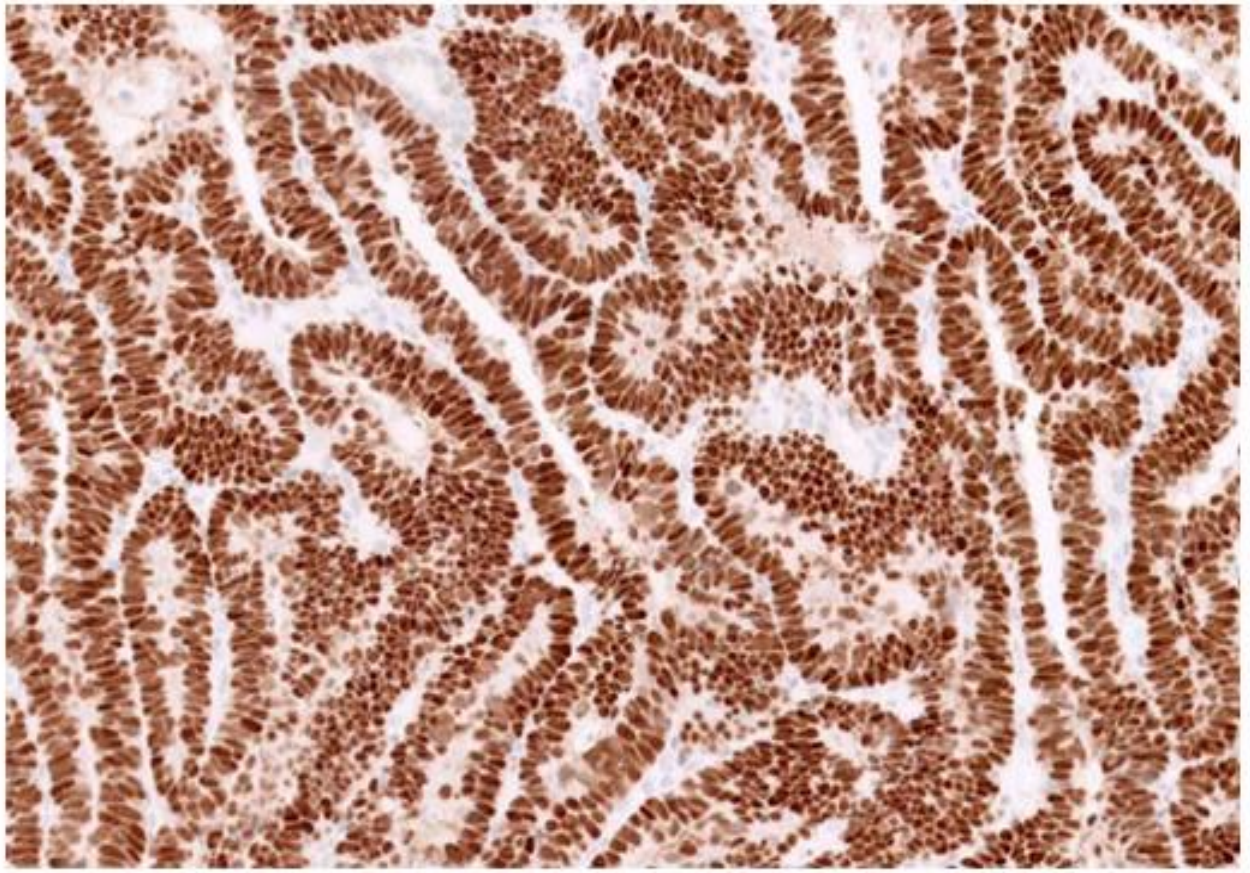
2. Serous carcinoma.

- Less common but far more aggressive.
- Not associated with unopposed estrogen or hyperplasia.
- Genetic: mutations in the TP53 tumor suppressor gene.
- Prognosis: strongly dependent on staging but because of its aggressive behavior → often high-stage disease with a poor prognosis.

Microscopic features



#Sheets and small papillae of endometrial serous carcinoma



#Strong and diffuse overexpression of p53

Tumors of the Myometrium

1. Leiomyomas (fibroids):

➢Benign tumors from the smooth muscle cells.

➢The most common benign tumor in females, 30-50% of women of reproductive age.

➢Estrogens stimulate the growth; shrink postmenopausally.

➢Often asymptomatic, most frequent sign is menorrhagia.

