

US Findings of First-Trimester Pregnancy

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Learning Objectives

1. Review normal embryonic development.
2. Recognize US diagnostic criteria of viable, uncertainly viable, and nonviable intrauterine pregnancies (IUPs).
3. Diagnose ectopic pregnancy and identify its various types.
4. Distinguish between the various types of benign gestational trophoblastic disease (GTD).

Introduction

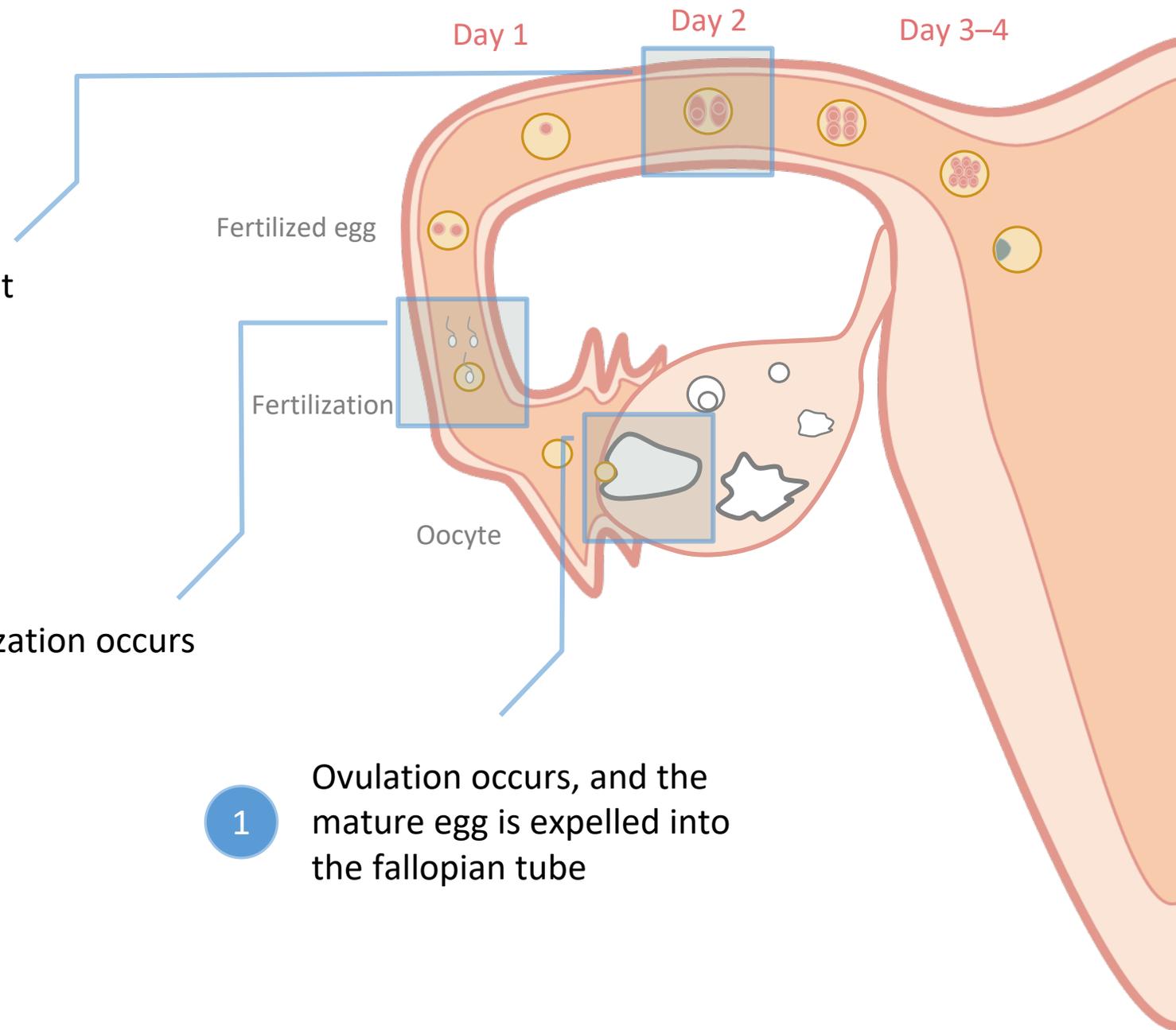
- *First trimester* is defined as the first 12 weeks of pregnancy
- It is a critical period when:
 - 80% of miscarriages occur¹
 - Ectopic pregnancy occurs, which is the leading cause of maternal death²
- US plays an important role in evaluating the viability of the early pregnancy and excluding ectopic pregnancy and GTD.

Fertilization

3 Embryo divides as it migrates to the endometrial cavity

2 Fertilization occurs

1 Ovulation occurs, and the mature egg is expelled into the fallopian tube

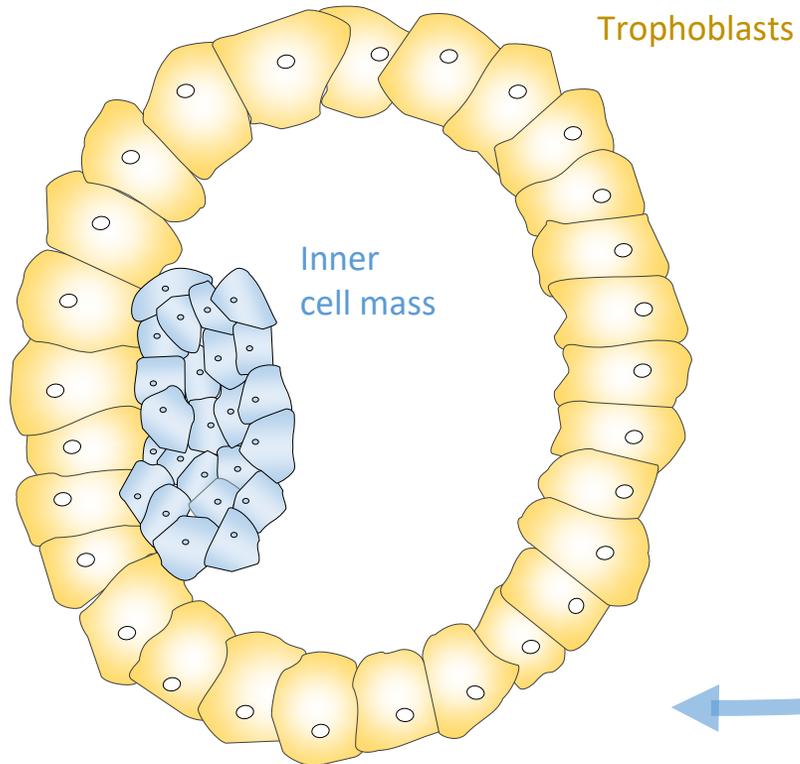
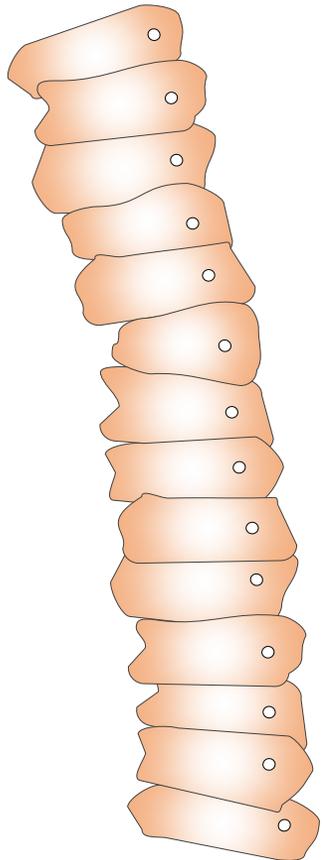


Blastocyst Stage

Blastocyst forms around 5 days after fertilization and contains:

- An **inner cell mass** (which forms the embryo)
- **Trophoblasts** (which give rise to the placenta)

Endometrium



Fertilized egg

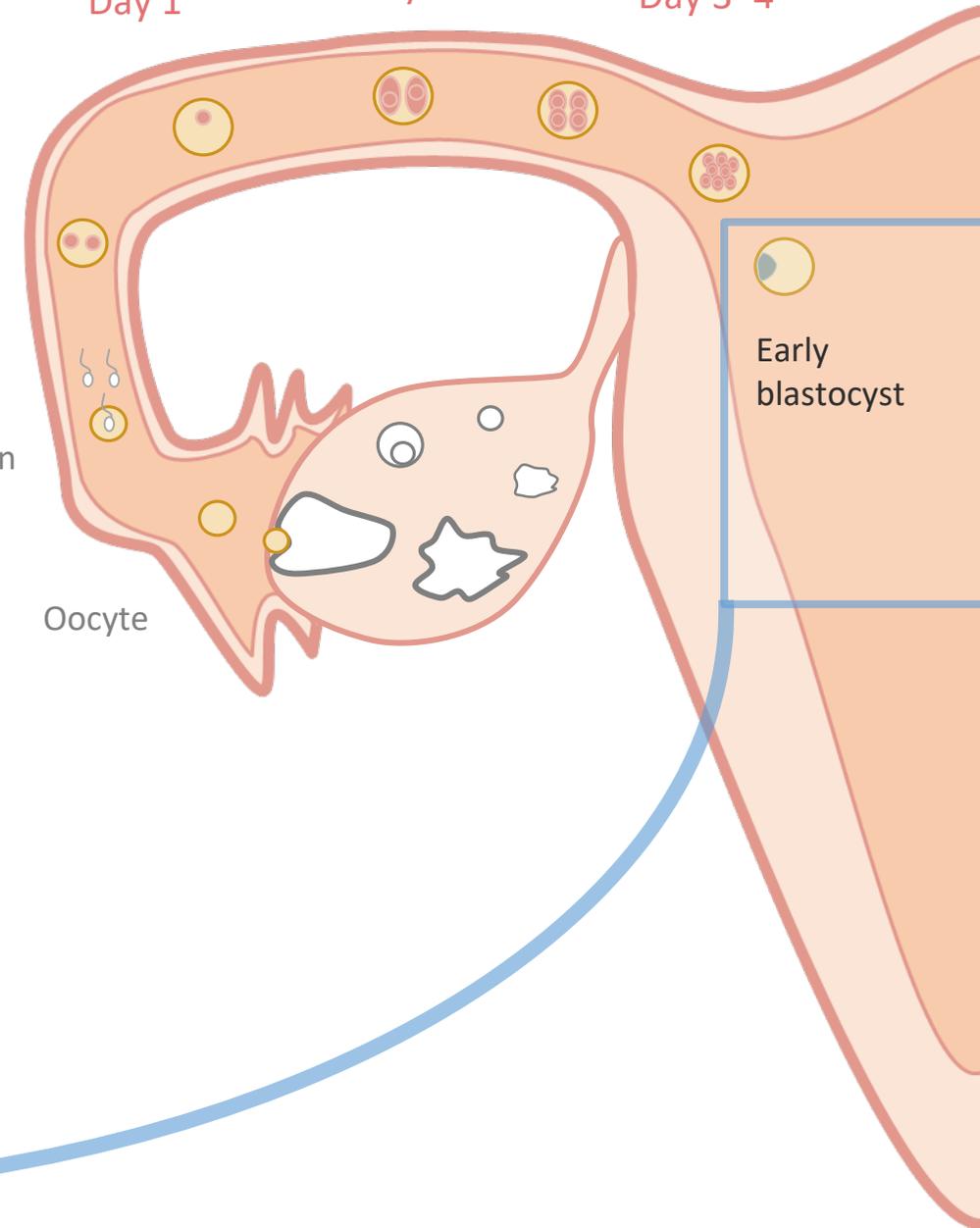
Fertilization

Oocyte

Day 1

Day 2

Day 3-4



Early blastocyst

Implantation

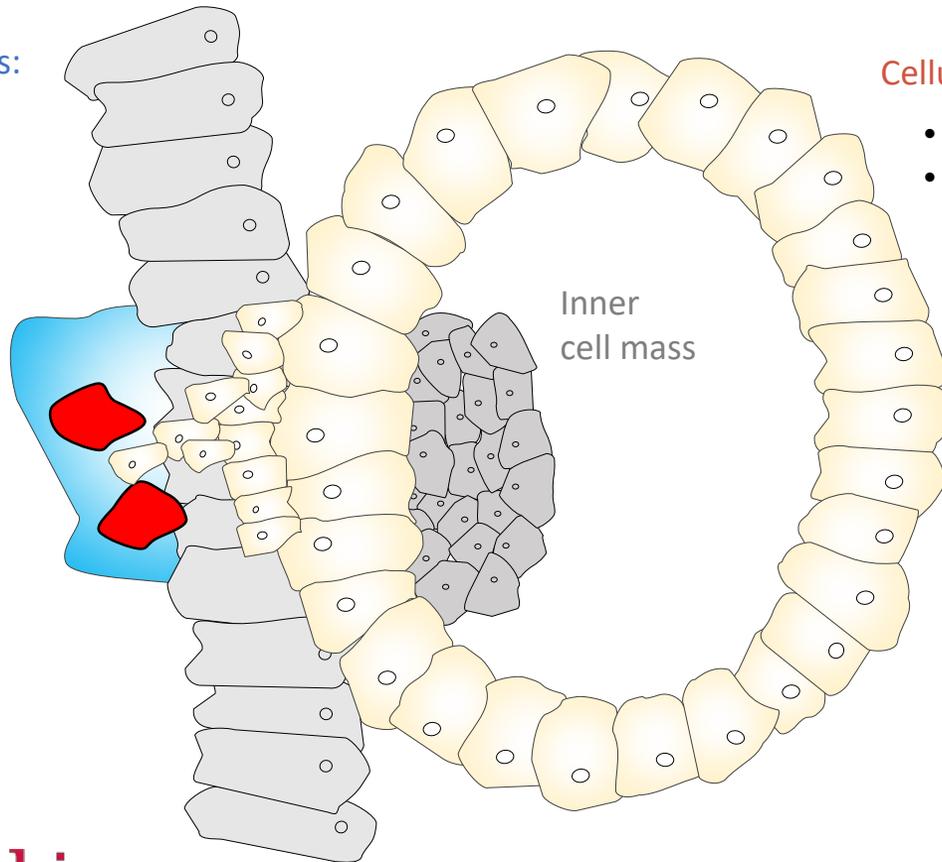
The blastocyst implants into the endometrium.

