Pregnancy Loss
Diagnosis and Care

Jennifer Braverman, MD, MA

Assistant Professor, Maternal Fetal Medicine

University of Colorado

SHAME, STIGMA AND SILENCE COURSE THROUGH OUR SOCIETY AS WOMEN GRIEVE AN ENVISIONED FAMILY MEMBER — TOO OFTEN MADE MORE COMPLICATED BY FEELINGS OF SELF-BLAME.

Objectives

- Sonographically diagnose and manage pregnancy loss
- Evaluate cause and recommend management for recurrent pregnancy loss
- Effectively counsel patients about pregnancy loss

Pregnancy loss is common

- About 10-20% of clinically recognized pregnancies end in pregnancy loss
  - 80% in the first trimester
  - IUFD is rare: 6.2 per 1000 births in the US
- Rates including losses before clinical recognition are probably 30-60%
- Approximately 1-3% of women will experience recurrent pregnancy loss

Etiologies of pregnancy loss – Before 20 weeks

- **Chromosomal anomalies (50%)**
- Congenital anomalies
  - Genetic and other (e.g. amniotic band)
- Uterine anomalies
  - Especially septate uterus
- Maternal infection/fever
  - TORCH: Toxo, Other, Rubella, CMV, HSV
  - Other: Syphilis, Varicella, Parvo, Listeria, Flu, ?Zika
- Maternal medical conditions
  - Endocrinopathy: Poorly controlled diabetes, thyroid dysfunction
  - Antiphospholipid antibody syndrome
- Teratogens
- Trauma (rare)
  - E.g. CVS/Amnio
- Unexplained
  - Small deletions/duplications/point mutations may account for some

Etiologies of recurrent early pregnancy loss

- Chromosomal abnormalities
  - Parental balanced translocations
- Uterine anomalies
  - Especially septate uterus
- Maternal medical conditions
  - Endocrinopathy: diabetes, thyroid
  - Antiphospholipid antibody syndrome

- **Unexplained (50%)**
  - Chromosomal
    - Maternal age-related, bad luck
    - Less selective endometrium hypothesis
  - Immunologic/Autoimmune?
    - Higher rate of positive ANA in pts with uRPL
    - Different immunophenotypes (make up of B-cells/T-cells/NK cells/macrophages)
  - Genetics?
    - GWAS suggest linkage to MHC genotypes and CNV in cadherin genes (Sonehara et al. 2024)
  - Metabolic?
    - Differences in apolipoprotein levels in patients with uRPL vs controls (Liu et al. 2024)

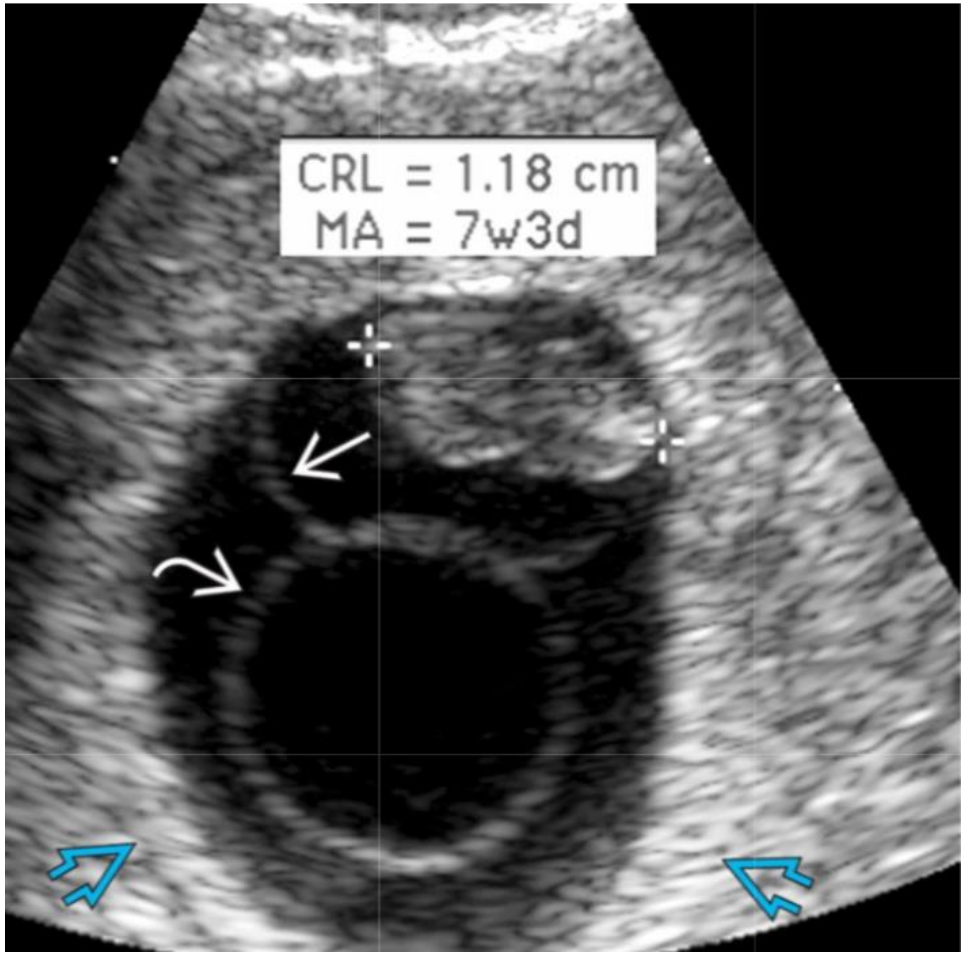
Etiologies of pregnancy loss – After 20 weeks