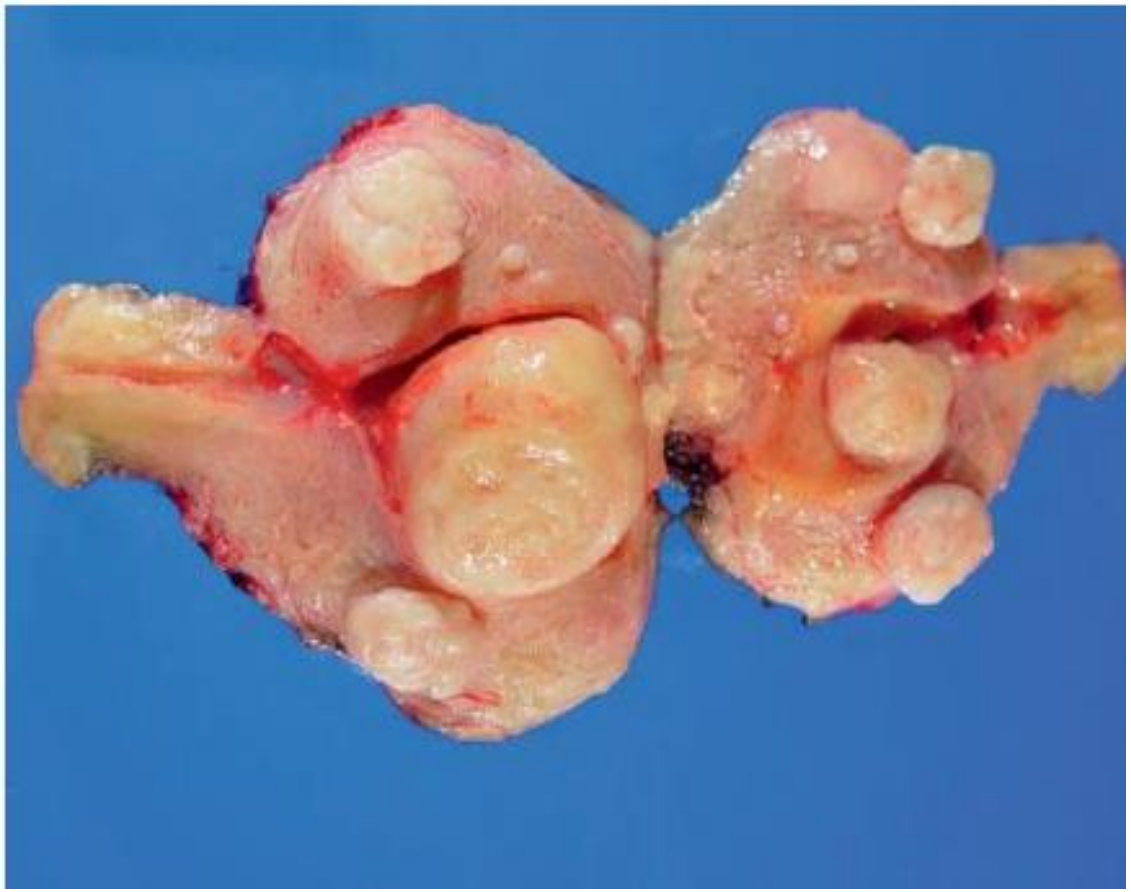
➢Rarely, if ever, transform into sarcomas, multiple lesions does not increase the risk of malignancy.

Gross morphology

sharply circumscribed, firm gray white masses with a characteristic whorled cut surface, often occur as multiple tumors.

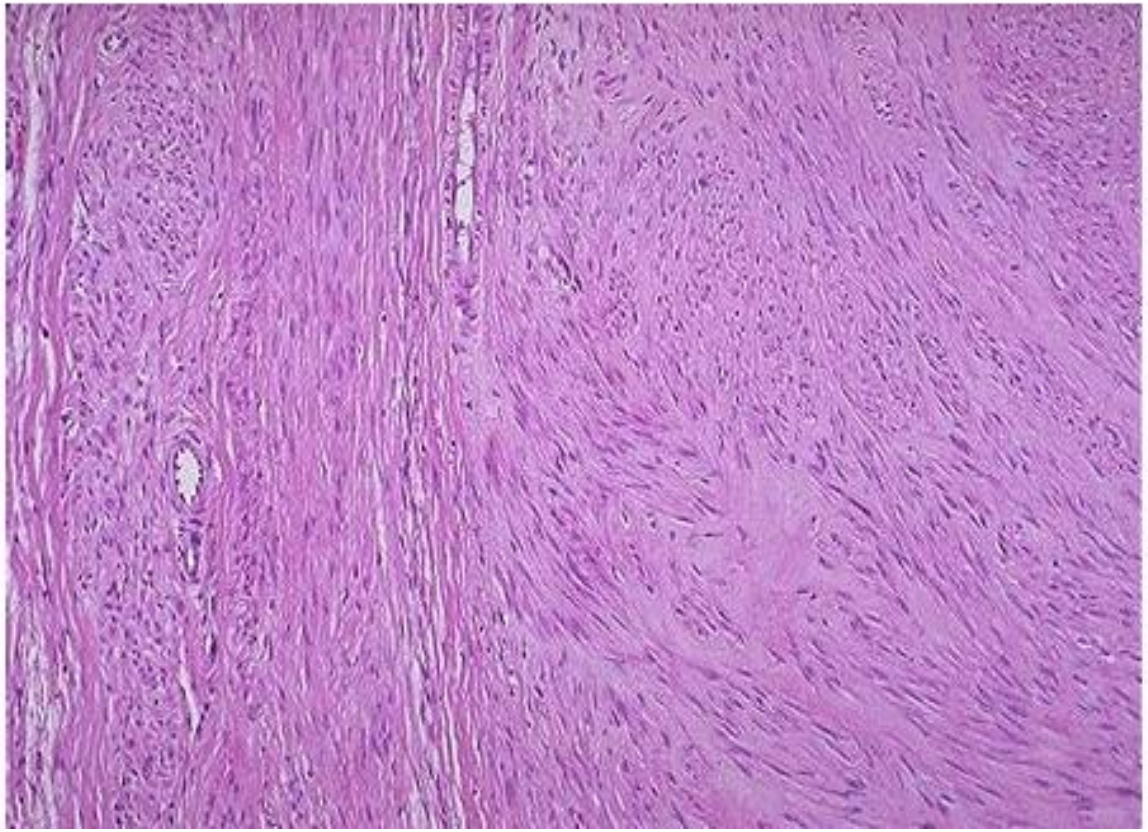
Possible location:

- Intramural.
- Submucosal.
- Subserosal.