During implantation, trophoblasts differentiate into **syncytiotrophoblasts** and **cellular trophoblasts**.

Endometrium

Syncytiotrophoblasts:

- Digest the endometrium to form lacunae (blood-filled spaces of maternal blood)
- Produce beta-human chorionic gonadotropin (β -hCG)

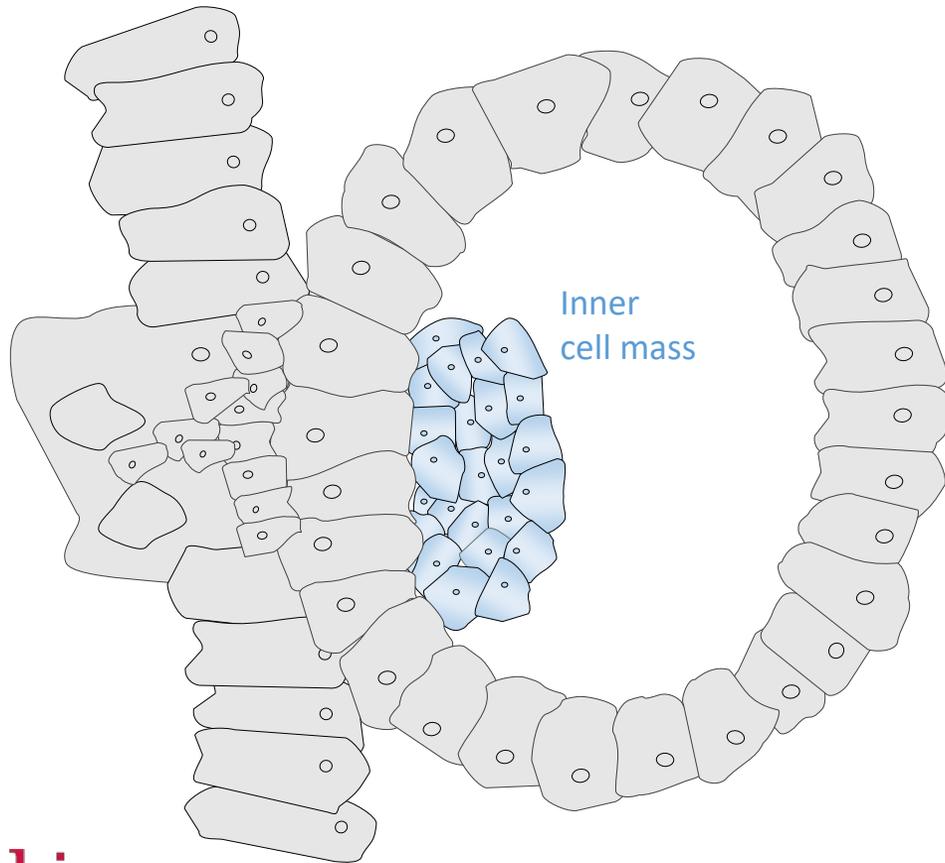


Cellular trophoblasts:

- Form chorionic villi
- Maternal blood from the lacunae bathes the chorionic villi, allowing for exchange of nutrients, waste, and gases between mother and fetus

Early Embryologic Development

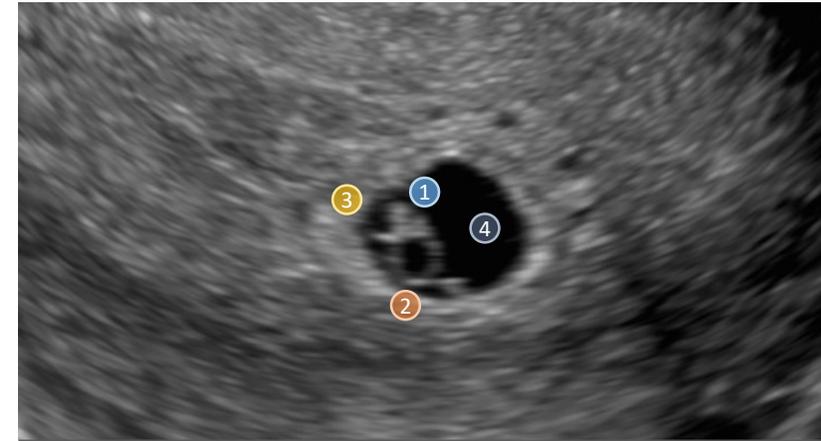
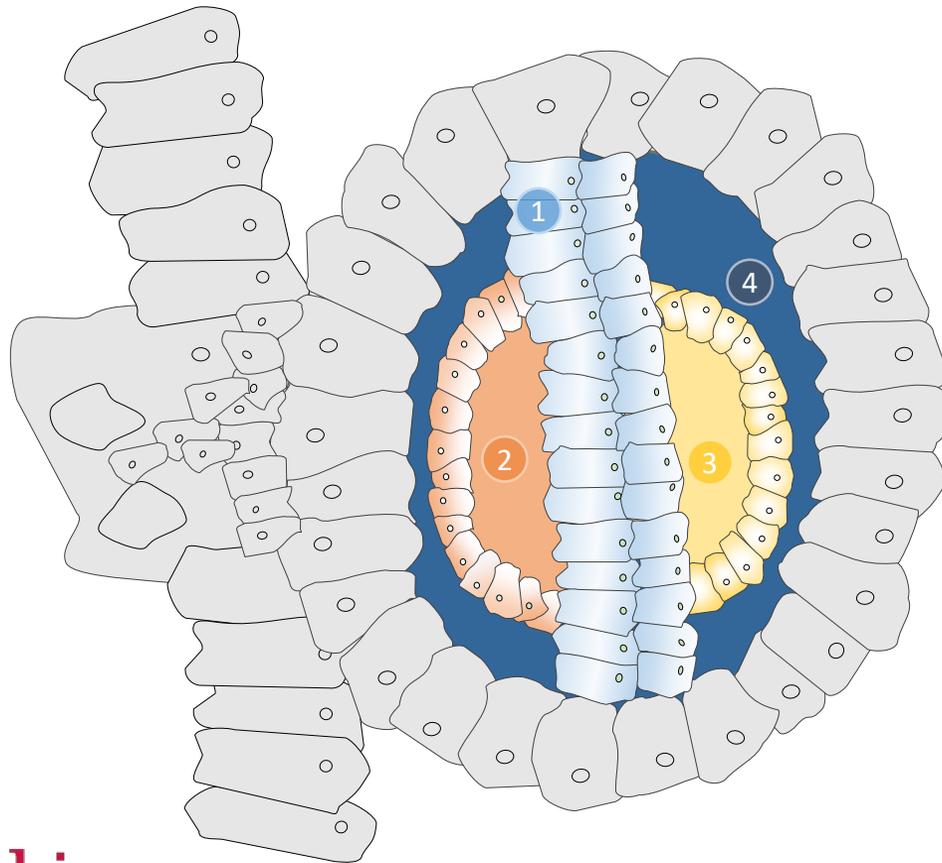
Endometrium



Inner cell mass pulls away from the proliferating trophoblasts.

Early Embryologic Development

Endometrium

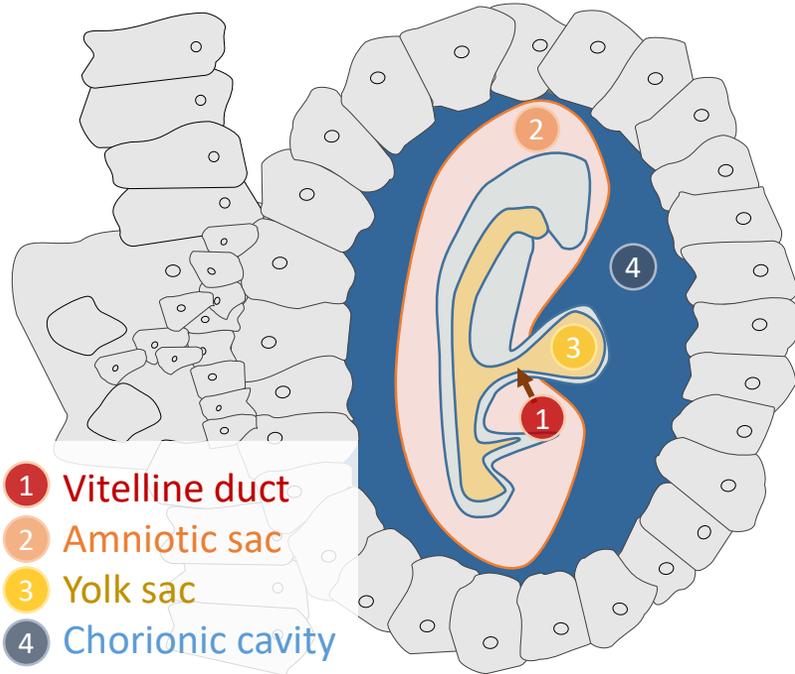


US image shows two cystic structures (2 3) flanking both sides of the fetal pole (1), representing the yolk sac and amniotic sac. These are surrounded by the chorionic cavity (4).

- 1 Inner cell mass pulls away from the proliferating trophoblasts.
- 2 An amniotic sac forms on one side.
- 3 A yolk sac forms on the other side.
- 4 Chorionic cavity surrounds the structures.

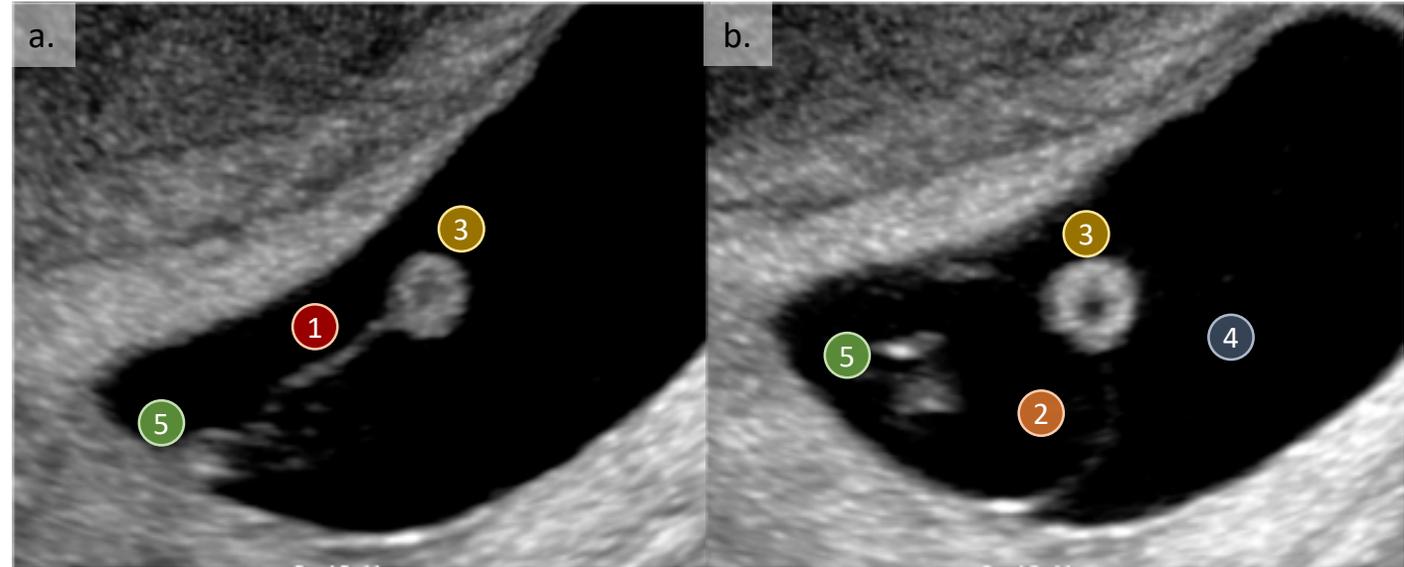
Early Embryologic Development

Endometrium



In early pregnancy, the vitelline duct (omphalomesenteric duct) can be seen. This vitelline duct connects the midgut to the yolk sac.

