Ectopic Pregnancy

**Clinical Cases Applicability:** Pregnancy of unknown location, Ectopic pregnancy

**Learning Objectives:**
1. Describe the normal histology of the fallopian tube
2. Understand the pathophysiology of ectopic pregnancy
3. Understand the pharmacology of methotrexate

**What is the function of the fallopian tube?**
Captures the ovulated ovum → provides environment for fertilization (typically in the ampulla) → transports zygote to the uterus typically within 3 days

**What are the segments of the fallopian tube?**
- Infundibulum – Most distal segment; Contains fimbriae → fingerlike extensions of the mucosal folds that project from the opening towards the ovary – “traps ovum”
- Ampulla – widened segment near the distal end; ↑ mucosal folds, common site of fertilization
- Isthmus – narrow segment adjacent to the uterine wall, contains few mucosal folds
- Interstitium – penetrates the uterine wall; ↓ mucosal folds, myometrium contributes to its muscularis

**What is the histology of the fallopian tube wall?** 3 layers: mucosa, muscularis, serosa (figure 1)
- Mucosa: lamina propria + simple columnar epithelium with 2 cell types: ciliated, columnar cells (aid in egg transport) & peg cells (non-ciliated secretory cells, produce substances that provide protection and nutrition for the ovum and sperm) (figure 1)
- Muscularis: inner layer circumferential, outer layer longitudinal smooth muscle (wave-like contractions)
- Serosa: highly vascular, continuous with visceral peritoneum.

**What occurs in normal implantation?** (figure 2)
Blastocyst (outer layer of cells = trophoblasts, inner cell mass → embryo) hatches out of the zona pellucida and is maintained initially by uterine secretions → Within 24 hours of hatching (~day 6), blastocyst implants in the uterine lining.

1) **Apposition** in which there is a loose connection between the trophoblast cells of the blastocyst to the endometrium
2) **Adhesion** in which the blastocyst is anchored to the endometrium and
3) **Invasion** in which trophoblasts invades maternal capillaries/vessels in the endometrium → extravasation of maternal blood and formation of lacunae (the intervillous space)

**What causes ectopic pregnancy?** 95% occur in the tube, 70% ampulla; other 5% include ovarian, abdominal, cervix and c-section scar
1) Delay or prevention of passage of fertilized oocyte to the uterine cavity from abnormal fallopian tube anatomy – prior ectopic, acute inflammation (chlamydia, PID), peri-tubal adhesions (surgery, endometriosis), salpingitis isthmica nodosa
2) May be factors inherent in the embryo result in premature implantation

**Why is rupture common in ectopic pregnancy?** No submucosa in the fallopian tube → rapidly proliferating trophoblasts invade through the epithelium and implants near or at the muscularis layer; invading expanding products of conception and associated hemorrhage can cause rupture of the tube.
- If the tube ruptures early (1st few weeks), the pregnancy is most likely located in the isthmic portion, whereas the ampulla is slightly more distensible

**How does methotrexate treat ectopic pregnancies?** (figure 3)
Folic acid antagonist competitively inhibits binding of dihydrofolic acid to the enzyme dihydrofolate reductase → inhibits rapidly dividing cells from making purine/pyrimidines → arrest of DNA, RNA, protein synthesis
Ectopic Pregnancy

Figure 1: Courtesy of Richard Lieberman MD

References:
- Tulandi, T. Ectopic pregnancy: epidemiology, risk factors, and anatomic sites. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (2017)

Liang A