1st Trimester Bleeding

Background:

1st trimester bleeding can represent a spectrum of problems of pregnancy, or can be normal (implantation bleeding). It can also be a sign of a significant abnormality in the pregnancy such as ectopic pregnancy or an imminent miscarriage. Accurately and correctly diagnosing the condition causing 1st trimester bleeding can be a diagnostic dilemma; and incorrect diagnosis can place the pregnant woman at risk. Ectopic pregnancy accounts for 6% of deaths[1] during pregnancy, thus accurate and timely diagnosis of pregnancy location is paramount when faced with a pregnant woman with 1st trimester bleeding. Diagnosis is not considered to be complete until the location and viability of the pregnancy is proven.

Current technology available, including high resolution ultrasound and serum quantitative β-HCG, allows for an algorithm to work through which enables the clinician to determine the reason for 1st trimester bleeding with a fair degree of accuracy. This algorithm will allow the clinician to detect several conditions, including, ectopic pregnancy, normal pregnancy, missed/inevitable abortion, complete abortion and normal pregnancy. However, there will remain some presumed diagnoses.

This algorithm assumes that a woman has a positive pregnancy test and is in the 1st trimester by last menstrual period dating criteria.

Diagnosis: See Diagnostic algorithm

Diagnostic Tools:

B-hCG- Produced by trophoblastic tissue. In a normal intrauterine pregnancy, it rises by at least 66% in 48 hours or 100% in 72 hours. This is considered an "optimal" rise. A sub-optimal rise suggests indicates a pregnancy with poor blood supply or growing abnormally. Be cautious though; 13% of ectopic pregnancies can have a normal slope.

This test varies slightly from lab to lab, so caution must be taken when interpreting β-hCG levels drawn from different labs. β-hCG levels can be correlated with ultrasound findings. The following is a graph[2] of "typical" *vaginal* ultrasound findings correlated with serum β-hCG in a normal pregnancy:

Vaginal ultrasound only

Gestational age	B-HCG (mIU/ml)	TVUS findings
4.5-5 weeks	<1,000	Possibly decidual reaction, possibly gestational sac
5 weeks	1,000-3,000	Gestational sac + decidual changes
5-6 weeks	>3,000	Yolk sac (+/- fetal pole)
6 weeks	10,000-20,000	Embryo with cardiac activity
7 weeks	>20,000	Embryonic torso/head

BUT

Be aware that 12% of normal pregnancies can have a sub-optimal slope

Be aware that 13% of ectopic pregnancies can have a normal slope

Unfortunately this correlation is not always absolute[1,3]. Thus, careful consideration must be taken when considering treatment based on β-hCG and ultrasound when near the zone of discrimination. For this reason, the attached algorithm uses as cutoff of 3000 for the "zone of discrimination." An increase of serum β-hCG of less than 53% in 48 hours raises suspicion of an abnormal pregnancy[6], but does not diagnose location.

For low β-hCG levels, <800, there should be little expectation of seeing a pregnancy even if it is in the uterus. This is a limitation of ultrasound imaging[4]. With low levels of hCG and no symptoms, the trend of β-hCG rise over serial tests will guide the clinician in decision making.

Progesterone- is created by the corpus luteal cyst. The pregnancy assumes production as it grows. In abnormal pregnancies and especially ectopic pregnancy, low progesterone production is the rule. A progesterone of <5 is considered diagnostic for ectopic pregnancy. >20 is consistent with IUP. From 5-20 is considered equivocal. Unfortunately, this is usually a reference test which takes 12-24 hours to return results. This may be a useful adjunct when serial β-hCG and ultrasound are inconclusive[4].

