GESTATIONAL TROPHOBLASTIC DISEASE

- Group of tumors typified by abnormal trophoblast proliferation
- Histologically :
  1. hydatidiform mole
     a) benign complete and partial mole
     b) malignant invasive mole

  2. non-molar trophoblastic malignant neoplasms
     a) choriocarcinoma
     b) placental site trophoblastic tumor
     c) epithelioid trophoblastic tumor

GESTATIONAL TROPHOBLASTIC DISEASE

.

PREMALIGNANT CONDITIONS

- Complete hydatidiform mole
- Partial hydatidiform mole

GTN/MALIGNANT GT DISEASE/PERSISTENT GT DISEASE

- Invasive mole
- Choriocarcinoma
- Placental site trophoblastic tumor
- Epithelioid trophoblastic tumor

MOLAR PREGNANCY

What is it?

Hydatidiform mole

HYDATIDIFORM MOLE

- Classical histological findings of molar pregnancy include *trophoblastic proliferation and villi with stromal edema*
- Hydropic degeneration and avascularity of chorionic villi..
- Degree of histological changes,karyotypic differences,absence or presence of embryonic elements ... a) complete mole
  b) partial mole
- GTN frequently follows complete hydatidiform mole

Hydatidiform mole

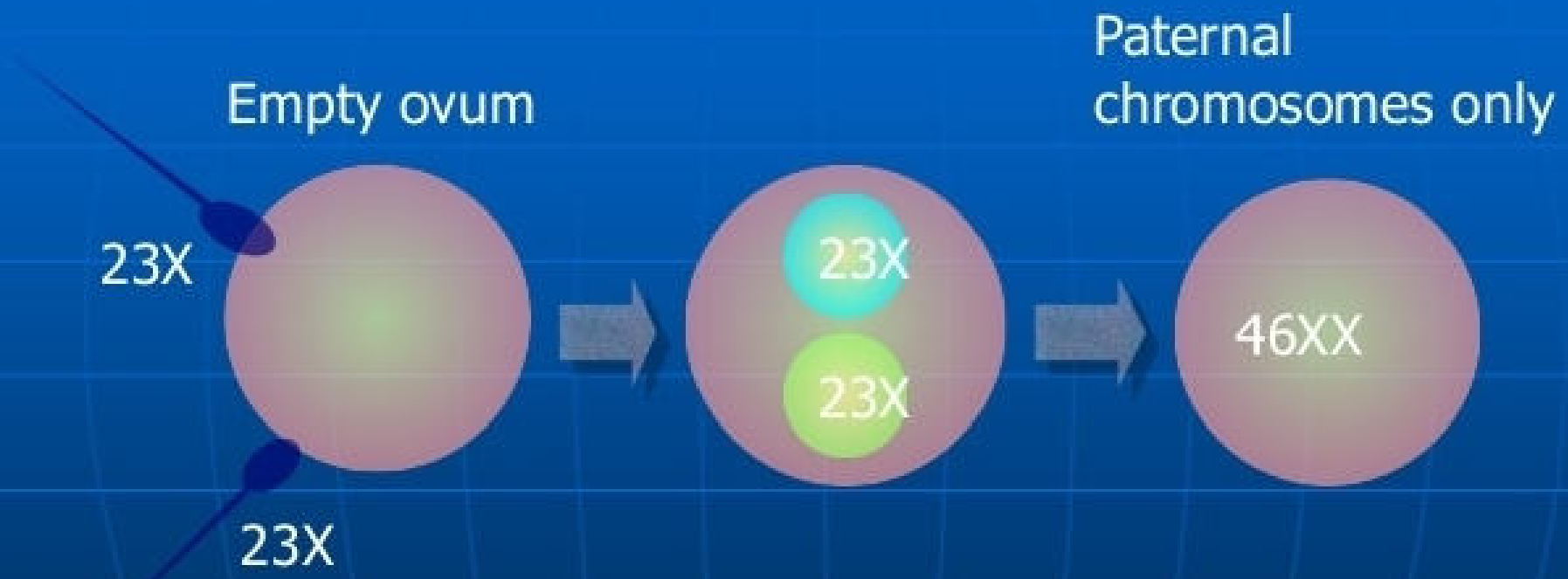
It is a neoplastic proliferation of the trophoblast in which the terminal villi are transformed into vesicles filled with clear viscid material.