- Congenital and genetic abnormalities
- Growth restriction and placental abnormalities
- Maternal medical conditions, including: diabetes, lupus, renal disease, cardiovascular disease, thyroid disease, cholestasis
- Hypertensive disorders and preeclampsia
- Infection including: parvo, syphilis, streptococcal infections, listeria, maternal sepsis
- Smoking
- Multiple gestations
- Placental abruption (due to trauma, drug use, hypertension, or unknown)
- **Unexplained**

Sonographic diagnosis of early pregnancy failure

Findings Diagnostic for Pregnancy Failure	Findings Suspicious for Pregnancy Failure
No heartbeat with CRL ≥ 7 mm	No heartbeat with CRL < 7 mm
No embryo with MSD ≥ 25 mm	No embryo with MSD 16-24 mm
Absence of embryo with heartbeat ≥ 14 days after GS without YS	Absence of embryo with heartbeat 7-13 days after GS without YS
Absence of embryo with heartbeat ≥ 11 days after GS with YS	Absence of embryo with heartbeat 7-10 days after GS with YS
	Empty amnion sign, no embryo ≥ 6 weeks after LMP
	Enlarged yolk sac > 7 mm
***ALL MEASUREMENTS BY TVUS**	Relatively small sac (< 5 mm difference between MSD and CRL)

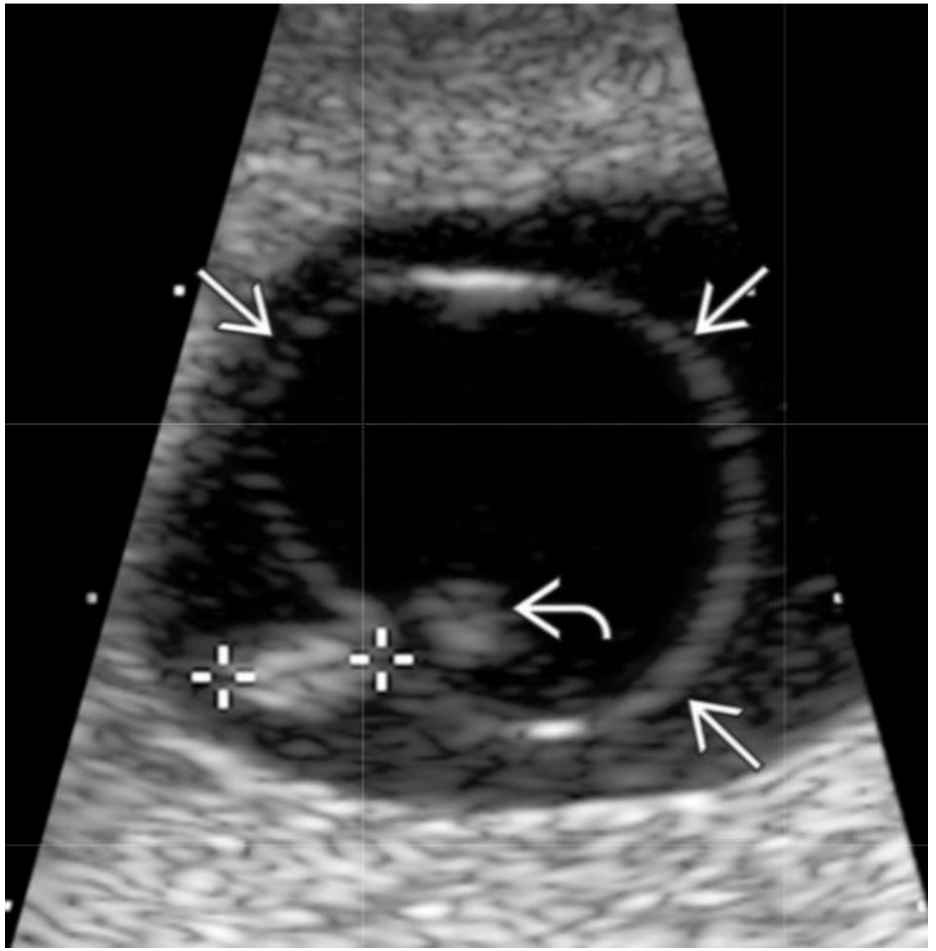
Sonographic diagnosis of early pregnancy failure



