Updates in Miscarriage Management

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9/20/2019

Outline

- Review of miscarriage management
- Medical management
  - Mifepristone
  - Regimen and follow up
- Implementation
  - Logistics
  - Support

Take Home Points

- Mifepristone is safe!
- Improves miscarriage management
- Effort needed to implement

Miscarriage or Early Pregnancy Loss

- Common
  - ~15% of clinically recognized pregnancies
- Prior to 12 weeks 6 days
  - Embryonic demise
  - Anembryonic gestation

Management Options

- Expectant management
- Medical management
- Surgical management
  - D&C

Medical Management

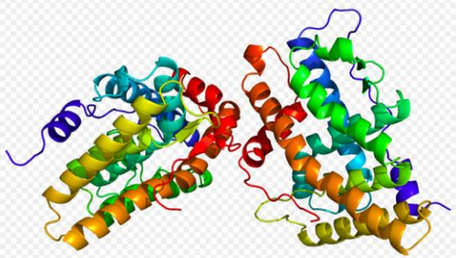
- Misoprostol
- Change in recommended regimen
- **Mifepristone** + Misoprostol
- ACOG supported

ACOG, Practice Bulletin No. 67

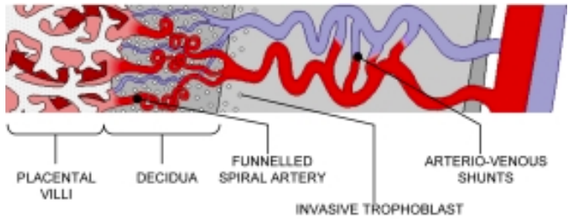
What is Mifepristone?