PATHOGENESIS ....

COMPLETE MOLE:

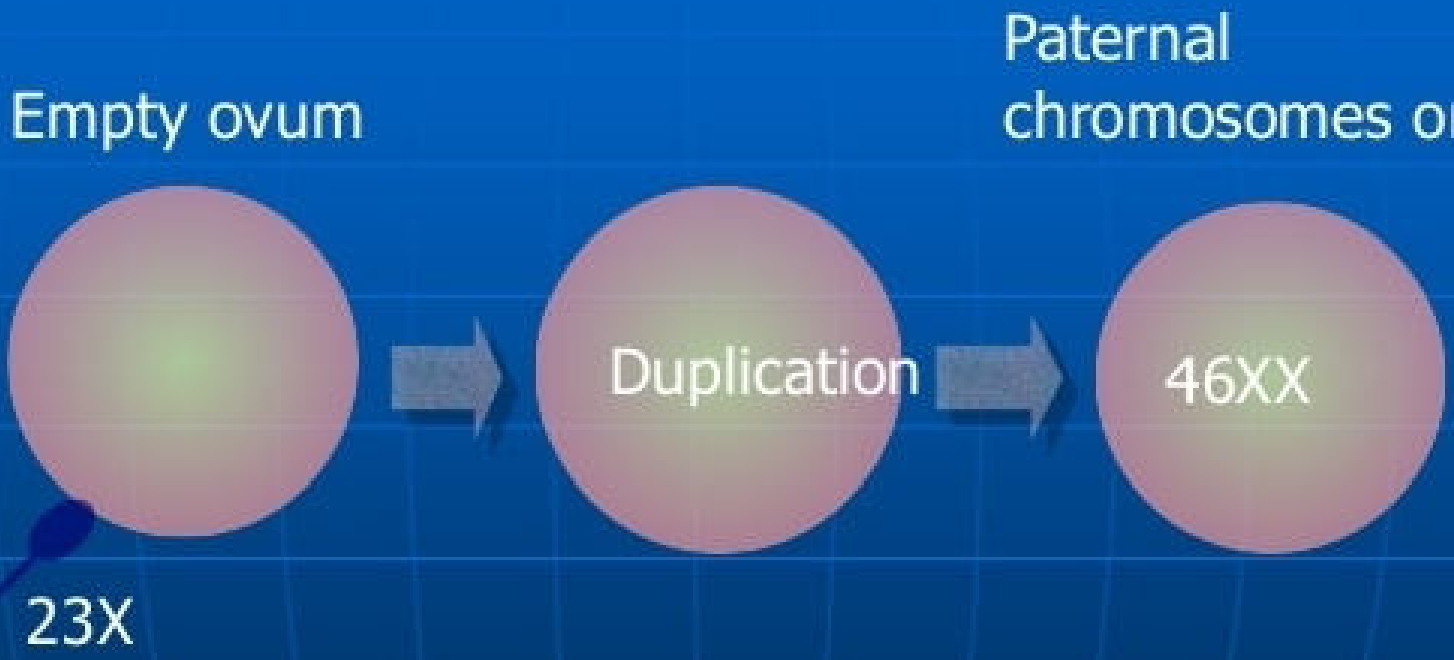
- duplication of chromosome of haploid sperm after meiosis ,following fertilization of inactivated or empty ovum; 46XX.
- ***androgenesis***.
- Less commonly chromosomal pattern 46XX and 46XY may occur due to **dispermic fertilization** of empty ovum ***dispermy***.
- paternal origin.
- Abnormal chorionic villi grossly appear as mass of clear vesicles.

