Pregnancy of Unknown Location

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Conflicts

- I have no conflicts to disclose

Clinical Scenario

- 22 yo G1 presents to the ER with spotting
- LMP unsure, ? Spotting 3 weeks ago, doesn't track cycles closely
- Was on OCP, but stopped it a while ago because she was doing a "cleanse"
- Positive UPT 3 days ago, hasn't seen her FD yet
- Desired pregnancy
- PMH: nothing major, +chlamydia when she was 16, treated, quit smoking recently, but still using a vape, no prior surgeries

Initial Evaluation

- Beta HCG: 450
- US: no IUP, no suspicious masses
- PE: unremarkable abdominal exam, speculum – scant brown blood, no CMT, anteverted uterus, non-tender adnexa

What to consider?

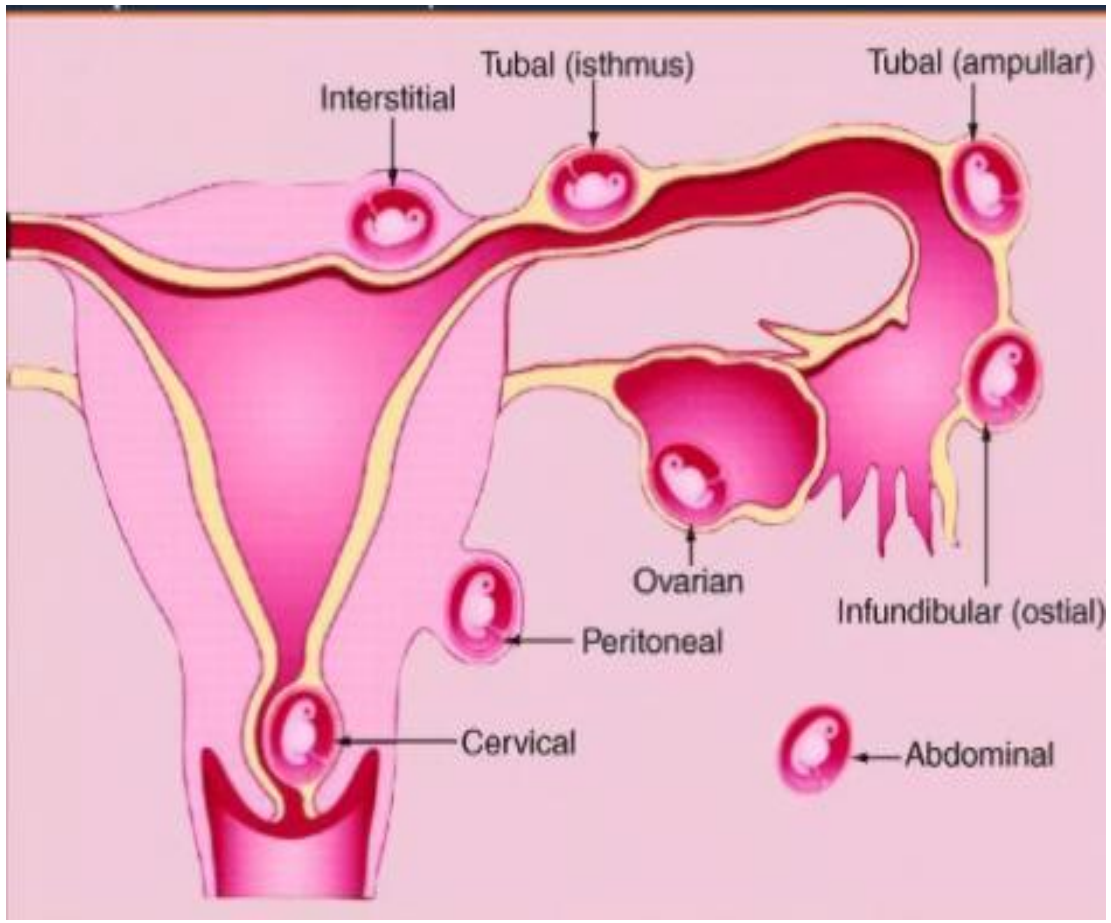
- Pregnancy of unknown location
- Why is it important?
  - Ectopic pregnancy – 1-2% of all pregnancies, but accounts for 75% of deaths in the 1st trimester and 9-13% of all pregnancy-related deaths
  - Approx 15% of patients being seen in the 1st trimester will have a PUL