- RU-486 or Mifeprex
- Anti-glucocorticoid
  - Potent anti-progestin

Mechanism of Action: Pregnancy



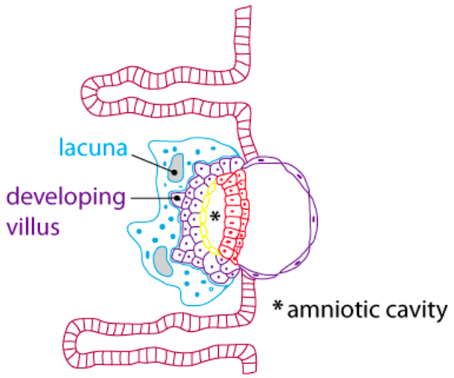
Binds progesterone receptor



Alters endometrium

Trophoblast separation

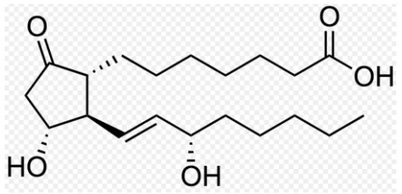
Prostaglandin release



↓ βHCG

Bleeding

Contractility & cervical ripening



Variety of Mifepristone Uses

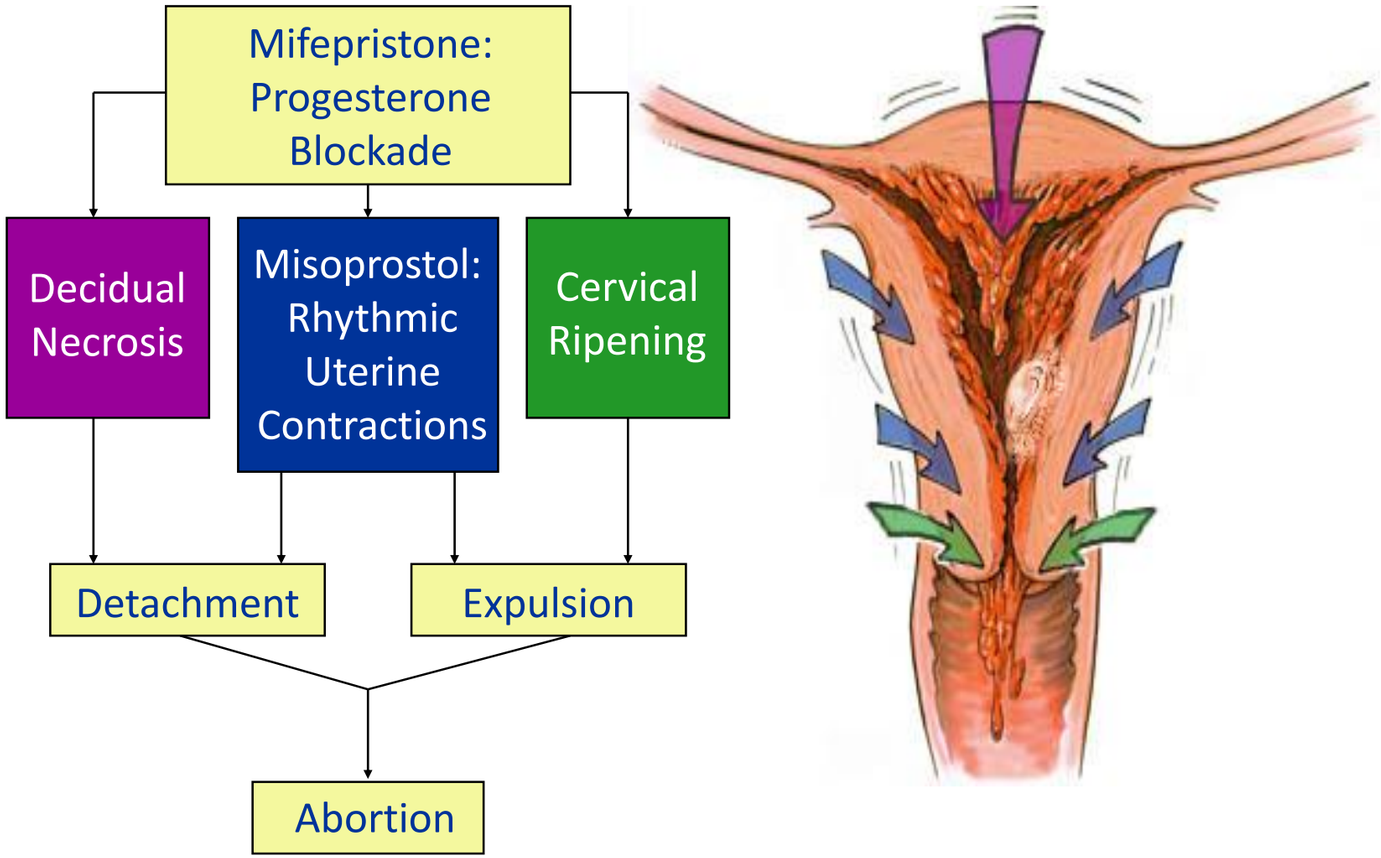
1. Cushing's Syndrome (Korlym)
2. Fibroids
3. Endometriosis
4. Emergency Contraception
5. Term cervical ripening
6. Medical abortion

Sartor et al, 1996; Kettel et al, 1998; Steinauer et al, 2004; von Hetzen et al, 2002; Wing et al, 2000

Use in Miscarriage Management

- Mifepristone
  - Progesterone blocker
- Misoprostol
  - Prostaglandin analogue

Mechanism of Action



Miscarriage Management

Primary Outcome: expulsion of gestational sac 1-3 days post-miso by TVUS

Schreiber et al, NEJM, 2018

Success Rates

Table 2. Clinical Outcomes among Women Who Received Medical Treatment for Early Pregnancy Loss.