Complete Mole, Pathogenesis



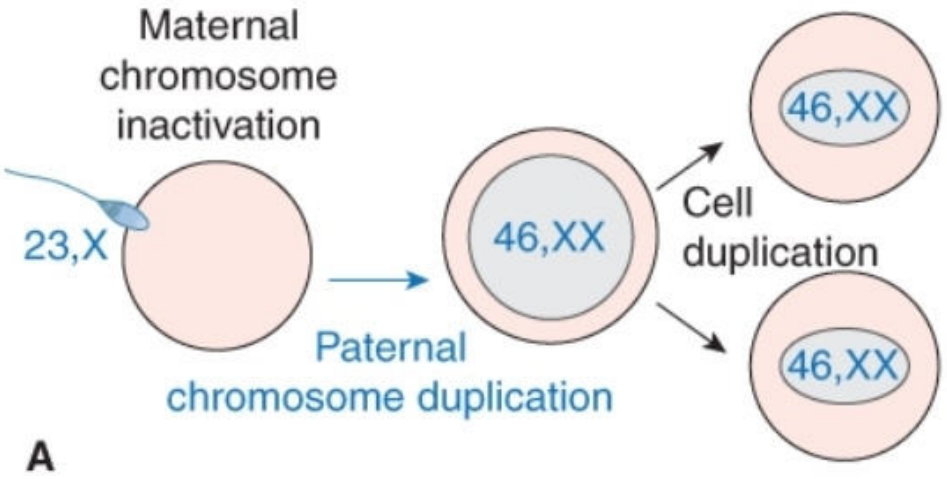
Dispermic diploidy

Complete Mole, Pathogenesis

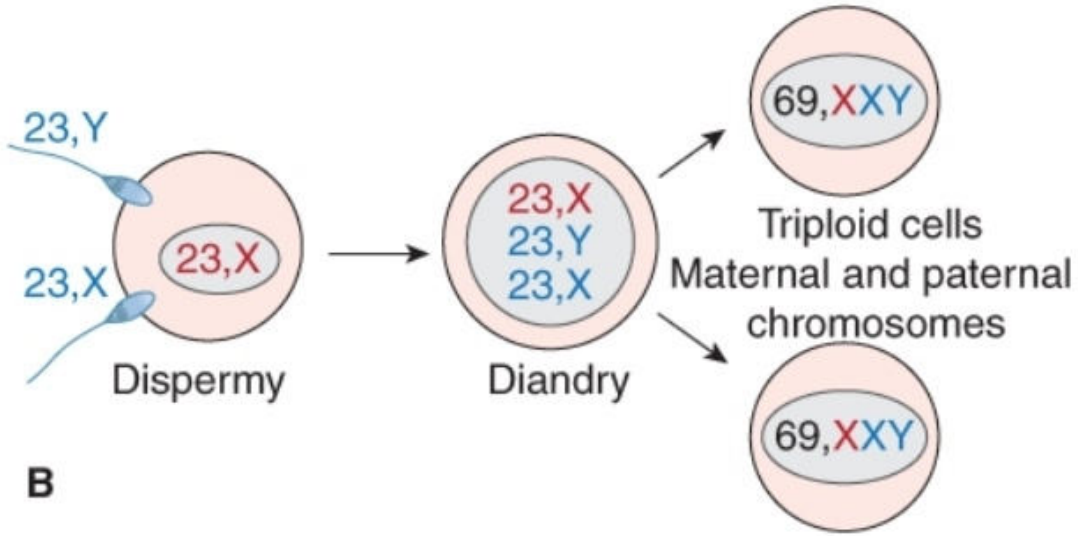


Diandric diploidy
Androgenesis

COMPLETE MOLE



PARTIAL MOLE



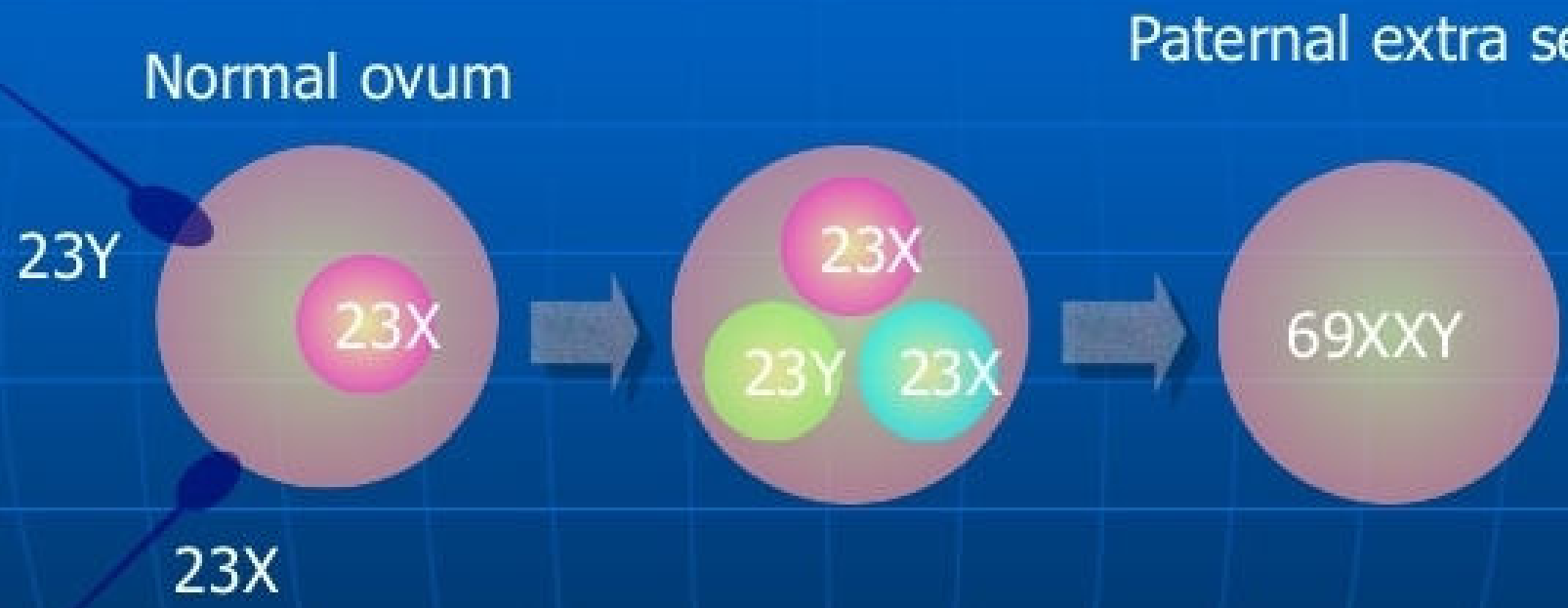
complete hydatidiform mole(CHM):

- the entire uterus filled with abnormal vesicles, no signs of fetus.

PARTIAL MOLE:

- triploid(69XXX or 69XXY);less commonly 69XYY.
- 2 sets of paternal haploid genes and 1 set of maternal haploid genes (dispermic fertilization) .This paternal contribution is called ***diandry*** .
- *Less frequently* a similar haploid egg may be fertilzed by an unreduced diploid 46XY sperm.
- Show some fetal tissue,at least an amniotic sac.
- Fetus with features of triploidy or tetraploidy (also seen) … IUGR,multiple malformation,dies earier.

Partial Mole, Pathogenesis



Dispermic triploidy

partial hydatidiform mole

- partial hydatidiform mole with evidence of a conceptus.

