I would like to thank Dr. Frank Sanderson for joining us for rounds today as well as for the expert opinion he has offered in preparation for this presentation.
Clinical Scenario

- 25 yo G3P1A1 with LMP Feb 27 2017 GA 6w1d by dates
- Presents with abdominal cramping & PV bleeding at 22:00

- Triage VS:
  BP:115/70  HR:80  T:36.5  O2:99%RA  RR:16  pain:5/10
Clinical Scenario

- Crampy pain since 13:00 across lower abdo
  - not isolated to RLQ or LLQ
- PV spotting started approx 18:00, soaked one pad so far

- Sure of LMP, periods have been regular
- No use of assisted reproductive technologies

- **PMHx:** term SVD 2013, SA at 10wk in 2015

- **Social hx:** Lives in Saint John, partner present at bedside

So the patient is brought into RAZ...

**Recall:** heterotopic is 1:7000 to 1:30 000 naturally conceived pregnancies, up to 1% with assisted reproductive technologies
Clinical Scenario

- O/E No acute distress, skin pink, cap refill brisk
- Spec: small amt pooling at posterior fornix, removed with one sponge, os has fishmouth appearance
- PV: uterus palp small, no adnexal masses or tenderness
- UPT +pregnancy
- B/W drawn for CBC, Type & Screen, and bHCG
- Patient offered Tylenol for pain

So the patient is brought into RAZ...
So you do a transabdominal bedside ultrasound and this is what you see...a **small** intrauterine gestational sac

*(actually this image is transvaginal, but for the case we’ll call it transabdominal 😊)*
Clinical Scenario

- Patient has improvement in pain while awaiting labs

- B/W results at 23:00:
  - Hb = 120
  - Type & Screen: O neg
  - bHCG = 1025

- How do you manage this patient?

So the patient is brought into RAZ...
An in depth review of the management of ectopic pregnancy is beyond the scope of today’s talk.
PREGNANCY OF UNKNOWN LOCATION
Ectopic Pregnancy

- Ruling out ectopic pregnancy is a critical issue in evaluation of the symptomatic patient in early pregnancy

- In women presenting to ED with abdominal pain or pv bleeding, prevalence of ectopic as high as 13%\(^1\)

- Well known sequelae of missed ectopic
  - Rupture, tubal infertility, possible death

- Sequelae of false positive diagnosis of ectopic
  - Termination of viable, desired pregnancy

So its critical to determine not only when ectopic is a possible diagnosis, but also not to jump to this diagnosis prematurely. The challenge is that there is a period of time during pregnancy when it may not be possible to definitively determine the location of pregnancy – this subset of patients represents a diagnostic and management dilemma

Ectopic Pregnancy

- Tools for diagnosis:
  - Quantitative βHCG
  - Bedside ultrasound
  - Comprehensive ultrasound

- Clinical suspicion

Clinical suspicion – suspect ectopic pregnancy even when signs and symptoms are subtle, including pv bleeding with no abdominal pain (RESOURCE??)
A normal gestational sac is rounded, with a thick echogenic rim, known as the double decidual sign.

Worth noting, while emergency physicians use the yolk sac to define an IUP<radiology literature uses the presence of a gestation sac to define IUP.

Sonographic findings in Ectopic

- Adnexal mass
  - Simple adnexal cyst - low probability ectopic if < 3mm (5%)
  - Complex adnexal mass – high probability ectopic (90%)².⁷
  - Most common location: ampullary or isthmic portion of fallopian tube (95% of ectopics)

- Isolated free fluid in the pelvis
  - Rarely the only sonographic finding

- Pseudogestational sac – seen in at most 10% ectopic

- Normal scan – 15 to 25%².⁸

Complex adnexal masses - include the tubal ring sign: a hyperechoic ring around a tubal gestational sac

Pseudogestational sac once thought to be very common, up to 20%. Now thought about 10% of ectopics have a pseudogestational sac. Seeing any fluid in the uterus carries a 99.5% chance of intrauterine pregnancy – all comers, not ED population

Of women with confirmed ectopic pregnancy, 15 to 25 % of initial scans are negative – empty uterus, no adnexal mass, no free fluid

Complex adnexal mass, distinct from uterus
See the endometrial stripe, and distinct separate mass
Important to look carefully, may be tempted to call it IUP once you see the fetal tissue
**Role of βHCG**

- βHCG levels in viable IUP, non viable IUP and ectopic pregnancy have considerable overlap

- What about the discriminatory zone?
  - 1981: Established as βHCG=6500 for trans abdominal US

- Annals of Emergency Medicine 2011:
  - For patients with non-diagnostic bedside US, serum hCG level is not helpful in differentiating intrauterine from ectopic pregnancy in symptomatic ED patients.

