GESTATIONAL TROPHOBLASTIC DISEASE

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Obstetrics & Gynecology

Gestational Trophoblastic Disease

- Spectrum of interrelated conditions
- All arise from the placenta
- Abnormal trophoblastic proliferation
- All secrete human chorionic gonadotropin (hCG)
  - *Excellent biomarker for disease progression and treatment response*

Gestational Trophoblastic Disease

Benign

- *Partial hydatiform mole*
- *Complete hydatiform mole*

Malignant

- *Invasive and metastatic mole*
- *Choriocarcinoma*
- *Placental Site Trophoblastic Tumor*
- *Epithelioid Trophoblastic Tumor*
- ***New:*** *Atypical placental site nodule*

Epidemiology

- Hydatiform mole (Benign)
  - *1/1000 pregnancies worldwide*
  - *High-income populations*
    - Complete moles: 1-3/1000
    - Partial moles: 3/1000
  - *More common at extremes of reproductive age (<15 and >45yo)*
  - *History of previous molar pregnancy → 10x risk* ****Biggest RF***
- Choriocarcinoma
  - *North America/Europe: 1/40,000*
  - *Southeast Asia/Japan: 3-4/40,000*

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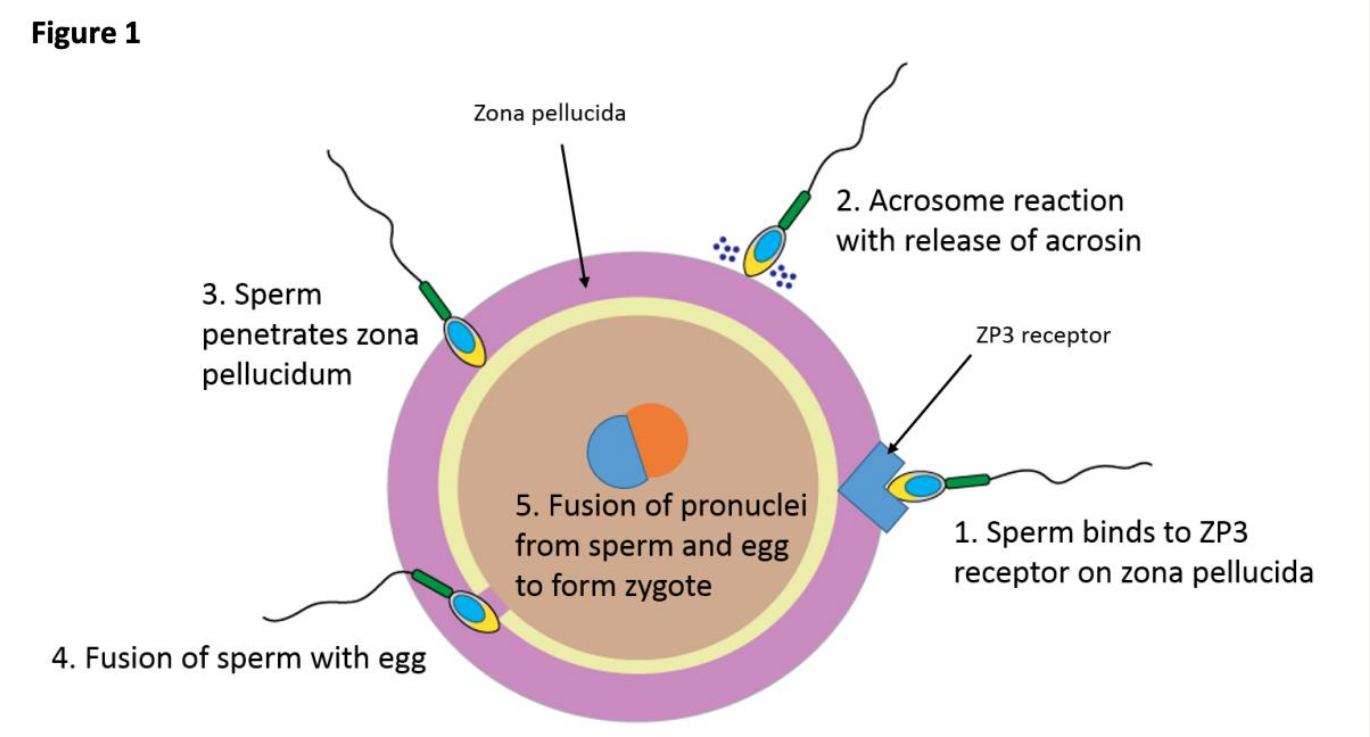
Review of Fertilization



1. Sperm head binds to zona pellucida (glycoprotein layer surrounding the oocyte)
2. **Acrosome reaction** = hydrolytic enzymes released at the head of the sperm
3. Penetration of the zona pellucida
4. Cell membrane of sperm and egg fuse
5. Sperm nucleus/cytoplasm released into the egg
6. Completion of second meiotic division by the 2' oocyte
7. Male and female pronucleus fuse to form **zygote**

Review of Fertilization

What prevents Dispermy??