Fetal hand demonstrating syndactyly. The fetus had a triploid karyotype, and the chorionic tissues were a partial mole

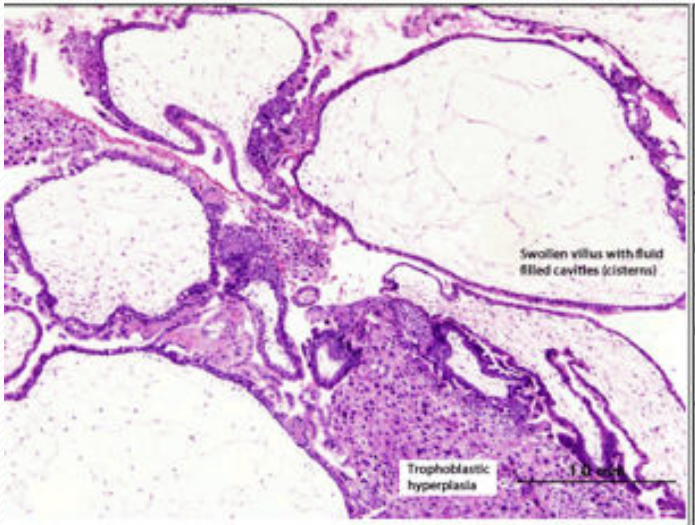
FEATURES OF COMPLETE AND PARTIAL HYDATIDIFORM MOLE

FEATURE	COMPLETE MOLE	PARTIAL MOLE
• KARYOTYPE	• 46,XX or -XY	• 69XXX or XXY
• CLINICAL PRESENTATION	• *MOLAR GESTATION*	• *MISSED ABORTION*
• *preliminary diagnosis*	• *50% LARGE for dates*	• *SMALL for dates*
• *uterine size*	• *25-30%*	• *RARE*
• *theca lutein cysts*	• *10-25%*	• *RARE*
• *medical complications*	• *>100,000 mIU/mL*	• *<100,000mIU/mL*
• *initial hcg levels*	• *15-20% of cases*	• *1-5% of cases*
• *rate of subsequent GTN*		

FEATURES OF COMPLETE AND PARTIAL HYDATIDIFORM MOLE

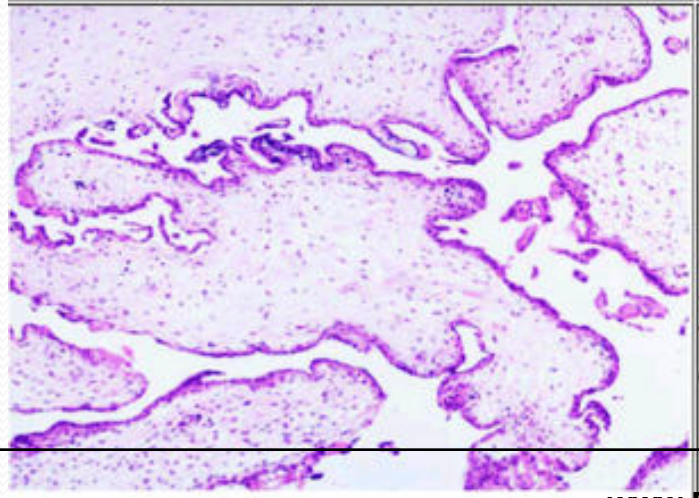
PATHOLOGY	COMPLETE MOLE	PARTIAL MOLE
EMBRYO-FETUS	*ABSENT*	*OFTEN PRESENT*
AMNION,FETAL RBCs	*ABSENT*	*OFTEN PRESENT*
VILLOUS EDEMA	*WIDESPREAD*	*FOCAL*
TROPHOBLASTIC PROLIFERATION	*SLIGHT TO SEVERE*	*FOCAL,SLIGHT TO MODERATE*
Trophoblast ATYPIA	*MARKED*	*MILD*
P57KIP2 immunostaining	*NEGATIVE*	*POSITIVE*
Scalloping of chorionic villi	*ABSENT*	*PRESENT*
Stromal inclusions	*ABSENT*	*PRESENT*

