



Updates in Miscarriage Management

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Family Planning

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

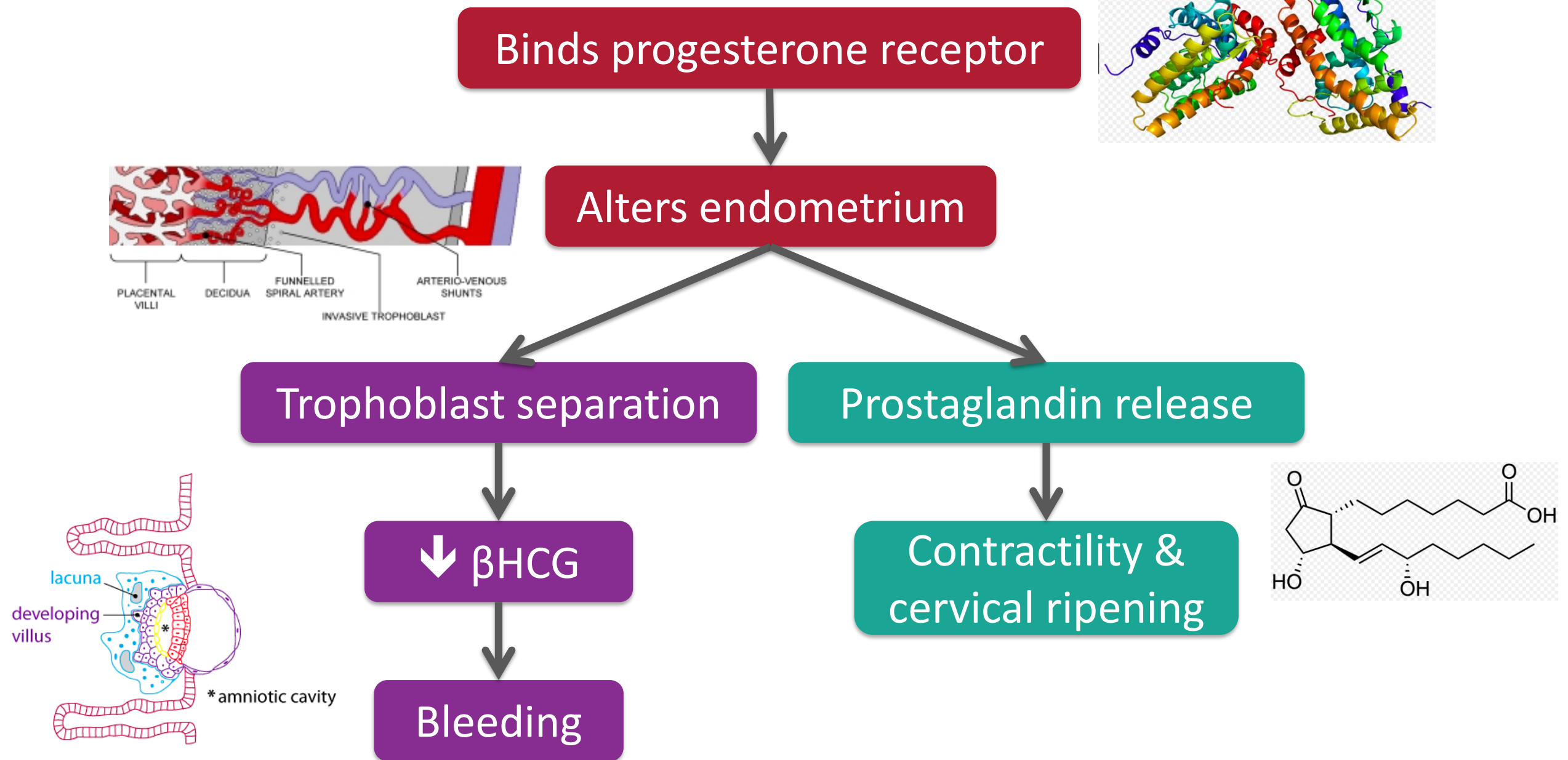
Medical Management

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

What is Mifepristone?

