Learning Objectives

- Understand use of HCG measurements and transvaginal ultrasound in evaluation of first trimester bleeding.
- Understand the diagnostic criteria, natural history and treatment options for early pregnancy loss (miscarriage).
- Describe the evaluation and treatment of ectopic pregnancy including common pitfalls leading to missed diagnoses.

Case

- 17-year-old woman comes to ED with complaint of cramping and bleeding. Her last menstrual period was 7 weeks ago. She had a home pregnancy test which was positive 1 week ago.
- How do you evaluate her?

First Trimester Bleeding

- Spontaneous abortion or threatened miscarriage
- Ectopic pregnancy
- Trophoblastic disease
- Other: cervical polyps, friable cervix, trauma, cervical cancer

Physical Exam

- Vital signs
  - Hemodynamically stable?
- Abdominal exam
  - Pain location, rebound, distension
- Speculum exam
  - Amount of bleeding
  - Tissue in cervical os or vagina
- Bimanual exam
  - Uterine size, adnexal tenderness
Does every woman with first trimester bleeding need an ultrasound?

- Yes per 2012 ACEP Clinical Policy guideline
- No level of HCG that is low enough to exclude potential for ruptured
- Level C Recommendation

Sept 2012 Annals of Emergency Medicine

18-year-old G1 PO presents with vaginal bleeding and no pain. HCG has gone from 1300 to 2100 in 48 hours. Empty uterus on ultrasound. What is her probable diagnosis?

1) Ectopic as HCG above discriminatory zone and empty uterus
2) Nonviable pregnancy due to slow HCG rise
3) Early twin pregnancy
4) Normal viable IUP

Epidemiology of early pregnancy loss

- One in four women will have a miscarriage during her lifetime
- 15-20% of diagnosed pregnancies result in abnormal pregnancies
- May only form a gestational sac (blighted ovum or anembryonic pregnancy) or demise may occur after embryo forms. Usually under 10 weeks gestational age

Terminology & clinical presentations of early pregnancy loss

- Threatened abortion: Bleeding with closed cervix and apparent viable pregnancy
- Incomplete abortion: Bleeding with passage of some but not all of POCs
- Inevitable abortion: Bleeding with a dilated cervix
- Complete abortion: All POCs have passed
- Missed abortion: Embryo without heartbeat without bleeding/cramping

Diagnosis of early pregnancy loss

- Ultrasound is primary and often only diagnostic approach needed
- Quantitative βhCG
  - Correlate with gestational age and ultrasound
  - 2 measurements, 48 hours apart – should at least increase by 53% but may not “double”
  - Falling or plateaued serial quantitative HCGs can diagnose a failing pregnancy loss but not the location

First Trimester Laboratory Tests

- Hematocrit
- Rh-give Rhogam to all Rh negative women with first trimester bleeding regardless of how early in pregnancy
First Trimester Bleeding

Transvaginal ultrasound diagnosis of miscarriage

- Anembryonic pregnancy: Gestational sac of >22 mm without pole or >20 mm without yolk sac OR if < 22 mm with no change on rescans 7 days later
- Missed abortion: Fetal pole of >6 mm by CRL without heart beat or if ≤6 mm no change in rescans 7 days later

Abdallah et al. Ultrasound Obstet Gynecol 2011

<table>
<thead>
<tr>
<th>Gestational age by LMP</th>
<th>Transabdominal Landmarks</th>
<th>Transvaginal Landmarks</th>
<th>Serum hCG mIU/ml IRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5 weeks</td>
<td>None</td>
<td>Possible gestational sac</td>
<td>1800</td>
</tr>
<tr>
<td>5 - 6 weeks</td>
<td>Gestational sac</td>
<td>Gestational sac, yolk sac</td>
<td>1800 - 3500</td>
</tr>
<tr>
<td>7 weeks</td>
<td>5-10 mm embryo</td>
<td>Same as transabdominal, with cardiac activity</td>
<td>&gt;20,000</td>
</tr>
</tbody>
</table>

HCG and Ultrasound Correlates

Normal gestational sac

- Round appearance
- Fundal location
- “Double decidual reaction” of echogenic area surrounding sac

7-week embryo

Crown rump length for dating

Menstrual age* (weeks) = CRL (cm) + 6.5

Anembryonic pregnancy

Over 22 mm gestational sac without an embryo

First Trimester Bleeding

Mixed hyperechoic and hypoechoic contents in the endometrial cavity of the fundus (arrowheads) represent decidual reaction/hemorrhage. Complete spontaneous abortion a few hours after the scan.