HISTOLOGY :

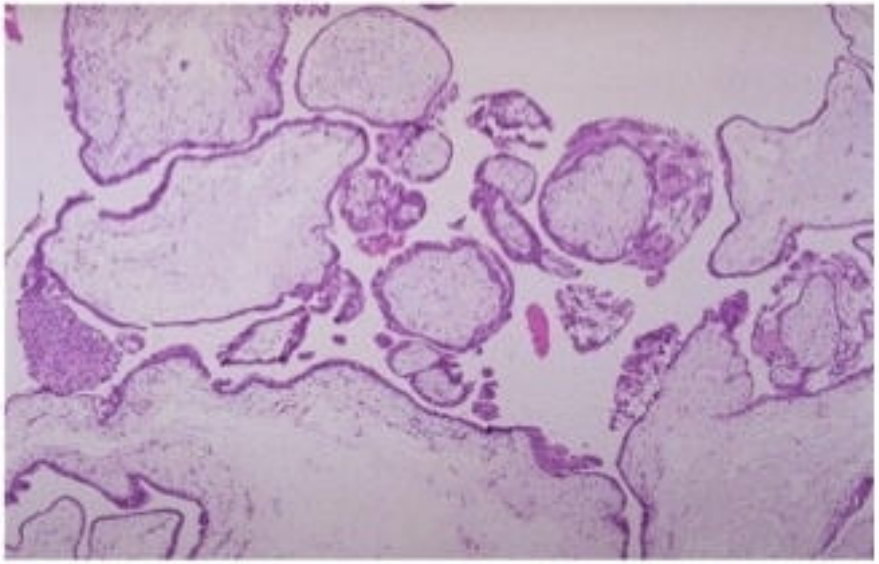


Click image for larger version

Microscopic - Complete Hydatidiform Mole.
This image shows edematous and dilated villi, with fluid-filled cavernous spaces (cisterns). The villi lack an organized vasculature. The spaces between villi show an expansion of trophoblastic tissue (trophoblastic hyperplasia).

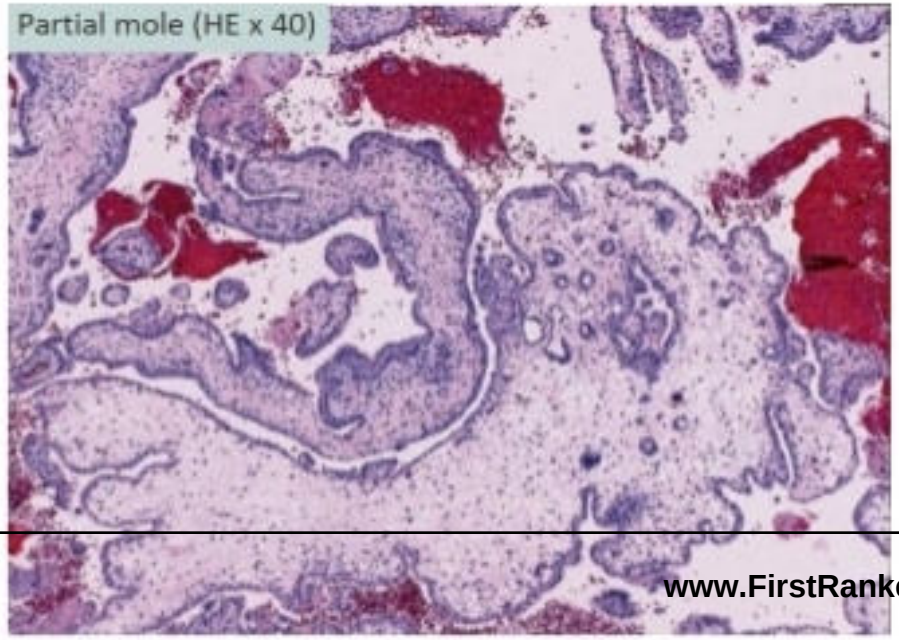


Microscopic - Partial Hydatidiform Mole.
Swollen villi with less extensive trophoblast expansion than with complete moles.



