Gestational Trophoblastic Disease

Clinical case applicability: Molar pregnancy, Gestational trophoblastic neoplasia

Learning Objectives:
1). Understand the physiologic stages of fertilization
2). Understand the pathogenesis of complete and partial molar pregnancy
3). Describe the differences in morphology between complete and molar pregnancy

What steps occur during fertilization? See figure 1
-Sperm head binds to zona pellucida (glycoprotein layer surrounding the oocyte) within 1 day of ovulation in the fallopian tube→acrosome reaction (hydrolytic enzymes released at the head of the sperm)→penetrates zona pellucida→cell membrane of sperm and egg fuse →sperm nucleus and cytoplasm released into egg→Completion of second meiotic division by the secondary oocyte; male & female pronucleus fuse to form zygote

What prevents dispermy (two sperm fertilizing an egg) after entry of the sperm?
1)Depolarization of egg cell membrane →prevents other sperm head from binding
2)Egg undergoes cortical reaction: enzymes released by egg → hardens the zona pellucida

What if the above mechanisms fail? What is the pathogenesis of molar pregnancy?
-Complete: chromosomes of ovum are absent or inactivated; haploid sperm duplicates its own chromosomes after meiosis (androgenesis), both sets of chromosomes are paternal → 46 XX
-Partial: 2 paternal haploid sets of chromosomes and 1 maternal haploid set (DISPERMY) → triploid 69 XXX, XXY or XYY (more rare)

What is gestational trophoblastic disease? Gestational trophoblastic neoplasm?
Tumors with abnormal trophoblast proliferation; Risks: extremes of age, prior history
1). Hydatiform moles: + villi & edematous immature placenta; *Types: complete, partial, invasive*
2). Non-molar trophoblastic neoplasms: lack villi; Types: *choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor*

GTN = subset of GTD with malignant sequelae, includes invasive moles & ALL the non-molar neoplasms
-Develop weeks-years following any type of pregnancy, but > common after complete mole
-Non-metastatic/low risk disease cured with single agent chemotherapy (methotrexate); High risk → combination chemotherapy

What are the differences between complete and partial molar pregnancies? See table 1
Complete: edematous villi & abnormal trophoblastic proliferation, NO fetal tissue – grossly appears like clear vesicles; "snowstorm" on ultrasound
Partial: focal and less advanced hydatidiform changes, CONTAINS fetal tissue

What causes hyperthyroid and preeclampsia in molar pregnancy? Rare because of early Dx & Tx
Hyperthyroid: Thyrotropin-like effects of hCG cause ↑T4 and ↓TSH
Preeclampsia: trophoblastic mass releases antiangiogenic factors that activate endothelial damage

How is GTD managed?
-Suction curettage with risk of intraoperative bleeding, particularly with large moles (IV access, blood banking support, uterotonic agents), consider hysterectomy in women >40 → ~1/3 will develop GTN
-Serial beta HCG levels (trophoblasts produce hcg)→helpful in diagnosis, management & surveillance
-Reliable contraception