βHCG levels in viable IUP, non viable IUP and ectopic pregnancy have considerable overlap - A single serum βHCG cannot distinguish
What about the discriminatory zone? Conceptually, βHCG below which pregnancy not visible on US
Annals 2011

For patients with nondiagnostic bedside ultrasonography, using a discriminatory hCG level of 3,000 mIU/mL to further assess for ectopic pregnancy showed sensitivity of 35% (95% confidence interval [CI] 18% to 54%) and specificity of 58% (95% CI 48% to 67%). Overall sensitivity of bedside pelvic ultrasonography for the detection of intrauterine pregnancy was 71% (95% CI 63% to 78%), and the specificity was 99% (95% CI 94% to 100%).

Role of $\beta$HCG

- In the setting of a symptomatic patient with empty uterus, low $\beta$HCG $< 1000$ does not rule out ectopic pregnancy
  - Ectopic pregnancy can occur at any $\beta$HCG
  - Rupture documented at very low $\beta$HCG$^{1,3}$

- For indeterminate US with $\beta$HCG between 2000 – 3000
  - 19 ectopic and 38 non-viable pregnancies for 1 viable pregnancy$^9$
  - Other studies have found no correlation

- Ectopic 70x more likely than viable IUP if $\beta$HCG $> 3000^{10}$
  - Another possibility: completed abortion

So how can we use the b-HCG?... In the setting of a symptomatic patient with empty uterus, a low $\beta$HCG $< 1000$ does not rule out ectopic pregnancy

**If anything, these figures further support the need to be suspicious of ectopic in pregnancy of unknown location with low bHCG**

   .....this study had 173 women
The American College of Emergency Physicians recommends: Proceed to TV US in symptomatic patients with βHCG less than 1000

If you hang your hat on the concept of a discriminatory zone, you may advocate avoiding or deferring ultrasound for βHCG < 1000. Particularly for us locally, one may perform a trans abdominal scan with No definitive IUP and βHCG = 1000. Are we done?

....ACEP’s 2017 updated policy on patients presenting to ED in early pregnancy would recommend to move forward with TVUS
One hundred and seventeen cases of ectopic pregnancy were reviewed. Thirty-seven cases met predetermined criteria of 'clinical stability' at first presentation. These patients waited a median 14 h for diagnostic ultrasound with 62% waiting more than 12 h. No adverse events occurred while waiting for this diagnostic study.

CONCLUSIONS: Preliminary results suggest that pregnant patients with abdominal pain and vaginal bleeding in the first trimester who meet specific low-risk clinical criteria could potentially have ultrasound delayed 12-18 h without risk of adverse event. Further prospective studies are warranted to confirm the safety of this strategy. They found no adverse events, defined as death or need for fluid bolus because of hemodynamic instability, in 37 patients despite a median delay to ultrasound of 14 hours (range 0 to 126 hours), with 62% of patients waiting 12 hours or longer. The mean b-hCG level in this group was 2,887 mIU/mL (range 85 to 26,000 mIU/mL), but the number of patients with a b-hCG level less than the discriminatory threshold was not provided.

According to the Association of Early Pregnancy Units guidelines, if no intrauterine or ectopic pregnancy or retained products of conception are seen on transvaginal ultrasound and the woman is asymptomatic at initial assessment, she can be managed conservatively. This is irrespective of the hCG discriminatory zone and additional ultrasound findings, such as a suspicious adnexal mass 3 cm. Conservative management involves re-estimation of serum hCG levels at 48 hours to determine the pattern of hCG change from the initial assessment. Further follow-up with hCG and transvaginal ultrasound can be arranged or therapeutic intervention made.15

Safety of discharge

- NJEM 2013:\(^3\)
  - there is limited risk in taking a few extra days to make a definitive diagnosis in a woman with a pregnancy of unknown location who has no signs or symptoms of rupture and no ultrasonographic evidence of ectopic pregnancy.