Failure of obliteration of the vitelline duct results in vitelline duct remnants such as the Meckel diverticulum.



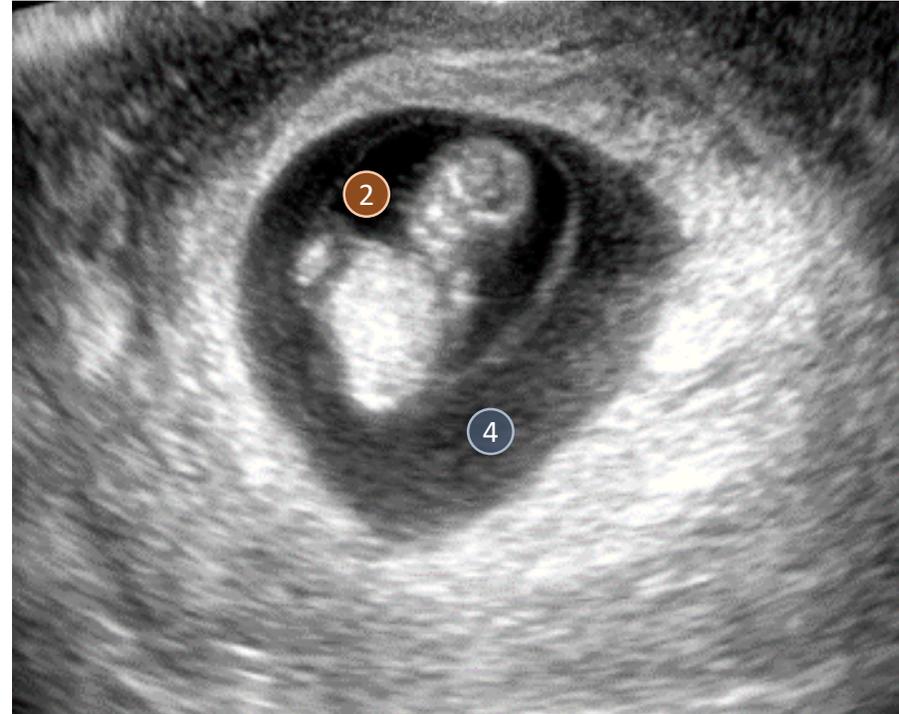
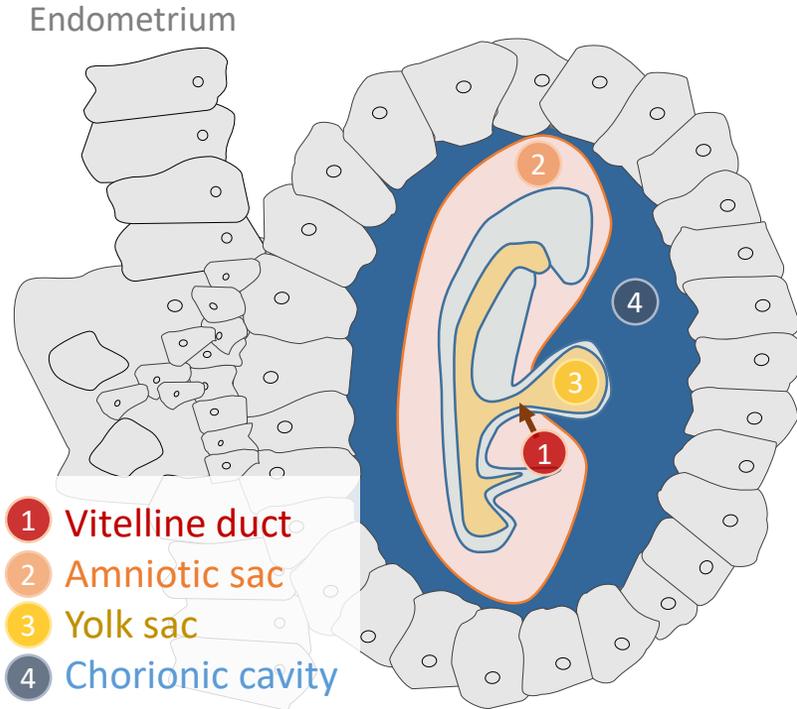
(a) US image shows the vitelline duct (1), which is seen connecting the fetal pole (5) to the yolk sac (3).

(b) US image shows the amniotic sac (2) surrounding the partially visualized fetal pole (5). These are surrounded by the chorionic cavity (4). The yolk sac (3) is also seen.

The amnion will eventually fuse with the chorion by 14 weeks gestation, and the chorionic cavity will obliterate.

Nonfusion of the chorion with the amnion after 14 weeks gestation is associated with fetal/chromosomal abnormalities.

Early Embryologic Development



US image shows fluid within the chorionic cavity that is gelatinous and as such contains diffuse internal echoes (4). This is in contrast to the more anechoic fluid of the amniotic sac (2).

This is considered normal and should not be mistaken for hemorrhage.

Timeline of Early Pregnancy

Gestational sac becomes visible
(5 weeks GA)



Embryo begins to show features and
rhombencephalon begins to form
(between 8–10 weeks GA)



Detailed anatomy
becomes more apparent
(12 weeks GA)



Gestational
Age (GA)

5 weeks

6 weeks

7 weeks

8 weeks

9 weeks

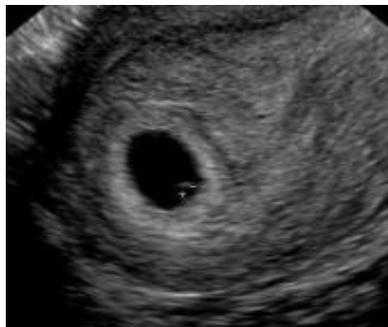
10 weeks

11 weeks

12 weeks

13 weeks

14 weeks



Yolk sac becomes visible
(5.5 weeks GA)



Fetal pole and heart motion become visible
(6 weeks GA)



Physiologic gut herniation completes
(begins at 6–8 weeks GA and completes at 12–13
weeks GA)



Yolk sac
no longer
visualized

Amnion fuses
with chorion
(14 weeks GA)

Gestational Sac

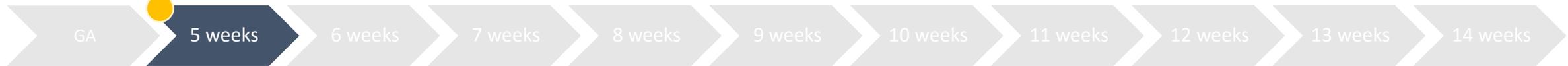
Gestational sac becomes visible
(5 weeks GA)



At 5–5 ½ weeks gestation, the gestational sac becomes visible.

With modern transvaginal US, any round or oval fluid collection visualized in a woman with a positive pregnancy test likely represents an intrauterine gestation and should be reported as such.³

It is less likely to be a decidual cyst or pseudogestational sac, which can be seen with ectopic pregnancies.



Terms such as *intradecidual sac sign* and *double decidual sac sign* were originally used to describe findings in the gestational sac at transabdominal US.

With the advent of transvaginal US, these signs were found to be absent in at least 35% of gestational sacs.³

Gestational Sac

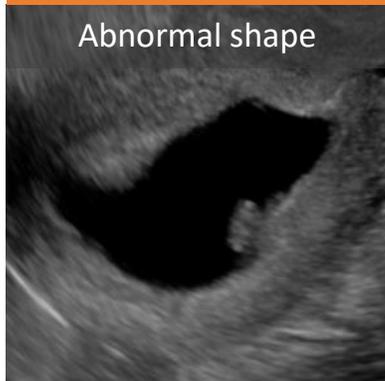
The gestational sac should be round or oval, appear smooth and well defined, have a decidua that is 2 mm or greater, and be positioned in the upper uterine body.⁴

Gestational sacs that deviate from this appearance are suspicious for abnormal pregnancies.⁴

US image shows a normal gestational sac



Abnormal Appearances of the Gestational Sac at US



Abnormal shape

Irregular margins and shape

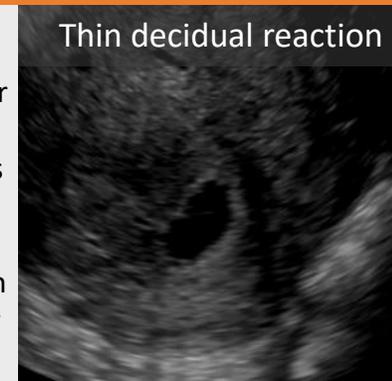
Associated with poor outcomes⁵



Small gestational sac

Normal mean sac diameter (MSD) should be greater than or equal to 5 mm larger than the crown rump length (CRL) at less than 9 weeks⁴

MSD less than 5 mm larger than the CRL is associated with poor outcomes⁶



Thin decidual reaction

Thin decidual reaction with weakly hyperechoic sac wall

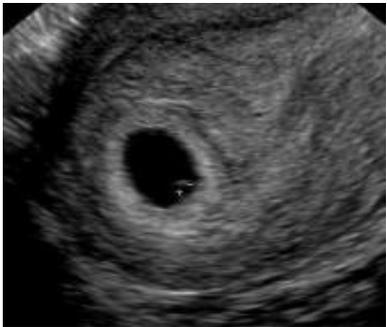
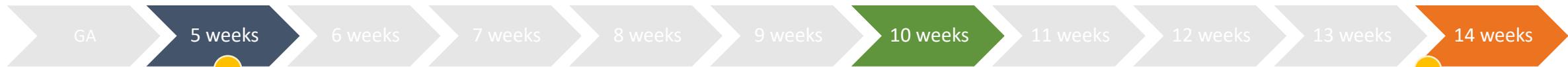
Associated with poor outcomes⁵

Yolk Sac

The yolk sac is the next structure to appear after the gestational sac, becoming visible at approximately 5.5 weeks GA.

The yolk sac gradually enlarges until 10 weeks GA, measuring up to 5–6 mm.

After 10 weeks, the yolk sac begins to shrink until it is no longer visualized beyond 14 weeks GA.

