EARLY PREGNANCY LOSS

ELYSE WATKINS, DHSC, PA-C, DFAAPA

Disclosures

I have no financial relationships to disclose.

Learning Objectives

- Differentiate between the various terms used to describe early pregnancy loss.
- Describe the key physical examination and diagnostic findings in a patient with an EPL.
- Utilize the best available evidence to create a diagnostic plan for a patient with a possible EPL.
- Create a management plan for a patient with a possible or confirmed EPL.

Terms

- **EPL: early pregnancy loss**
- A **nonviable intrauterine pregnancy** (IUP) diagnosed up to 12w 6d gestation
  - Used to be called spontaneous abortion (SAb)
  - Now used for variants of incomplete abortion, complete abortion, and anembryonic pregnancy

Term	Definition
Threatened abortion	closed cervical os, viable IUP on ultrasound
Incomplete abortion	dilated cervical os, nonviable IUP on ultrasound, POC retained in uterus
Complete abortion	Closed cervical os, no POC on ultrasound, symptom resolution
Anembryonic pregnancy	No embryo development on ultrasound
Recurrent early pregnancy loss	Loss of two or more pregnancies in first trimester

IUP: intrauterine pregnancy
POC: products of conception

Incidence

- Occurs in approximately 10% of all pregnancies (ACOG)
- Risk of an EPL is 80% by age 45 years + (ASRM)
- Females with 3+ losses: 40% risk of subsequent loss (Magnus et al)

Etiology of EPL

- Up to 80% of all EPLs are due to a chromosomal aberration

Chromosomal Abnormality	Definition/ Examples	Incidence (%)
Single autosomal trisomy	One additional autosomal chromosome present, Examples: Trisomy 16), Trisomy 21 (Down syndrome), Trisomy 22	64.6
Triploidy	Three sets of chromosome in each cell, Example: 69XXX	13.1
Monosomy X	An X chromosome is missing, Example: Turner syndrome	10.4
Chromosomal rearrangements	Chromosomal deletions, duplications, inversions, translocations	5.2

Risk Factors for EPL

- **Infection:** CMV, HIV, rubella, dengue fever (*Flavivirus*), malaria, syphilis
- **Uterine anomalies**
- **Subchorionic hematoma**
- **IUS *in situ***
- **Factor V Leiden/prothrombin gene mutation**
- **Antiphospholipid syndrome** (anticardiolipin antibodies IgG and IgM)

Risk Factors for EPL

- **Uncontrolled chronic disease** (especially T1, T2 diabetes, hypo- and hyperthyroidism)
- **Hx EPL**
- **Maternal age:**
  - slightly increased for women < 20 years
  - increased significantly > 30 years (>50% risk by 45 years)
  - Lowest risk of miscarriage at age 27 years

Modifiable Risk Factors

- Alcohol use
- High BMI
- Tobacco use
- Cocaine use
- NSAID use (especially >2 wks use)

Common presenting signs and symptoms

- Vaginal bleeding
- Pelvic cramping/pain
- No symptoms!
- Nausea, vomiting, breast tenderness, painless vaginal spotting usually **NOT** associated with EPL
  - N/V (particularly hyperemesis) is associated with molar pregnancy

Physical examination

- **Assess hemodynamic status!**
- **Perform speculum exam**
  - What to look for/document
- **Perform bimanual exam**
  - What to palpate/document
- **Fetal heart tones/cardiac activity?**
  - External fetal doptone vs ultrasound

Labs and Imaging

- **Quantitative β-HCG, CBC, and Rh** status
  - Note on β-HCG: need to correlate with ultrasound findings!
  - β-HCG should double within 48-72 hours
- **Serum progesterone** < 35 nmol/L suggestive but not diagnostic of EPL

Imaging

- Transvaginal ultrasound
- Must correlate with β-HCG

Ultrasound finding	β-HCG (mIU/mL)
Gestational sac	**390 - 3510**
Yolk sac	**1094 - 17716**
Fetal pole	**1394 - 47685**

Imaging: Ultrasound Findings to Dx EPL (SRU)

Mean gestational sac ≥25 mm with no embryo
Crown-rump length ≥ 7 mm with no cardiac activity
Empty gestational sac by 12w6d gestation
Absence of embryo with cardiac activity ≥ 2 wks after a previous ultrasound showed a GS without a YS
Absence of embryo with cardiac activity 11 days after a previous ultrasound showed a GS with a YS

Important Notes

- Fetal heart rate <100 bpm: re-evaluate in 7-10 days
- Subchorionic hemorrhage: re-evaluate in 7-10 days
- If unsure of diagnosis:
  - **Repeat HCG** in 48 – 72 hours if the patient is stable
  - **Repeat ultrasound** in 7 – 10 days if the patient is stable

Expectant Management

- If hemodynamically stable, < 13w6d, and afebrile, **expectant management** can be considered.
  - Expectant management: 80% will expel POC on their own especially if symptomatic
  - If the patient is Rh negative, administer **Rho(D) immunoglobulin**.