Figure 1

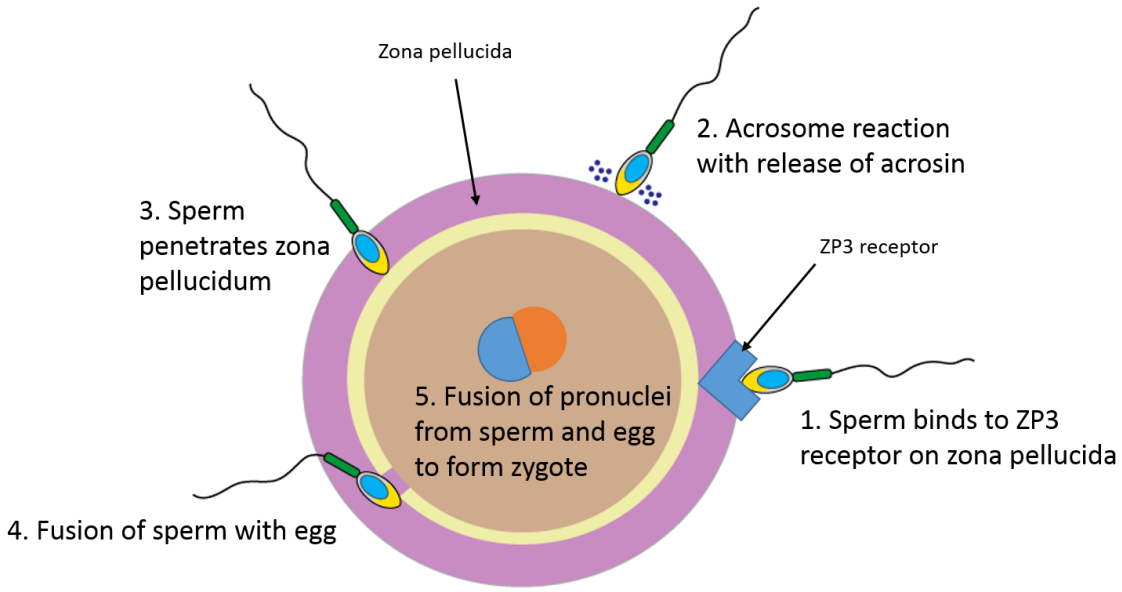

Figure 2

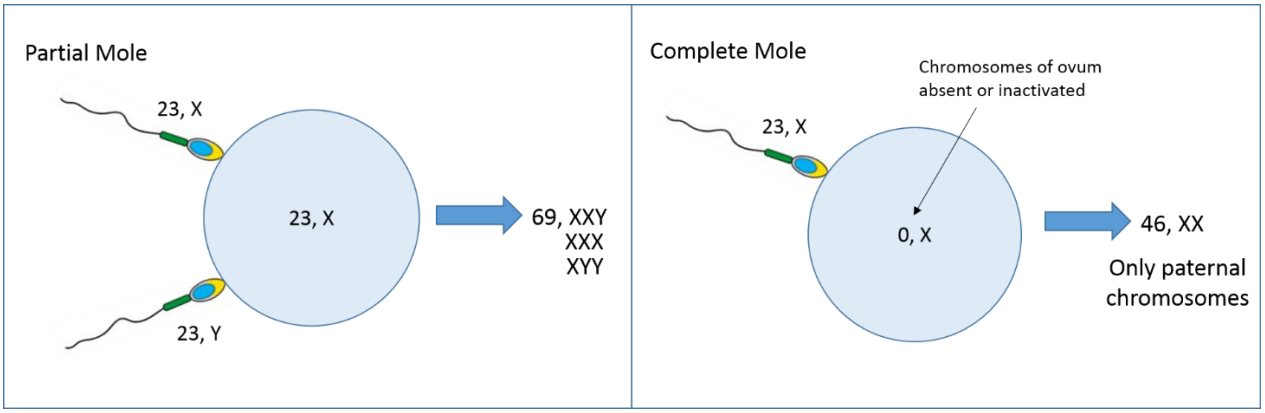

Table 1

	Beta HCG	Uterine size	Theca-lutein cysts	Complications*	Subsequent GTN
Complete	>100,000	S>D	25-30%	Uncommon	15-20%
Partial	<100,000	S<D	Rare	Rare	1-5%

*Complications: preeclampsia, hyperemesis, hyperthyroidism, anemia

References:
-Cunningham F, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS. “Gestational Trophoblastic Disease.” *Williams Obstetrics, Twenty-Fourth Edition* New York, NY: McGraw-Hill; 2013.
-Cunningham F, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, Casey BM, Sheffield JS. "Chapter 5. Implantation and Placental Development." *Williams Obstetrics, Twenty-Fourth Edition*. New York, NY: McGraw-Hill; 2013.
-"Chapter 9. Reproductive Physiology." *Medical Physiology: The Big Picture* Eds. Jonathan D. Kibble, and Colby R. Halsey. New York, NY: McGraw-Hill, 2014.