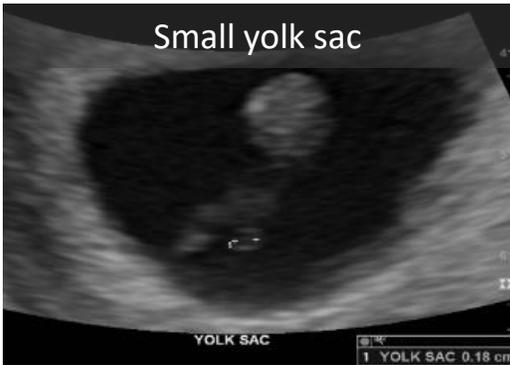


Yolk sac becomes visible
(5.5 weeks GA)

Yolk sac
no longer
visualized

Yolk Sac

Variable and Abnormal Appearances of the Yolk Sac at US



Small yolk sacs visualized in very early pregnancy (before expected shrinking after 10 weeks)

- Scant knowledge of outcomes
- Limited study showed a sac less than 2 mm is associated with poor outcomes⁷
- Prudent to recommend close follow-up



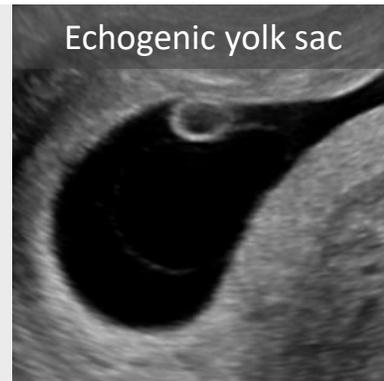
Large yolk sac (> 5–6 mm)

- Associated with increased risk of demise⁸



Abnormal in early pregnancy if the embryo had been present while the yolk sac was involuting

Generally associated with embryonic demise⁹



Internal echoes within the yolk sac anecdotally are not associated with poor outcomes¹⁰

Differential diagnosis: calcified yolk sac (calcified rather than echogenic material in the yolk sac), which is associated with failed IUP¹¹



Wrinkled margins and indented walls

Effect on outcomes is a topic of debate, but more recent studies suggest no change in outcomes¹⁰

Yolk Sac

Visualization of multiple yolk sacs is the earliest sign of a multigestational pregnancy.¹²

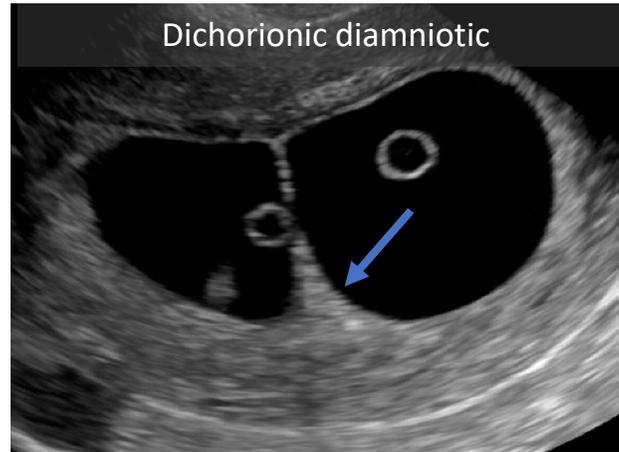
The number of yolk sacs matches the number of amniotic sacs if the embryos are alive.¹²

The first trimester is the easiest time to determine chorionicity and amnionicity of a multigestational pregnancy.¹³



US image shows a single chorionic cavity without an intervening membrane (monochorionic).

Two yolk sacs (1, 2) are identified (diamniotic).



US image shows two chorionic cavities (dichorionic), which are divided by a thick triangular-shaped membrane (arrow). This is referred to as the twin peak sign or lambda (λ) sign.¹⁴

Two yolk sacs are identified (diamniotic).



US image shows two embryos (1, 2).

One chorionic cavity is visualized (monochorionic).

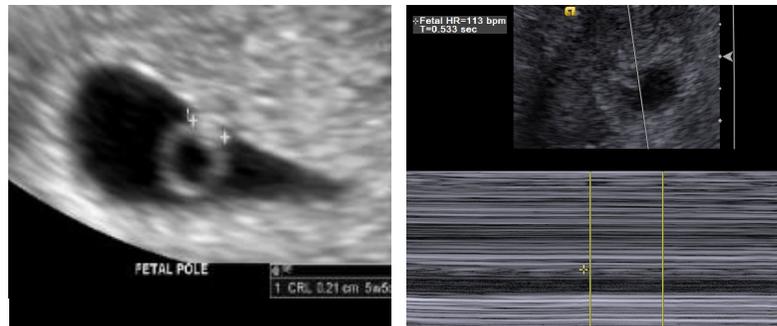
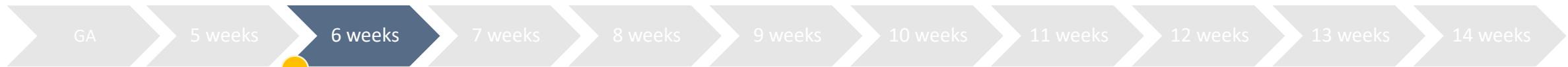
One yolk sac is also identified (monoamniotic).

Fetal Heart Rate

Fetal heart motion is usually detectable around 6 weeks GA (usually visible as soon as the embryo is detectable).

The lower limit of normal for fetal heart rate (FHR) is 100 beats per minute (bpm) (at GA < 6.2 weeks) and 120 bpm (at GA > 6.2 weeks).¹⁵

An FHR less than or equal to 90 bpm in the first trimester carries a dismal prognosis.¹⁵



Fetal pole and heart motion become visible (6 weeks GA)

FHR

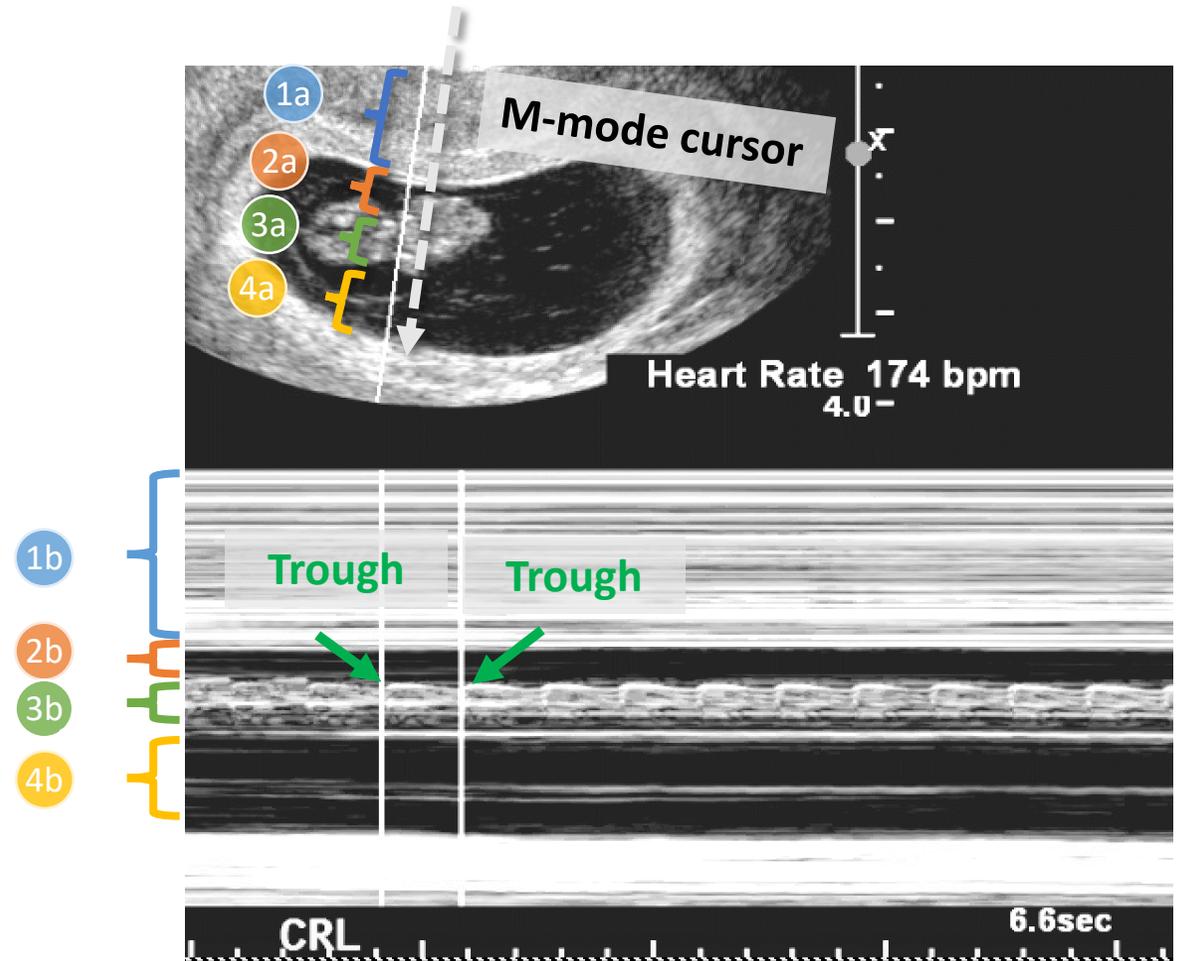
M-mode is used to measure FHR.

M-mode US image displays motion along a chosen US line. For example, the hyperechoic area (1a) on the grayscale US image corresponds to a hyperechoic area (1b) on the M-mode image. The hypoechoic areas (2a, 4a) on the grayscale US image correspond to the hypoechoic areas (2b, 4a) on the M-mode image.

The echoes encountered along the chosen US line are mapped over time, creating the M-mode image.

At depth of (3b), rhythmic echoes are noted, representing movement of the beating heart (3a).

FHR is calculated by measuring the distance from trough to trough of two subsequent waves.



FHR

M-mode is the preferred US mode over color and pulsed (spectral) Doppler US.

Color and pulsed-wave Doppler US are associated with higher power output (Table).

Although there is no evidence that color and pulsed-wave Doppler US are harmful, all but brief insonation is not recommended during the embryonic period.¹⁶

Spectral Doppler US should only be employed when there is a clear benefit-risk advantage and both thermal index ($TI < 1$) and examination duration are kept low.¹⁷

Table: Comparison of Spatial Peak–Temporal-Average Intensity (I_{SPTA}) between US Modes¹⁸

US Mode	I_{SPTA} (mW/cm ²)
M-mode	121
Color Doppler	344
Pulsed Doppler	1659
mW = milliwatt	

Fetal Rhombencephalon

US image shows that the embryo begins to show features and rhombencephalon begins to form (between 8–10 weeks GA)



The fetal rhombencephalon (which forms the medulla, pons, and cerebellum) is visible between 8 and 10 weeks GA.

It appears as a rounded anechoic structure in the posterior brain (**arrow**).

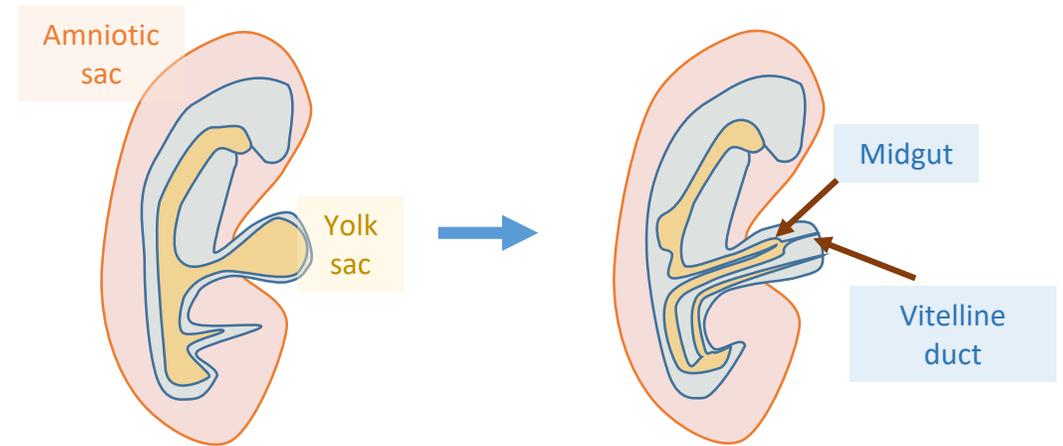
This is a normal finding and should not be misinterpreted as a condition.

Physiologic Herniation of Bowel

Physiologic gut herniation occurs normally beginning from 6 to 8 weeks GA.

The bowel then undergoes a 270° counter-clockwise rotation and returns into the abdominal cavity around 12–13 weeks GA.

This is a normal finding prior to 12–13 weeks GA and may be mistaken for gastroschisis or omphalocele.



US image shows a completed physiologic gut herniation (begins 6–8 weeks GA, completes 12–13 weeks GA)

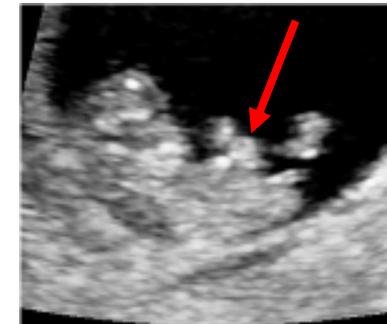
Physiologic Herniation of Bowel¹⁹

US findings:

- Manifests as an abdominal wall mass at the base of the umbilical cord
- Should be 4–7 mm in a fetus with a CRL of 19–41 mm

Abnormal US findings:

- Should not be present after 12–13 weeks
- Should not be seen with a CRL greater than 44 mm
- Should be smaller than the fetal abdomen



A small echogenic mass is visualized in the anterior abdominal wall (**arrow**), representing a physiologic herniated bowel.

US image shows a completed physiologic gut herniation (begins 6–8 weeks GA, completes 12–13 weeks GA)

Assessment of GA²⁰

Determination of GA is more accurate the earlier US is performed.