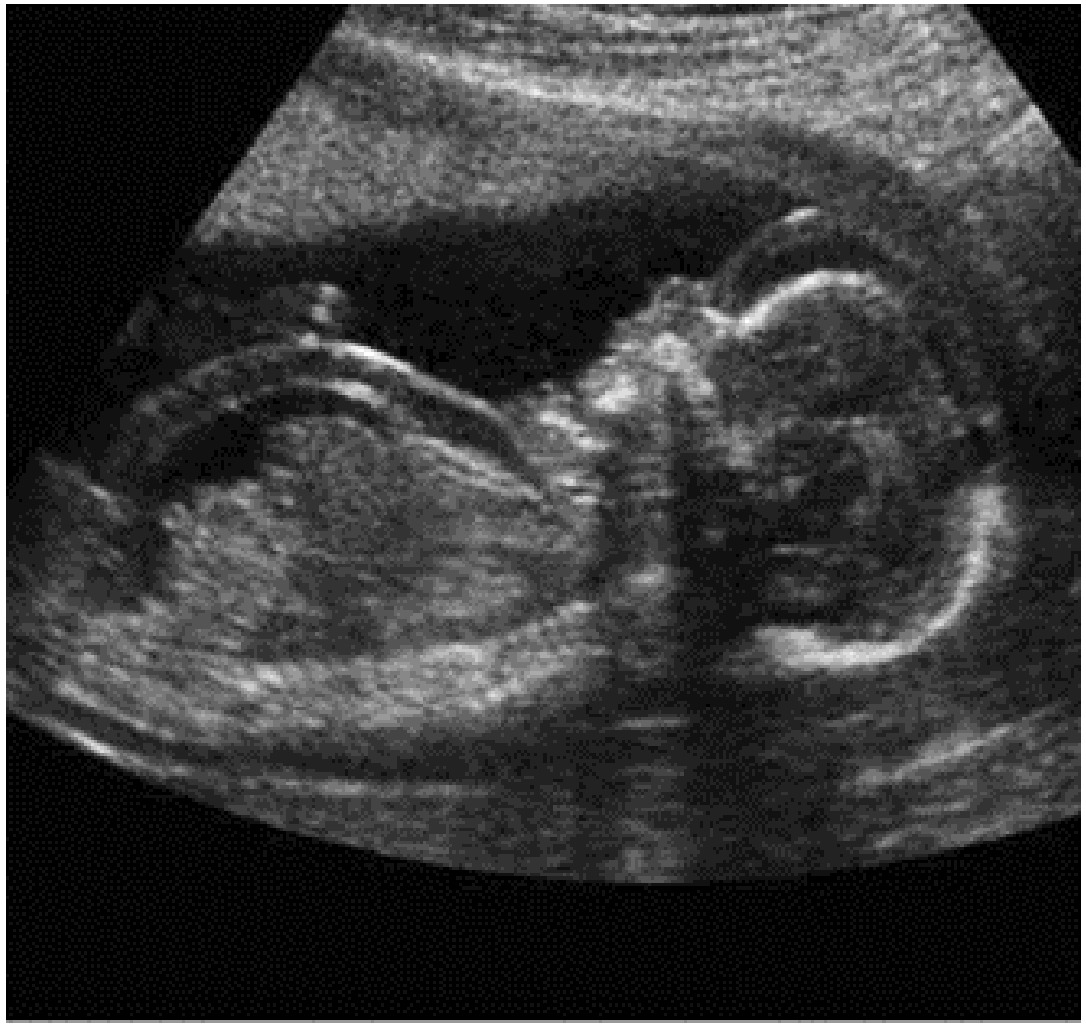
←**CRL ≥ 7 mm with no FHM,** enlarged YS, expanded amnion sign

Expanded amnion sign →

Pay attention to CRL vs YS



Sonographic diagnosis of intrauterine fetal demise



- No heartbeat
- Can use color and/or pulse wave Doppler, and consider transvaginal imaging if visualization is difficult
- Helpful to obtain biometry, evaluate for obvious malformations or hydrops

Management of first trimester pregnancy loss

Options are expectant, surgical, or medical management

- Expectant management
  - ~80% of patients will have complete passage without intervention (within 8 wks)
  - Unpredictable timing, may have significant bleeding/cramping
- Surgical management: Suction dilation and curettage (D&C)
  - More immediate completion, less follow-up
  - Can be done in office or OR, with sedation or general anesthesia

Management of first trimester pregnancy loss

- Medical management
  - Compared to expectant, ↓ time to expulsion, ↑ rate of complete expulsion without surgery
  - Mifepristone 200 mg PO followed by misoprostol 800 mcg PV 24 hours later has highest rate of completion. (SFP Guidelines: Can give the misoprostol vaginally or buccally 7-48 hours after mifepristone).
  - Misoprostol alone also effective, but takes longer and higher risk of failure and need for surgical management
    - ACOG: 800mcg PV with one repeat dose as needed between 3 hours and 7 days after first dose.
    - SFP: 600-800mcg PV or buccally, at least 2 doses at least 3 hours apart.
    - Vaginal is faster with less risk of diarrhea compared to buccal/sublingual.

After first trimester pregnancy loss

Rh D prophylaxis for Rh- patients was previously recommended due to theoretical risk of alloimmunization and low risk of harm, but **guidelines have changed**!

- 2020 pilot study (n=37): Patients undergoing uterine aspiration before 11w3d. None had post-procedure fetal RBC levels above estimated threshold for sensitization.
- 2023 multicenter prospective cohort study (n= 506): Patients undergoing abortion at <12w0d. 99.8% had postabortion fetal RBC levels below estimated threshold for sensitization. (Horvath et al. *JAMA*. 2023).
- ACOG, SFP, WHO, RCOG, and SOGC now recommend **against** routine use at <12w0d. (ACOG says it may be provided on patient request after shared decision making).

No available data on optimal follow up (Symptoms? Ultrasound? Trending βHCG?)