Outcome	Mifepristone-Pretreatment Group (N = 148)	Misoprostol-Alone Group (N = 149)	Relative Risk (95% CI)*
	number (percent)		
Gestational sac expulsion by the first follow-up visit: treatment success†	124 (83.8)	100 (67.1)	1.25 (1.09–1.43)‡
Gestational sac expulsion by the second follow-up visit at day 8	132 (89.2)	111 (74.5)	1.20 (1.07–1.33)
With 1 dose of misoprostol	130 (87.8)	106 (71.1)	
With 2 doses of misoprostol	2 (1.4)	5 (3.4)	
Gestational sac expulsion by the 30-day telephone call	135 (91.2)	113 (75.8)	1.20 (1.08–1.33)
With 1 dose of misoprostol	130 (87.8)	106 (71.1)	
With 2 doses of misoprostol	5 (3.4)	7 (4.7)	
Uterine aspiration§	13 (8.8)	35 (23.5)	0.37 (0.21–0.68)

NNT = 6.8

* Relative risks were adjusted for trial site with use of the Mantel–Haenszel method.
† Treatment success was defined as gestational sac expulsion with one misoprostol dose by the first follow-up visit and no additional intervention within 30 days after treatment.
‡ The rate of treatment success by the first follow-up visit was significantly higher in the mifepristone-pretreatment group than in misoprostol-alone group (P<0.001).
§ Indications for uterine aspiration included participant request and clinical recommendation.

Schreiber et al, NEJM, 2018

Gestational Age Limitations

	No. participants (%)	Treatment Success	
		Mifepristone	Misoprostol
10-12 wk	18 (6)	70.0%	75.0%

Schreiber et al, NEJM, 2018

Regimen

Patient Selection

- Medical history
- 10 weeks or less gestation*
  - **Based on SIZE**

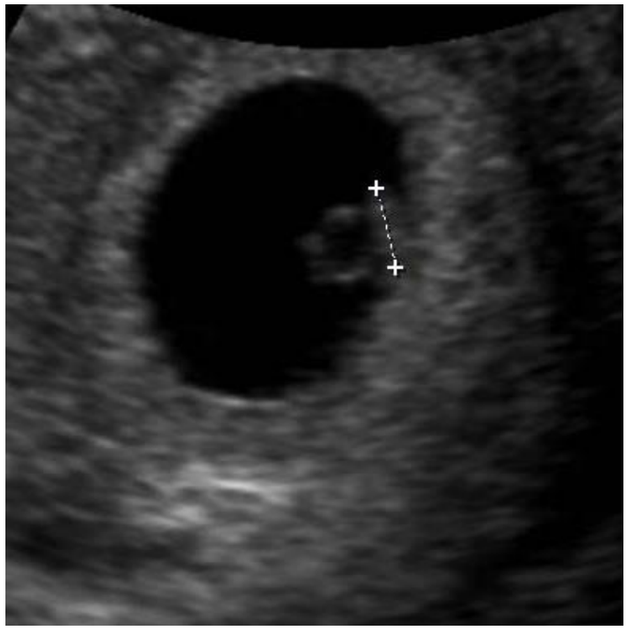
*Exceptions can be made up to 12 weeks

Contraindications to Medical Management

- Anemia (Hgb <9)
- Chronic adrenal failure
- Porphyrias
- Ectopic pregnancy
- Long-term corticosteroid therapy
- Anticoagulation therapy
- IUD in place (take it out)

