MALE GENITAL SYSTEM

WHO classifications of testicular tumors

I. Germ cell tumors derived from germ cell neoplasia in situ

A) Non-invasive germ cell neoplasia

- Germ cell neoplasia insitu
- Specific forms of intratubular germ cell neoplasia

B) Germinoma family of tumors

Seminoma

c) Non-seminomatous germ cell tumors

embryonal carcinoma

Yolk sac tumor

Trophoblastic tumor : choriocarcinoma, epithelioid TT

Teratomas

D) Other germ cell tumors

Mixed germ cell tumors

II. Germ cell tumors unrelated to germ cell neoplasia in situ

Yolk sac tumor

spermatocytic tumor

Teratomas

III Sex cord stromal tumors

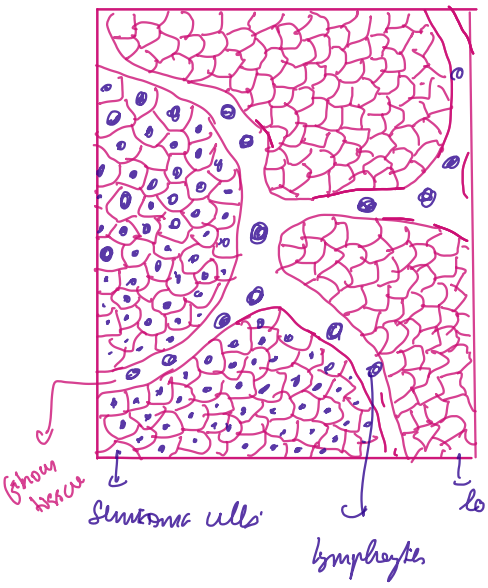
Leydig cell tumor

Sertoli cell tumor

Mixed sex cord-stromal tumor

Seminoma

- Member of germinoma family of tumors
- m/c malignant tumor of testis
- 4th decade
- Undescented testis harbours seminoma more frequently
- ↑ hCG & PLAP



GROSS : * Enlarged testis (10 times)

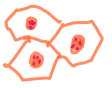
* maintains the normal contour, since tumor rarely invades tunica
* Large tumor replaces entire testis

Small tumor appears as circumscribed mass

C/S : ~~homogenous~~, grey, white lobulated appearance

M/S : Seminoma cells

- lies in cords, sheets or colums forming lobules
- Tumor cells - uniform in size with clear cytoplasm + well defined cell borders
- Cytoplasma contains variable amt of glycogen (PAS +)
- Nuclei centrally located, large, hyperchromatic, (-2 prominent nucleoli



- Stroma is delicate fibrous tissue which divides tumor into lobules.
- Shows lymphocytic infiltration

genetic alterations in Seminoma :

- Isochrome p12
- mutations in (KIT)
- KIT amplification

Prognosis :

* Extremely radiosensitive
* lymph node metastasis seen
* Hematogenous spread late
* But prognosis

CRYPTORCHIDISM

Etiology :

* Mechanical factors : short sc, narrow inguinal canal, adhesions to peritoneum
* Genetic factors : trisomy 13, maldev of scrotum
* Hormonal factors : Abnorm in hypothalamo-pituitary - testicular axis, androgens

Pathology :

Gross : small, firm, fibrotic

M/c :

Seminiferous tubules

- loss of germ cells, leaving mostly spermatogonia & spermatids
- thickened BM & reduced tubule size
- Advanced cases shows severly damaged tubules with only sertoli cells

Interstitial stroma

- Increased fibrous tissue
- Presence of leydig cells in small clusters

Cf :