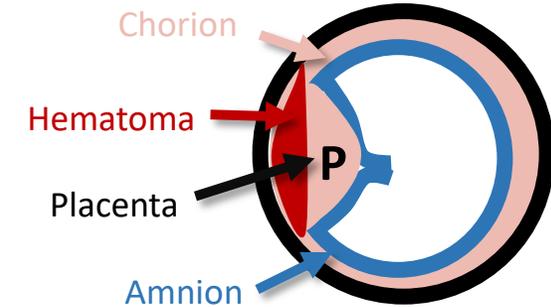
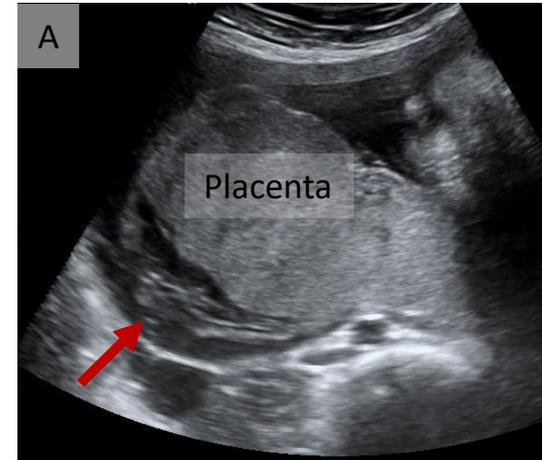
- MSD measurements are not recommended for estimating due date.
- CRL is the most accurate method to establish GA (up to and including 13 6/7 weeks of gestation).
- Beyond a CRL of 84 mm (14 weeks, 0 days), dating on the basis of CRL becomes less accurate, and other second-trimester biometric parameters should be used. These parameters (biparietal diameter, abdominal circumference, head circumference, and femur length) are used to determine the arithmetic US age.
- At a GA of 8 6/7 weeks or less (based on last menstrual period [LMP]), US dating should be used if the LMP dating and US dating differ by more than 5 days.
- At a GA between 9 0/7 weeks and 13 6/7 weeks (on the basis of the LMP), US dating should be used if the LMP dating and US dating differ by more than 7 days.
- The estimated due date (EDD), if based on US dating, should be based on the earliest US examination of a CRL measurement. Changes to the EDD should be reserved for rare circumstances.

Perigestational Hemorrhage

Perigestational hemorrhage refers to hemorrhages that occur around the fetus. Subchorionic hemorrhages are the most common type but are not the only type.

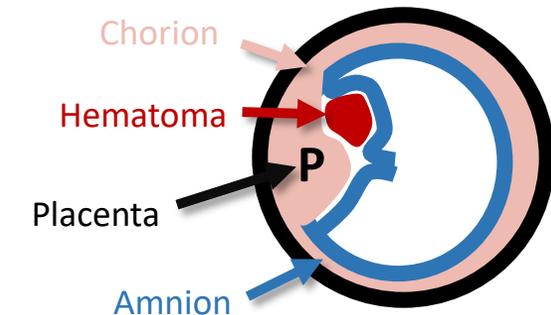
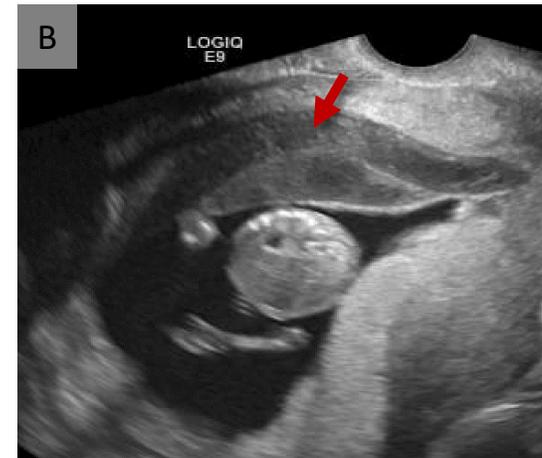
Retroplacental hematoma (Figure A)

- Illustration (right) demonstrates a retroplacental hematoma.
- US image (left) shows a hematoma (arrow) that separates the placenta from the uterine wall.
- The source of bleeding is probably from the spiral arteries.
- The term *placental abruption* is usually reserved for after 20 weeks GA.²¹
- Frequency of fetal demise is 50%.²²



Subamniotic hematoma (Figure B)

- Illustration (right) demonstrates a subamniotic hematoma.
- US image (left) shows a hematoma (arrow) that is contained within the amnion and chorion and extends anteriorly to the placenta, but it is limited by the reflection of the amnion on the placental insertion site of the umbilical cord.
- This results from the rupture of the chorionic vessels.
- This is a rare entity.



Subchorionic Hemorrhage

Subchorionic hemorrhage is a frequent cause of first- and second-trimester bleeding.

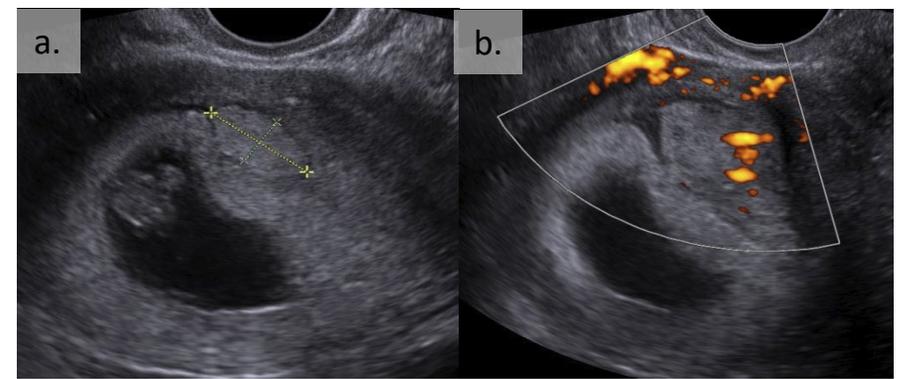
Occurs when blood collects between the chorion and uterine wall

Vaginal bleeding may occur if the blood leaks to the cervical canal.

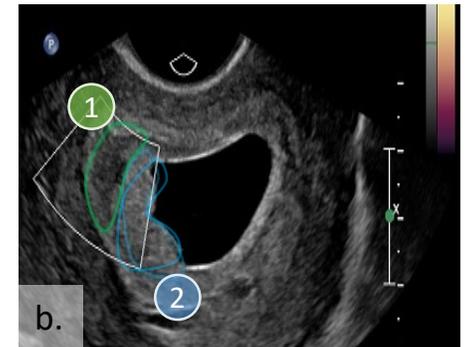
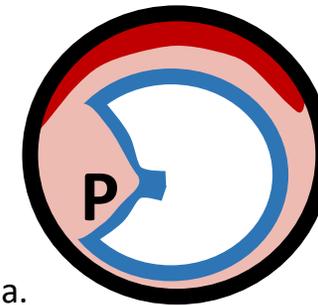
Outcomes are dependent on the size of the subchorionic hemorrhage, maternal age, and GA of the fetus (discussed in the next slide).

US findings:

- Crescentic collection of variable echotexture elevates the chorionic membrane
- Echotexture varies depending on the age of the blood
 - Acute: hyperechoic (may be difficult to delineate from the chorion)
 - Subacute to chronic: decreasing echogenicity over time
- May be considered a marginal subchorionic hemorrhage if the hematoma extends to the margin of the placenta



Acute subchorionic hemorrhage. US image (a) and color Doppler US image (b) show a small collection deep to the chorion that appears hyperechoic and is potentially difficult to differentiate from the chorion. The hyperechoic appearance suggests an acute hemorrhage.



(a) Illustration demonstrates a subacute marginal subchorionic hemorrhage. *P* = placenta. (b) US power Doppler image shows a collection deep relative to the chorion, with a hypoechoic fluid collection (1) along the margin of the placenta (2), representing a marginal subchorionic hemorrhage. The hypoechoic appearance suggests a subacute hemorrhage.

Subchorionic Hemorrhage

Table. Subchorionic Hemorrhages and the Risk of Spontaneous Abortion

Factor	Risk of Spontaneous Abortion*	Crude Relative Risk
Size of hemorrhage		
Small	7.7%	1
Medium	9.2%	1.2
Large	18.8%	2.4
Maternal age		
< 35 y	7.3%	1
≥ 35 y	13.8%	1.9
GA		
> 8 wk	5.9%	1
≤ 8 wk	13.7%	2.3

Note.—*Overall rate of all spontaneous abortions in this study was 9.3%.

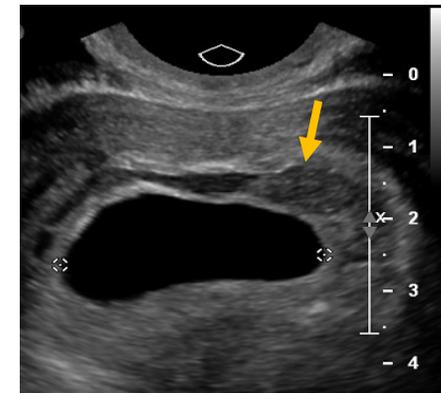
Source.—Data are from reference 23.

The relative risk of spontaneous abortion from subchorionic hemorrhage is dependent on the size of the hemorrhage, maternal age, and gestational age.²³

The relative risk increases with large subchorionic hemorrhage, a maternal age of 35 years or more, and a GA less than or equal to 8 weeks.²³

In this study, the size of subchorionic hemorrhage was defined as:

- Small: hemorrhage surrounds less than one-third of the chorion
- Medium: hemorrhage surrounds one-third to one-half of the chorion
- Large: hemorrhage surrounds more than two-thirds of the chorion



US image shows a hypoechoic collection (arrow) that surrounds slightly less than two-thirds of the chorion, representing a medium-sized subchorionic hemorrhage.

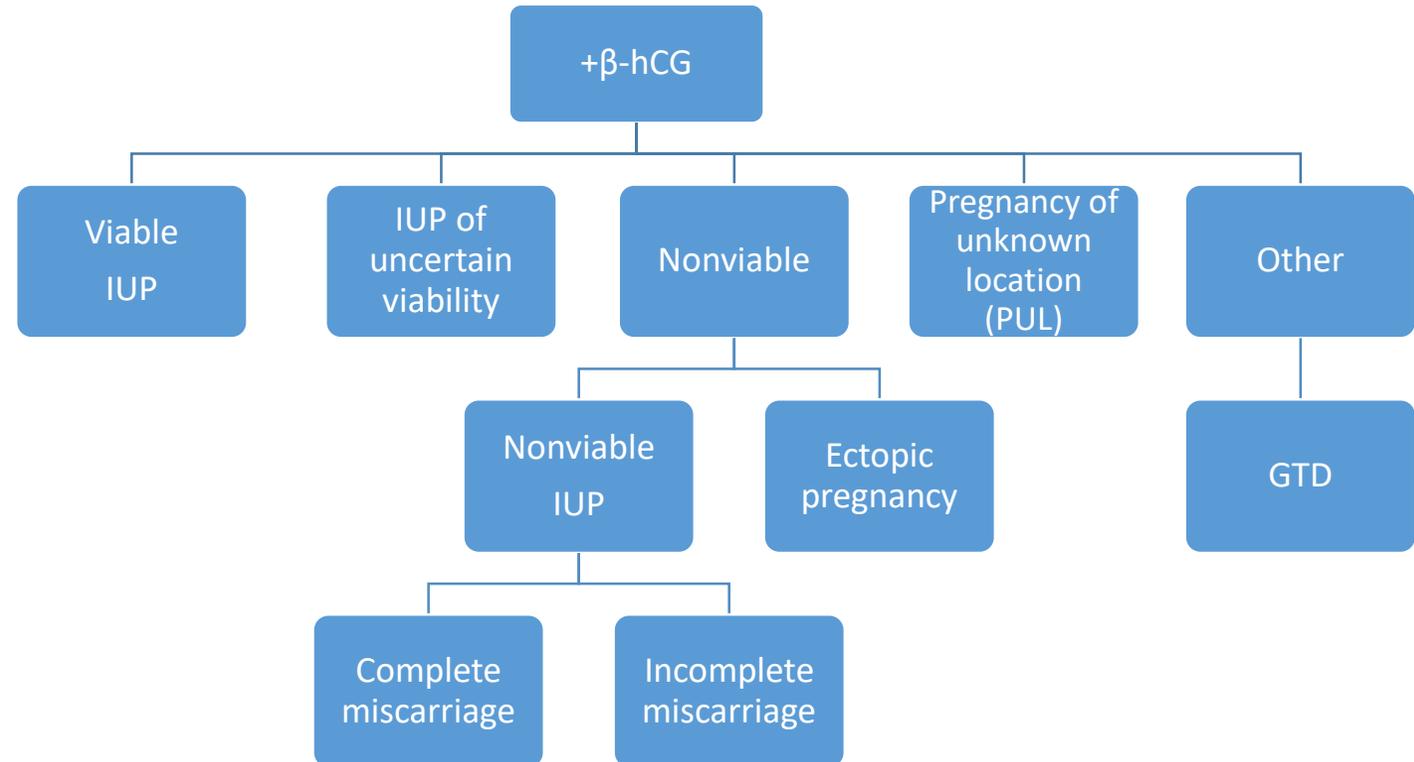
Algorithm of First-Trimester Pregnancies

In early pregnancy, US is important to first confirm an IUP.