Differential Diagnosis

- PUL – a working diagnosis, not a final one!
- Indicates a situation with a positive pregnancy test without US findings to establish location
- Possible final diagnoses
  - 1. IUP (either viable or not) ~30-40%
  - 2. Ectopic pregnancy ~8-14%
  - 3. Pregnancy with location never identified (spontaneous resolution) ~50-70%

Ectopic pregnancy

- Any pregnancy outside the uterus
- 98% will be tubal
- Less frequent sites:
  - Cesarean scar 1/2000
  - Abdominal 1/5000
  - Ovarian 1/7000
  - Cervix, rudimentary horn – rare



Assessment of PUL

- Full assessment can require multiple visits and repeat testing with close follow up
- Delay in treatment can cause adverse outcomes, BUT early treatment could harm a viable, desired pregnancy
- Clear communication with the patient is important
- Protocols to rule out ectopic may not always rule in a viable IUP

Risk Factors

- Tubal scarring → multiple surgeries, PID
- Smoking
- Previous ectopic (~10% recurrence rate)
- ART
- IUD*** (not really)

Diagnosis – serial Beta HCG

- Needs to correlated with the patient's symptoms and history
- Minimum sufficient increase for an IUP is 66% in 48hrs, typically for a viable IUP will see 100% increase or more
- Progesterone has limited utility but can be helpful in very early cases
- US can definitively diagnose ectopic, but can't definitively rule it out
  - IUP with a yolk sac should be visible by 5-6 weeks gestation]
  - Discriminatory zone – varies amongst institutions
- When all else fails, uterine aspiration +/- laparoscopy should be considered to confirm location of pregnancy

Management of Tubal Ectopic

- Expectant – rarely used, but may be appropriate for asymptomatic patients with a low beta HCT
  - Spontaneous resolution in 96% of patients with HCG<175
  - Failure to resolve in 93% of patient with HCG>2000

Criteria for expectant management of tubal pregnancy

Symptoms	Asymptomatic	Any symptoms
Initial β-hCG	<1000 IU/L	≥1000 IU/L
Change in β-hCG in 48 h	Decreasing (≥15%–20%)	Plateau *or* increase
Adnexal appearance on US	No significant hematosalpinx *and* no fetal heart rate	Large hematosalpinx *or* detectable fetal heart rate
Free fluid on US	No significant free fluid	Hemoperitoneum
Patient characteristics	• Agreeable to participation in close follow-up • Understands and accepts potential risks of failure • Counselled on signs and symptoms requiring emergency care • Can access emergency care	• Barriers to understanding diagnosis or risks • Potential barriers to participating in follow-up • Poor access to emergency care • Requests active treatment

Medical Management - Methotrexate

- Folic acid antagonist – inhibits DNA synthesis in rapidly dividing cells
- Initially used to treat GTN
- Multi dose vs single/double dose

Single Dose Protocol

- Day 1 – Serum Beta HCG, 50mg/m2 MTX IM
- Day 4 – Serum Beta HCG
- Day 7 – Serum Beta HCG – If >15% drop from day 4, treatmentis successful, follow HCG to zero. If <15% drop, give next dose and repeat protocol
- If still <15% drop on second week of treatment day 4->7, consider surgery
- Proceed to surgery for s&s of rupture

Who is a good candidate?

Criteria	Consider MTX	Use MTX with caution	Use MTX with extreme caution
Vital signs	Normal	–	Abnormal
Abdominal pain	None	Mild/transient	Significant or persistent
β-hCG	<1500 IU/L	1500–5000 IU/L	>5000 IU/L
Adnexal mass size	<35 mm	–	≥35 mm
Appearance	Empty gestational sac or heterogeneous mass	Yolk sac with or without fetal pole	Fetal heart rate seen
Free fluid on ultrasound	None/minimal	Simple and/or confined to pelvis	Echogenic or large