Histological features

- Bundles of smooth muscle cells mimicking the appearance of normal myometrium

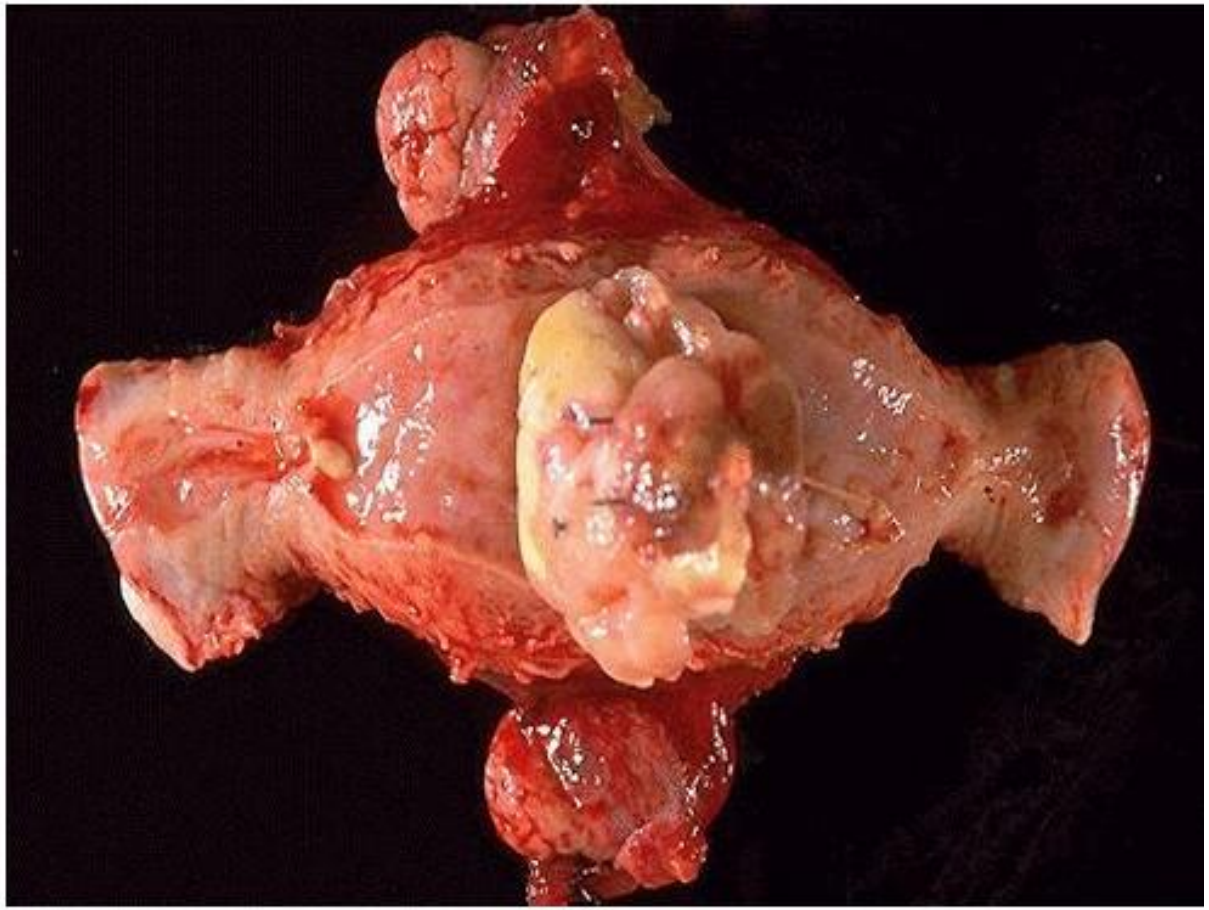


2. Leiomyosarcoma

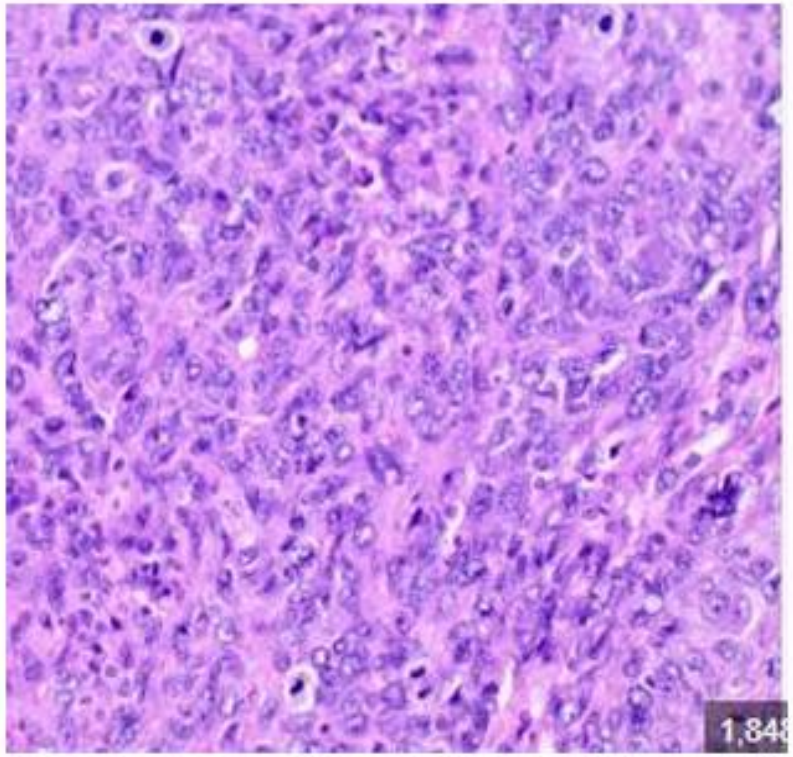
➢Malignant counterpart of Leiomyoma.
➢Always arise de novo (not from previous Leiomyoma)
➢Solitary and mostly in postmenopausal women.
➢Recurrent is common & many metastasize, typically lungs.