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

Mechanism of Action: Pregnancy



Variety of Mifepristone Uses

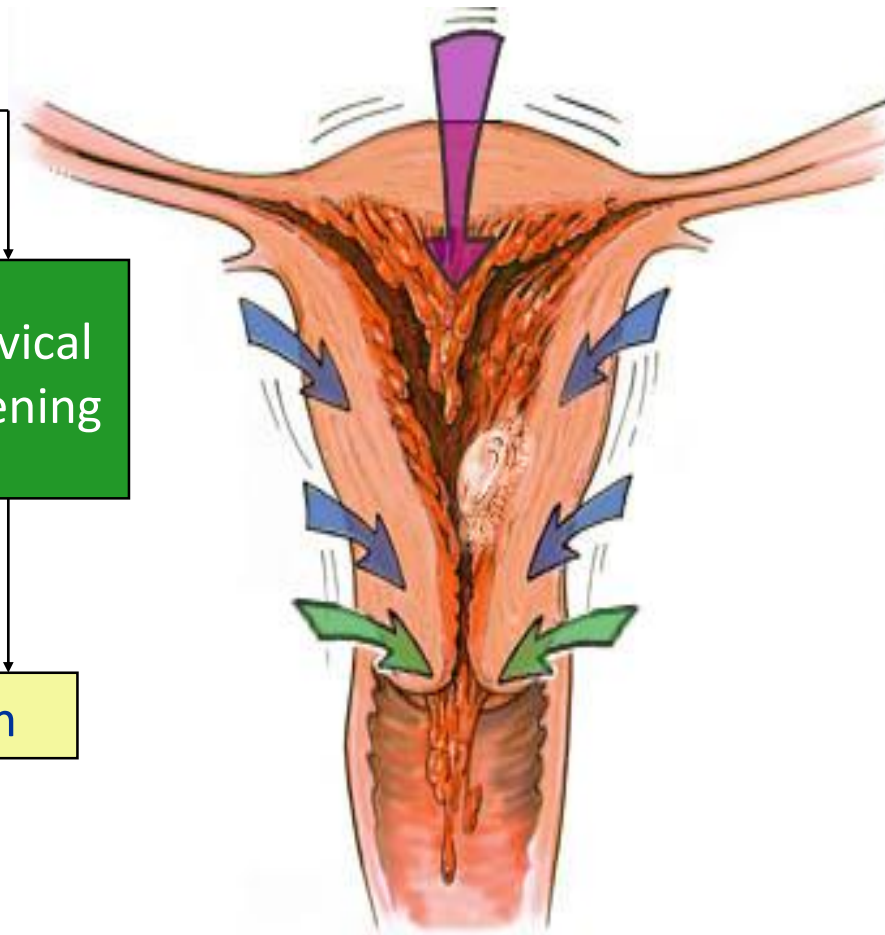
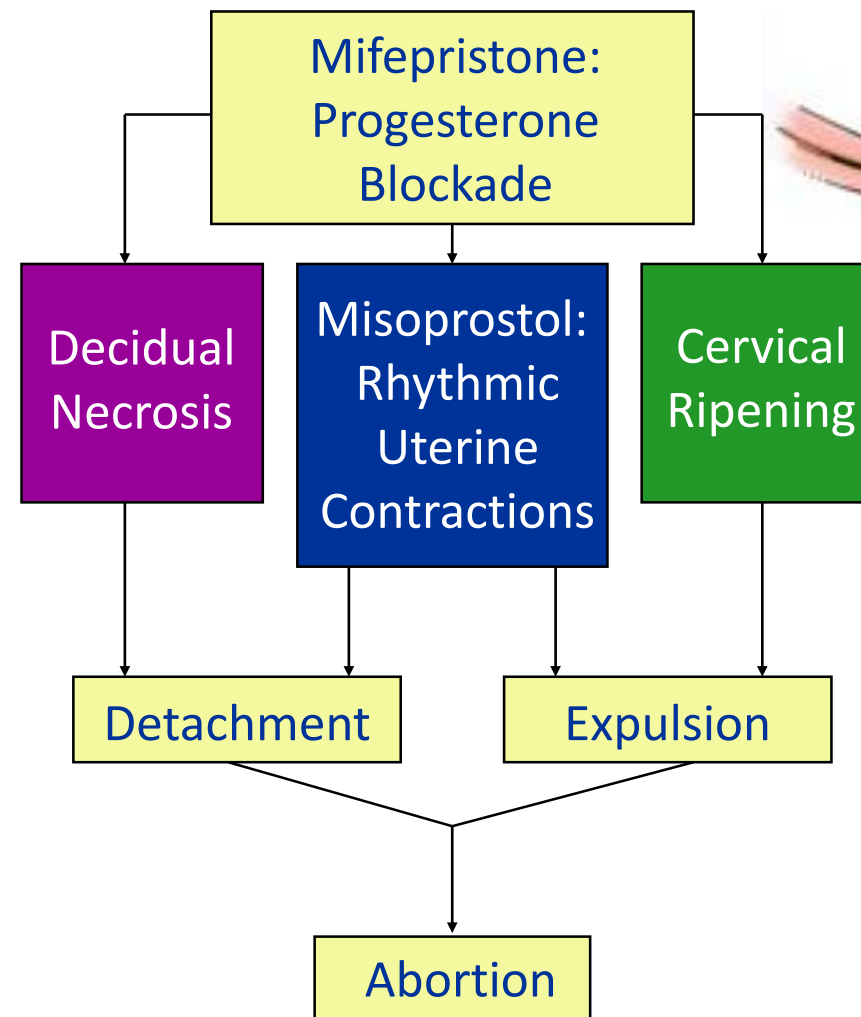
1. Cushing's Syndrome (Korlym)
2. Fibroids
3. Endometriosis
4. Emergency Contraception
5. Term cervical ripening
6. Medical abortion