Ability to follow up	No identified barriers, agreeable to follow-up	Potential barriers: language, social, geographic	Unable or unwilling to follow up
Labs	Normal CBC, Cr, ALT	• Mild anemia or thrombocytopenia • Slight elevation in ALT or Cr (no more than 2 times upper limit of normal)	Significant abnormalities in any of CBC, Cr, or ALT
Patient medical history	Healthy	• Mild anemia or thrombocytopenia • Refuses blood transfusion	• Infection (TB, HIV) • Immunosuppression • Breastfeeding • Liver or renal disease • Bone marrow suppression • Blood dyscrasias • Pulmonary fibrosis • GI or oral ulcers • Heterotopic pregnancy
β-hCG change in 48 h pretreatment (if available)	<20% increase in 48 h	>50% increase in 48 h	Rapidly increasing (mirroring IUP)

Surgical Management

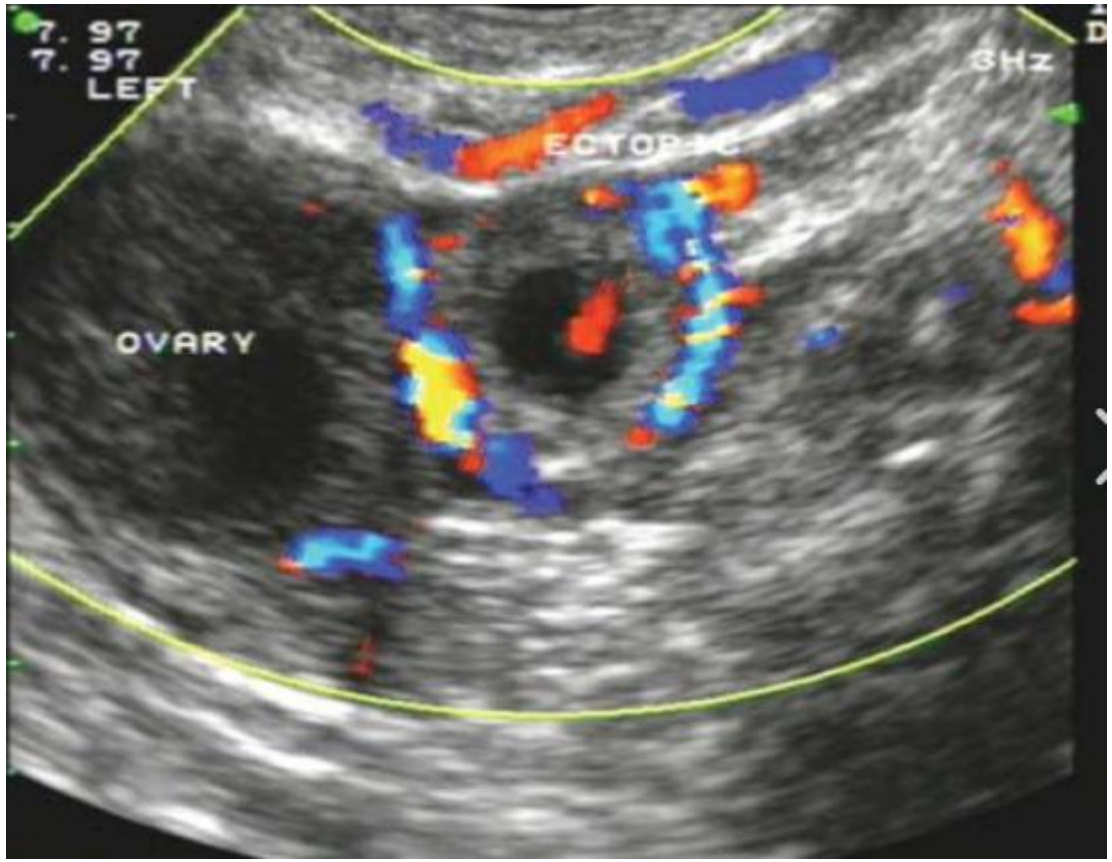
- Salpingectomy vs Salpingostomy
- Salpingectomy: no/low risk of persistence, dec risk of recurrent ectopic, possible dec in future fertility
- Salpingostomy: inc future fertility in women w/ contralateral tube damage, but no evidence in women normal opposing tube; risk of persistence is relatively high –requires follow up labs, possible inc risk of recurrence