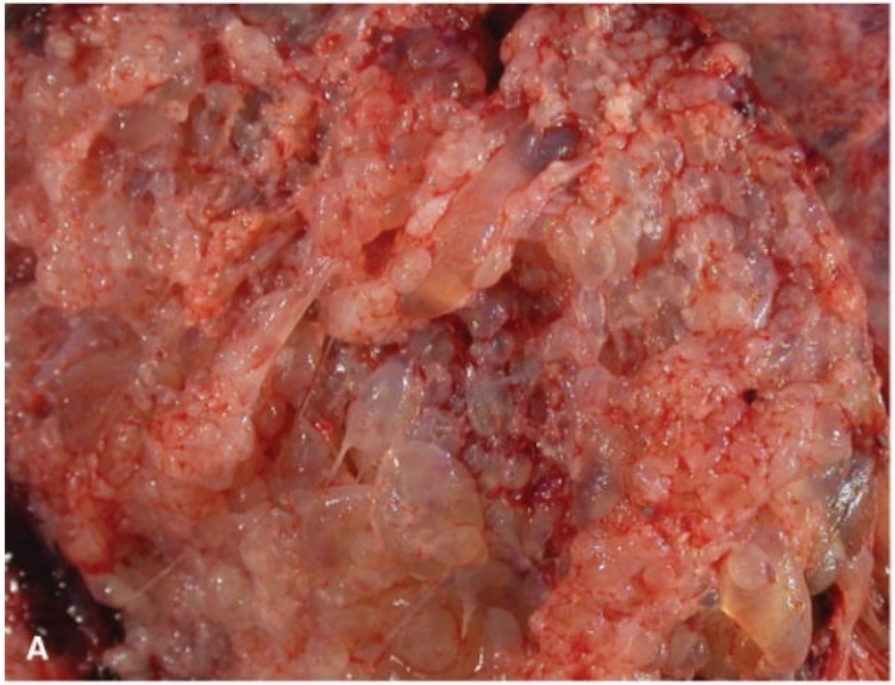
The microscopic of complete mole:

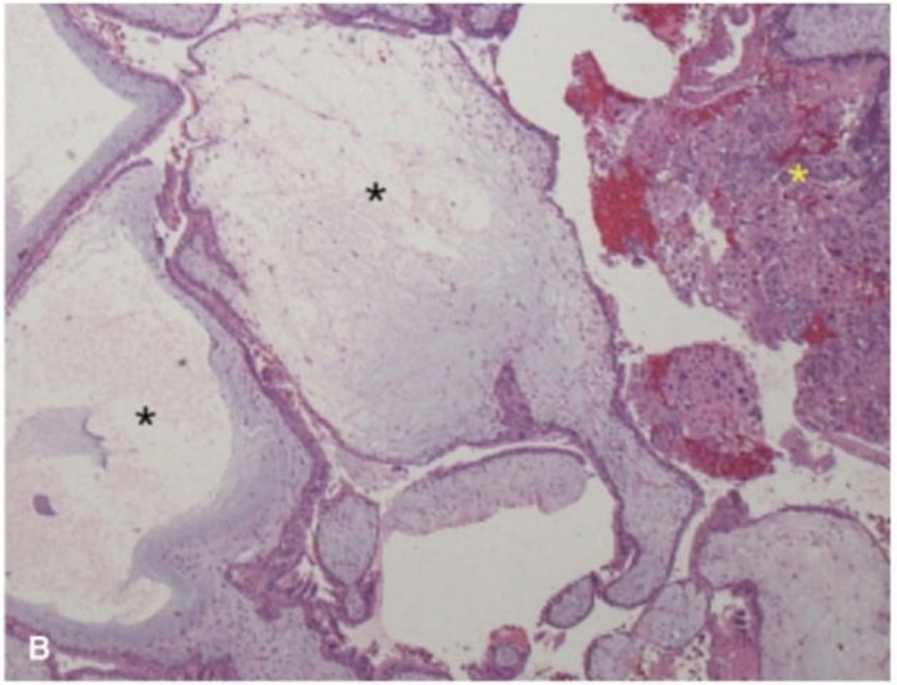
- Hyperplasia of trophoblastic cells
- Hydropic swelling of all villi
- Vessels are usually absent