→ Infertility

→ malignancy

Premalignant lesions of penis : Bowen disease & bowenoid papules

Female genital system

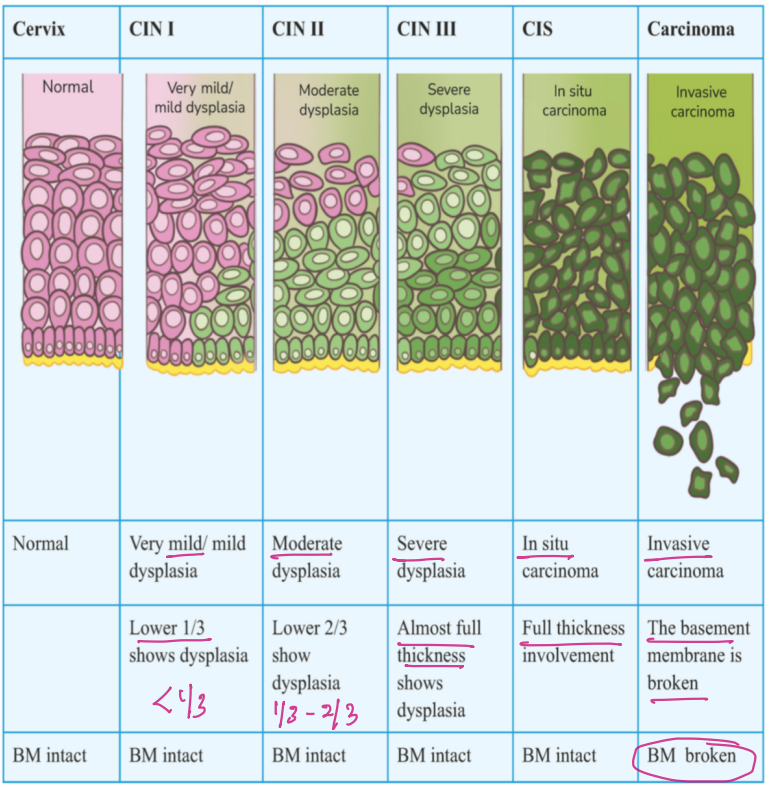
Squamous intraepithelial lesion (SIL)
Cervical intraepithelial neoplasia (CIN)] → CIS → ICC

⇒ ° Dysplasia – loss of polarity / lack of maturation
↳ Atypical cytological changes in the layers of sq. epithelium (progressive changes)

° Carcinoma-in-situ : full thickness (layers) involved
(above the basement membrane)

CIN → Classification to group various grades of dysplasia & CIS
[grade I – III]

CIN-I : less than 1/3rd (<1/3 (mild dysplasia)
CIN-II : 1/3 – 2/3 (moderate dysplasia)
CIN-III : Almost full thickness
CIS :- full thickness
Carcinoma : BM broken



* The Bethesda system : for reporting cervical & vaginal cytopathology

CIN → L-SIL → CIN-1
CIN → H-SIL → CIN-2, 3

Atypia full thickness : CIS

Etiopathogenesis

1) Epidemiological studies

* women having early age sexual activity
* " " multiple sexual partners
* women with persistent HPV infection
* multiparous, smoking, use of OCP, HIV etc.

2) Virological studies

- Human papilloma virus (HPV) : strongly implicated in cervical cancer.

3) Molecular studies

- HPV-16 & 18 inactivates tumor suppressory genes, TP53, RB-1 gene

"use of pap smear followed by colposcopy-directed biopsy" → diagnosis.

Invasive cervical cancer

- 4th m/c cancer in women
- declining due to increased use of pap smear technique
- RF & etiological factors same as CIN

Pathology

Gross → 3 type of patterns : fungating, ulcerating, infiltrating

↓

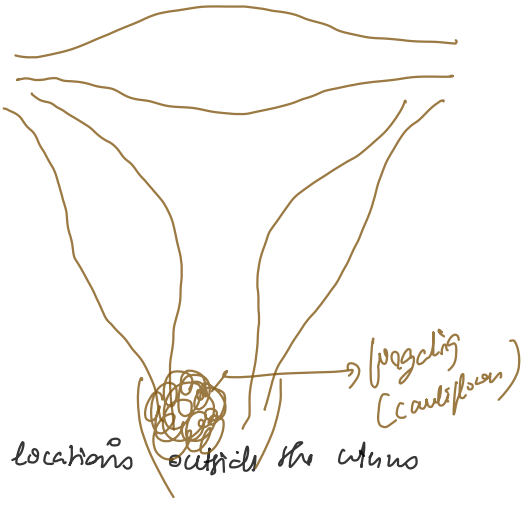
appears

cauliflower-like

m/s → • Squamous cell carcinoma (2 patterns)

- m/c : moderately differentiated non-keratinizing large cell type
- well differentiated keratinizing
- Poorly differentiated squamous cc

- Adenocarcinoma (gland)
  - well differentiated mucus-secreting/ clear cell type containing glycogen but no mucin
  - Poor prognosis
- Neuroendocrine carcinoma
  - Small cell undifferentiated carcinoma