- SFP recommends all patients be offered in-person follow up but should not be required.
- If ultrasound used to confirm completion, absence of gestational sac is all that is required
- No surgery required for asymptomatic women with thickened endometrial stripe

Management of second trimester pregnancy loss

- Options are medical or surgical management
- Medical management
  - Mifepristone 200 mg PO, then misoprostol 800 mcg PV 24-48 hours later, then misoprostol 400 mcg every 3 hours up to 5 doses (91% completion in 24 hours)
  - Misoprostol alone also effective, but takes longer and higher risk of failure and need for surgical management
  - Risks include retained products of conception, need for D&C, bleeding, infection
  - High-dose misoprostol can be used even in patients with 1 prior cesarean (risk of uterine rupture 0.28%)

Management of second trimester pregnancy loss

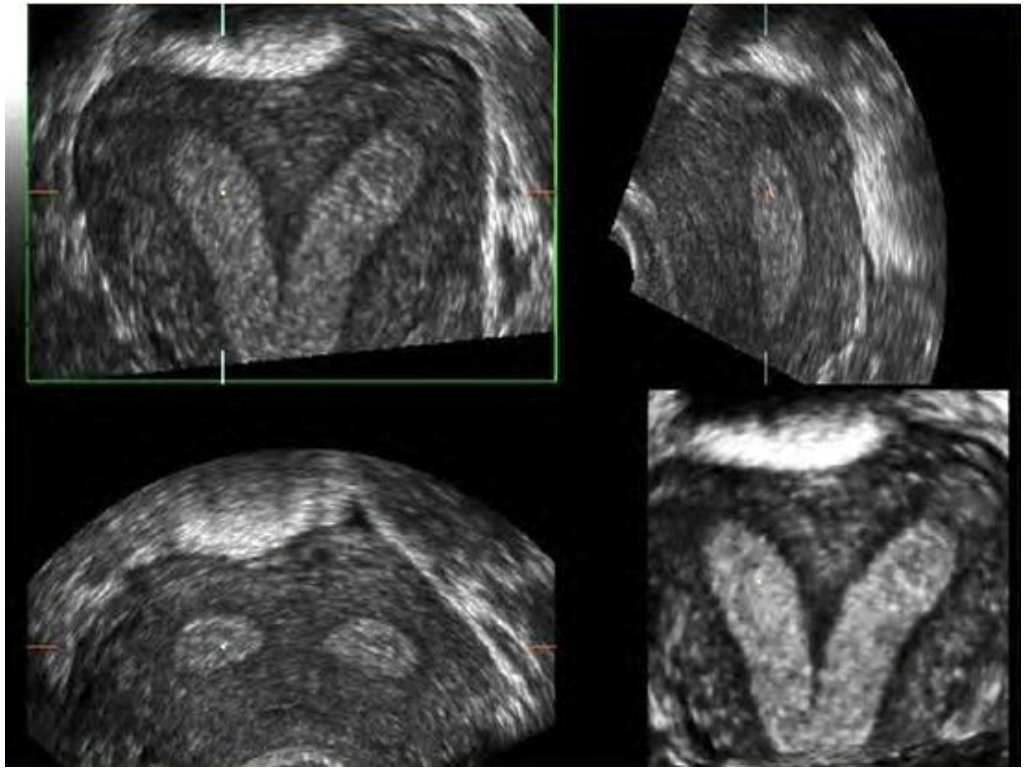
- Surgical management: Dilation and evacuation (D&E) – Up to ~24-26 weeks
  - Requires cervical preparation with dilators the day before the procedure
  - Grasping forceps used to remove fetus and pregnancy tissue through the cervix
  - Done under ultrasound guidance in the OR
  - Risks include retained products of conception, uterine perforation, bleeding, infection

Management of third trimester pregnancy loss

- Induction of labor
  - Often 12 to 48 hours, longer with higher gestational age
- Anesthesia options include IV pain medications, epidural
- May require D&C for retained placenta (more common in second trimester losses)
- About 24-hour hospital stay after delivery

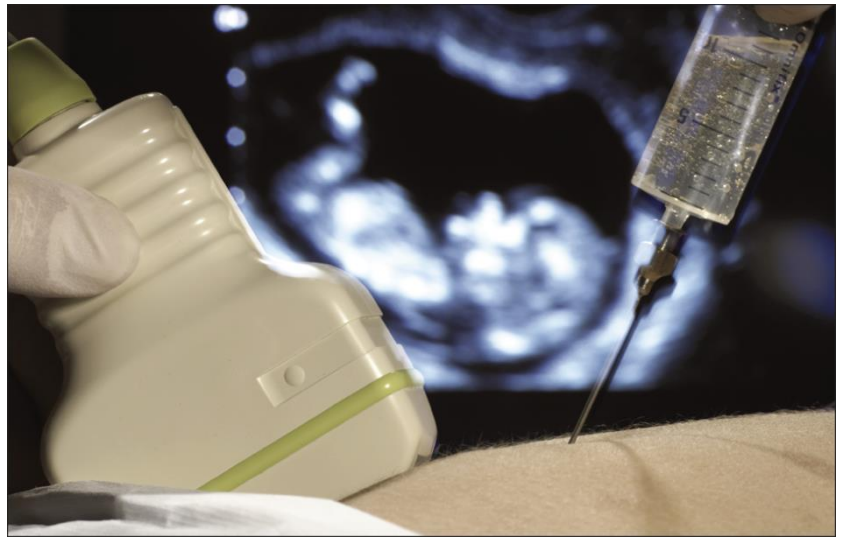
Work-up of early and recurrent pregnancy loss