Non-Tubal Ectopic Pregnancy

- Ovarian
- Cesarean Scar
- Interstitial (Cornual)
- Cervical
- Abdominal

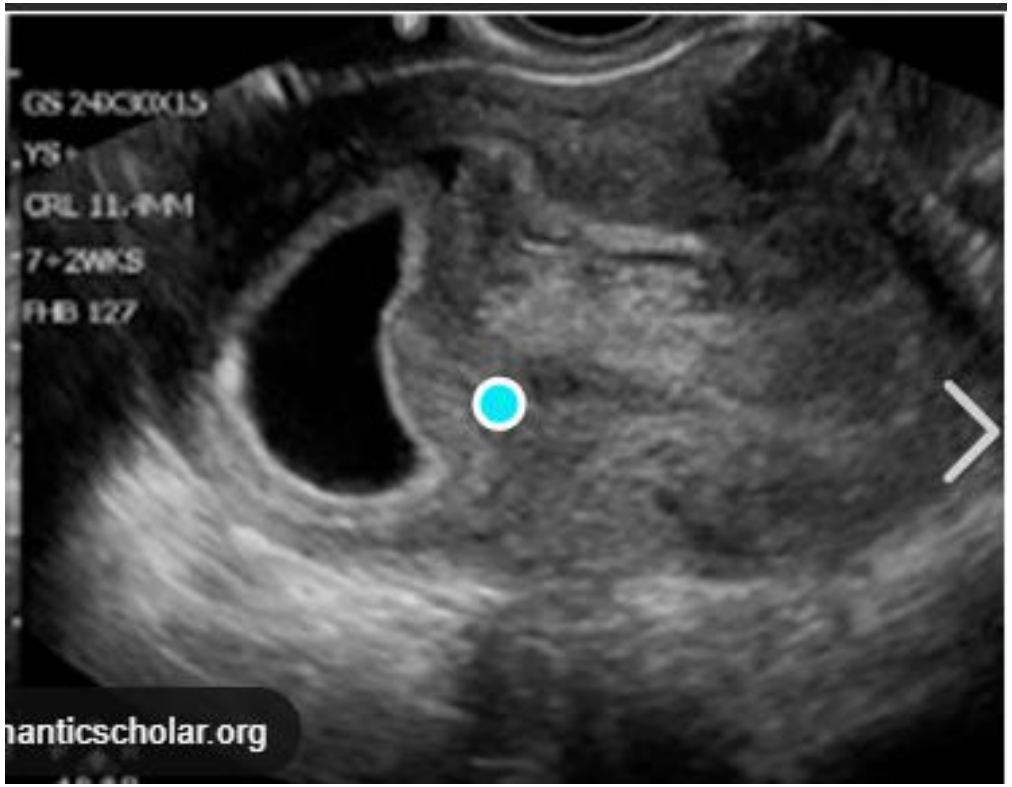
Ovarian Ectopic

- Hard to distinguish from tubal, sometimes not clear until laparoscopy
- Single dose MTX
- Surgical, usually USO