Patient Selection and Intake

- Pregnancy dating
  - LMP
  - Ultrasound
  - Pelvic exam
- Contraceptive plan

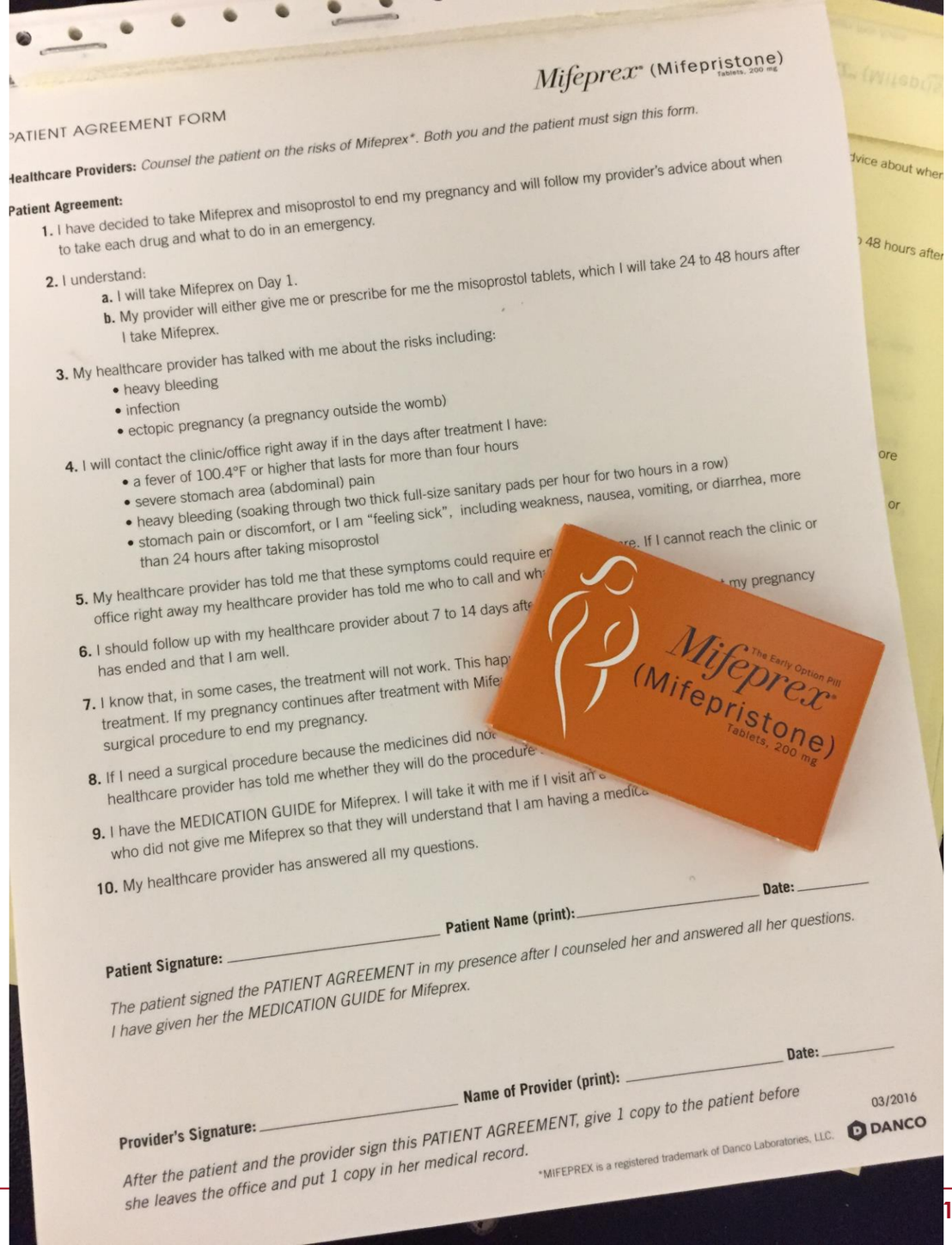


First!

- Provide Patient Medication Guide
- Sign Patient Agreement Form
- Print all materials online:

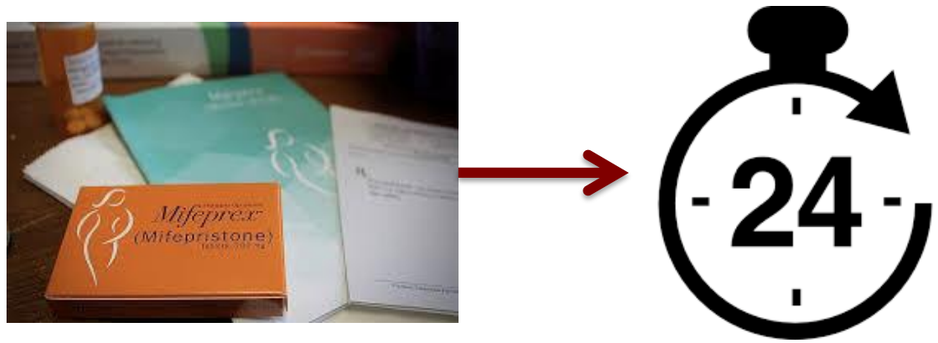
https://www.earlyoptionpill.com/for-health-professionals/patient-support-materials/