- *Depolarization of egg cell membrane → prevents other sperm head from binding*
- *Egg undergoes cortical reaction: enzymes released by the egg → hardens the zona pellucida*

What if this mechanism fails?

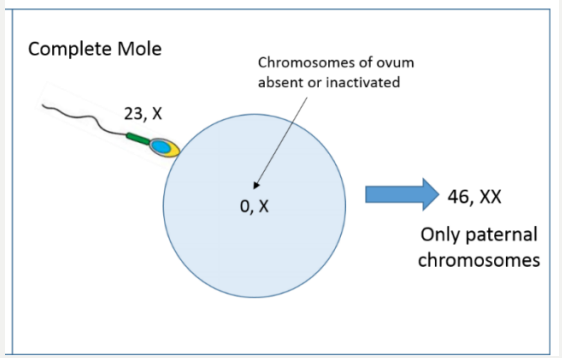
Molar pregnancy!!

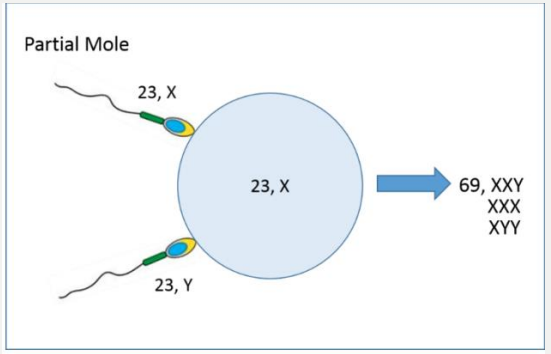
Hydatiform Moles

	Partial Mole	Complete Mole
Karyotype	69XXX, 69XXY	46XX, 46XY

<u>Complete Moles</u>
- Diploid Chromosomes
- Fertilization of “empty” egg by 1-2 sperm
- All chromosomes derived from the father
  - “Complete-ly Male”
- Monospermic or dispermic fertilization

<u>Partial Moles</u>
- Triploid karyotype
- Fertilization of “normal” egg by 2 sperm
- 2 sets of dad + 1 set of mom





Hydatiform Moles

	Partial Mole	Complete Mole
Karyotype	69XXX, 69XXY	46XX, 46XY
Pathology		
Fetus/Fetal parts	Present	Absent
Amnion, fetal RBCs	Present	Absent
Villous edema	Variable, Focal	Diffuse
Clinical Presentation		
Diagnosis	Missed abortion	Molar gestation
Uterine size	Small for gestational age	50% larger for gestational age
Post-molar malignant sequelae	<5%	6-32%

Molar Pregnancy: Clinical Presentation

- Ultrasound findings (typically in 1T)
- Vaginal bleeding or passage of vesicles
- Uterine enlargement (size > dates)
- Pregnancy complications