Transvaginal ultrasound (TVUS)- Is considered the standard for evaluation of 1st trimester pregnancy. As an ultrasound probes moves away from its target, the accuracy decreases by a factor of 4:1. The closer the probe is to the target, the more accurate the imaging is. With current ultrasound and hCG assays, the "zone of discrimination" is an hCG level >3000. This means that at 3000 and above, at least the sac should be visible in the uterus. Below 3000, a pregnancy may be so small as to not be visible on imaging. For **abdominal imaging**, the zone of discrimination is >6500. Current literature is clear that the quality of imaging is directly correlated with the skill and experience of the ultrasonographer/interpreter[4,5]. If skilled and experienced operators in vaginal ultrasonography are not available, consider transferring the patient to a facility with a higher level of care. Diagnosis of an intrauterine pregnancy can only be accomplished with specific images.

Terminology

'Indeterminate' is a term used in clinical practice that has led to confusion. Some practitioners have used the term to mean 'pregnancy of indeterminate site' while others mean 'pregnancy of indeterminate viability'[7]. The term 'indeterminate' should no longer be used, and should be replaced with the two separate terms below.

Both terms should only be used after assessment by TVS. [7, 9]

'Pregnancy of unknown location': No signs of either intra- or extrauterine pregnancy or retained products of conception in a woman with a positive pregnancy test. [3]

Pregnancy of 'uncertain viability': Intrauterine sac (16-24 mm mean diameter) with no obvious fetus; or crown–rump length <7 mm with no obvious fetal heart activity.
In order to confirm or refute viability, a repeat scan at a minimal interval of 11 days is necessary.

Findings diagnostic of Pregnancy Failure by Transvaginal Ultrasound

-CRL $\geq$ 7mm with no fetal cardiac motion
-Mean sac diameter $\geq$ 25 mm and no embryo
-Absence of embryo with fetal cardiac motion $\geq$ 2 wks after a scan that showed a gestational sac without a yolk sac
-Absence of embryo with fetal cardiac motion $\geq$ 11 days after a scan that showed a gestational sac with a yolk sac

Management: See Algorithm

Based on input from the local provider, an OB/GYN consultant, and the patient, one of the first decisions is where the patient is best managed.

Transfer to tertiary care:

The following are treatment options that warrant a transfer to a care center with emergent surgical capability:

A. **Patient elects methotrexate management**- There is a guideline to follow for HCG trends (see **Medical management** below). Additionally, until the HCG reaches 0, there is risk of rupture and a surgical emergency.
B. **Patient elects surgical management-**Requires a facility with surgical capability.

C. **Patient is symptomatic**- This patient is either a surgical emergency or will likely become one very soon. Transfer to closest care center emergently. Coordination with care center is paramount to patient care.
D. **Unclear Clinical picture**- Diagnostic dilemmas should be transferred to a facility with consultants and is capable of medical and/or surgical management

Management of Ectopic Pregnancy- varies based on several factors. Ideally all management schemes for ectopic pregnancy will occur in a facility with emergent surgical capability. The decision to use medical or surgical management will depend on the physician, the patient, the symptoms and the availability of care in geographical location. Even if medical management is chosen, the patient is still at risk for becoming a surgical emergency and this treatment does not obviate the need for referral to a tertiary care facility for the duration of treatment. Duration of treatment means definitive surgical management and/or following serum hCG to an undetectable level.

Conservative management- With hCG<400 and decreasing with no symptoms, a patient with first trimester bleeding may be observed and the hCG followed to 0. If a decreasing hCG plateaus (stops decreasing) or rises, or the patient becomes symptomatic, the patient should be treated medically or surgically as indicated.

Medical management- For ectopic pregnancy or presumed ectopic pregnancy only
Please see ANMC Ectopic Pregnancy Management: Tubal and interstitial
http://home1.anmc.org/qaweb/guidelines/index.cfm?fuseaction=osList.main&strSection=Obstetrics
Warrants transfer to a tertiary care center.

Surgical management- At the discretion of the findings, the patient and the physician. For an identified ectopic (ultrasound imaging shows), diagnostic/operative laparoscopy with salpingostomy/salpingectomy is indicated. However, in certain situations, methotrexate may also be considered. In comparing systemic methotrexate with tube-sparing laparoscopic surgery, randomized trials have shown no difference in overall tubal preservation, tubal patency, repeat ectopic pregnancy, or future pregnancies[6].