- Explain wording on form



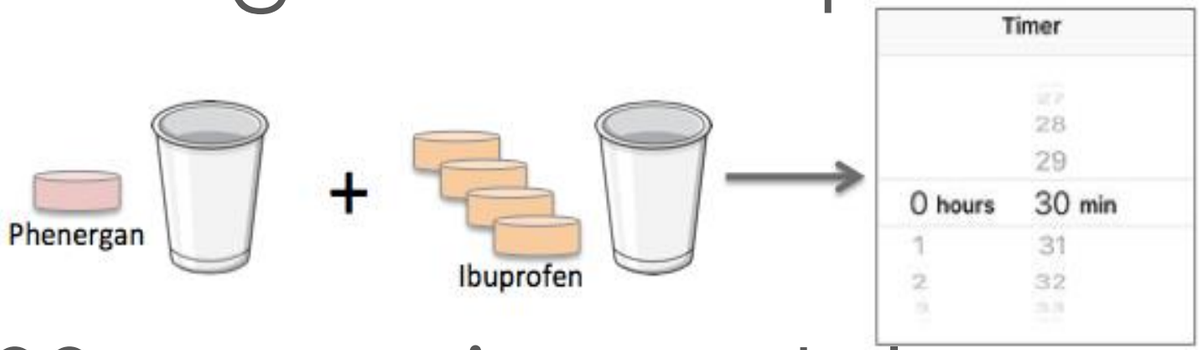
Regimen

1. Give 200mg mifepristone PO **in clinic**
2. Patient waits 24-48 hours

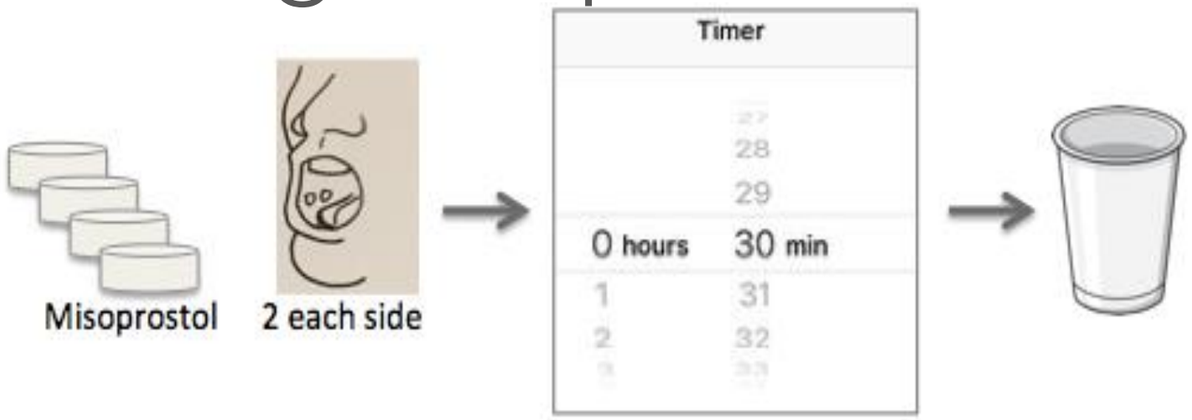


At Home – 24-48 hours later

1. Take phenergan and ibuprofen



1. Place 800 mcg misoprostol



Pain Management

- Ibuprofen
  - 800mg q8hrs
- Norco or Percocet
  - 5/325, 1 tab q6hrs prn
  - No evidence to support its routine prescription
- Supportive measures

