

Advanced Concepts: First Trimester Pregnancy Complications - Managing Ectopics, Gestational Trophoblastic Disease, and Spontaneous Abortion Diagnostic Challenges

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The content of my material/presentation in this CME activity will include discussion of unapproved or investigational uses of products or devices as indicated: We will discuss effective and evidence-based regimens using methotrexate to treat ectopic pregnancies. Methotrexate is FDA-approved for other uses and is used off-label to manage ectopic pregnancy.

The logo for FMX, consisting of the letters 'FMX' in a bold, white, sans-serif font, set against a dark orange background with diagonal white stripes.

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Dr. Pierce is a graduate of Rush Medical College in Chicago, Illinois. She completed her residency at the University of Illinois-Chicago Advocate Illinois Masonic Medical Center Family Medicine Residency and a reproductive health care and advocacy fellowship at the Reproductive Health Access Project in New York, New York. Dr. Pierce enjoys practicing the full scope of family medicine, from newborns to geriatric patients. Her passion is reproductive health care, helping women and families plan when and whether to have children, and subsequently helping them have the healthiest pregnancies and babies possible.

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Dr. Johnston is a graduate of Brown University's Alpert Medical School in Providence, Rhode Island. She completed her residency at Lawrence Family Medicine Residency, Massachusetts, and participated in the Physicians for Reproductive Health Leadership Training Academy. At Lawrence Family Medicine Residency, she coordinates the women's health rotation and the women's health area of concentration. Her areas of interest include the empowerment of women, reproductive health access, immediate postpartum long-acting reversible contraception provision, and political action. Dr. Johnston served as the 2018 women's delegation co-convenor and delegate for the National Conference of Constituency Leaders (NCCL). In addition, she has leadership roles at the state level, including serving as the family medicine representative on the Massachusetts Department of Public Health Perinatal Advisory Committee and the Special Legislative Commission on Postpartum Depression.

FMX

Learning Objectives

1. Describe medical management of ectopic pregnancy, including initial management, followup, patient inclusion criteria, and when obstetrical consultation is necessary.
2. Explain management of gestational trophoblastic disease
3. Accurately diagnose the causes in less straightforward cases of early pregnancy bleeding.

FMX

Audience Engagement System



FMX

Case 1

-Mary is a 24 yo G2P1 comes in after a positive pregnancy test at home. She has a history of PCOS and very irregular menses, unsure of her LMP. This is a desired pregnancy.

-Notes 2 days of vaginal spotting

-Initial HCG 1900. Progesterone 5ng/mL

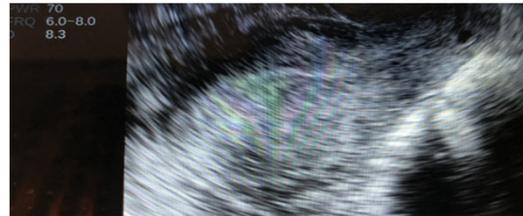
-Repeat HCG 48 hours later 1575



2 days later.....

Patient presents to the ER with severe pelvic pain and was diagnosed with an ectopic pregnancy.

Was there a clue?



Poll Question 1

All of these 48 hour HCG values are associated with an ectopic pregnancy **except**....

1. HCG decreases 18%
2. HCG decreases 25%
3. HCG increases 30%
4. HCG increases 25%

HCG rise and fall in 48 hours

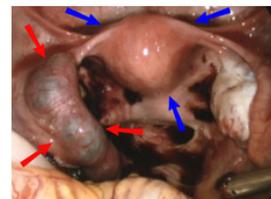
- ❖ Viable pregnancy: increase >53%
- ❖ Spontaneous abortion: decrease >21-35%
- ❖ Ectopic pregnancy: rise or fall in HCG less than these values

Seeber, BF, Barhhart KT. Suspected ectopic pregnancy. Obstet Gynecol 2006 Feb;107(2 Pt 1):399-413.

Progesterone's role?

<6ng/mL excludes a viable pregnancy

low levels DO NOT distinguish intrauterine from ectopic pregnancy



Verhaegen J, Gallos ID, van Mello NM, et al. Accuracy of a single progesterone test to predict early pregnancy outcome in women with pain or bleeding: meta-analysis of cohort studies. BMJ. 2012;345:e6077.