- No specific work-up after one early pregnancy loss
  - Antiphospholipid antibody testing if morphologically normal fetus dies at 10+ weeks
- Recurrent pregnancy loss work-up:
  - Evaluation of uterine cavity (e.g., SHG or HSG)
  - Genetic evaluation of products of conception
  - Parental karyotypes
  - Prolactin, TSH, hemoglobin A1c
  - Antiphospholipid antibody testing after three consecutive unexplained losses before 10 weeks



Work-up of intrauterine fetal demise

- Most important components
  - Fetal autopsy
  - Pathology examination of placenta, cord, and membranes
  - Genetic evaluation: Amnio has sightly higher yield than fetal tissue

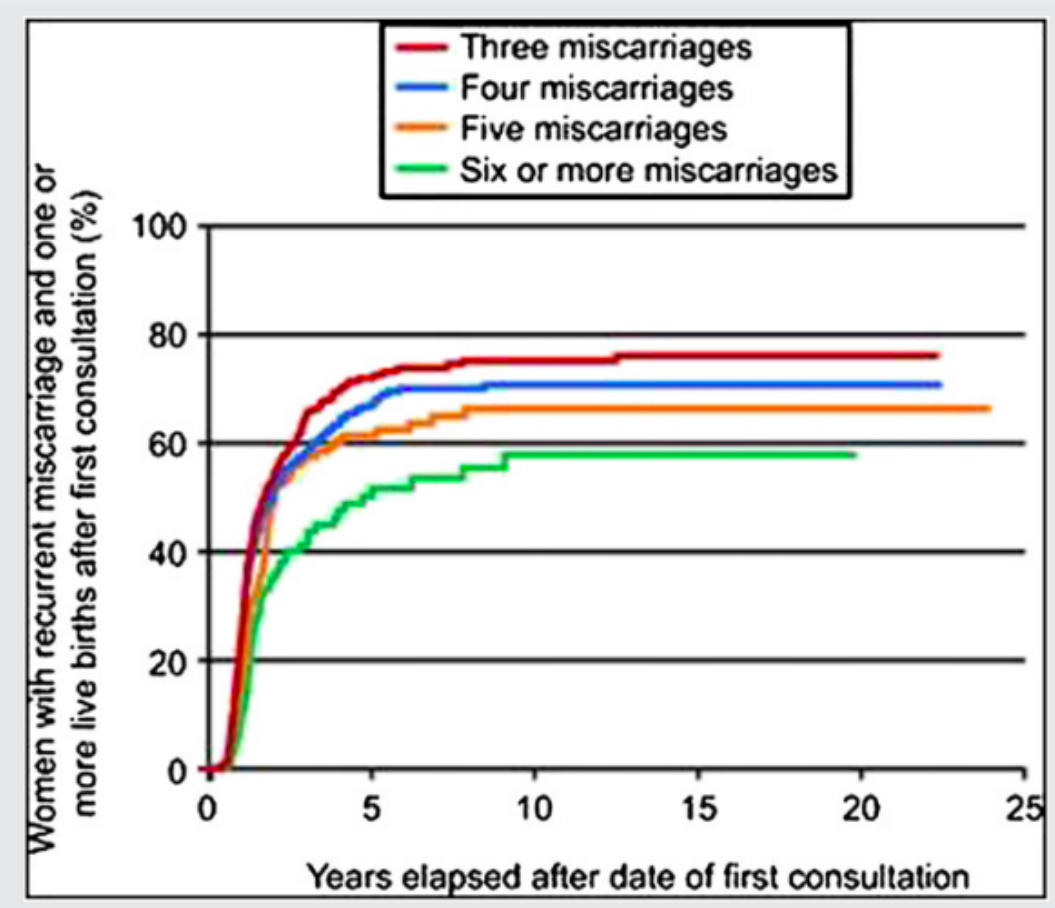


- Maternal evaluation
  - Kleihauer-Betke
  - Antiphospholipid antibodies
  - Syphilis screening

  - In selected cases
    - Antibody screen
    - Toxicology screen
    - TSH, Glucose screening
    - Parental karyotype

Prognosis after early and recurrent pregnancy loss

- One early pregnancy loss does not increase the risk in subsequent pregnancies
- After 2 or 3 early pregnancy losses, risk is 24-29%
- After 4 or more: 31-33%
- Recurrence risk is age dependent