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

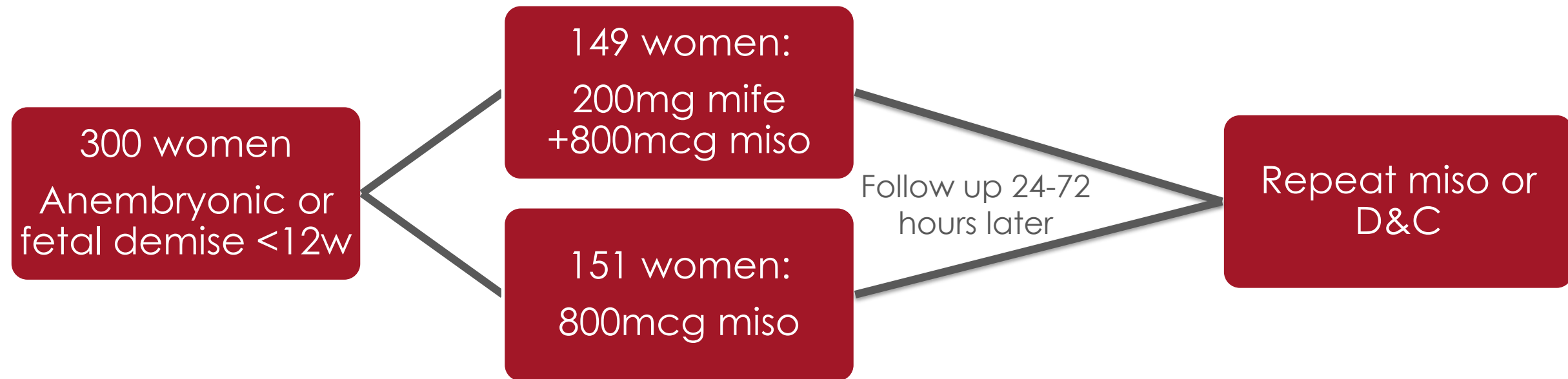
Use in Miscarriage Management

- Mifepristone
 - Progesterone blocker
- Misoprostol
 - Prostaglandin analogue

Mechanism of Action



Miscarriage Management



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

Success Rates

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

Outcome	Mifepristone-Pretreatment Group (N = 148) <i>number (percent)</i>	Misoprostol-Alone Group (N = 149) <i>number (percent)</i>	Relative Risk (95% CI)*
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

Mifeprex® (Mifepristone)
Tablets, 200 mg

PATIENT AGREEMENT FORM

Healthcare Providers: Counsel the patient on the risks of Mifeprex®. Both you and the patient must sign this form.