- Progression of hCG values over a period of 48 hours provides valuable information:\(^{13}\)
  - If failure to fall by 15%
  - And failure to rise by 55%
  - ...most likely diagnosis is ectopic pregnancy


This concept is supported in the 2016 SOGC Guideline on Ultrasound Evaluation of First Trimester Complications of Pregnancy.
A reasonable approach

In the pregnant patient with vaginal bleeding and / or abdominal pain:

- Always perform bedside US to establish definitive IUP
- Do not rule out ectopic pregnancy in patients with empty uterus and βHCG < 1000
- Do obtain a comprehensive TVUS when bedside US does not confirm IUP regardless of βHCG
**A reasonable approach**

**In the pregnant patient with vaginal bleeding and / or abdominal pain:**

- When TVUS is delayed or remains non-diagnostic, involve obstetrician to aid in risk stratification and management

- Reliable, hemodynamically stable patients may be discharged with follow up
  - Expedited TVUS (next day)
  - Repeat βHCG in 48h

**In the pregnant patient with vaginal bleeding and / or abdominal pain:**

When TVUS is delayed or remains non-diagnostic, involve obstetrician to aid in risk stratification and management

Reliable, hemodynamically stable patients may be discharged with follow up
- Expedited TVUS (next day)
- Repeat βHCG in 48h

The patient will require appropriate discharge instructions, advising of the continuing possibility of ectopic pregnancy. She should be advised to return to ED immediately if bleeding or abdominal pain or presyncope occur. For patients presenting from remote locations or those who may not be reliable, consider admission while awaiting repeat b-HCG
Back to the case…

- 25 yo G3P1A1 with LMP Feb 27 2017 GA 6w1d by dates
- Abdominal cramping & PV bleeding, vitals stable

- Transabdominal US: gestational sac, NDIUP

- B/W results at 23:00:
  - Hb = 120   Rh: O neg   βHCG=1025

- Minimal pv spotting since arrival to ED, pain controlled with Tylenol

- How do you manage this patient?
### Back to the case…

- You suspect threatened abortion, but recognize that ectopic not ruled out
- No US available after hours

- Obstetrics consulted to review case
  - There are 6 patients in case room and about to go to c-section, discusses case on phone

- Together, decided it is safe to discharge with instructions to return for TVUS in AM and serial βHCG at 48h
  - Specific discharge instructions to return immediately if bleeding/pain/presyncope
  - As patient is Rh(-) she is given a dose of Rhogam

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The patient is reliable and will be going home to her partner, she lives near the hospital.
DIAGNOSIS & MANAGEMENT OF EARLY PREGNANCY LOSS
In the first trimester, the terms spontaneous abortion, miscarriage and early pregnancy loss are used interchangeably.

There is risk associated with diagnosing early pregnancy loss too early due to risk of false positive – risk of intervening on a viable pregnancy.

Early pregnancy loss is diagnosed using ultrasound, with attention to serial bHCG and time-based criteria for diagnosis.
A normal gestational sac is rounded, with a thick echogenic rim, known as the double decidual sign

**Worth noting, while emergency physicians use the yolk sac to define an IUP**, **radiology literature uses the presence of a gestation sac to define IUP.**

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CRL=5mm has a false positive rate of 8.3%, gest sac of 16mm has false positive rate of 4.4%


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**Ultrasound diagnosis of EPL**

*Old guidelines (pre-2011)*

- Embryonic demise: crown rump length $\geq 5$mm w no FHR
- Anembryonic pregnancy: gestational sac with mean gestational diameter $\geq 16$mm with no embryo

- **Recently challenged in two large prospective studies**\(^{15, 16}\)
  - Due to inter-observer variability
- Dating by LMP is unreliable, must allow $\frac{1}{2}$ wk variation even when sure of dates\(^{14}\)
Criteria are from the Society of Radiologist in Ultrasound (American) in 2011 and endorsed by both ACOG and SOGC

The FHR is typically visible as soon as embryo visible, therefore CRL < 7mm with no FHR is suggestive but not diagnostic of early pregnancy loss.