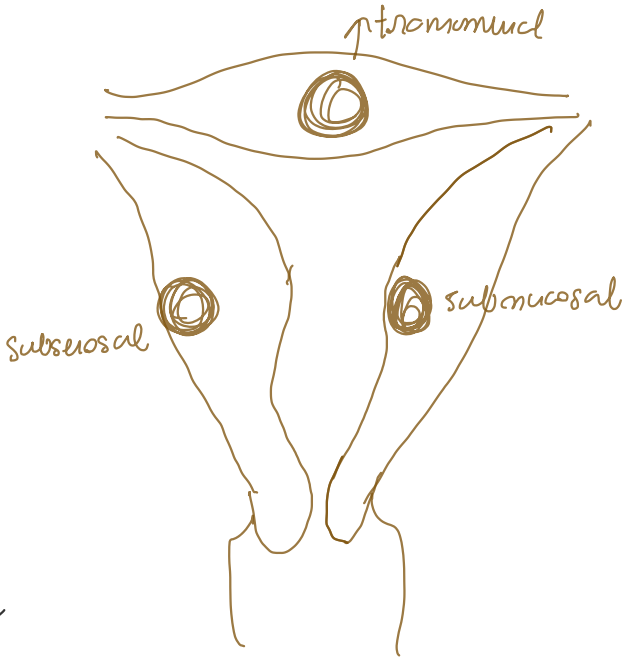
Endometriosis

- Presence of endometrial glands & stroma in abnormal locations outside the uterus

3 theories :

* Transplantation / regurgitation theory : ectopic endometrial tissue is transplanted from uterus to an abnormal location by way of fallopian tubes due to regurgitation of menstrual blood
* metaplastic theory : by metaplasia of coelomic epithelium
* Vascular or lymphatic dissemination.

Cysts - in ovary → chocolate cyst



Leiomyoma (fibroids)

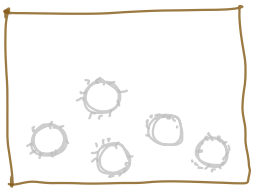
- m/c uterine tumors
- smooth muscle origin
- Benign
- c/f depends on size & location
- Cause : unknown but possible : oestrogen

location : within myometrium - intramural

serosa (subserosal)

underneath the endometrium - submucosal

gross : multiple, circumscribed, firm, nodular, grey white masses



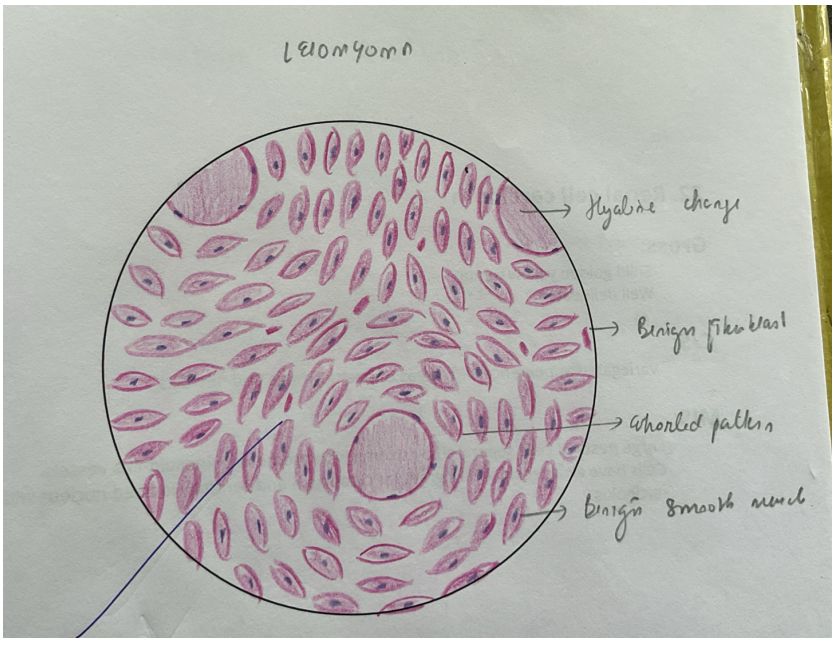
c/s : whorled

m/s : composed of 2 elements

↳ whorled bundles of smooth muscles & variable amt of CT

smooth muscle cells : uniform in size & shape, abundant cytoplasm & central oval nuclei

appearance altered by { - hyalin degeneration, cystic degeneration, infarction, calcification, infection, suppuration, necrosis & fatty change