10 weeks of amenorrhea presents with intermittent vaginal bleeding. TVUS shows a relatively small-sized embryo (arrow) compared with the gestational sac. No cardiac activity was demonstrated on pulsed Doppler.

Management of early pregnancy loss (miscarriage)

- Uterine curette introduced in 1843
- D and C advocated in late 18th century to decrease hemorrhage and chance of sepsis
- Dilation and curettage has been standard management for over 50 years
- Edwards and Carson report prompts increased MVA use in USA in 1997
- Misoprostol introduced for medical management of EPL in 2001-2004

Expectant management

Risks
- Infection
- Need for urgent uterine aspiration
- Hemorrhage/blood transfusion

Benefits
- Avoid risks (albeit rare) of uterine aspiration including perforation
- Decrease risk of excess curettage (Asherman’s syndrome)
- Patient preference to avoid procedure
- Cost

Contraindications to expectant management

- Excess blood loss
- Infection
- Inability to access an emergent uterine aspiration
- Patient choice – aspiration should be option for all women

Myths of expectant management

- Acceptable for limited time only
- Disseminated intravascular coagulation is concern
- Infection likely
First Trimester Bleeding

Why was D and C the standard for miscarriage in recent past?

• Septic abortion was common and serious problem prior to legalization of abortion
• Women with post unsafe abortion routinely said they were “miscarrying”
• Septic abortion now rare and usually benign course of miscarriage has become apparent

Success of expectant management

• Casikar et al followed 227 women who agreed to expectant management after miscarriage dx
• After 14 days spontaneous resolution/completion occurred in 61%
• 71% incomplete miscarriage, 53% missed abortion with empty sac and 35% missed abortion with fetal pole

Casikar et al Ultrasound Obst Gynecol 2010

Psychosocial factors in decision making: qualitative study

• Women may need more time and information than usually provided after initial diagnosis to make decision
• Women choosing surgery usually got adequate counseling
• Women choosing expectant management needed more info about miscarriage process

Ogden. BJOG 2004; 111:463-7

Key Counseling Issues

• Woman needs to know that miscarriage is not her fault
• Nothing she did caused this to happen
• Very important to give this information to her partner, too.
• Remember – Half of pregnancies are unintended – not everyone is sad to lose a pregnancy

Surgical options

• Sharp curettage (D and C) no longer an acceptable option due to higher complication rates
• Vacuum aspiration includes manual vacuum aspiration (MVA) vs. electrical pump aspiration

Uterine aspiration

Electric Suction Machine
First Trimester Bleeding

**MVA Instruments and Supplies**

- Inexpensive
- Small
- Portable
- Quiet
- Specimen likely to be intact
- May require reloading of suction

**Manual Vacuum Aspiration vs. Electric Vacuum Aspiration**

- **MVA**
  - More costly, but longer life
  - Bulky
  - Less Portable
  - Noisy
  - Fragmentation of specimen
  - Constant Suction

- **EVA**

**Why deal with this in the ED? Can we just send everyone home or to the OR?**

- MVA in ED/labor ward vs. suction D and C (EVA) in OR
- Waiting time reduced by 52%
- Procedure time reduced from mean 33 to 19 minutes
- Costs reduced by 41% ($1404 to $827, P < .01) for all three outcomes

  - Blumenthal PD, Remsburg RE. Int J Gynecol Obstet 1994; 45: 261-267

**Dilating the Cervix**

- Necessary when the cervical canal will not allow passage of appropriate cannula
- Gently dilate with dilators or cannula of increasing size.
- Or, give misoprostol several hours before the procedure.

**Inserting Cannula**

- Holding cannula with fingertips, gently insert through the cervix with a rotating motion.