The Mean sac diameter of 25 mm with no embryo is 100% specific for EPL

<table>
<thead>
<tr>
<th>Findings Diagnostic of Pregnancy Failure</th>
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</thead>
<tbody>
<tr>
<td>Crown–rump length of ≥7 mm and no heartbeat</td>
</tr>
<tr>
<td>Mean sac diameter of ≥25 mm and no embryo</td>
</tr>
<tr>
<td>Absence of embryo with heartbeat ≥2 wk after a scan that showed a gestational sac without a yolk sac</td>
</tr>
<tr>
<td>Absence of embryo with heartbeat ≥11 days after a scan that showed a gestational sac with a yolk sac</td>
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</tbody>
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Criteria are from the Society of Radiologists in Ultrasound Multispecialty Consensus Conference on Early First Trimester Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy, October 2012.
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- When findings are suspicious for but not diagnostic of EPL, a follow up US in 7 – 10d is recommended

<table>
<thead>
<tr>
<th>Findings Suspicious for, but Not Diagnostic of, Pregnancy Failure</th>
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<tbody>
<tr>
<td>Crown–rump length of &lt;7 mm and no heartbeat</td>
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<tr>
<td>Mean sac diameter of 16–24 mm and no embryo</td>
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<tr>
<td>Absence of embryo with heartbeat 7–13 days after a scan that showed a gestational sac without a yolk sac</td>
</tr>
<tr>
<td>Absence of embryo with heartbeat 7–10 days after a scan that showed a gestational sac with a yolk sac</td>
</tr>
<tr>
<td>Absence of embryo ≥6 wk after last menstrual period</td>
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<tr>
<td>Empty amnion (amnion seen adjacent to yolk sac, with no visible embryo)</td>
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<tr>
<td>Enlarged yolk sac (&gt;7 mm)</td>
</tr>
<tr>
<td>Small gestational sac in relation to the size of the embryo (&lt;5 mm difference between mean sac diameter and crown–rump length)</td>
</tr>
</tbody>
</table>
Panel A shows an embryo with a crown–rump length (between the plus signs, indicating calipers) of 7.1 mm. No cardiac activity was seen on realtime ultrasonography.

For reflection – this is a measurement of millimeters, so subject to inter-observer variability

Panels B and C show a gestational sac with a mean diameter of 27.7 mm (average of 35.4 mm, 19.7 mm, and 28.1 mm), with no visible embryo. SAG denotes sagittal view, and COR coronal view.
Time based criteria include:
Absence of embryo with heartbeat 7–13 days after a scan that showed a gestational sac without a yolk sac
Absence of embryo with heartbeat 7–10 days after a scan that showed a gestational sac with a yolk sac
Absence of embryo ≥6 wk after last menstrual period
Panel D shows an intrauterine gestational sac with a yolk sac, and Panel E (a scan obtained 2 weeks later) shows a yolk sac but no embryo within the gestational sac.
Use of βHCG

- Serum βHCG becomes positive at implantation
  - Day 21 or 22 post LMP (Day 8 post conception)

- Early pregnancy: βHCG doubling time 1.4 – 2.1 days
  - Minimum of 55% rise over 48h in viable pregnancy3,14,14

- βHCG plateaus at approx. 8 to 12 wks, then declines

- For early pregnancy < 7-8 wk gestation, serial βHCG can support a US diagnosis of spontaneous abortion
  - βHCG falling > 15% in 48h confirms non-viable pregnancy

Serum βHCG becomes positive at implantation
Day 21 or 22 post LMP
Day 8 post conception
Positive serum βHCG >15
Note: urine preg+ at βHCG = 30

A Single or serial βHCG may be used to add support to US diagnosis of non viable pregnancy
Suggested approach from SOGC:

Management of Early Pregnancy Loss

- Expectant management
- Medical management with misoprostol
- Surgical management with suction curettage

Note: Spontaneous abortion is medically common, and its emotional impact is often underestimated.

Note: Spontaneous abortion is medically common, and its impact is often underestimated. We often deal with these patients in the time-pressured environment of RAZ, and while we may be glad that the patient does not have an ectopic pregnancy, to the patient it may be one of the worst days of her life.