Gross features

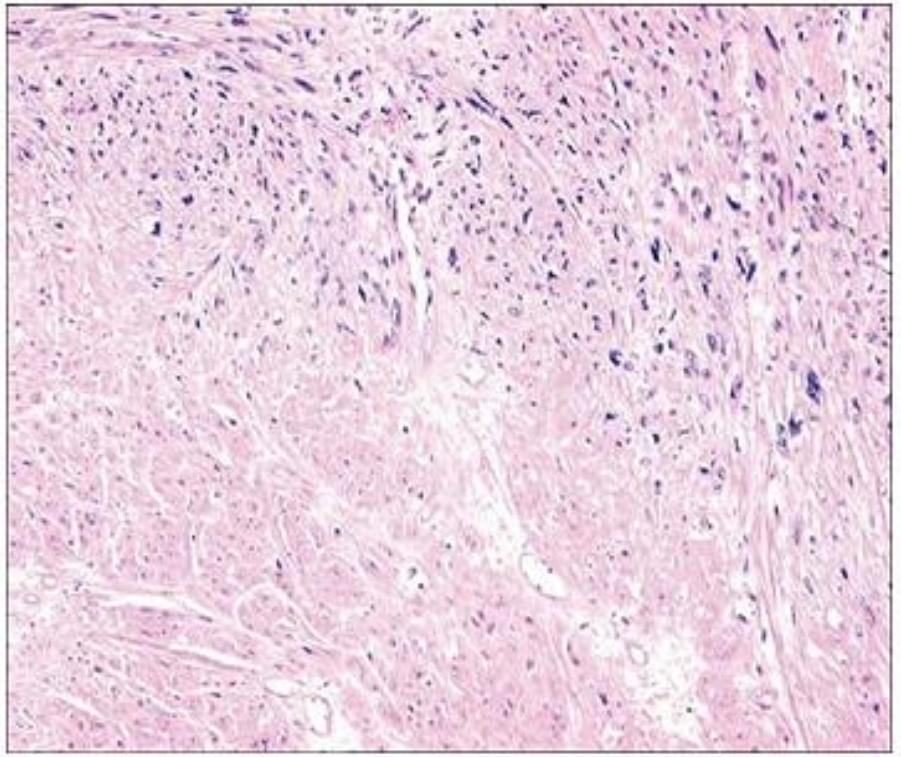
soft, hemorrhagic, necrotic masses.
Irregular borders.



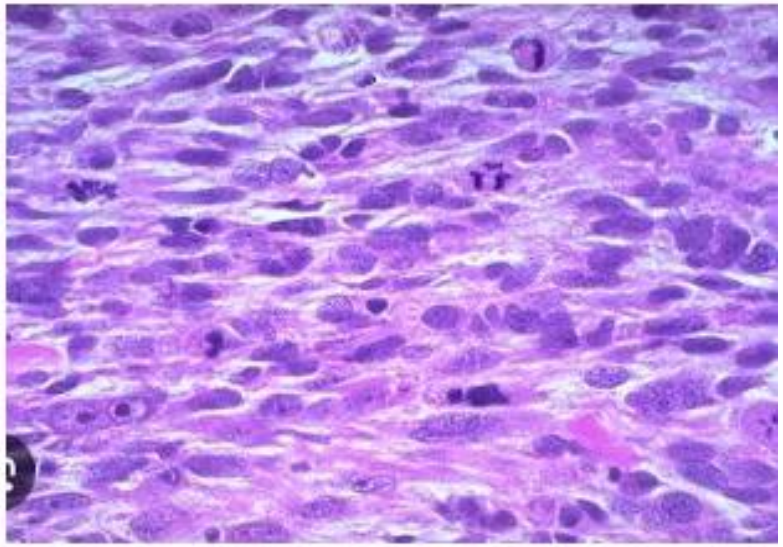
Microscopic features
Diagnostic features of leiomyosarcoma:



cytologic atypia

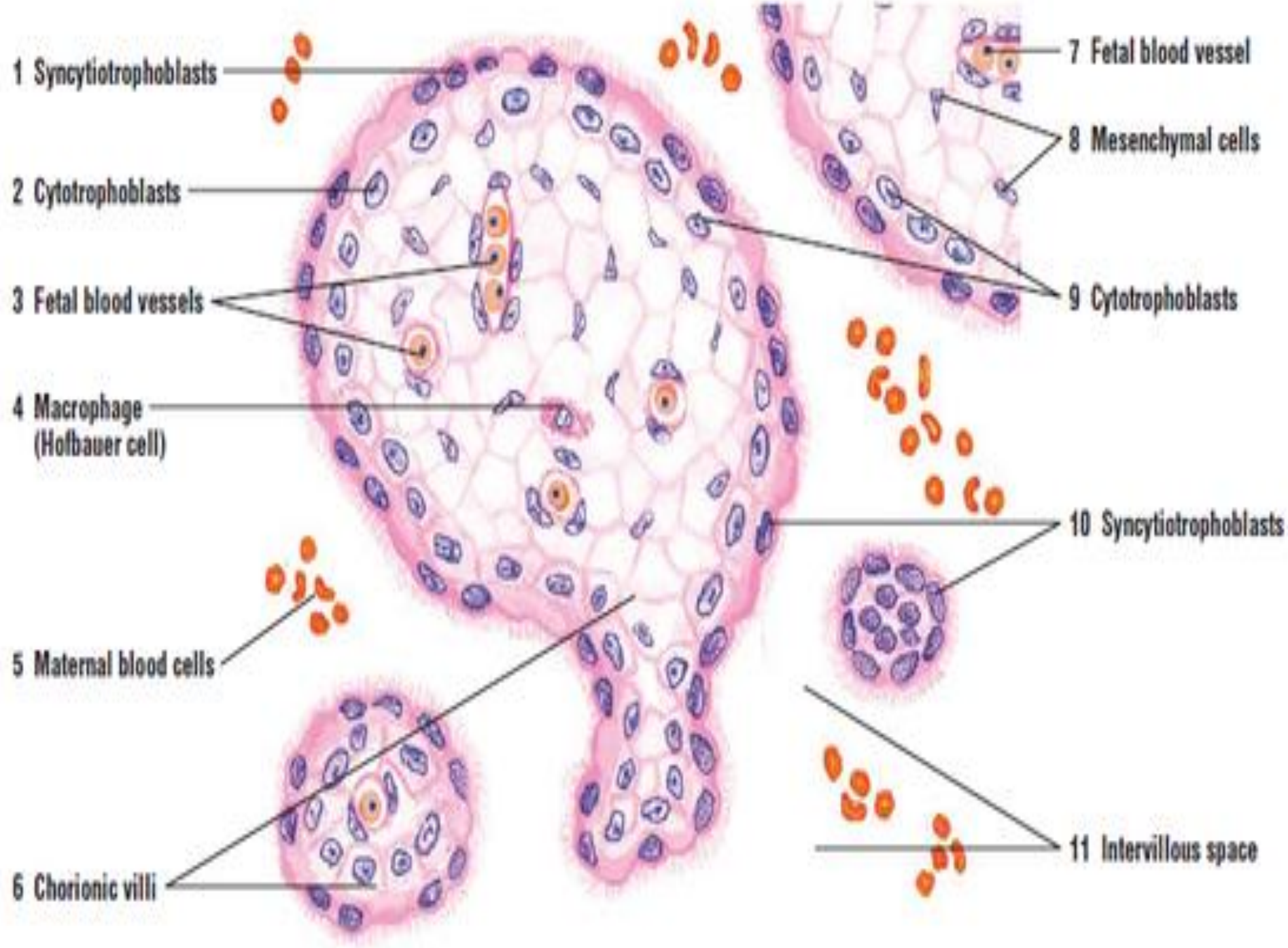


tumor necrosis



mitotic activity

Placental disc histology



Gestational trophoblastic disease

An abnormal proliferation of fetal trophoblast cells. (normal cells of placenta in pregnancy)

In early embryo trophoblast cells form chorionic villi → in time they make the placenta (provide a large contact area between fetal & maternal circulations to allow gas & nutrient exchange).

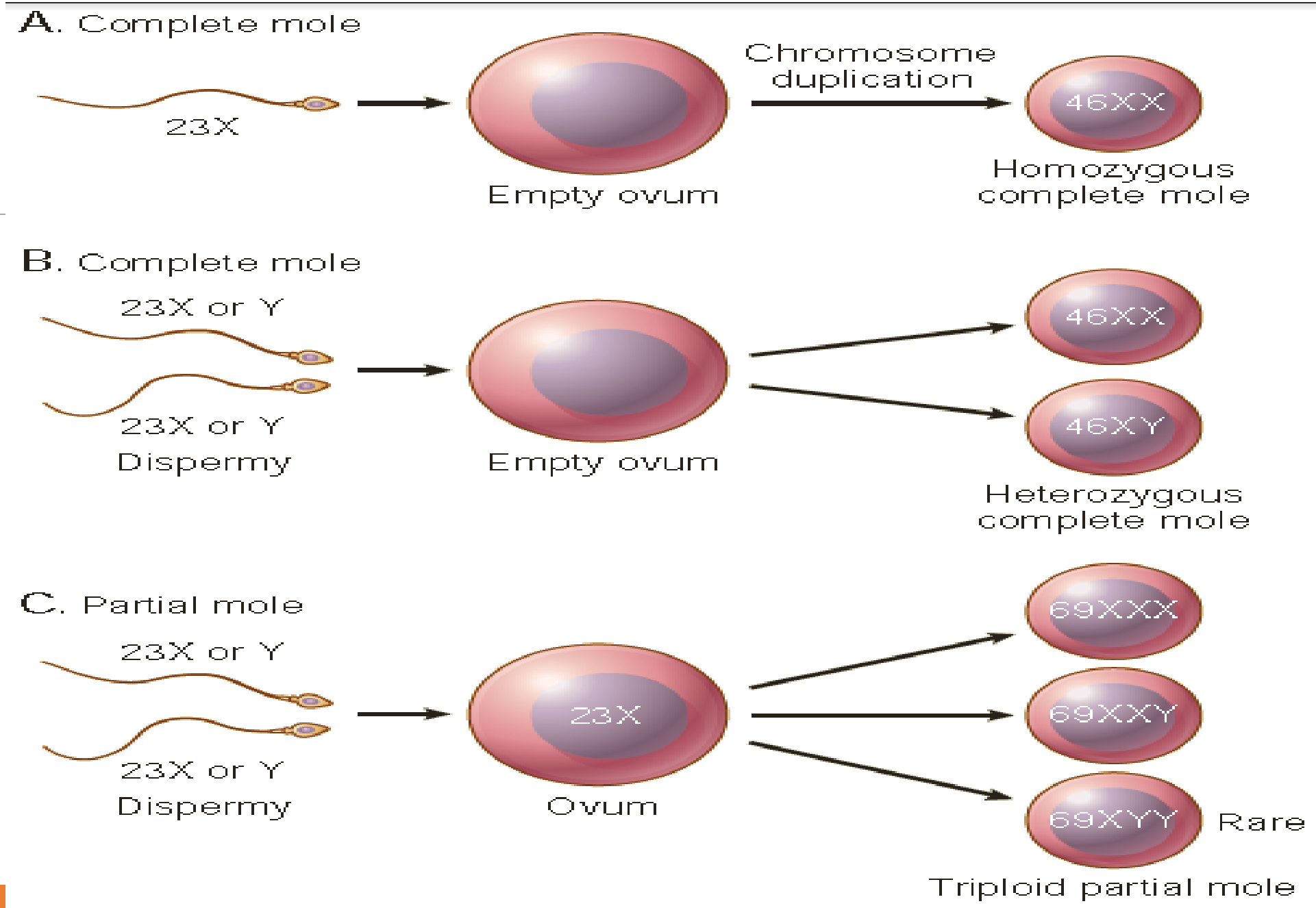
All elaborate human chorionic gonadotropins (hCG) → detected in the blood & urine at levels higher than those found during normal pregnancy. (diagnosis, follow up).

Hydatidiform Mole - Pathogenesis

An abnormal gestational process due to abnormal fertilization with an excess of paternal genetic material, two forms:

1-Complete mole: an empty egg fertilized by two spermatozoa (or a diploid sperm) → diploid karyotype containing only paternal chromosomes.