Prognosis after intrauterine fetal demise

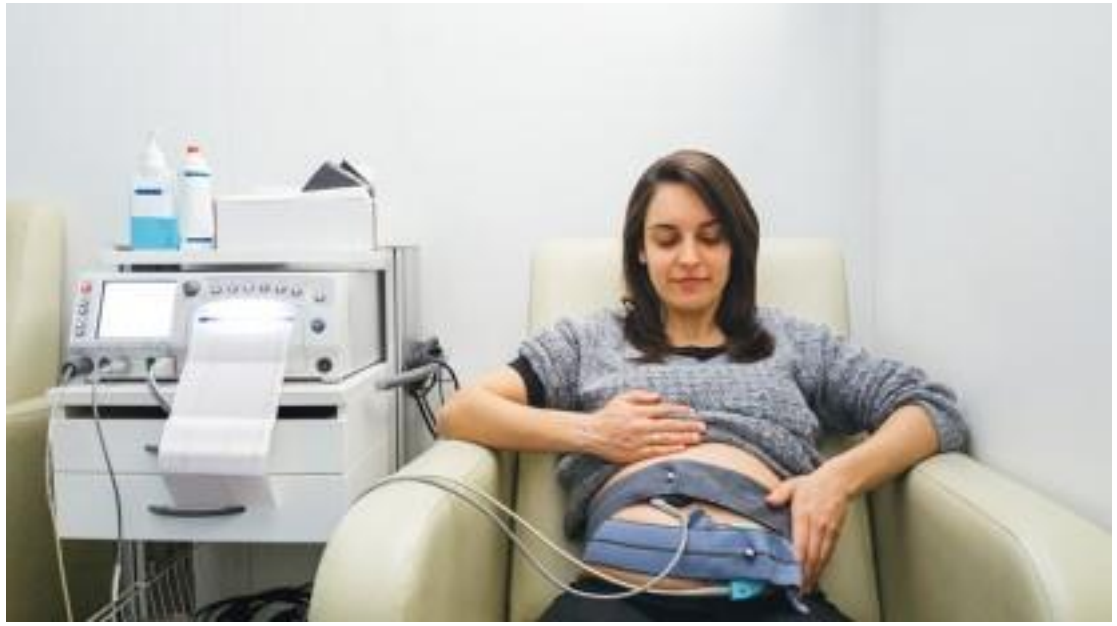
- Risk of recurrent IUFD depends on etiology.
- In low-risk women with unexplained IUFD, recurrence risk is 8-10/1000. That means there is at least a 99% chance of live birth.
- Most of risk is before 37 weeks
- Risk of loss after 37 weeks 1-2/1000
- Risk of IUFD actually much higher in women with a prior live birth of baby with preterm IUGR: 21/1000
- Risk of recurrent IUFD higher in women with diabetes, hypertension, other comorbidities

Management in the next pregnancy

- If one early loss, routine care
- If recurrent pregnancy loss
  - Stray-Pedersen and Stray-Pedersen (1984): 195 couples with 3+ early pregnancy losses.
  - Intervention group: psychological support, weekly ultrasounds and visits, and instructions to avoid heavy lifting, travel, sex
  - Intervention group: 85% live birth rate, control group: 36%
- If findings consistent with antiphospholipid antibody syndrome
  - Lovenox or unfractionated heparin and low dose aspirin

Management in the next pregnancy

- If IUFD
  - Dating ultrasound in first trimester
  - Growth ultrasound at or after 28 weeks
  - Kick counts at 28 weeks if desired
  - Antenatal surveillance at 32 weeks or 1-2 weeks earlier than prior stillbirth
  - Consider delivery at 37 to 39 weeks



- Consideration of need for behavioral health services

Interventions that are not evidence-based

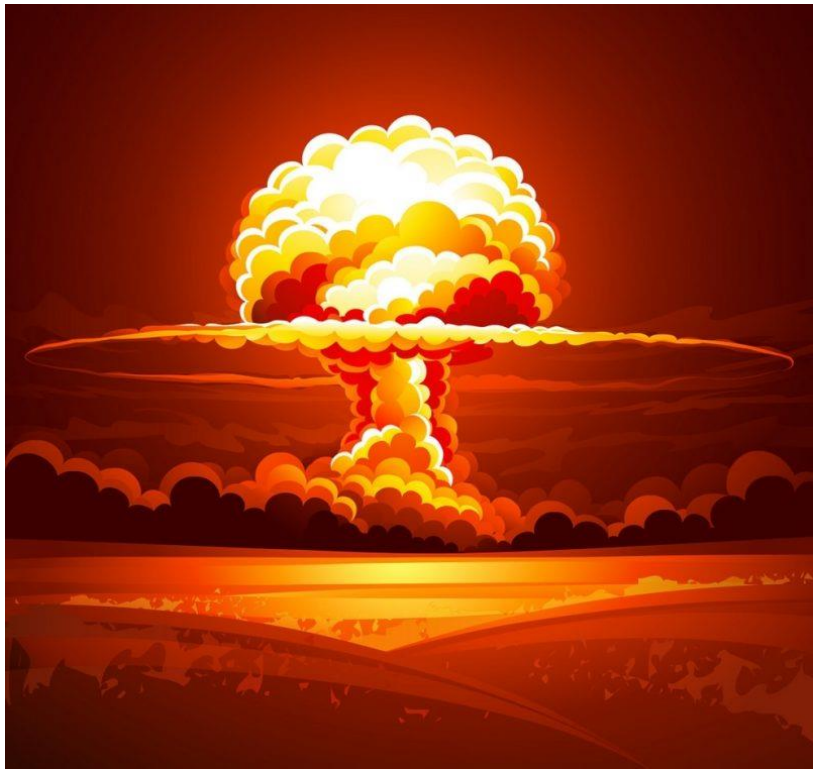
- Progesterone
  - No benefit in preventing RPL in PROMISE RCT (2015): 66% LBR progesterone vs. 63% placebo
  - Unless there is concomitant 1st trimester bleeding: PRISM RCT (2019): 72% LBR progesterone vs. 57% placebo
- IVIg, IV intralipids, IV lymphocyte immunotherapy
- Hydroxychloroquine
- Steroids
- Antihistamines
- Filgrastim/Pegfilgrastim
- Enoxaparin/Aspirin (in the absence of antiphospholipid syndrome)
  - Aspirin may often still be indicated for preeclampsia risk reduction