Once an IUP has been confirmed, it is important to determine the viability of the pregnancy.

It is important to distinguish between:

- Findings definitive for pregnancy failure
- Findings that are suspicious but not definitive for pregnancy failure, which will require follow-up testing to establish a definitive diagnosis²⁴

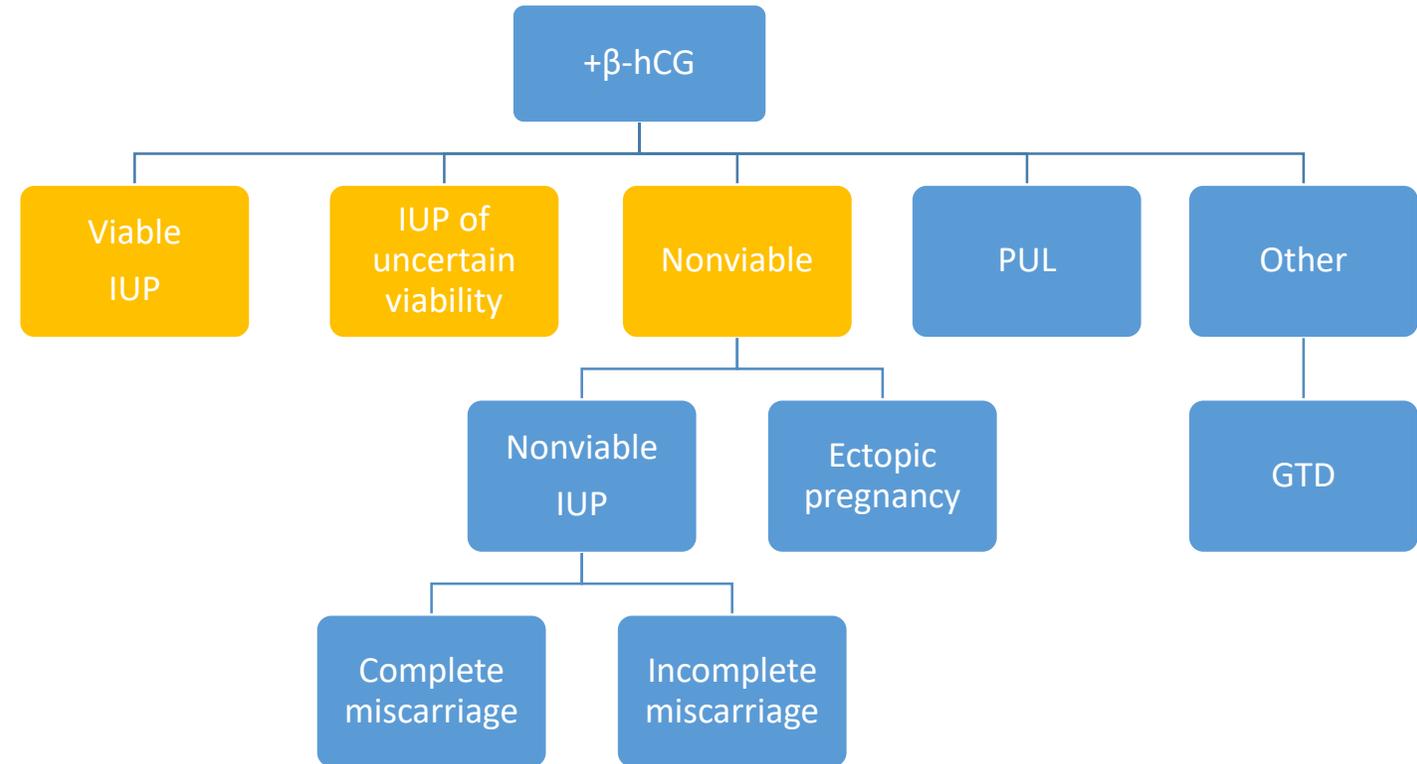


Determining Viability

In 2012, the criteria for diagnosing nonviability were made more stringent to virtually eliminate false-positive US results.³

In general, false-positive results at US of the first-trimester pregnancy have worse consequences than false-negative results.

- False-positive results:
 - Diagnosing a viable pregnancy as nonviable may result in interventions that would harm a viable IUP.
- False-negative results:
 - Diagnosing a nonviable pregnancy as viable may result in short treatment delay.
 - Diagnosing an ectopic pregnancy as a PUL, which causes a short treatment delay in a stable woman with good follow-up, is less harmful than a false-positive diagnosis of ectopic pregnancy, which would harm a viable IUP.



Determining Viability

The criteria most often used to diagnose pregnancy failure are:

- Absence of cardiac activity by the time the embryo has reached a certain length (1).
- Absence of an embryo by the time a gestational sac has grown to a certain size (2).
- Absence of an embryo after a certain point in time (3).

Findings Diagnostic of Pregnancy Failure³

- 1 CRL \geq 7 mm and no heartbeat
- 2 MSD \geq 25 mm and no embryo
- 3a Absence of embryo with heartbeat \geq 2 weeks after a US scan that showed a gestational sac without a yolk sac
- 3b Absence of an embryo with a heartbeat \geq 11 days after a US scan that showed a gestational sac with a yolk sac

Pregnancy Failure

The criteria most often used to diagnose pregnancy failure are:

- Absence of cardiac activity by the time the embryo has reached a certain length (1).
- Absence of an embryo by the time a gestational sac has grown to a certain size (2).
- Absence of an embryo after a certain point in time (3).

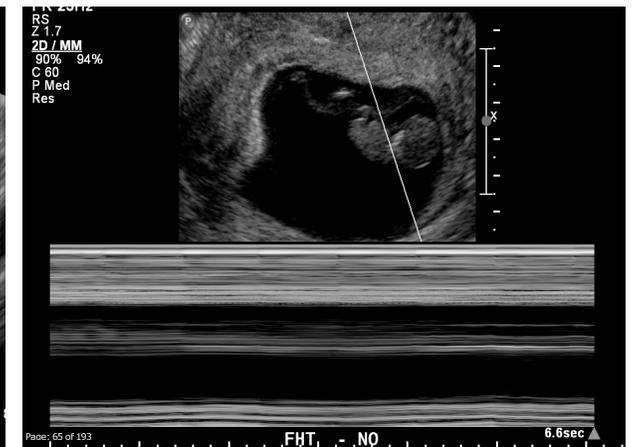
US (a) and M-mode (b) images show a CRL of 24 mm and no heartbeat, compatible with pregnancy failure.

Findings Diagnostic of Pregnancy Failure³

- 1 CRL \geq 7 mm and no heartbeat
- 2 MSD \geq 25 mm and no embryo
- 3a Absence of embryo with heartbeat \geq 2 weeks after a US scan that showed a gestational sac without a yolk sac
- 3b Absence of an embryo with a heartbeat \geq 11 days after a US scan that showed a gestational sac with a yolk sac



a



b

Pregnancy Failure

The criteria most often used to diagnose pregnancy failure are:

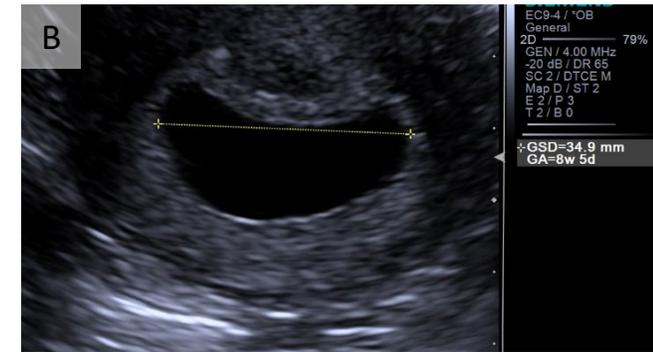
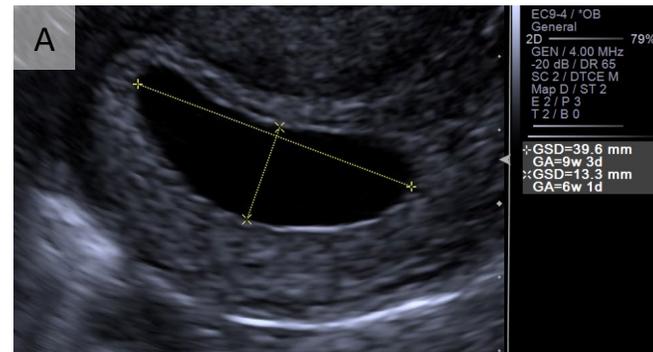
- Absence of cardiac activity by the time the embryo has reached a certain length (1).
- Absence of an embryo by the time a gestational sac has grown to a certain size (2).
- Absence of an embryo after a certain point in time (3).

US images show an MSD of 29.3 mm with no embryo, compatible with pregnancy failure.

This is also referred to as an anembryonic pregnancy, where a gestational sac forms without an embryo. This is also sometimes referred to as a blighted ovum.

Findings Diagnostic of Pregnancy Failure³

- 1 CRL \geq 7 mm and no heartbeat
- 2 MSD \geq 25 mm and no embryo
- 3a Absence of embryo with heartbeat \geq 2 weeks after a US scan that showed a gestational sac without a yolk sac
- 3b Absence of an embryo with a heartbeat \geq 11 days after a US scan that showed a gestational sac with a yolk sac



Pregnancy Failure

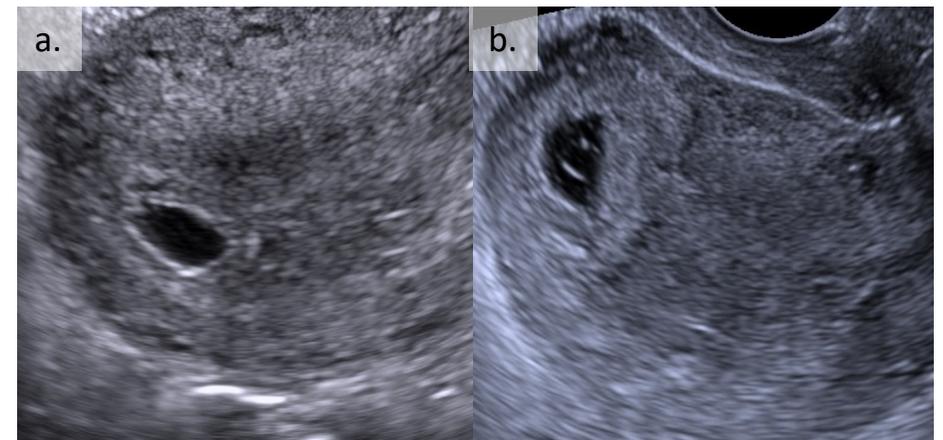
The criteria most often used to diagnose pregnancy failure are:

- Absence of cardiac activity by the time the embryo has reached a certain length (1).
- Absence of an embryo by the time a gestational sac has grown to a certain size (2).
- Absence of an embryo after a certain point in time (3).

Initial US image (a) shows a gestational sac without a yolk sac. Follow-up US image (b) obtained 2 weeks later shows a yolk sac with absence of an embryo with a heartbeat, compatible with pregnancy failure.

Findings Diagnostic of Pregnancy Failure³

- 1 CRL \geq 7 mm and no heartbeat
- 2 MSD \geq 25 mm and no embryo
- 3a Absence of embryo with heartbeat \geq 2 weeks after a US scan that showed a gestational sac without a yolk sac
- 3b Absence of an embryo with a heartbeat \geq 11 days after a US scan that showed a gestational sac with a yolk sac



Pregnancy Failure

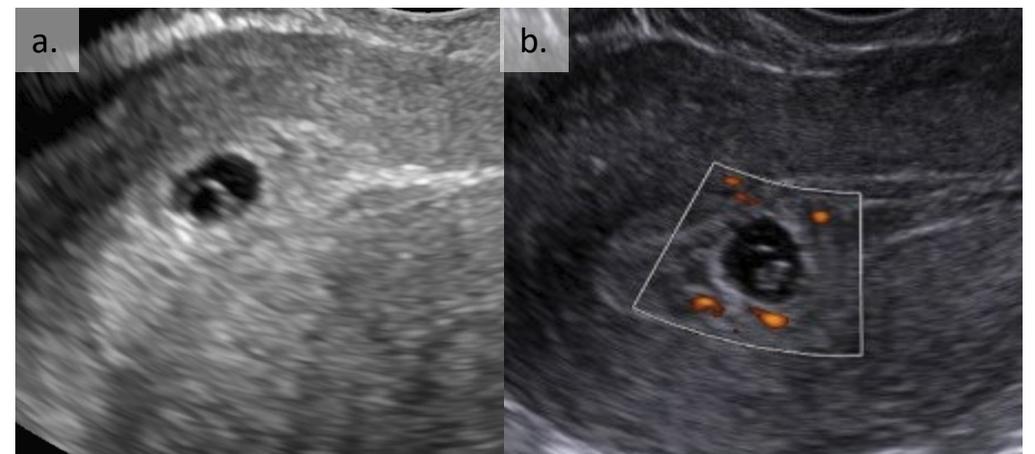
The criteria most often used to diagnose pregnancy failure are:

- Absence of cardiac activity by the time the embryo has reached a certain length (1).
- Absence of an embryo by the time a gestational sac has grown to a certain size (2).
- Absence of an embryo after a certain point in time (3).