**Releasing the Pinch Valve**

When the pinch valve is released, the vacuum is transferred through the cannula to the uterus.
First Trimester Bleeding

Aspirating uterine contents

- Move the cannula gently back and forth, rotating the syringe.
- Do not withdraw cannula aperture(s) beyond cervical os.
- Do not grasp syringe by the plunger arms.
- Blood, tissue, and bubbles will flow through the cannula into the syringe.

Introducing MVA in your ER or urgent care practice

- Training: Easy to adopt if already doing electric suction D and C
- Equipment: MVA syringe ($30 reusable) and suction curret(s) ($1 each)
- Ultrasound: Useful to ensure completion but not essential. $20,000. Billable
- Patient handouts/forms

Misoprostol for early pregnancy failure

- Vaginal misoprostol appears to have success rates between 80-90% depending on whether bleeding and cramping has already begin
- The reason women choose it – still feels somewhat natural yet the expulsion timing is more predictable

Misoprostol for miscarriage

- 800 mcg miso administered vaginally on Day 1 with repeat on Day 3 if incomplete and Vacuum on Day 8 if still incomplete
- 71% complete by Day 3
- 84% complete by Day 8
- Anembryonic gestation success rate 81%
- Embryonic or fetal death 88%
- Incomplete or inevitable abortion 93%
- Zhang et al NEJM 8/25/05

Buccal & Sublingual Use

- Mostly been studied with the use of induced medical abortion
- Sublingual has faster absorption than buccal*
- Buccal as effective as vaginal in induced medical abortion up to 56 days’ gestation
- Sublingual as effective as vaginal misoprostol in induced medical abortion up to 63 days’ gestation
- Buccal used most often currently given recent deaths associated with medication abortion

*Schaff, EA et al 2005
*Tang, OS et al 2006
Middleton, T et al 2005

Side effects of misoprostol

- Bleeding – typically lasts up to 2 weeks with spotting till next period. Call for “heavy bleeding” defined as soaking a pad every hour for more than 2 hours.
- Cramping – usually starts within the first few hours. NSAIDs can be used
- Fevers and/or chills – common side effect. If lasts >24 hours, evaluate for infection
- Nausea and vomiting – more common after oral misoprostol. Should resolve in 6 hours
- Diarrhea – also more common after oral miso and should resolve in 24 hours.
First Trimester Bleeding

**Patient precautions**
- Call for "heavy bleeding" defined as soaking a pad every hour for more than 2 hours.
- The patient does not need to bring products of conception back to the physician.
- If no passage of tissue occurs (the patient has not bled as much as a period) within 12-24 hours, the patient may repeat 800 mcg dose.
- Follow-up plan: If no passage of tissue occurs by 1-2 weeks consider referral for aspiration vs. continued expectant management.

**What do you need to start using misoprostol in your practice?**
- Uterine aspiration plan if unsuccessful or heavy bleeding (same plan as expectant management?)
- Patient handouts/clinical guidelines
- On call system familiar with misoprostol
- Follow-up plan: confirm completion with HCG drop of 50% expected 48-72 hours after passage of tissue or transvaginal ultrasound with absence of sac
- The patient does not need to bring products of conception back to the physician.

**Which is better or safer: aspiration, medication or waiting?**
- Cochrane 2010 compared to miso to expectant and found each equal found.
- Cochrane 2012 compared aspiration to expectant and found more unplanned surgery with expectant (obvious?) and transfusion (1.4% vs. 0%). Infection and psychological outcomes similar and cost less with expectant.

**Antibiotics indicated?**
- Yes for uterine aspiration based on abortion date – optimal is pre-procedure
- Doxycycline 200 mg the night before (up to 12 hrs) or 1 hour prior to procedure appears optimal
- Metronidazole alternative if allergic
- Society of Family Planning Guideline Contraception April 2011

**Pain and bleeding**
- Tell her she does not have ectopic and schedule a prenatal visit within a week.
- HCG above discriminatory zone so to OR for diagnostic laparoscopy.
- HCG above discriminatory zone so offer methotrexate.
- Give ectopic precautions and return for HCG in 48 hours.