OB/Gyn Consultation needed:

- Varies by hospital
- When ectopic is diagnosed
- May be a specific HCG ex. 5000
- When surgical treatment is required

Role of uterine aspiration

- Pregnancy of unknown location (PUL)
 - used diagnostically
 - If chorionic villi are found the evaluation is complete
- Want to avoid methotrexate if not needed
 - Presumptive treatment does not decrease cost or complications with PUL
 - Debate about length of time after treatment to delay pregnancy
- Do not see expected HCG drop after first dose of MTX and this is a PUL

Contraindications for Methotrexate

Relative

- Cardiac activity
- Gestational sac size >4cm
- HCG >2000m IU/mL
- Alcoholism

Absolute

- Severe asthma
- Active peptic ulcers
- Breastfeeding
- Creatinine clearance <50ml/min/1.73m²
- Sensitivity to methotrexate
- Hematologic problems

ACOG practice bulletin no.94: medical management of ectopic pregnancy. Obstet Gynecol. 2008;111 (6):1481.

1 or 2 doses?

- Single dose regimen is the simplest
- Increased success with 2 doses if HCG > 3600-5000 mIU/mL
- Faster resolution with 2 doses (25.7 days vs. 31.9 days)

Methotrexate

- Day 1
 - Single dose 50 mg/m²
- Day 4 and 7
 - Repeat HCG levels
- Repeat Mtx if <15% decrease
- Measure HCG to 0



Expectant Management

- Appropriate if low and decreasing HCG
- No ectopic on ultrasound or <3 cm mass
- Extensive counseling is needed
- Risk of tubal rupture at any HCG
- Follow HCG weekly until 0

Poll Question 2

Which does NOT increase the risk of ectopic pregnancy?

1. IUD use
2. Pregnancy with ART (assisted reproductive technology)
3. Prior ascending pelvic infection
4. History of ectopic pregnancy

What about IUDs?

IUD's reduce the risk of all pregnancies but...
53% pregnancies that occur with an IUD in place are ectopic.



Tubal ectopic pregnancy. ACOG Practice Bulletin No. 193. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e91-103.

Ectopic pregnancy learning points

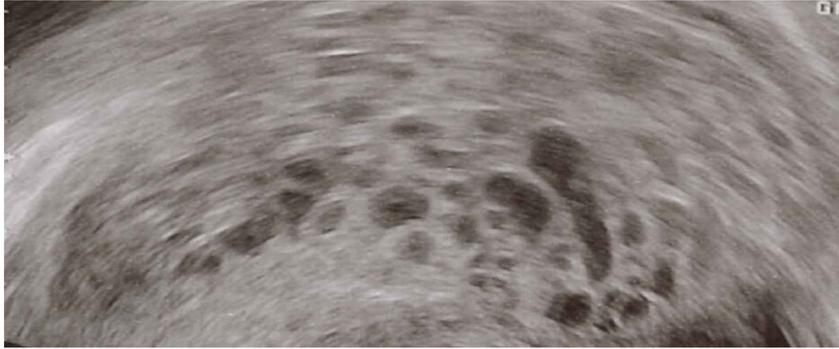
- Minimum decline with a miscarriage at 48 hours is 21-35%
- There can be rupture at any HCG level
- HCG should decrease by >15% from day 4-7
- Always document ectopic precautions

Barash, J., Buchanan, E., Hillson, C. Diagnosis and Management of Ectopic Pregnancy. *Am Fam Physician*. 2014;90 (1):34-40.

Case #2

- Simone is a 34 yo G3P2 presents with a positive home pregnancy test. Worried that she might have twins as she has had more morning sickness than in previous pregnancies.
- Her exam reveals a uterus larger than expected by her LMP 6 weeks ago.

POCUS



Gestational Trophoblastic Disease

- Irregular vaginal bleeding (most common)
- Hyperemesis
- Uterine enlargement out of proportion to gestational age
- Early failed pregnancy

ACOG practice bulletin no.53: Diagnosis and Treatment of Gestational Trophoblastic Disease. Obstet Gynecol. 2004;103:1365-77.

Poll Question 3

What is the preferred treatment?

1. Misoprostol and mifepristone
2. Suction curettage
3. Sharp curettage
4. Medical induction of labor

Management of Molar Pregnancy

- ❖ Suction curettage
- ❖ Rhogam is needed for partial but not complete moles
- ❖ Hysterectomy may be preferred to reduce sequelae
- ❖ Serial HCG measurements

Gestational trophoblastic disease (GTD)

Partial Mole

- 90% are triploid, evidence of a fetus

Complete Mole

- 75-80% are diploid, no fetal tissue

Gestational Trophoblastic Neoplasia

- persistent GTD

Follow up care

HCG should be measured within 48 hours of treatment, then q 1-2 weeks until levels drop and monthly for at least 6 months (to 12 Months).