US image (a) obtained during an initial examination shows a gestational sac with a yolk sac. Follow-up US image (b) obtained 11 days later shows an embryo without a heartbeat, compatible with pregnancy failure.

Findings Diagnostic of Pregnancy Failure³

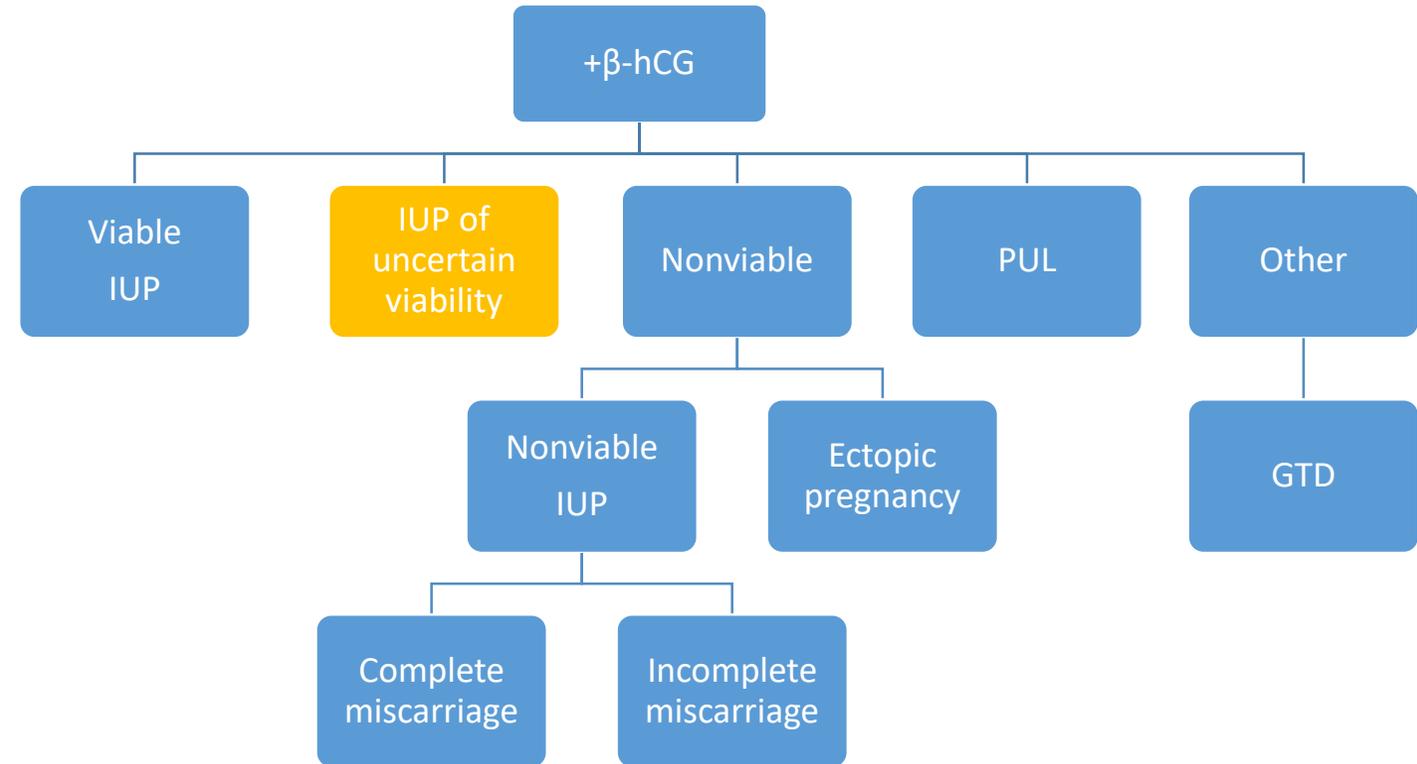
- 1 CRL ≥ 7 mm and no heartbeat
- 2 MSD ≥ 25 mm and no embryo
- 3a Absence of embryo with heartbeat ≥ 2 weeks after a US scan that showed a gestational sac without a yolk sac
- 3b Absence of an embryo with a heartbeat ≥ 11 days after a US scan that showed a gestational sac with a yolk sac



Intrauterine Pregnancy of Uncertain Viability

If an intrauterine gestational sac does not show an embryonic heartbeat or definitive findings of pregnancy failure, the pregnancy is considered to be of uncertain viability.

If there is suspicion of pregnancy failure, a follow-up US performed within 7–10 days to reassess viability is generally appropriate.³



IUP of Uncertain Viability

The Society of Radiologists in Ultrasound consensus findings that are suspicious for but not diagnostic of pregnancy failure are listed in the table.

If there is any suspicion of pregnancy failure, a follow-up US performed in 7–10 days to reassess viability is generally appropriate.³

US Findings Suspicious for but not Diagnostic of Pregnancy Failure

CRL < 7 mm and no heartbeat

MSD 16–25 mm and no embryo

Absence of embryo with heartbeat 7–13 days after a US scan that showed a gestational sac without a yolk sac

Absence of embryo with heartbeat 7–10 days after a US scan that showed a gestational sac with a yolk sac

Absence of an embryo \geq 6 weeks after last menstrual period

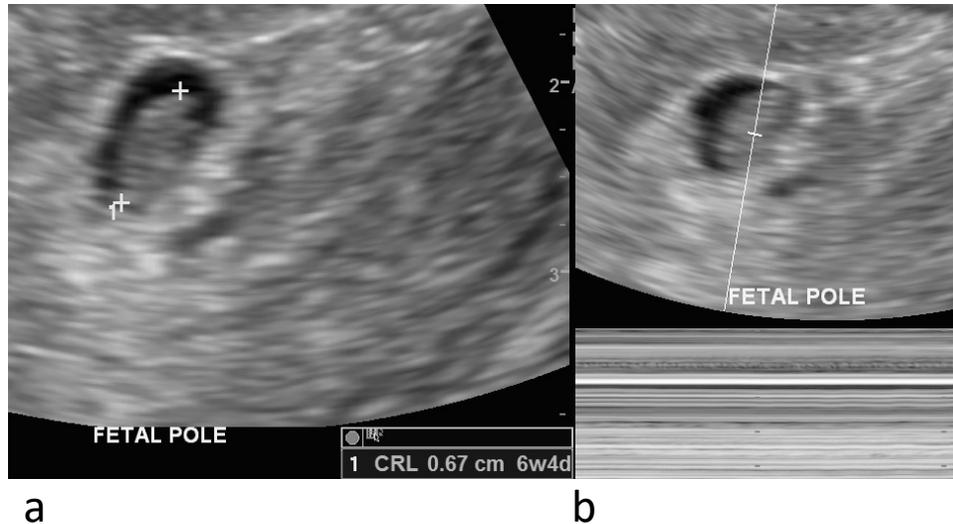
Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5-mm difference between MSD and CRL)

Note.—Data are from Reference 3.

IUP of Uncertain Viability



(a) US image of an IUP shows a CRL of less than 7 mm. (b) M-mode image shows no fetal heartbeat. The gestational sac is also small, as demonstrated by the large embryo in relation to the gestational sac.

These findings are suspicious for but not diagnostic of pregnancy failure.

US Findings Suspicious for but not Diagnostic of Pregnancy Failure

CRL < 7 mm and no heartbeat

MSD 16–25 mm and no embryo

Absence of embryo with heartbeat 7–13 days after a US scan that showed a gestational sac without a yolk sac

Absence of embryo with heartbeat 7–10 days after a US scan that showed a gestational sac with a yolk sac

Absence of an embryo \geq 6 weeks after last menstrual period

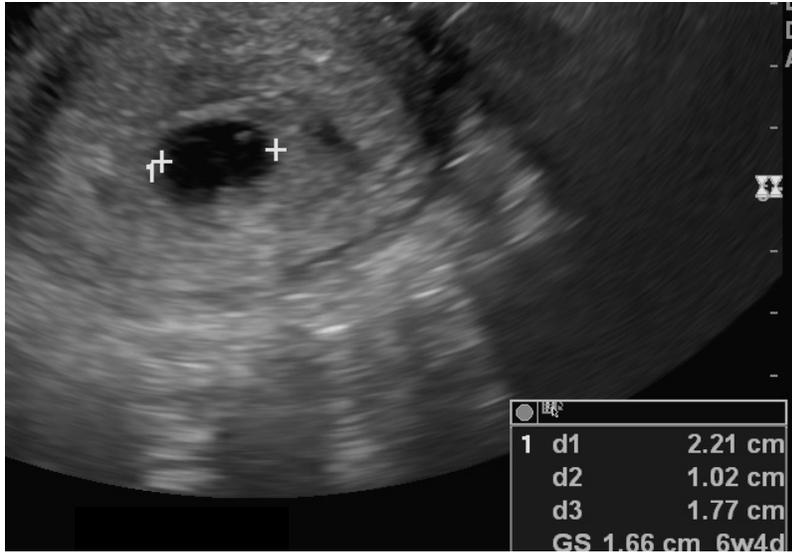
Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5-mm difference between MSD and CRL)

Note.—Data are from Reference 3.

IUP of Uncertain Viability



US image of an IUP shows an MSD (length + height + width/3) of 16.6 mm without an embryo.

This finding is suspicious for but not diagnostic of pregnancy failure.

US Findings Suspicious for but not Diagnostic of Pregnancy Failure

CRL < 7 mm and no heartbeat

MSD 16–25 mm and no embryo

Absence of embryo with heartbeat 7–13 days after a US scan that showed a gestational sac without a yolk sac

Absence of embryo with heartbeat 7–10 days after a US scan that showed a gestational sac with a yolk sac

Absence of an embryo \geq 6 weeks after last menstrual period

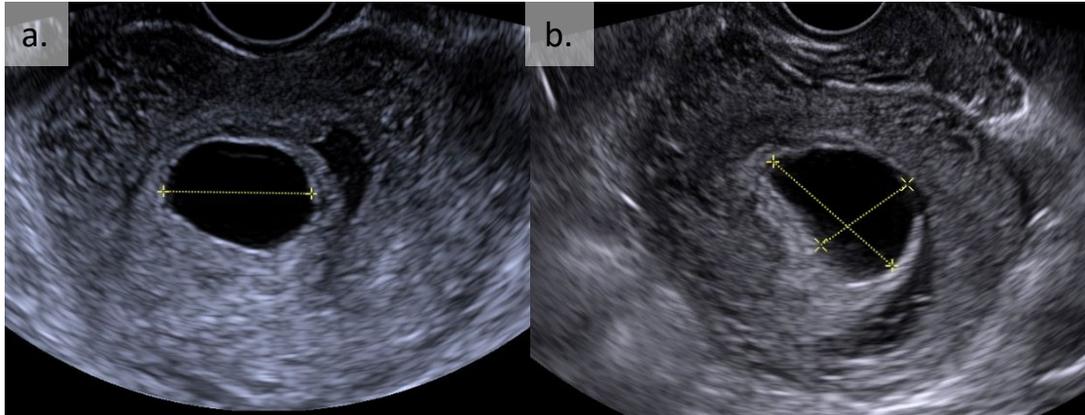
Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5-mm difference between MSD and CRL)

Note.—Data are from Reference 3.

IUP of Uncertain Viability



(a) US image obtained during the initial examination shows a gestational sac without an embryo or yolk sac. **(b)** Follow-up US image obtained 9 days later shows no embryo with a heartbeat.

This finding is suspicious for but not diagnostic of pregnancy failure.