**Ectopic Pregnancy**
- Pregnancy outside the uterus – Usually in fallopian tube.
- Occurs in >1:100 pregnancies.
- Second most common cause of maternal mortality.
- Early diagnosis critical!
First Trimester Bleeding

Risk Factors for Ectopic

- History of previous ectopic pregnancy ***
- Prior tubal surgery ***
- Prior tubal infection(s) **
- Contraceptive IUD in place **
- Progestin-only contraception
- Infertility
- Smoking
- Age <18 or >35 years
- Many occur in women with no risk factors!

Jurkovic BMJ 2011; 342

Presentation of Ectopic

- Vaginal bleeding is most common presentation but absent in 10-20%
- Pain usually follows bleeding but absent in 10%
- Ruptured ectopic – peritoneal signs and hemodynamic instability

Diagnosis of Ectopic

- Failure of βhCG to rise appropriately is common but HCG pattern in ectopic overlaps with viable IUP and miscarriage
- Ultrasound (transvaginal)
  - IUP rules out ectopic except rare heterotopic
  - No gestational sac + βhCG>1800 highly suggestive
  - Gestational sac / embryo outside of uterus confirms ectopic
  - Pitfalls: pseudogestational sac, ruptured corpus luteum
- Laparoscopy – gold standard

Ectopic Pregnancy – Extrauterine Mass

Discriminatory zone reconsidered

- Reviewed 690 first tri pregnancies with vaginal bleeding and/or pelvic pain with HCG and transvaginal ultrasound within 6 hours
- 50% of the time a gestational sac could be seen when HCG >879 and 90% of the time when HCG >1918
- 99% discriminatory level was 3510 – much higher than currently used

Obstet Gynecol 2013;121:65–70

Ectopic on ultrasound
First Trimester Bleeding

### Extrauterine Signs of Ectopic

<table>
<thead>
<tr>
<th>Finding</th>
<th>Risk of Ectopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>No mass or free fluid</td>
<td>20%</td>
</tr>
<tr>
<td>Any free fluid</td>
<td>71%</td>
</tr>
<tr>
<td>Echogenic mass</td>
<td>85%</td>
</tr>
<tr>
<td>Moderate to large amount of fluid</td>
<td>95%</td>
</tr>
<tr>
<td>Echogenic mass with fluid</td>
<td>100%</td>
</tr>
</tbody>
</table>

Mahony et al. JUM1985;4:221-228

### Diagnostic pitfalls

- **Missing ectopic pregnancy**
  - Assuming miscarriage when IUP not demonstrated
  - Chronic ectopic
  - Poor follow-up
- **Treating IUP with methotrexate**
  - Missing gestational sac on ultrasound
  - Misinterpretation of HCG pattern
  - Mistake corpus luteal cyst for ectopic

### Medical Management: methotrexate

- Safe, effective, less costly than surgery
- Equal or better fertility preservation
- Criteria for use:
  - Stable vital signs, few symptoms
  - No contraindication to drug
  - Unruptured ectopic
  - Absence of embryonic cardiac activity
  - Ectopic mass <4cm
  - $\beta$hCG levels <5000 mIU/ml (relative)

### Methotrexate Dosing

- Single dose IM regimen with 1 mg/kg or 50 mg/m2
- Obtain serum $\beta$hCG on 4th and 7th day post-treatment
  - Follow until level reaches < 5 mIU/ml (3-4 wks)
- Document 15% or greater drop between days 4 and 7
- Alternative 2-dose regiment may be more effective

### Surgical Management

- Traditional mainstay of treatment
- Conservative – conservation of tube
- Exirpative – removal of tube
- Criteria for selecting surgery
  - Unstable vital signs or hemoperitoneum
  - Uncertain diagnosis
  - Advanced ectopic pregnancy
  - Unreliable follow-up
  - Contraindication to expectant management or methotrexate

### Summary

- Diagnosis of miscarriage or ectopic relies on ultrasound and HCG and may require serial visits.
- Expectant management or medical (misoprostol) or surgical intervention (uterine aspiration) are appropriate with EPL based on patient choice.
- Education and close follow-up are essential for medical & expectant management of miscarriage
- Ectopic pregnancy remains significant cause of maternal mortality – be vigilant!