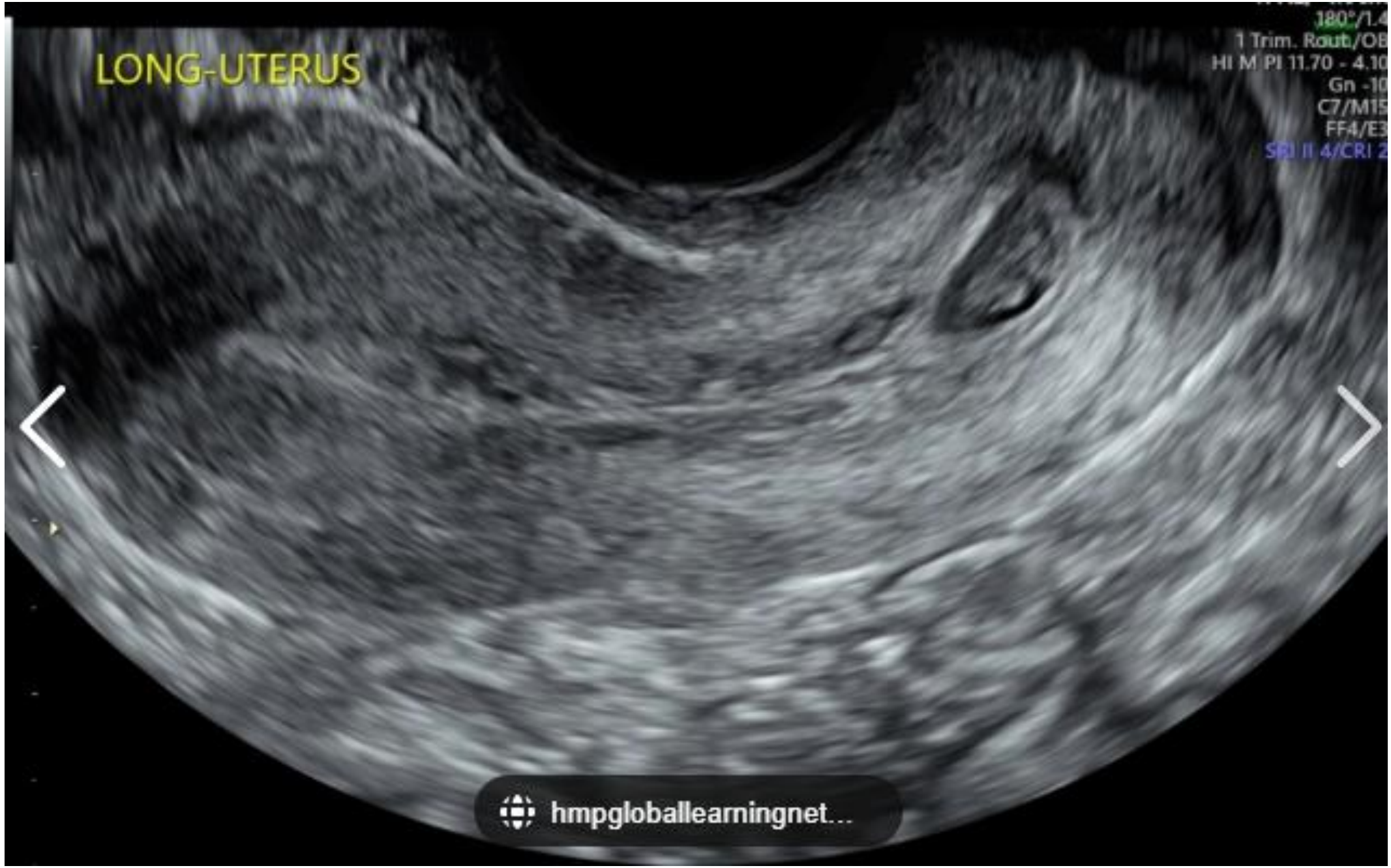
Interstitial Ectopic

- Single dose or Multi-dose MTX
- Local injection of MTX
- Surgical → cornuotomy, wedge resection