Teratoma ovary

- Composed of different types of tissue derived from 3 germ cell layers : ecto, endo, mesoderm in varying proportions
- Cytogenetic studies → tumors arise from a single germ cell (ovum) after the 1st meiotic div

3 types : Mature (benign, dermoid cyst), Immature (malignant), Monodermal (specialized)

Mature (benign) teratomas

- Majority
- Predominant ectodermal elements
- dermoid cyst (aka)
- solid & benign

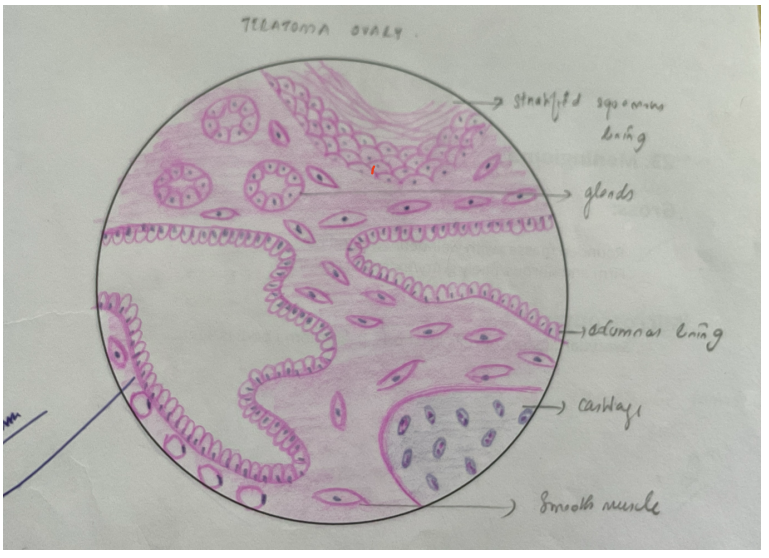
gross → Unilocular cyst - cyst wall thin

c/s → cyst is filled with greasy with keratin, sebum, fat, hair, teeth

m/s → Ectodermal, endodermal, mesodermal derivatives

Cyst wall - stratified squamous epithelium

- Sebaceous glands, sweat glands, hair follicles, skin with appendages, tooth, cartilage, bone, resp epithelium, fat, colonic mucosa, glial tissue



Immature (malignant) teratomas

- Rare
- Solid tumors that contains immature / embryonal structures

gross : Unilateral solid mass

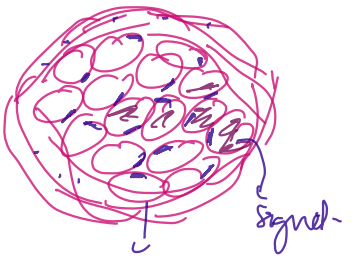
c/s : hemorrhages, necrosis, tiny cysts, heterogenous admixture

m/s : may show mature tissues, most of it composed of immature tissues

Monodermal/specialized : examples : Struma ovarii, Carcinoid tumor, Struma-carcinoid.

Krukenberg tumor

- Bilateral tumor metastatic to the ovaries by transcoelomic spread
- m/c 2° gastric carcinoma



Gross: large, rounded / kidney shaped, firm, multinodular masses

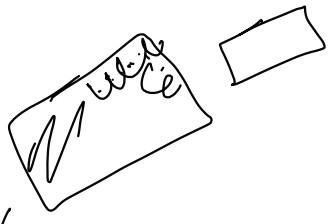
m/s: mucin filled signet ring cells

Gestational trophoblastic neoplasms

- Benign: Hydatidiform mole
- Malignant: Choriocarcinoma

Hydatidiform mole

- Abnormal placenta
  - enlarged, edematous, hydropic change of villi (which becomes vesicular)
  - Circumferential trophoblastic proliferation



- non-invasive
  - complete
  - partial
- Invasive

C/F: ↑ uterine size, vaginal bleeding, toxemia

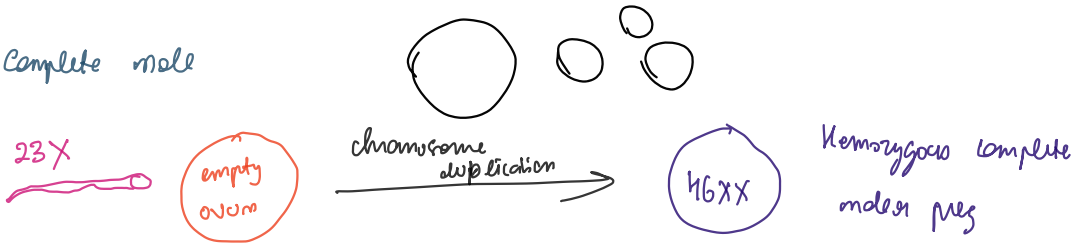
determination of β-hCG (↑)