Patient Counseling

- Cramping
  - Starts 30-60 minutes after misoprostol
- Bleeding
  - Can be heavy, clots to lemon size
- Worst point: 4 hours after taking tablets (average)
- Bleeding for 1-2 weeks (light)

Follow up

- Phone call in 3 to 5 days
- Day 3 to 14 follow up ultrasound
- Day 3 to 14 serum HCG
  - Requires HCG draw on day of mifepristone
  - F/u draw can be done at any lab
  - Decrease by >50% from Day 1

Contraception

- Pills, patch, ring, depo: start within 5 days
- Nexplanon: place at time of mifepristone
- IUD: place at follow up

Side Effects

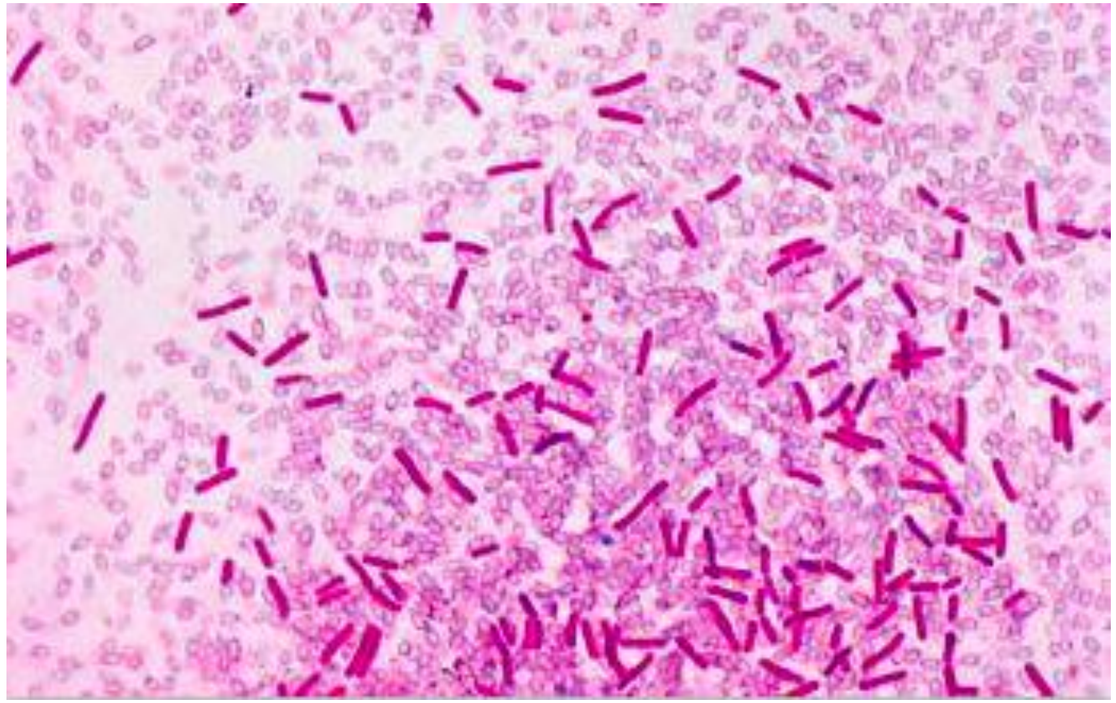
- Misoprostol related
  - Fever
  - Chills
  - Nausea/vomiting
  - Diarrhea