For the patient who choses surgery instead of methotrexate, for the "presumed" ectopic pregnancy which is suspected, but not imaged, a suction D&C with frozen section of the tissue is warranted. If there are no chorionic villi, the patient should undergo laparoscopy. For **unstable** patients, laparotomy is indicated.

Post-treatment care- If there is no tissue for pathologic diagnosis, then the HCG should be followed to zero. If a falling hCG plateaus or rises, the patient should be referred to a tertiary care center for evaluation.

Key Points:

Make certain that the timing of serum hCG draws are clearly 48 hours or 72 hours apart. A difference in as little as 12 hours can falsely demonstrate a sub-optimal slope.

Timely diagnosis. Treating suspected ectopic pregnancies at the earliest definitive diagnosis may prevent significant morbidity (hemorrhage from rupture, etc). Once there is enough clinical data to make an accurate diagnosis, treatment should be rendered.

Treatment too early. Be wary of making a decision with an unclear clinical picture. It is possible to treat a "normal" pregnancy accidentally. If there is an unclear picture, contact the OB/GYN consultant on-call.

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Other useful resources concerning 1st trimester bleeding:

COCHRANE DATABASE (Accessed 7/6/18)

Miscarriage

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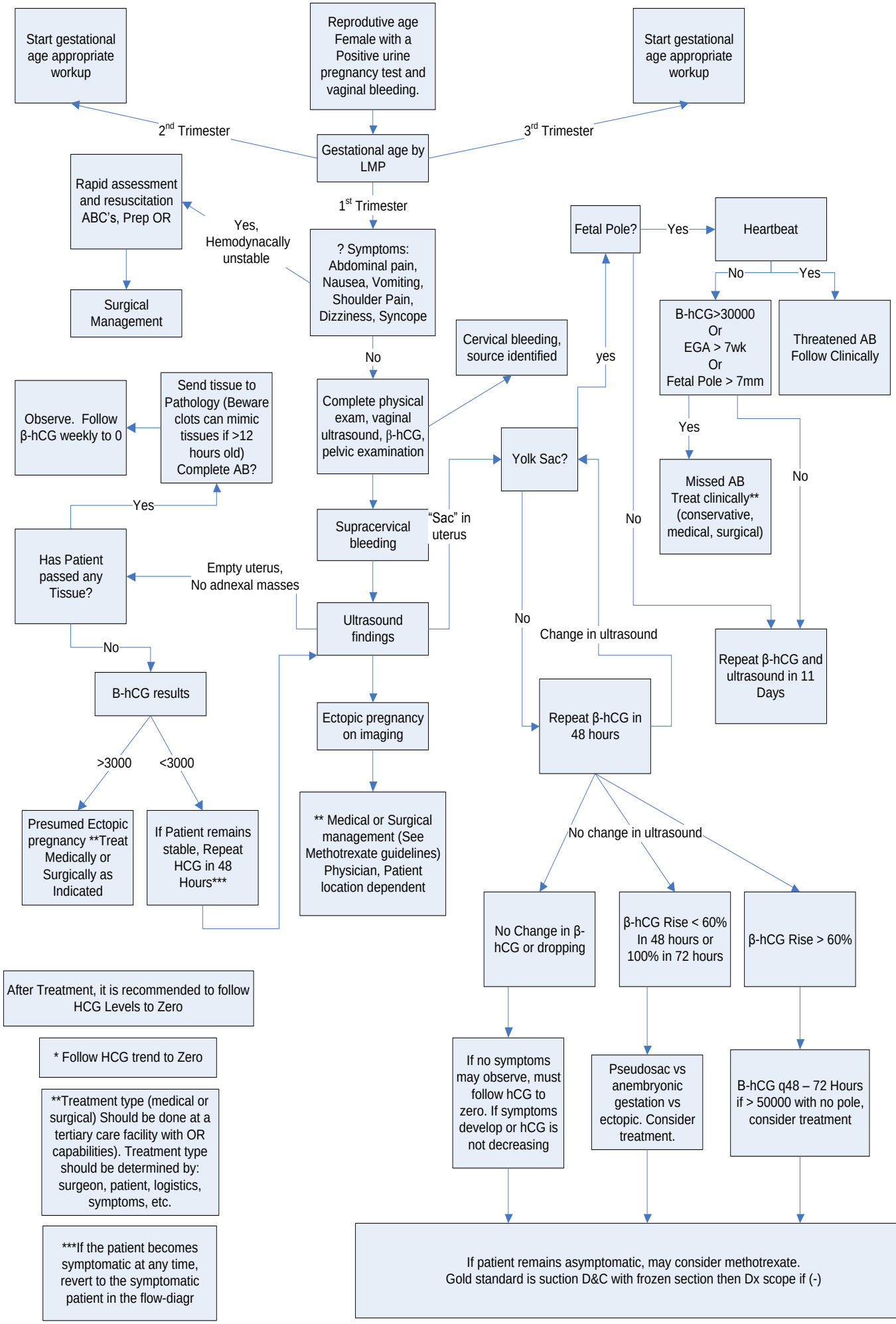
Reprodutive age Female with a Positive urine pregnancy test and vaginal bleeding.
Gestational age by LMP
2nd Trimester
3rd Trimester
Start gestational age appropriate workup
Start gestational age appropriate workup
1st Trimester
Rapid assessment and resuscitation ABC's, Prep OR
Surgical Management
Yes, Hemodynacally unstable
? Symptoms: Abdominal pain, Nausea, Vomiting, Shoulder Pain, Dizziness, Syncope