2-Partial mole: a normal egg is fertilized by two spermatozoa (or a diploid sperm) → triploid karyotype with a dominance of paternal genes.


A. Complete mole
23X
Empty ovum
Chromosome duplication
46XX
Homozygous complete mole
B. Complete mole
23X or Y
23X or Y
Dispermy
Empty ovum
46XX
46XY
Heterozygous complete mole
C. Partial mole
23X or Y
23X or Y
Dispermy
23X
Ovum
69XXX
69XXY
69XYY
Rare
Triploid partial mole

Hydatidiform Mole – Epidemiology & clinical

-Incidence complete hydatidiform mole is about 1 to 1.5 per 2000 pregnancies(higher in Asian)

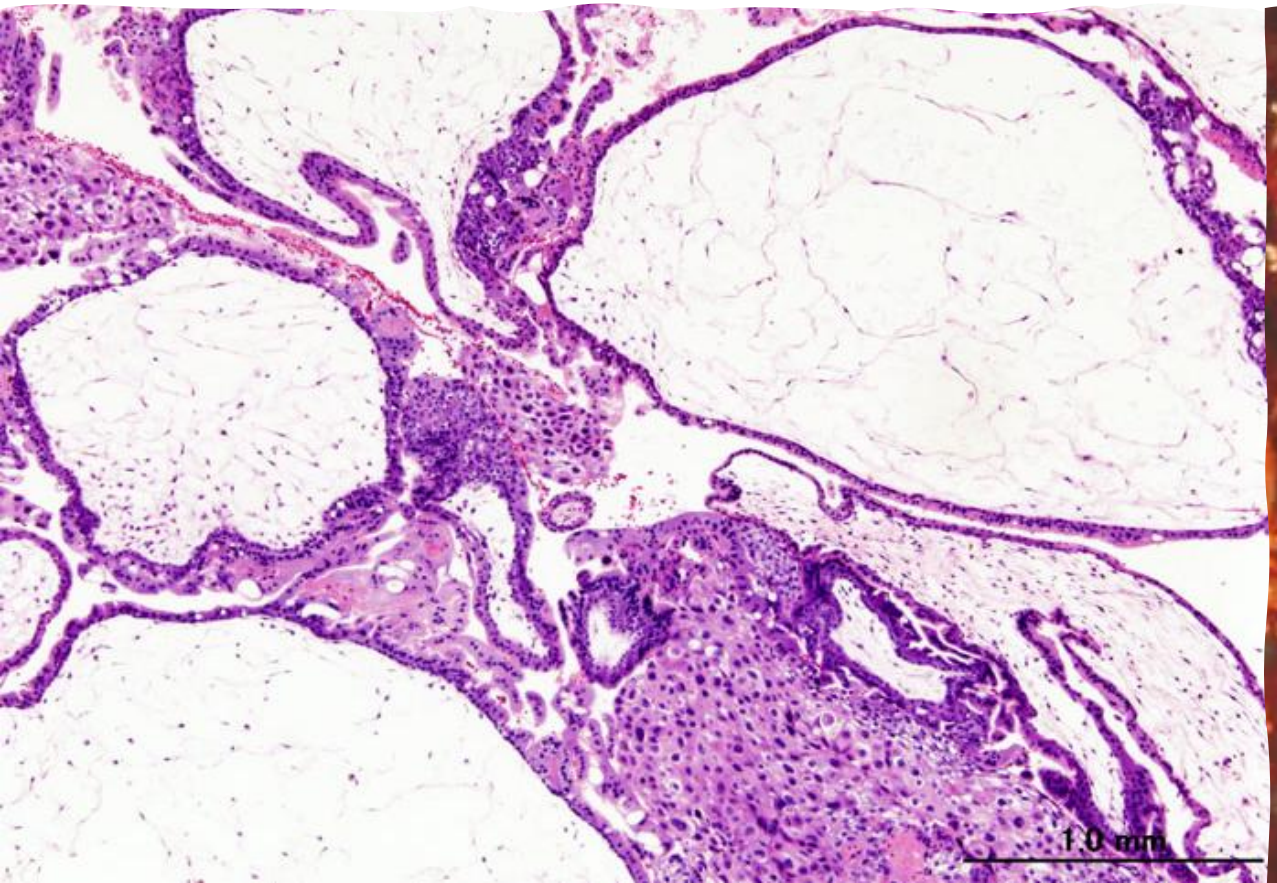
-Most common before 20 & after 40 years (maternal age)