Coomarasamy et al. 2015, Coomarasamy et al. 2019, Achilli et al. 2018, Lima et al. 2025

COMPASSION GOES A LONG WAY AS WOMEN TRUDGE THROUGH THE MURKINESS OF MOURNING. BE MINDFUL. EXPRESS EMPATHY. HIGHLIGHT CARE. SHY AWAY FROM STATEMENTS THAT BEGIN WITH "AT LEAST..." INQUIRE RATHER THAN ADVISE. FEELING HEARD CREATES A SENSE OF EMOTIONAL SAFETY AND EMPHASIZES THE NORMALIZATION OF GRIEF.

Counseling Strategies

- Ask the patient if you can tell them what you are seeing
- Consider asking if they'd like family to leave the room



- Give a "warning shot"
  - "I don't have good news"
  - "I'm sorry to tell you this"
  - "Unfortunately"
- Give the news
  - "I don't see a heartbeat."
  - "I don't see an embryo."
  - "The baby's heart is not beating."

Responding to emotions

- Acknowledge the emotion
  - “I can tell that this is not what you were expecting.”
  - “I know this is really unbelievable.”
  - “I can see how upsetting this is.”
- Legitimate the emotion
  - “I think anyone in this situation would be shocked.”
  - “A lot of people in your shoes would feel angry.”
  - “It’s ok to cry.”

Responding to emotions

- Empathize with the emotion
  - “I imagine that this is completely overwhelming.”
  - “This is really hard. I wish that things were different.”
  - “I am so sorry you are going through this.”

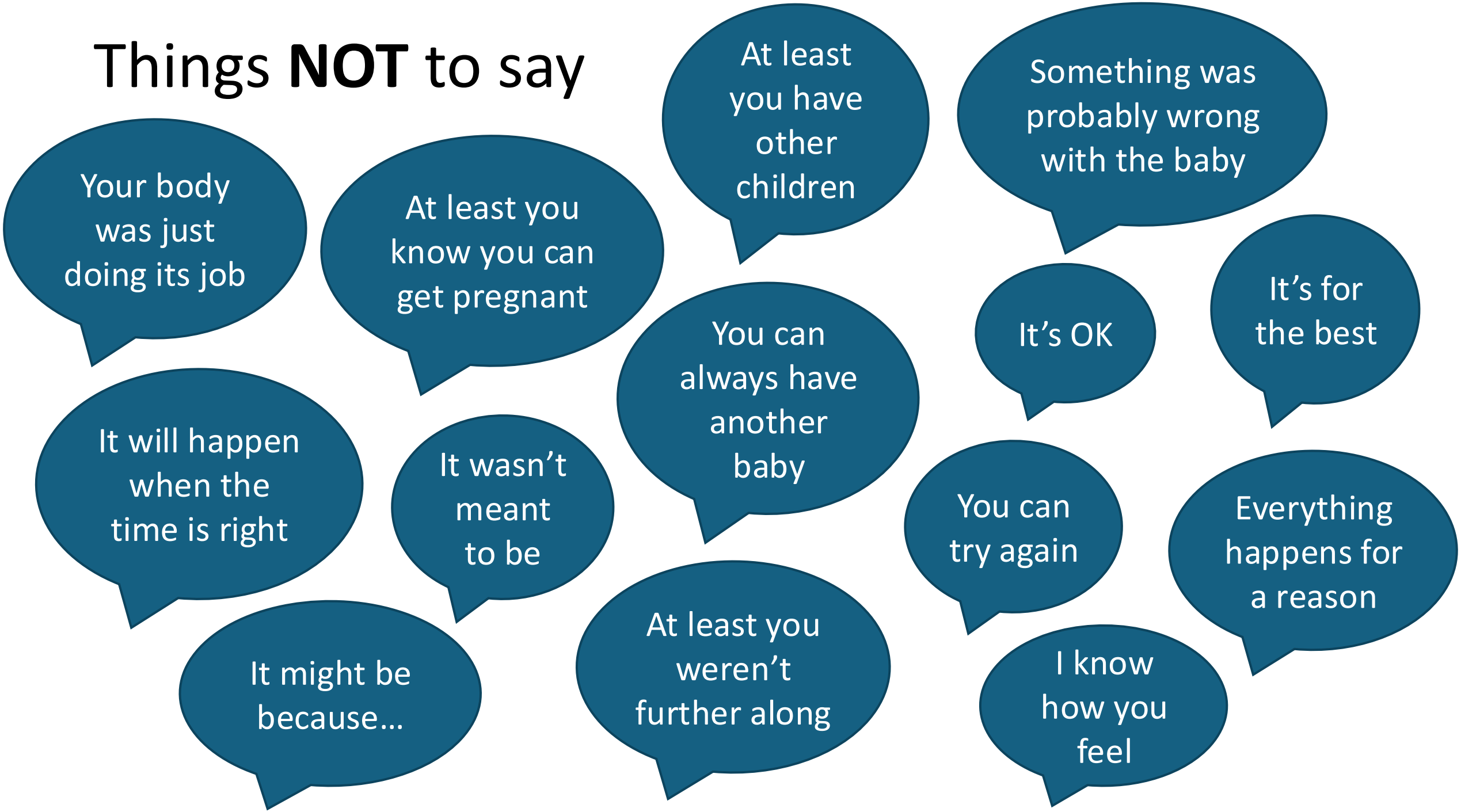
- Provide support
  - “Can I call someone for you?”
  - “Take as much time as you need.”
  - “Do you want me to sit with you?”