No
Complete physical exam, vaginal ultrasound, β-hCG, pelvic examination
Cervical bleeding, source identified
Send tissue to Pathology (Beware clots can mimic tissues if >12 hours old) Complete AB?
Observe. Follow β-hCG weekly to 0
Yes
Has Patient passed any Tissue?
Empty uterus, No adnexal masses
No
B-hCG results
>3000
<3000
Presumed Ectopic pregnancy **Treat Medically or Surgically as Indicated
If Patient remains stable, Repeat HCG in 48 Hours***
Supracervical bleeding
"Sac" in uterus
Ultrasound findings
Ectopic pregnancy on imaging
** Medical or Surgical management (See Methotrexate guidelines) Physician, Patient location dependent
Yolk Sac?
yes
No
Change in ultrasound
Repeat β-hCG in 48 hours
No change in ultrasound
No Change in β-hCG or dropping
β-hCG Rise < 60% In 48 hours or 100% in 72 hours
β-hCG Rise > 60%
If no symptoms may observe, must follow hCG to zero. If symptoms develop or hCG is not decreasing
Pseudosac vs anembryonic gestation vs ectopic. Consider treatment.
B-hCG q48 – 72 Hours if > 50000 with no pole, consider treatment
If patient remains asymptomatic, may consider methotrexate.
Gold standard is suction D&C with frozen section then Dx scope if (-)
Fetal Pole?
Yes
Heartbeat
No
Yes
B-hCG>30000 Or EGA > 7wk Or Fetal Pole > 7mm
Threatened AB Follow Clinically
Yes
Missed AB Treat clinically** (conservative, medical, surgical)
No
No
Repeat β-hCG and ultrasound in 11 Days
After Treatment, it is recommended to follow HCG Levels to Zero
* Follow HCG trend to Zero
**Treatment type (medical or surgical) Should be done at a tertiary care facility with OR capabilities). Treatment type should be determined by: surgeon, patient, logistics, symptoms, etc.
***If the patient becomes symptomatic at any time, revert to the symptomatic patient in the flow-diagr