Patient Agreement:

1. I have decided to take Mifeprex and misoprostol to end my pregnancy and will follow my provider's advice about when to take each drug and what to do in an emergency.
2. I understand:
 - a. I will take Mifeprex on Day 1.
 - b. My provider will either give me or prescribe for me the misoprostol tablets, which I will take 24 to 48 hours after I take Mifeprex.
3. My healthcare provider has talked with me about the risks including:
 - heavy bleeding
 - infection
 - ectopic pregnancy (a pregnancy outside the womb)
4. I will contact the clinic/office right away if in the days after treatment I have:
 - a fever of 100.4°F or higher that lasts for more than four hours
 - severe stomach area (abdominal) pain
 - heavy bleeding (soaking through two thick full-size sanitary pads per hour for two hours in a row)
 - stomach pain or discomfort, or I am "feeling sick", including weakness, nausea, vomiting, or diarrhea, more than 24 hours after taking misoprostol
5. My healthcare provider has told me that these symptoms could require emergency care. If I cannot reach the clinic or office right away my healthcare provider has told me who to call and when to call.
6. I should follow up with my healthcare provider about 7 to 14 days after treatment. If my pregnancy continues after treatment with Mifeprex, I will have a surgical procedure to end my pregnancy.
7. I know that, in some cases, the treatment will not work. This happens if my pregnancy continues after treatment with Mifeprex. I will have a surgical procedure to end my pregnancy.
8. If I need a surgical procedure because the medicines did not work, my healthcare provider has told me whether they will do the procedure.
9. I have the MEDICATION GUIDE for Mifeprex. I will take it with me if I visit another healthcare provider who did not give me Mifeprex so that they will understand that I am having a medication.
10. My healthcare provider has answered all my questions.

Patient Signature: _____ **Date:** _____

Patient Name (print): _____

The patient signed the PATIENT AGREEMENT in my presence after I counseled her and answered all her questions. I have given her the MEDICATION GUIDE for Mifeprex.


Provider's Signature: _____ **Date:** _____

Name of Provider (print): _____

After the patient and the provider sign this PATIENT AGREEMENT, give 1 copy to the patient before she leaves the office and put 1 copy in her medical record.

*MIFEPREX is a registered trademark of Danco Laboratories, LLC.