- Partial mole

- Hydropic villi and trophoblastic hyperplasia are less conspicuous in partial mole.
- Fetal tissues like erythrocyte may be found.
- Scalloping of chorionic villi and trophoblastic stromal inclusions.





Complete mole .....

INCIDENCE AND AETIOLOGY :

- Varies with ethnic differences : Asians > Caucasions. (3)
- Maximum in orientals like chineese and japaneese
- Extremes of age : adolescents and 36-40 years (2)
  :>40yrs (10)
- Previous mole. : complete mole - .9% risk
  -2 prior complete mole -20% have 3rd
  : partial mole - .3% risk
- Sporadic (vast majority)
- Familial syndrome of recurrent hydatidiform mole-rare.
- Role of other factors –less clear.

SYMPTOMS...

- Amenorrhea of varying duration
- Passage of vesicles per vaginum
- Bleeding per vaginum
- Nausea and vomiting ...

more pronounced with complete than partial mole as gestation advances

SIGNS...

- **Uterus :** *50% cases-enlarged; larger than period of amenorrhea; softer*

  :35% corresponds to gestational period

  :15% it may be smaller

- **Fetal heart sounds** *wont be heard with complete mole.*
- **Hyperemesis**

• **Theca lutein cysts** *felt in ovaries(50%cases) most common with complete mole*

- Larger moles are more likely to develop cysts: overstimulation of luteal elements by hCG.

- Theca lutein cysts-PT Disease

- regress following evacuation(expectant management preferred)

-rarely undergo torsion, infarction and hemorrhage

-oophrectomy -extensive infarction after untwisting .

Fig. 20.2: Bilateral lutein cysts in association with hydatidiform mole

- **Thyrotoxicosis--***thyrotrophic like effect of hCG .*
  - *free T_4 THYROXINE- inc;TSH-decrease*
  - *mimicked by bleeding and sepsis from infected products.*

- **Respiratory distress** –*due to embolisation*

- *PARTIAL MOLE may not present with classic features of a complete mole.*

  Vaginal bleeding *is a usual symptom*.

  Many a times- **incomplete or missed abortion**

- **Uterine bleeding-**

-spotting or profuse hemorrhage
-almost always with untreated molar pregnancy
-may preceed spontaneous molar abortion or follows an intermittent course for weeks to months

- **Fe deficiency anemia** *–advanced moles with concealed uterine hemorrhage*

- **Pre-eclampsia/eclampsia:**

  - *Early onset pre-eclampsia (HTN <20wks –important to rule out hydatidiform mole)*

  - *Severe pre-eclampsia/eclampsia-common with advanced molar pregnancy.....seldom seen today...early diagnosis evacuation*

    (***exception- normal fetus+complete mole in continuing twin gestations*** severe pre-eclampsia mandates preterm delivery...)

HYDATIFORM MOLE

CLINICAL FEATURES

Vaginal bleeding (anemia)	97%
Excessive uterine size	50%
Theco-lutein ovarian cysts	50%
Preeclampsia	27%
Hyperemesis	25%
Hyperthyroidism	7%
Trophoblastic embolization (respiratory distress)	2%

TWIN PREGNANCIES…

- **Chromosomally normal fetus + complete diploid molar pregnancy**
- **Single partial molar pregnancy + abnormal fetus**
- **Amniocentesis and fetal karyotyping-confirmation**
- **Survival of normal fetus depends on associated comorbidity from molar component**…pre-eclampsia and hemorrhage necessitates preterm delivery…