Ultrasound findings– Molar Pregnancy

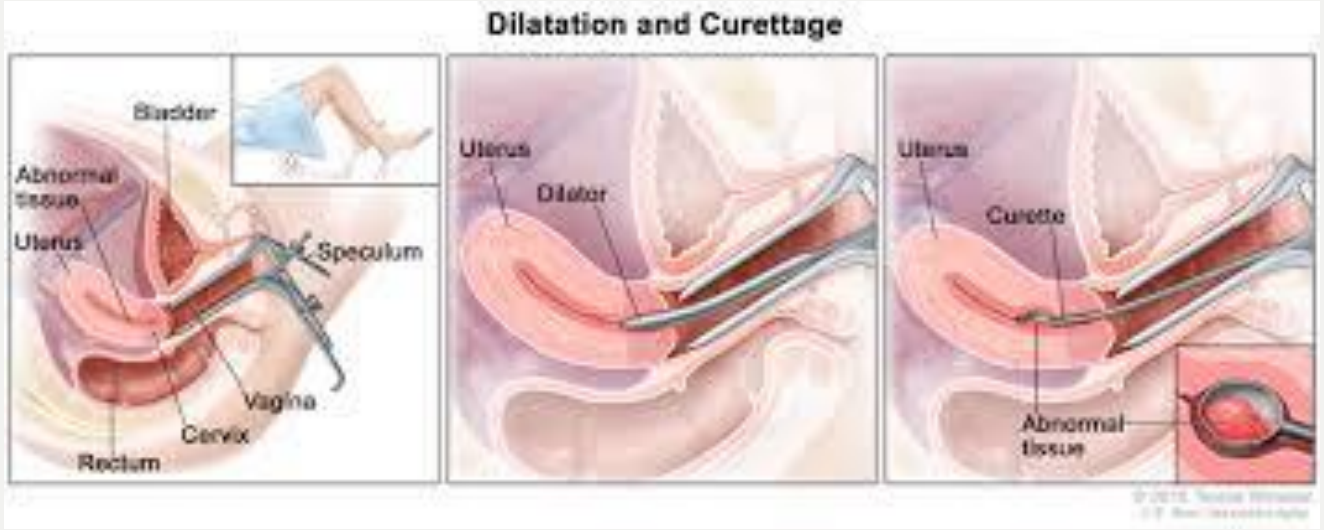
- Ultrasound findings (typically in 1T)
  - *Classic….*
    - Honeycomb, “snowstorm” appearance
  - *Usually…*
    - Deformed gestational sac
    - Absence of fetal parts
    - Cystic appearance of the placenta
    - ~spontaneous abortion

Clinical Presentation – Molar Pregnancy

- Pregnancy Complications
  - *Preeclampsia*
  - *Hyperemesis gravidarum*
  - *Hyperthyroidism*

Management – Molar pregnancy

- Suction evacuation and curettage under ultrasound guidance
- Increased risk of bleeding d/t increased uterine size
  - *IV Pitocin during procedure*
  - *Uterotonics available*
  - *Blood products available*
  - *Adequate IV access*
- Hysterectomy is alternative
  - *Childbearing complete*
  - *Life-threatening bleeding*
- Rhogam for Rh- woman



Surveillance – Molar Pregnancy

- Follow-up hCG monitoring q1-2 weeks until normalization of hCG
- Monthly hCG measurements x 6 months after normalization
- Recommend reliable form of contraception

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***Malignant = Gestational Trophoblastic Neoplasm = GTN*

GTN: Clinical Presentation/Diagnosis

- 50% occur after **molar pregnancy**
- 50% occur after **spontaneous abortion, ectopic pregnancy, term pregnancy**

GTN after Molar Pregnancy

- Asymptomatic
- hCG surveillance →
- Placenta pathology

Box 1 FIGO criteria for diagnosis of postmolar gestational trophoblastic neoplasia.

- When the plateau of hCG lasts for four measurements over a period of 3 weeks or longer; that is, days 1, 7, 14, 21.
- When there is a rise in hCG for three consecutive weekly measurements over at least a period of 2 weeks or more; days 1, 7, 14.
- If there is a histologic diagnosis of choriocarcinoma.

Abbreviation: hCG, human chorionic gonadotropin.

GTN: Clinical Presentation/Diagnosis

- 50% occur after **molar pregnancy**
- 50% occur after **spontaneous abortion, ectopic pregnancy, term pregnancy**