Medical Management

- If the patient is Rh negative, administer at least 50 mcg of **Rho(D) immunoglobulin**
- **Misoprostol 800 micrograms vaginally**
  - May repeat one dose as needed in 3 hours after the initial dose and within 7 days if no response
- **Mifepristone 200 mg** orally 24 hours before misoprostol
- Combined tx increases expulsion rate without surgical intervention (Schreiber et al)

Medical Management

- **Methylergonovine** 0.2 mg PO every 6 – 8 hours can help with bleeding.
  - Increase in bleeding requires prompt evaluation!
- **Pain medications** as appropriate.

Medical Management

- If using **misoprostol/mifepristone**, repeat ultrasound in 7 – 10 days to ensure POC have been expelled.
  - If not, and pt is afebrile and not bleeding, can repeat misoprostol dose.

Surgical Management

- **Surgical intervention:**
  - Retained POC
  - Increase bleeding/hemorrhage
    - > 2 maxi pads/hour x 2 hours
  - Sepsis
  - Patient unable to tolerate medical/expectant management

Surgical management

- **Suction curettage** is superior to sharp curettage
- Can be done in the outpatient setting with local anesthetics +/- conscious sedation (Dalton et al)
- Can use doxycycline 200 mg PO one hour before procedure

Post-Loss Issues

- Abstain from vaginal intercourse for 1-2 weeks (low evidence)
- No evidence regarding when patient can try to conceive again

Post-Loss Issues

- Work-up for recurrent EPL (van Dijk et al)
  - After 2nd or 3rd loss?
  - Ultrasound imaging
  - Thyroid testing
  - Parental karyotyping – weak evidence
  - Antiphospholipid antibodies linked to EPL
    - Tests: lupus anticoagulant (LAC), anticardiolipin (aCL) antibody, and anti-beta-2glycoprotein I antibody.
    - Anticoags/ASA not recommended to prevent EPL unless +antiphospholipid antibody syndrome

Patient Education

- Grief reaction
- Blame
- Future pregnancy
- Modifiable risk factors

Question 1

A patient presents to the ED at 5w6d based on her LMP. She is c/o spotting. Which of the following is the best next step in evaluating the patient?

a. Diagnose a threatened abortion and have her follow up with her ob/gn in the morning.

b. Perform an ultrasound to check for viability.

c. Order a quantitative HCG.

d. Perform a focused history and physical exam.

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Question 2

Which of the following statements is most true regarding early pregnancy loss (EPL)?

a. The majority of patients with an EPL will have anticardiolipin antibodies.

b. Most EPLs are due to maternal factors, such as smoking tobacco.

c. The most common etiology for EPL is a chromosomal aberration.

d. Patients who experience one EPL are 80% more likely to have another.

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Question 3

Which of the following findings can definitively be used to diagnose an EPL?

a. Empty mean gestational sac of 10 mm

b. No yolk sac by 5w6d

c. Empty mean gestational sac 26 mm

d. No cardiac activity on initial imaging by 6w0d

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References

- American College of Obstetricians and Gynecologists. Practice Bulletin 200: Early Pregnancy Loss. 2018. https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2018/11/early-pregnancy-loss
- Magnus MC, Wilcox AJ, Morken N, Clarice R, Weinberg CR, Håberg SE. Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study. BMJ 2019;364:l869–l1876.
- Doubilet PM, Benson CB, Bourne T, Blaivas M, Barnhart KT, Benacerraf BR, et al. Diagnostic criteria for nonviable pregnancy early in the first trimester. Society of Radiologists in Ultrasound Multispecialty Panel on Early First Trimester Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy. N Engl J Med 2013;369:1443–51.
- Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Practice Committee of the American Society for Reproductive Medicine. *Fertil Steril.* 2012;98:1103–11

References

- Hendricks E et al. First trimester bleeding: Evaluation and Management. *Am Fam Physician*. 2019 Feb 1;99(3):166-174.
- Schreiber CA, Creinin MD, Atrio J, Sonalkar S, Ratcliffe SJ, Barnhart KT. Mifepristone pretreatment for the medical management of early pregnancy loss. N Engl J Med 2018;378:2161–70
- Dalton VK, Harris L, Weisman CS, Guire K, Castleman L, Lebovic D. Patient preferences, satisfaction, and resource use in office evacuation of early pregnancy failure. Obstet Gynecol 2006;
- Myrthe M van Dijk, Astrid M Kolte, Jacqueline Limpens, Emma Kirk, Siobhan Quenby, Madelon van Wely, Mariëtte Goddijn, Recurrent pregnancy loss: diagnostic workup after two or three pregnancy losses? A systematic review of the literature and meta-analysis, *Human Reproduction Update*, Volume 26, Issue 3, May-June 2020, Pages 356–367, https://doi.org/10.1093/humupd/dmz048