Adapted from Quill et al.

More counseling tips

- Use the patient's own words (if they have words for what happened)
  - Miscarriage preferred to spontaneous abortion by most but **NOT** all women
  - Some people dislike the terms chemical pregnancy or rainbow baby
- Be aware that they may feel sad, but may also feel other emotions (shock, denial, anger, guilt, **relief**)
- Offer to provide images now, or later
- Emphasize that it is not their fault

Things **NOT** to say



www.perinatalgrief.com

How to take care of yourself

- Find a way to honor the lost pregnancies
  - Light a candle, grow a plant, say a prayer, make a donation, volunteer your time…
  - Mark October 15th on your calendar – Pregnancy and Infant Loss Remembrance Day
- Take the time to feel your feelings
  - Go for a walk, do yoga, talk with a friend, eat ice cream, meditate, take a bath, draw or paint, journal…
- Employee Assistance Program, Therapy

References

Achilli C, Duran-Retamal M, Saab W, Serhal P, Seshadri S. The role of immunotherapy in in vitro fertilization and recurrent pregnancy loss: a systematic review and meta-analysis. *Fertil Steril*. 2018;110(6):1089-1100. doi:10.1016/j.fertnstert.2018.07.004

Coomarasamy A, Williams H, Truchanowicz E, et al. A Randomized Trial of Progesterone in Women with Recurrent Miscarriages. *N Engl J Med*. 2015;373(22):2141-2148. doi:10.1056/NEJMoa1504927

Coomarasamy A, Devall AJ, Cheed V, et al. A Randomized Trial of Progesterone in Women with Bleeding in Early Pregnancy. *N Engl J Med*. 2019;380(19):1815-1824. doi:10.1056/NEJMoa1813730

Early pregnancy loss. ACOG Practice Bulletin No. 200. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;132:e197–207.

Evaluation and treatment of recurrent pregnancy loss: a committee opinion. The Practice Committee of the American Society for Reproductive Medicine. Fertil Steril 2012;98(5):1103-1111.

"Five Things You Should Know About Recurrent Miscarriages." *USC Fertility*, 5 Nov. 2009, uscfertility.org/5-things-know-recurrent-miscarriages/.

Lima J, Guerreiro J, Ângelo-Dias M, et al. Efficacy of therapeutic interventions for idiopathic recurrent pregnancy loss: a systematic review and network meta-analysis. *Front Med (Lausanne)*. 2025;12:1569819. Published 2025 May 14. doi:10.3389/fmed.2025.1569819

Liu K, Xu X, Sun L, et al. Proteomics profiling reveals lipid metabolism abnormalities during oogenesis in unexplained recurrent pregnancy loss. *Front Immunol*. 2024;15:1397633. Published 2024 Aug 8. doi:10.3389/fimmu.2024.1397633

Management of stillbirth. ACOG Practice Bulletin No. 102. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:748-761.

Monticciolo I, Guarano A, Inversetti A, Barbaro G, Di Simone N. Unexplained Recurrent Pregnancy Loss: Clinical Application of Immunophenotyping. Am J Reprod Immunol. 2024 Oct;92(4):e13939. doi: 10.1111/aji.13939. PMID: 39392245.

Quilll T, et al. Delivering Bad News. DocCom Module 33. *DocCom*, Drexel University College of Medicine, webcampus.drexelmed.edu/doccom/db/readDocComDemo.aspx?m=33.

Second-trimester abortion. ACOG Practice Bulletin No. 135. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013;121:1394-1406

Sonehara K, Yano Y, Naito T, et al. Common and rare genetic variants predisposing females to unexplained recurrent pregnancy loss. *Nat Commun*. 2024;15(1):5744. Published 2024 Jul 17. doi:10.1038/s41467-024-49993-5

Stray-Pedersen B, Stray-Pedersen S. Etiologic factors and subsequent reproductive performance in 195 couples with a prior history of habitual abortion. *Am J Obstet Gynecol*. 1984;148(2):140-146. doi:10.1016/s0002-9378(84)80164-7

Tarleton JL, Benson LS, Moayedi G, Trevino J; with the assistance of Leah Coplon, Anitra Beasley, and Elise Boos on behalf of the Society of Family Planning Clinical Affairs Committee. Society of Family Planning Clinical Recommendation: Medication management for early pregnancy loss. *Contraception*. 2025;144:110805. doi:10.1016/j.contraception.2024.110805

Woodward PJ, Kennedy A, & Sohaey R. (2016). *Diagnostic Imaging: Obstetrics* (3rd ed.). Philadelphia, PA: Elsevier.

Zucker J and Alexander-Tanner R. "Grieving a Miscarriage: An Illustrated Discussion." *The New York Times*,14 Mar. 2017, www.nytimes.com/2017/03/14/well/family/grieving-a-miscarriage-an-illustrated-discussion.html.

Questions?

Jennifer Braverman, MD, MA

Jennifer.Braverman@cuanschutz.edu