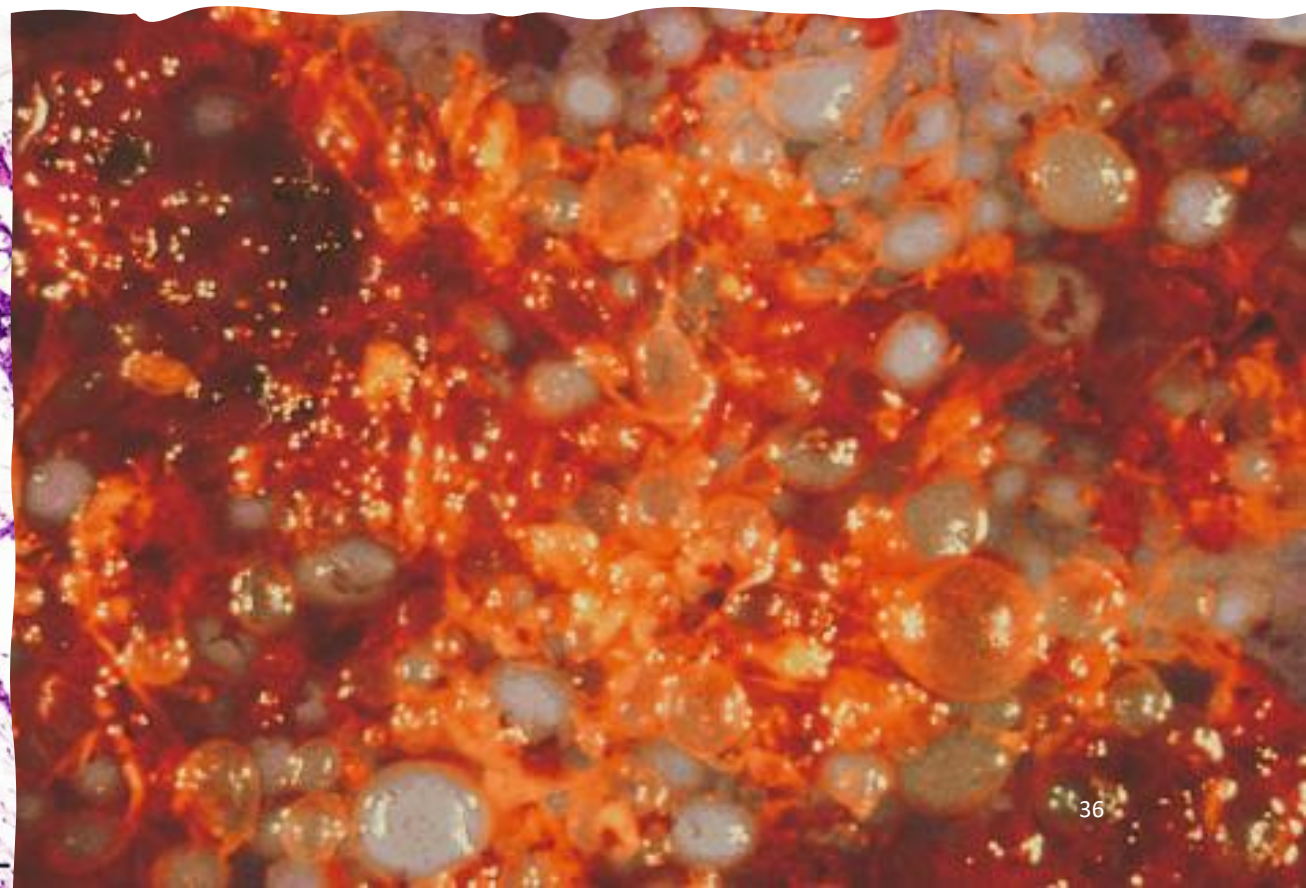
-History of Mole increases the risk for molar disease in subsequent pregnancies.

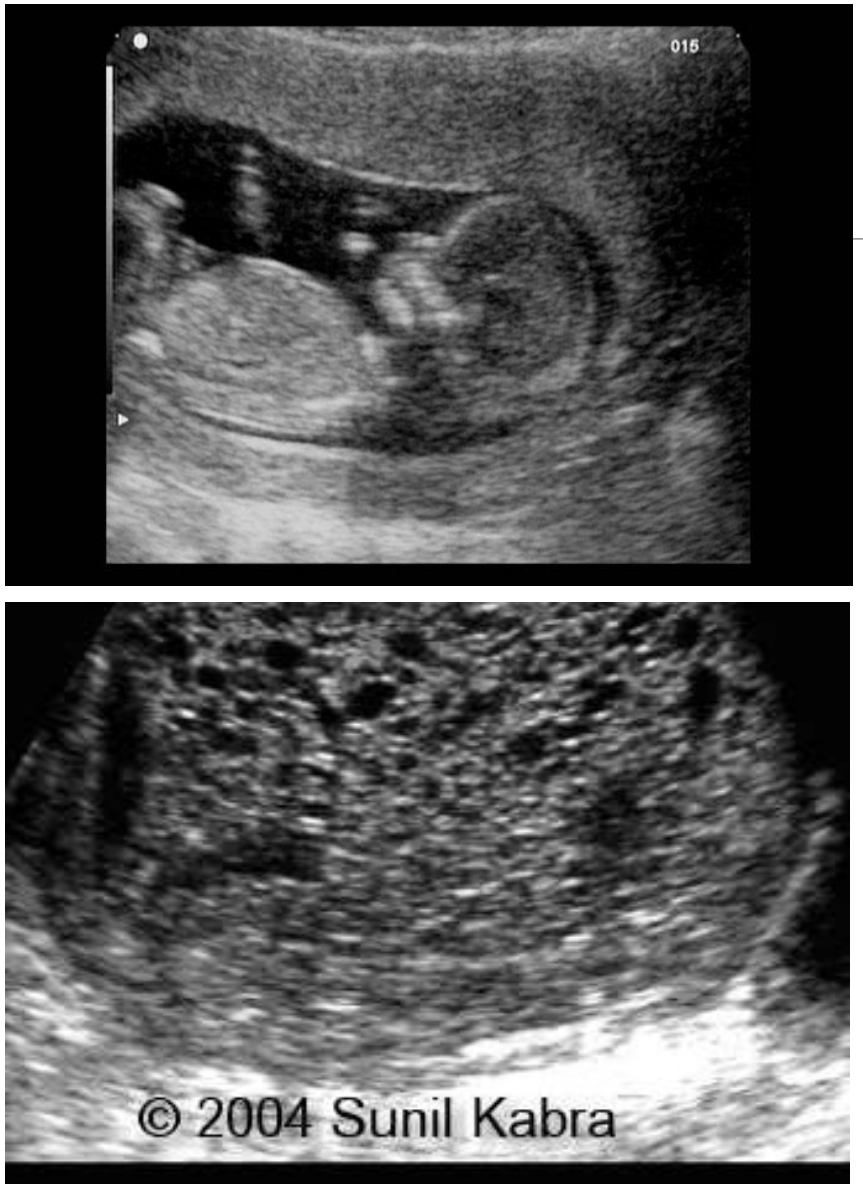
-Presentation: At 12-14 weeks of pregnancy during investigation for a gestation “too large for dates,”. +both moles → Hyperemesis, elevation of hCG in maternal blood & no fetal heart sounds.