Mifepristone FDA Black Box Warning

- Added in 2004
  - Atypical bacterial infections
  - Bleeding

Bacterial Infection

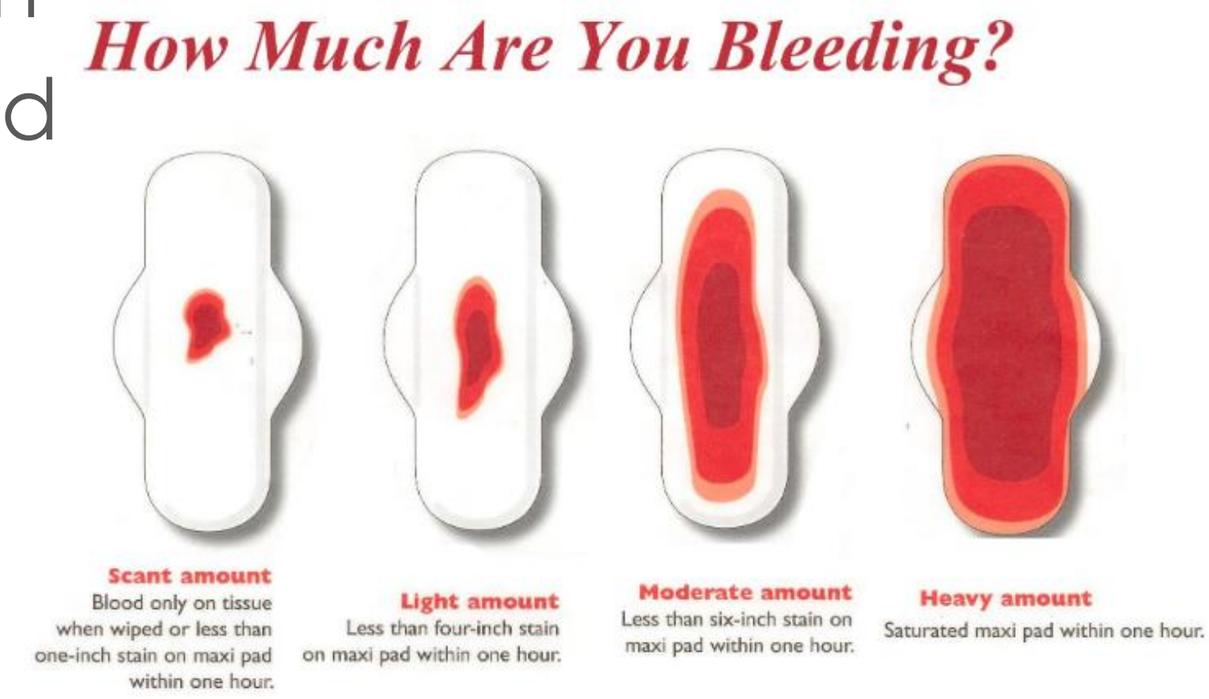
- *Clostridium sordelli*
  - 9 deaths (2000 to 2012)
  - Vaginal misoprostol
- General infection rate
  - 0.01-0.5%



Dempsey, Clin Obstet Gyn, 2012; Fischer et al, NEJM, 2005; Meites et al, NEJM, 2010; Chen and Creinin, Obstet Gynecol, 2015

Bleeding

- Prolonged heavy bleeding
  - After medical abortion
  - 0.03-0.6% require blood transfusion
  - 0.049% require D&C



Chen and Creinin, Obstet Gynecol, 2015; Hausknecht, Contraception, 2003

Implementation

REMS

- Risk Evaluation and Mitigation Strategy
  - Drugs with serious safety concerns
  - Ensures benefits outweigh risks
  - Different for different drugs

Mifepristone REMS

- Registered ordering provider
- Mifeprex Patient Medication Guide
- Mifeprex Patient Agreement Form
- Dispensed in clinic, medical office, hospital
- Taken in presence of provider

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FOR HEALTH PROFESSIONALS

HEALTH
UNIVERSITY OF UTAH

Implementation success

- University of Utah wide
- Protocol creation
- Teamed with pharmacy

We are here to help!

- Family Planning Division
  - David Turok, MD
  - Lori Gawron, MD
  - Jen Kaiser, MD
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Questions?

Thank you!