Gestational Trophoblastic Neoplasia (GTN)

- ❖ May occur after a molar pregnancy, a non-molar pregnancy, or a live birth
- ❖ **Vaginal bleeding** is the most common presenting symptom for diagnosis after an abortion, miscarriage, or birth
- ❖ 1 study showed the median time between pregnancy and choriocarcinoma was 5-6 months

Tidy JA, Rustin GJ, Newlands ES, Foskett M, Fuller S, Short D, Rowden P. Presentation and management of choriocarcinoma after nonmolar pregnancy. Br J Obstet Gynaecol. 1995 Sep;102(9):715-9.

When should Gyn-onc be consulted?

- At diagnosis of the molar pregnancy?
- After routine uterine evacuation?
- If her HCG plateaus or increases?

Contraception after a Molar Pregnancy

- Hormonal contraceptives are safe during period of HCG follow up
- IUDs are safe unless there is persistent levels or malignant disease
- Higher risk of IUD expulsion after molar evacuation c/w second trimester uterine size

MENU CDC Contraception 2016

Gestational trophoblastic disease [§]	—
a. Suspected gestational trophoblastic disease (immediate postevacuation)	—
i. Uterine size first trimester	>
ii. Uterine size second trimester	>
b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)	—
i. Undetectable/non-pregnant β -hCG levels	>
ii. Decreasing β -hCG levels	>
iii. Persistently elevated β -hCG levels or malignant disease, with no evidence or suspicion of intrauterine disease	>
iv. Persistently elevated β -hCG levels or malignant disease, with evidence or suspicion of intrauterine disease	>

MENU CDC Contraception 2016

b. Confirmed gestational trophoblastic disease (after initial evacuation and during monitoring)

iv. Persistently elevated β -hCG levels or malignant disease, with evidence or suspicion of intrauterine disease

Method	Category		Clarification Evidence Comment SPR Info
	Init.	Cont.	
Cu-IUD	4 [†]	2 [†]	>
LNG-IUD	4 [†]	2 [†]	>
Implants	1 [†]		>
DMPA	1 [†]		>
POP	1 [†]		>
CHCs	1 [†]		>

Case #3

- Mary, a 28 yo who presents with vaginal bleeding “like a period”. She is 6 months remote from an uncomplicated vaginal delivery at 39 weeks.



Case continues

- Her exam revealed a normal vaginal canal with scant red blood in the vault. Uterus was non-tender, no signs of infection.
- HCG 3000
- Ultrasound with empty gestational sac
- She elects medication management



Case continues...

You have given her Mifepristone 200mg in the office and have prescribed 800 mcg of misoprostol.

She calls after 24 hours and reports no bleeding. What is the next step?

35

Troubleshooting medication management

No bleeding

- May repeat misoprostol 24-48 hours if no bleeding
- Aspiration procedure can be offered

Vomiting

- Can prescribe zofran to take prior to the mifepristone
- Dose can be repeated, consider if less than 20 minutes
- Have the patient take the misoprostol vaginally if nauseous

36

Case #4

Emily is a 35 yo G4P1 who had a positive home pregnancy test 4 weeks ago. Her menses were irregular and she is unsure about an LMP. She comes into your office with vaginal spotting.

Early pregnancy bleeding

- Subchorionic hematoma
- Infection
- Ectopic
- Miscarriage
- GTD

Case continues...

Minimal dark blood noted in the vaginal vault. Her HCG is 5000. The patient is unable to get to her scheduled ultrasound. Her HCG 2 days later is 6750. She has had not further bleeding.

Poll Question 4

What do you tell her?

1. You are not worried about an ectopic because the HCG increased.
2. This must be an ectopic because the HCG increase was so small.
3. This is definitely a miscarriage.
4. You need more testing, this could still be a viable pregnancy.

Vanishing Twins

- Incidence: 10-40% of all twin pregnancies
- Mean 2-day hcg increase was lower (114.3% vs. 128.8%)
- 2.2% had 2 day increases < 53% and had a live birth
- 80% of those with a 2 day increase <53% had a 3rd level >53%

Considerations

- ❖ Consider a 3rd HCG level to follow a trend
- ❖ There are outliers
- ❖ 35% 48 hour hcg increase includes more of the outliers

Take home points

1. Viable pregnancy: generally hcg increases >53%
2. Spontaneous abortion: hcg decrease >21-35%
3. Ectopic pregnancy: rise **or** fall in HCG less than these values
4. Contraception including IUDs are safe following a molar pregnancy
5. HCG levels needed for any bleeding 6 weeks following any pregnancy to rule out GTN
6. Consider a 3rd HCG level if considering vanishing twins

Recommended Practice Changes

1. Manage ectopic pregnancies safely and confidently in the family medicine office when appropriate patient criteria are met.
2. Manage some cases of gestational trophoblastic disease and be comfortable with contraceptive management.
3. Diagnose the cause of early pregnancy bleeding when laboratory or ultrasound findings are not initially diagnostic.

Contact Information

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Questions