Hydatidiform Mole – Morphology

Uterine cavity is expanded by friable mass (**Grape-like villi**) composed of thin-walled, cystically dilated chorionic villli covered by varying amount of atypical chronic epithelium.







Hydatidiform Mole – Ultrasound snow storm

Hydatidiform Mole – treatment & prognosis

Tx: surgical evacuation of the uterine cavity & close follow up with serum hCG.

The majority of moles do not recur after thorough curettage, 10% of complete moles are invasive

No more than 2-3% give rise to choriocarcinoma **(usually complete, rarely partial).**

So partial mole has much better prognosis

Feature	Complete Mole	Partial Mole
Karyotype	46,XX (46,XY)	Triploid (69,XXY)
Villous edema	All villi	Some villi
Trophoblast proliferation	Diffuse; circumferential	Focal; slight
Atypia	Often present	Absent
Serum hCG	Elevated	Less elevated
hCG in tissue	++++	+
Behavior	2% choriocarcinoma	Rare choriocarcinoma

Gestational Choriocarcinoma

A very aggressive malignant tumor, arises from gestational chorionic epithelium or, less frequently, from totipotential cells within the gonads (as a germ cell tumor).

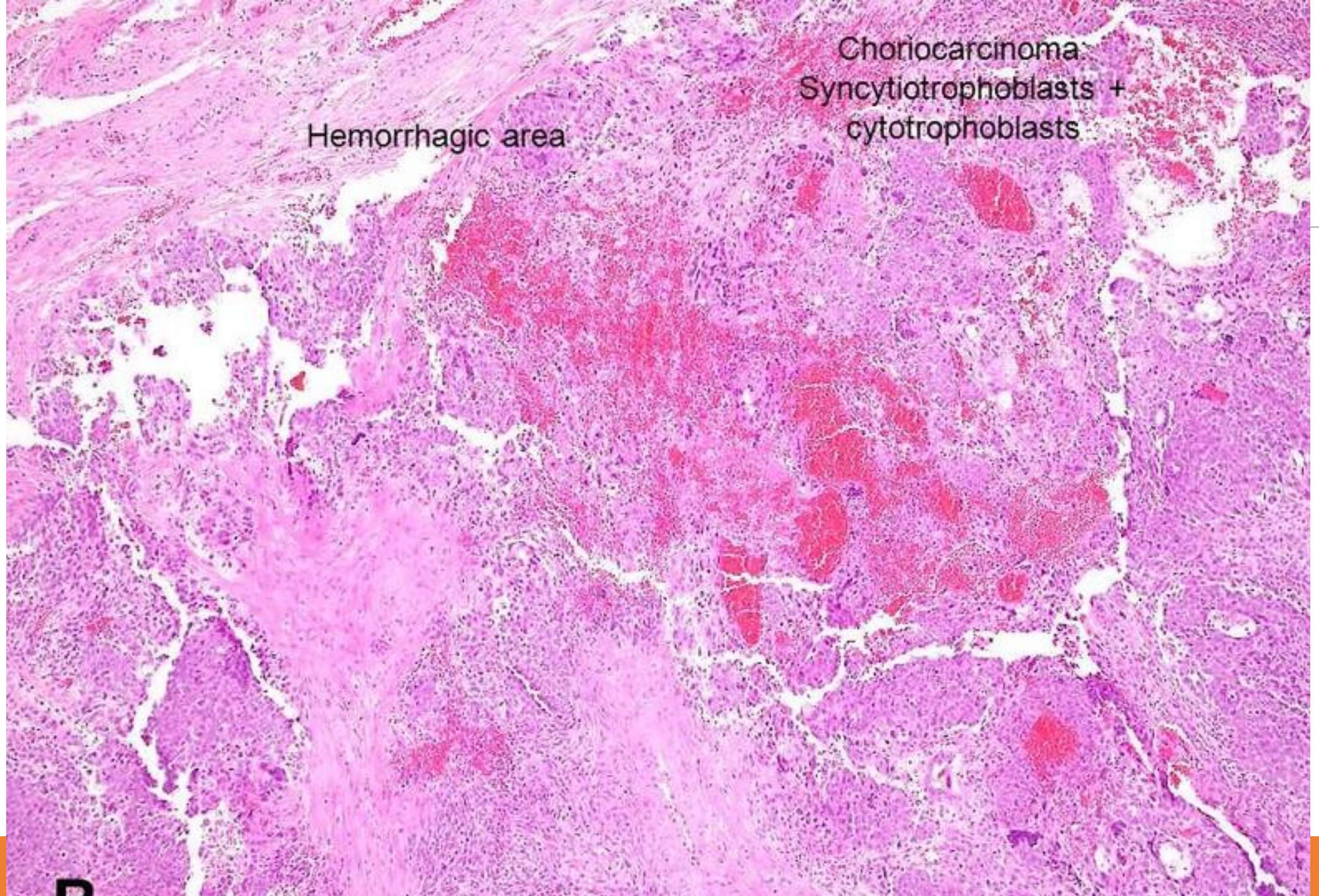
Rare tumor (higher in Asian)

Most common before 20 & after 40 years (maternal age)

50% from complete moles; 25% after an abortion, 25% after an apparently normal pregnancy

- **Presentation**: a bloody, brownish discharge, very high hCG absence of marked uterine enlargement (not like mole)
- **Gross**: hemorrhagic, necrotic uterine masses.
- **Microscopic:** In contrast with hydatidiform moles chorionic villi are not formed; the tumor is composed of anaplastic cuboidal cytotrophoblasts & syncytiotrophoblasts

- **Very aggressive disease.**
- At diagnosis widespread vascular (hematogenous) spread usually the lungs & brain.
- Lymphatic invasion is uncommon.
- Despite the extremely aggressive of placental choriocarcinoma → sensitive to chemotherapy.
- By contrast, response to chemotherapy in gonads choriocarcinomas is poor.


Choriocarcinoma
Syncytiotrophoblasts +
cytotrophoblasts
Hemorrhagic area