So it’s essential that we have these conversations in a tactful, empathic manner. – and vital that we are able to provide upfront info on treatment option. Even better – print a handout for the patient.

ACOG handout: http://www.acog.org/-/media/For-Patients/faq090.pdf
Expectant management

- Limited to first trimester up to 12w6d
  - Contraindicated if: infection, hemorrhage

- Successful to complete expulsion in 80% women

- Expect moderate to heavy bleeding

- Confirmation: typically with US
  - Absence of gestational sac and endometrial thickness < 30mm
  - Serial βHCG alternative if limited US access

Limited to first trimester up to 12w6d
C/I if: infection, hemorrhage, severe anemia, bleeding disorder
Successful to compete expulsion in 80% women - Possibly more effective in women already experiencing bleeding
Expect moderate to heavy bleeding - Counsel that surgery or medication may be necessary if complete expulsion not achieved
Confirmation: typically with US - Absence of gestational sac and endometrial thickness < 30mm, Serial βHCG alternative if limited US access
Medical Management

- Same criteria as expectant (<12w6d, medically stable)

- Sample protocol
  - Misoprosol 800 mcg pv, may repeat in 48h if no result
  - Ibuprofen for pain control
  - RhoGAM within 72h of first dose if Rh(-)

- US in 7-14d to document complete expulsion
  - Or serial βHCG

Same criteria as expectant (<12w6d, medically stable) –
Success rate of medical mgmt about 95% for incomplete abortion, 88% for fetal
death and 80% for anembryonic pregnancy
Good option for woman wishing to shorten duration to expulsion but wishing to
avoid surgical evacuation - Also more control over when bleeding occurs, Reduces
need for D&C by 60%
Sample protocol - Misoprosol 800 mcg pv, One repeat dose prn, no earlier than 3h
after first dose and within 7d, Ibuprofen for pain control, RhoGAM within 72h of
first dose if Rh(-)
US in 7-14d to document complete expulsion - Or serial βHCG
Counsel re: what is too much bleeding? Soaking 2 maxi pads per hours for 2
consecutive hours – if this occurs return to ED
If misoprostol fails, patient may opt for expectant or surgical management
Surgical Management

- Traditional approach

- Urgent surgical evacuation if:
  - Hemodynamic instability, hemorrhage, infection

- Preferable if woman desires more immediate completion and less follow up

- All 3 methods result in complete evacuation in most patients with similar adverse event rates
  - Hemorrhage: 0.5 – 1%, Infection: 1 – 2%

Success rate of D&C approaches 99%
Suction curettage may be performed in an office setting
Futher management issues

- Prevention of allo-immunization for Rh(-) mother:
  - RhoGAM 50mcg within 72h of dx of miscarriage

- Delayed conception → no benefit

- May resume contraception immediately after completion of spontaneous abortion
  - IUD may be placed at time of surgical evacuation

Prevention of allo-immunization for Rh(-) mother: - RhoGAM 50mcg within 72h of dx of miscarriage Or immediately following surgical management, If 50mcg dose not available, use full 300mcg dose

Delayed conception? → no benefit

  Avoid intercourse 1-2 wk after passage of tissue to reduce infection (not evidence based)

May resume contraception immediately after completion of spontaneous abortion
  IUD may be placed at time of surgical evacuation
Diagnosis of early pregnancy loss is made as she has absence of embryo with heartbeat 7–13 days after an ultrasound scan that showed a gestational sac without a yolk sac
Additionally, bHCG is falling
Take home points

- Do obtain a comprehensive TVUS when bedside US does not confirm IUP regardless of βHCG

- Do not rule out ectopic pregnancy in patients with empty uterus and βHCG < 1000
  - Clinical judgment: safe discharge planning vs admission
  - Low threshold to involve Obs-Gyn for these cases

- Early pregnancy loss is diagnosed by US when:
  - CRL >/= 7mm with no FRH
  - Mean sac diameter >/= 25mm and no embryo

- Expectant, medical and surgical management are equally effective and safe in treatment of EPL
  - Patient preference may guide decision making

Added take home point:
- It can take 3 to 4 visits over 1 – 2 weeks to make a final diagnosis of ectopic pregnancy or early pregnancy loss
- These cases require team work with the patient’s obstetrical provider
References


References