Cervical Ectopic

- Multidose MTX (usually inpatient)
- MTX injection
- Embolization of uterine/cervical arteries
- Suction curettage
- Hysterectomy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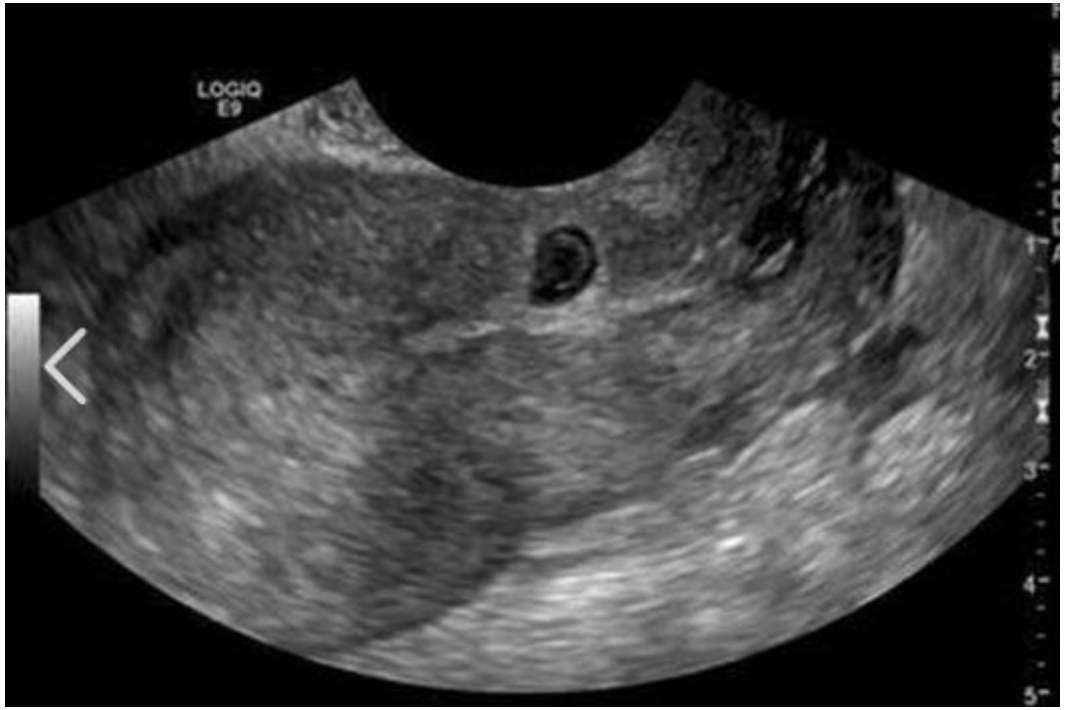
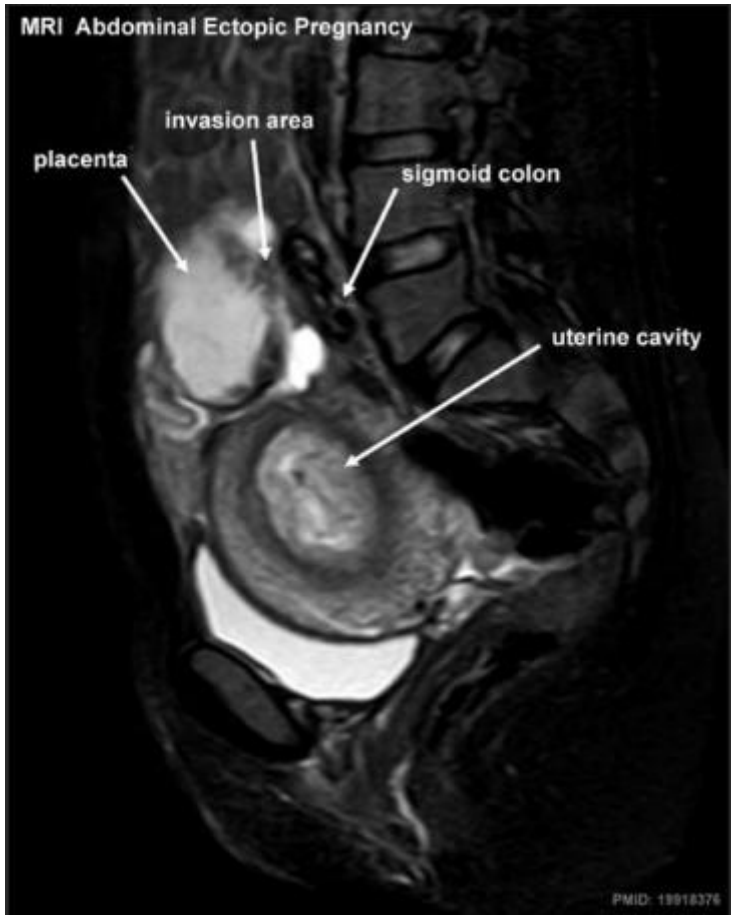
Cesarean Scar



- Single or Multidose MTX
- Direct MTX injection
- Uterine artery embolization
- Surgical → Suction curettage, hysteroscopic excision, laparoscopic wedge resection (depends on site).
- Occasionally may become an IUP, but has a high risk of abnormal placentation/placenta accreta