Complete mole	Partial mole
○ Uterus enlarged, grape like vesicles with clear watery fluid	○ No enlargment of uterus
○ Rarely macerated (fetal maceration) fetus (−)	○ Partially developed foetus (+)
m/s → ★ large, acellular, round, edematous villi	m/s ★ villi show edematous change
★ ↓ed vascularity of villous	★ Trophoblastic proliferation
★ Trophoblastic proliferation	3n/4n
2n - empty ova + duplicate chromosome sperm	
p57 −	p57 +

TABLE 25.11 Comparative features of major forms of gestational trophoblastic disease.

	FEATURE	COMPLETE MOLE	PARTIAL MOLE	GESTATIONAL CHORIOCARCINOMA
1.	*Karyotype*	46, XX or rarely 46, XY	Triploid, i.e. 69, XXY or 69, XXX	46, XY or variable
2.	*Clinical findings*			
	i) Diagnosis	Mole	Missed abortion	Abortion; molar, ectopic or normal pregnancy
	ii) Vaginal bleeding	Marked	Mild	Marked, abnormal
	iii) Uterus size	Large	Small	Generally not bulky
3.	*hCG levels*			
	i) Serum hCG	High	Low	Persistently high
	ii) ~~hCG in tissues~~	~~Marked~~	Mild	Localised in syncytiotrophoblast only
4.	*Embryo*	Not present	May be present (often present)	Not present
5.	*Gross appearance*			
	i) Vesicles	Large and regular present	Smaller and irregular present	No vesicles
	ii) Villi			Always absent
6.	*Microscopy*			
	i) Villous size	Uniform	Variable	None present
	ii) Hydropic villi	All	Some	None
	iii) Trophoblastic proliferation	Circumferential, all three (cytotrophoblast, intermediate trophoblast and syncytiotrophoblast)	Focal, syncytiotrophoblast only	Cytotrophoblast, intermediate cytotrophoblast and syncytiotrophoblast, bizarre forms
	~~iv) Atypia~~	~~Minimal~~	~~Minimal~~	~~Marked~~
	v) Blood vessels	Generally absent	Present	Lack of new blood vessels formation. Trophoblast lined pseudovascular channels present
	vi) Necrosis	Absent	Generally absent	Present
	vii) ~~IHC for P57~~	~~Negative~~	~~Positive~~	~~Positive~~
7.	*Persistence after initial therapy*	20%	7%	May metastasise rapidly if not treated
8.	*Behaviour*	2% may develop choriocarcinoma	Choriocarcinoma almost never develops	Survival rate with chemotherapy 70%

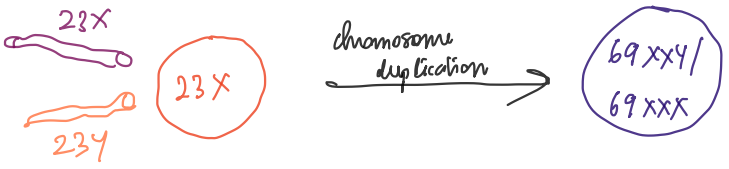
Complete mole



Homozygous complete molar preg

Heterozygous complete mole pregnancy

Partial mole



Triploid partial molar pregnancy

Gestational choriocarcinoma

- highly malignant
- widely metastasis tumor of trophoblast
- can happen following hydatidiform mole, spontaneous abortion, normal pregnancy, ectopic pregnancy.
- c/f: Vaginal bleeding

- high HCG levels.
- haematogenous metastasis early

PATHOLOGY:

GROSS → haemorrhage, necrosis, fleshy mass
- may be small often like a clot in uterus

M/S → no villi / vesicles
Masses of highly anaplastic & bizarre trophoblasts (all 3 - syncitio, cyto, intermediate)
haemorrhage & necrosis +
invades underlying myometrium & other structures

Treatment: Respond very well to chemotherapy.
hysterectomy & chemotherapy