03/2016 **DANCO**



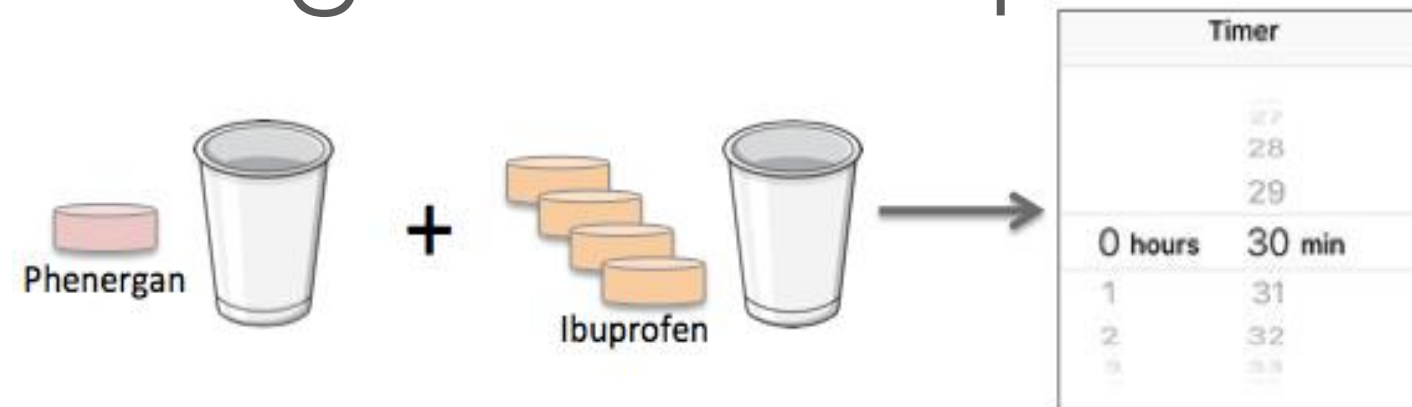
Regimen

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%

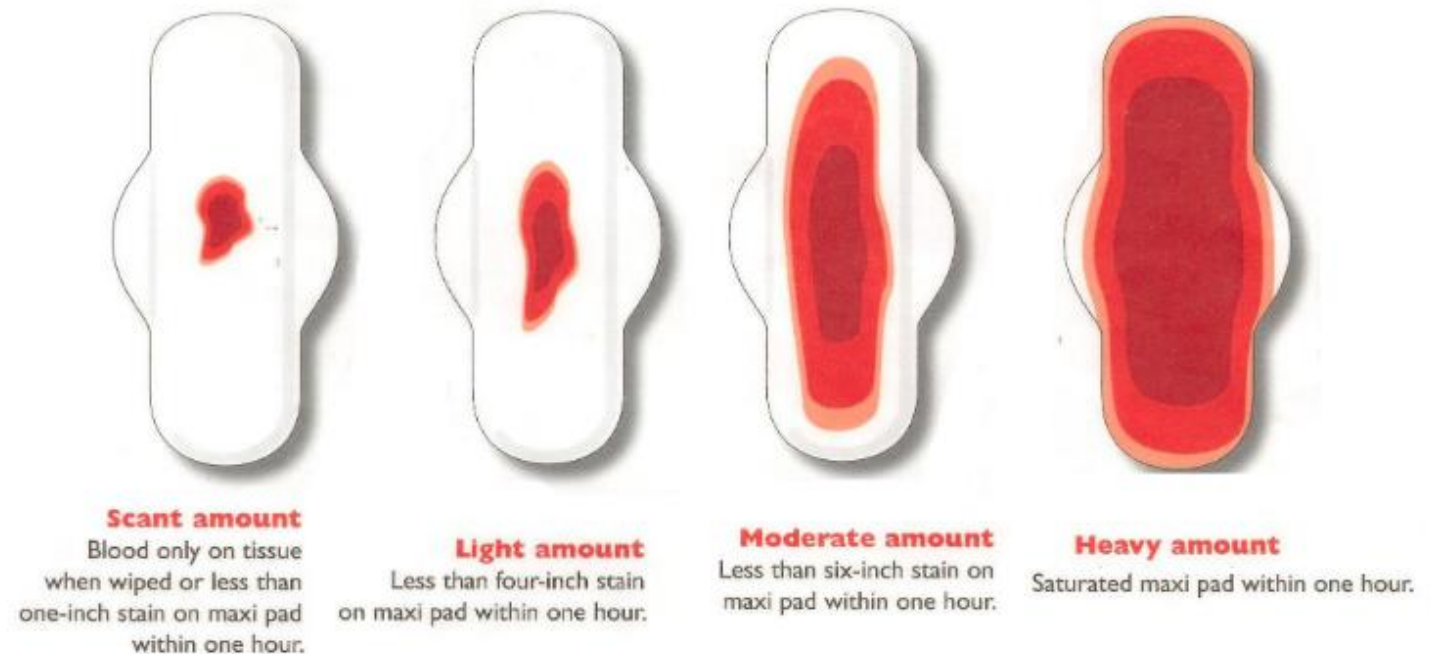


Dempsey, Clin Obstet Gyn, 2012; Fischer et al, NEJM, 2005; Meites et al, NEJM, 2010; Chen and Creinin, Obstet Gynecol, 2015

Bleeding

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

How Much Are You Bleeding?



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

www.earlyoptionpill.com/for-health-professionals



FOR HEALTH PROFESSIONALS

FOR PATIENTS

PRESCRIBING INFORMATION

IMPORTANT SAFETY INFO



What is Mifeprex?

Is Mifeprex right for me?

How do I get Mifeprex?

What can I expect?



FOR HEALTH PROFESSIONALS



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
 - Jennifer.Kaiser@hsc.utah.edu
 - Jessica Lewis-Caporal, NP
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Take Home Points

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Questions?

Thank you!