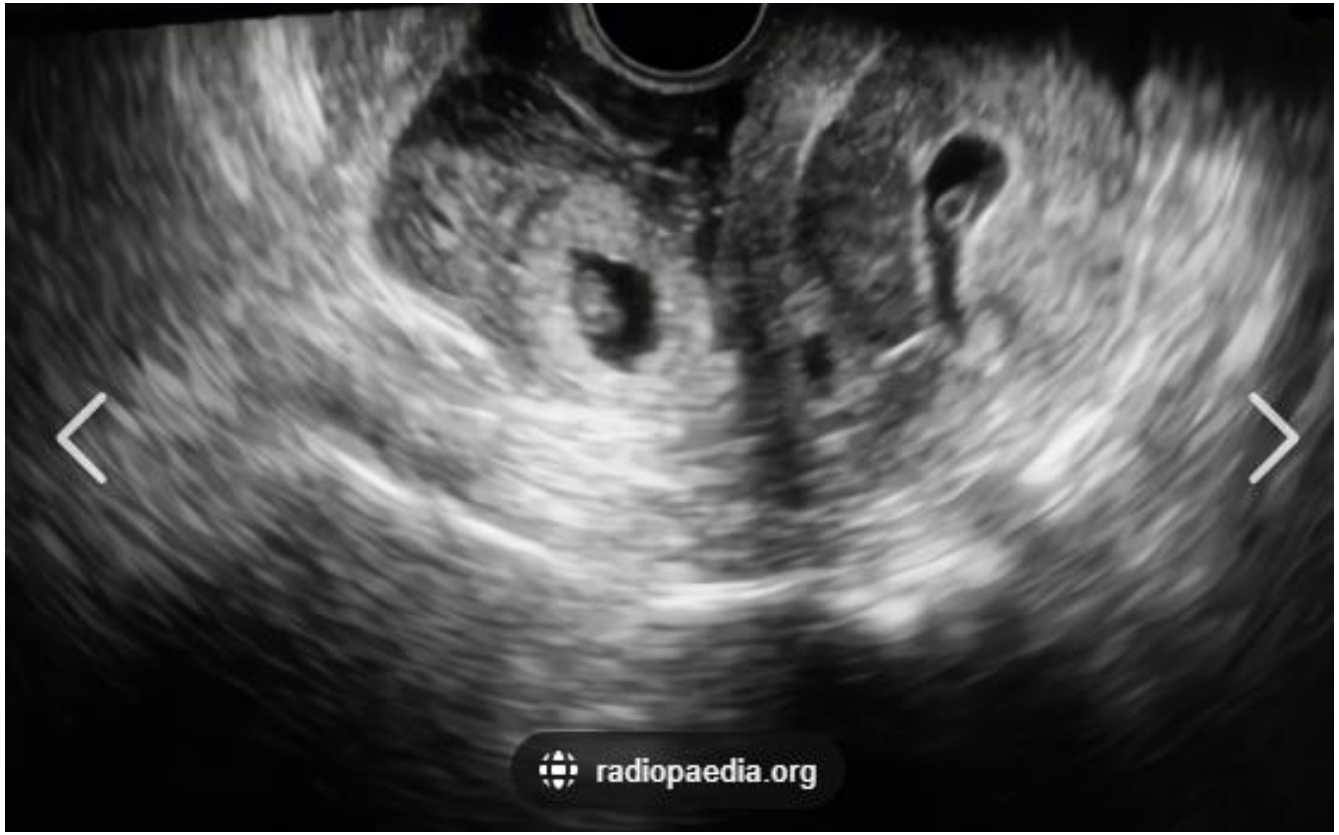
Abdominal Ectopic

- 1.3% of all ectopics, 8x greater fatality rate (hemorrhage)
- Multidose MTX
- Laparoscopy/laparotomy
  - Excision of pregnancy tissue
  - Delivery of fetus



Heterotopic Pregnancy

- 1/30000 spont, 1/1000 ART
- Surgical management (avoid MTX)



To rhogam or not to rhogam?

- Poor data to be certain
- Expert opinion leans towards administering rhogam
- Should be given within 72hours of any bleeding event or rupture of ectopic

Our patient

- Repeat bHCG 48hrs later is 625 (←450)
- Still having spotting and cramping
- Repeat US done – no significant change, no free fluid

- Counselled about options and prefers MTX – given 1st dose
- Follow up on day 4 is 700 → Are you concerned?

- Day 7 bHCG 550
- Having some increased cramping
- Is she sufficiently treated?
- What is her recommended follow up?

Future pregnancies

- 10% recurrent rate overall for another ectopic
- Early bHCG x2 should be considered with initial UPT

Questions??

Thank you!