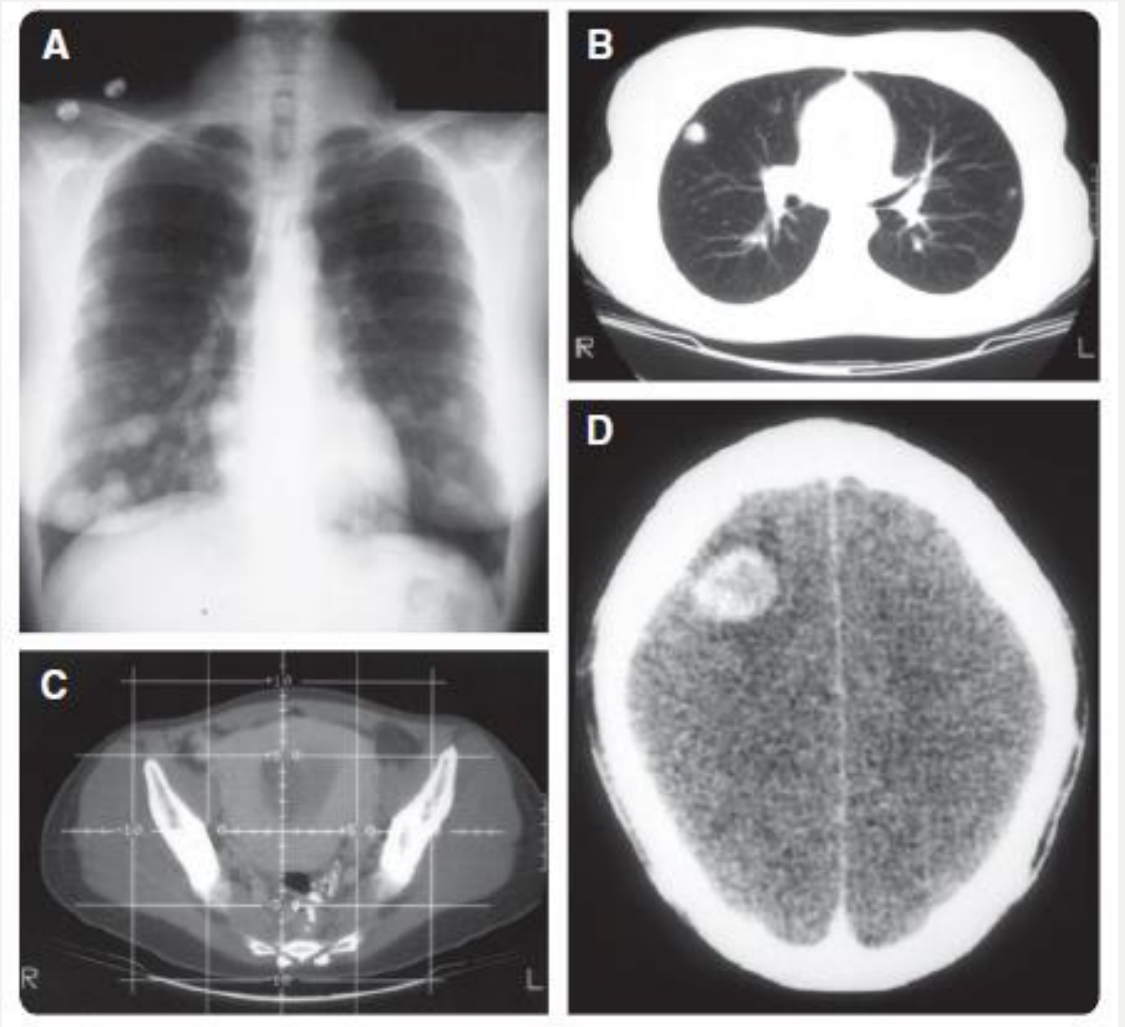
GTN after Non-Molar Pregnancy

- Abnormal vaginal bleeding
- Metastatic site bleeding (liver, spleen, intestines, lung, brain)
- Pulmonary symptoms
- Neurologic signs

Box 2 Tools for investigation of gestational trophoblastic neoplasia.

- Chest X-ray is appropriate to diagnose lung metastases and can be used for counting the number of lung metastases to evaluate the risk score. Lung CT may be used.
- Liver metastases may be diagnosed by ultrasound or CT scanning.
- Brain metastases may be diagnosed by MRI or CT scanning.

Metastatic Lesions



GTN: Staging

TABLE 1 FIGO staging and classification for gestational trophoblastic neoplasia.

FIGO Stage	Description
I	Gestational trophoblastic tumors strictly confined to the uterine corpus
II	Gestational trophoblastic tumors extending to the adnexae or to the vagina, but limited to the genital structures
III	Gestational trophoblastic tumors extending to the lungs, with or without genital tract involvement
IV	All other metastatic sites

GTN: Management

- Chemotherapy
  - ***Low-risk*** → *Single-agent chemotherapy (Methotrexate, Actinomycin-D)*
  - ***High-risk*** → *Multi-agent chemotherapy (Etoposide, Methotrexate, Actinomycin-D, cyclophosphamide, vincristine).* → *"EMA-CO"*
- ?Hysterectomy → consider if uncontrolled uterine bleeding
- ?Radiation therapy → limited role
- PSTT, ETT
  - *Less chemosenstitive*
  - *Hysterectomy is primary mode of treatment*
- Surveillance
  - *hCG monitoring q1 month x 12 months*
  - *Recommend reliable form of contraception*

THANK YOU!