US Findings Suspicious for but not Diagnostic of Pregnancy Failure

CRL < 7 mm & no heartbeat

MSD 16–25 mm and no embryo

Absence of embryo with heartbeat 7–13 days after a US scan that showed a gestational sac without a yolk sac

Absence of embryo with heartbeat 7–10 days after a US scan that showed a gestational sac with a yolk sac

Absence of an embryo \geq 6 weeks after last menstrual period

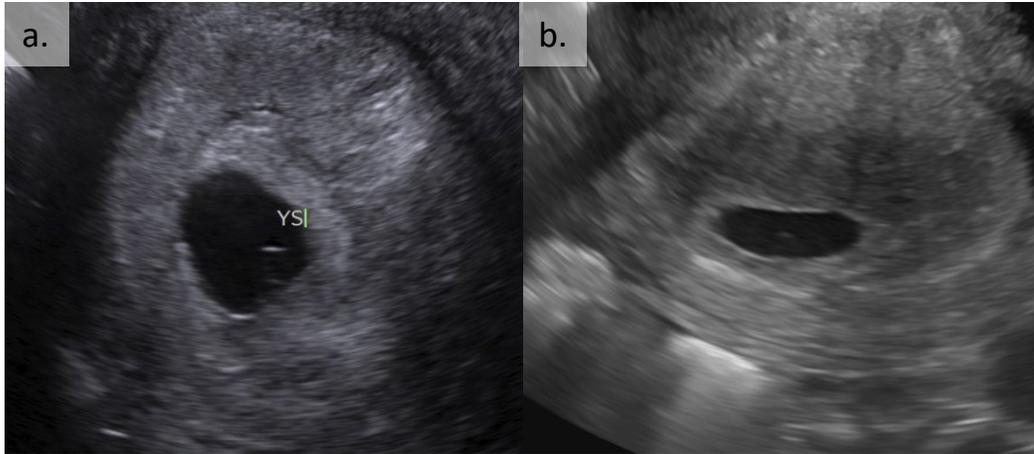
Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5-mm difference between MSD and CRL)

Note.—Data are from Reference 3.

IUP of Uncertain Viability



(a) US image obtained during initial examination shows a gestational sac with a yolk sac but no embryo. **(b)** Follow-up US image obtained 7 days later shows no embryo with a heartbeat.

This finding is suspicious for but not diagnostic of pregnancy failure.

US Findings Suspicious for but not Diagnostic of Pregnancy Failure

CRL < 7 mm and no heartbeat

MSD 16–25 mm and no embryo

Absence of embryo with heartbeat 7–13 days after a US scan that showed a gestational sac without a yolk sac

Absence of embryo with heartbeat 7–10 days after a US scan that showed a gestational sac with a yolk sac

Absence of an embryo \geq 6 weeks after last menstrual period

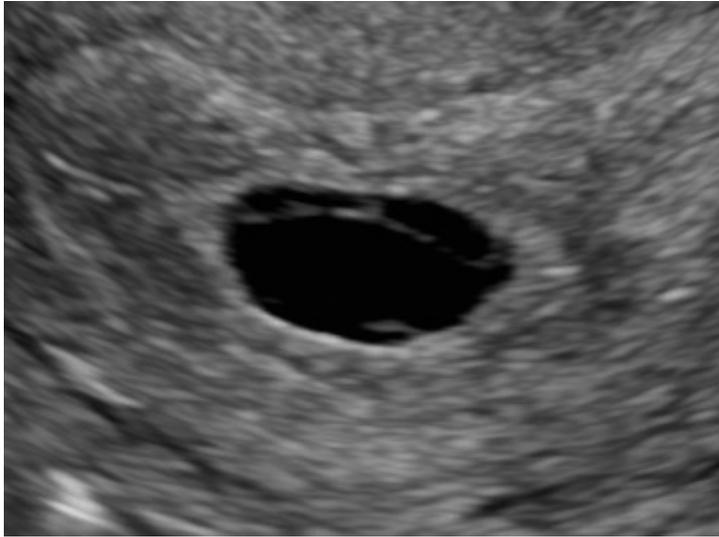
Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5-mm difference between MSD and CRL)

Note.—Data are from Reference 3.

IUP of Uncertain Viability



US image shows a gestational sac and amniotic sac without an embryo, reflecting an empty amnion.

This finding is suspicious for but not diagnostic of pregnancy failure.

US Findings Suspicious for but not Diagnostic of Pregnancy Failure

CRL < 7 mm and no heartbeat

MSD 16–25 mm and no embryo

Absence of embryo with heartbeat 7–13 days after a US scan that showed a gestational sac without a yolk sac

Absence of embryo with heartbeat 7–10 days after a US scan that showed a gestational sac with a yolk sac

Absence of an embryo \geq 6 weeks after last menstrual period

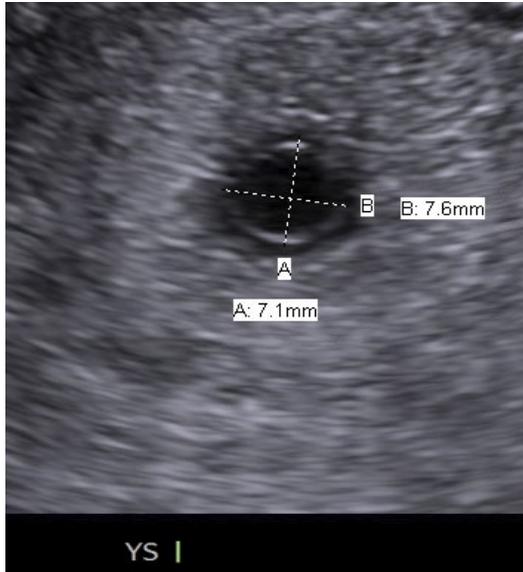
Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5-mm difference between MSD and CRL)

Note.—Data are from Reference 3.

IUP of Uncertain Viability



US image shows a large yolk measuring greater than 7 mm, which is suspicious for but not diagnostic of pregnancy failure.

Findings Suspicious for but not Diagnostic of Pregnancy Failure

Crown rump length < 7 mm & no heartbeat

Mean sac diameter 16-25 mm and no embryo

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 an embryo ≥ 6 weeks after last menstrual period

Empty amnion (amnion adjacent to yolk sac, no visible embryo)

Enlarged yolk sac (> 7 mm)

Small gestational sac (< 5 -mm difference between MSD and CRL)

Note.—Data are from Reference 3.

Retained Products of Conception

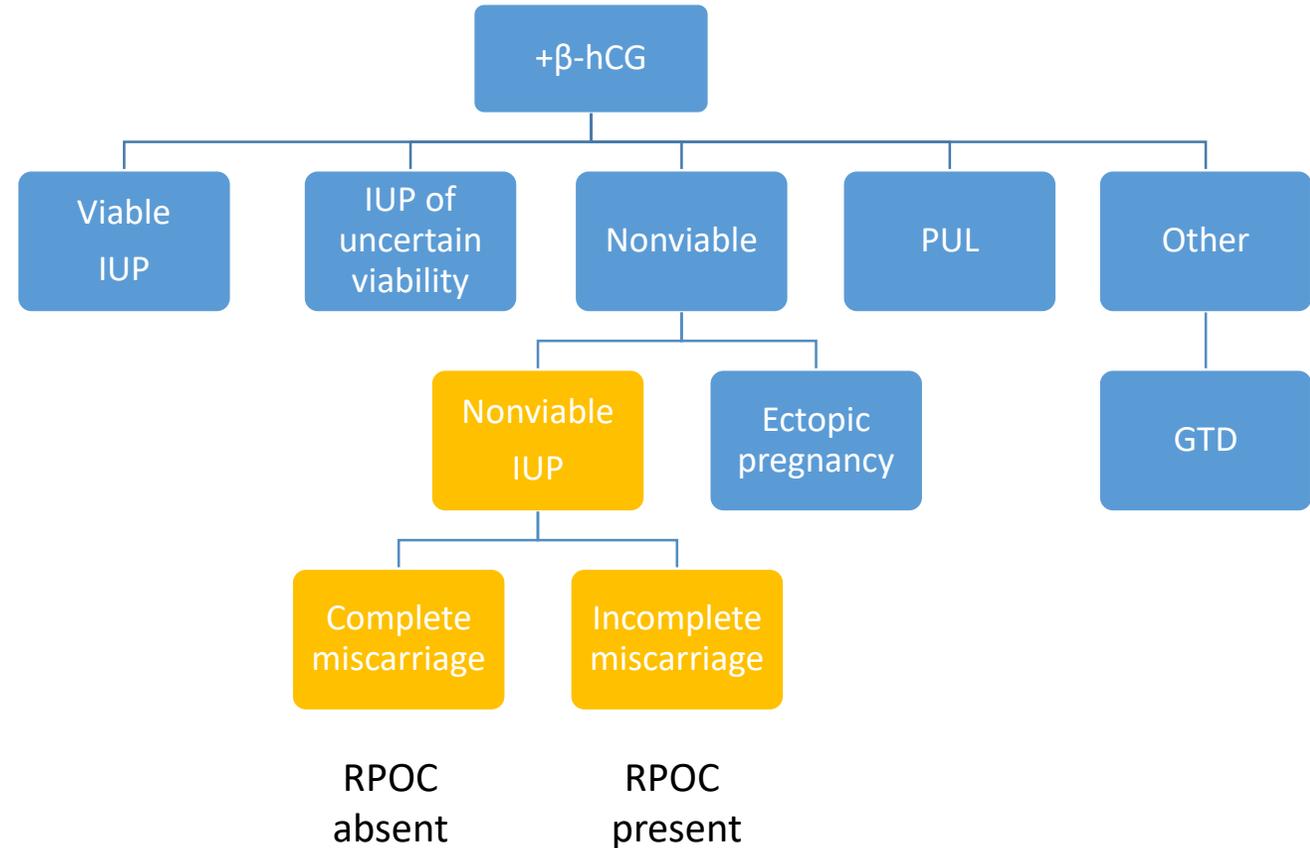
When evaluating for passage of a nonviable fetus, it is important to evaluate for retained products of conception (RPOC).

The presence of RPOC differentiates a complete miscarriage (no RPOC present) from an incomplete miscarriage (RPOC present).

Patients with RPOC often present with postpartum hemorrhage.²⁵

RPOC occurs more frequently in cases of medical termination of pregnancy and second-trimester miscarriage.²⁵

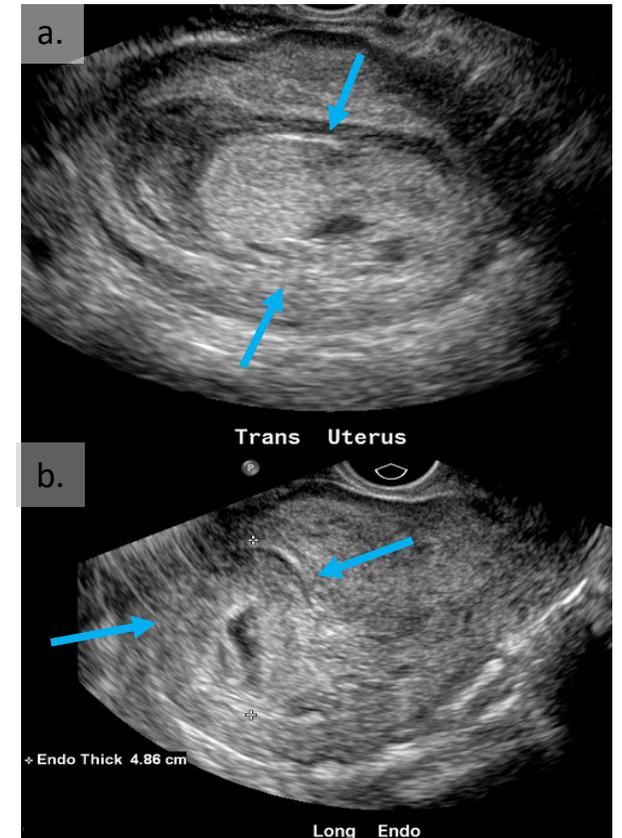
Treatment includes the administration of prostaglandin E1 analogs, dilation and curettage, or hysteroscopic removal.



RPOC

Gray-scale US findings:

- Thickened endometrial echocomplex (EEC)
 - Most sensitive finding for RPOC
 - Using 10-mm cutoff
 - 80% sensitivity
 - 20% specificity
 - 63%–80% negative predictive value (NPV) if EEC is less than 10 mm²⁵
- Endometrial mass
 - Defined as a structure seen in two orthogonal planes, separate from the endometrium
 - Sensitivity: 29%–79%
 - High positive predictive value (PPV, 80%)²⁵



Gray-scale transverse (a) and longitudinal (b) US images of a postpartum patient show a thickened EEC (arrows).

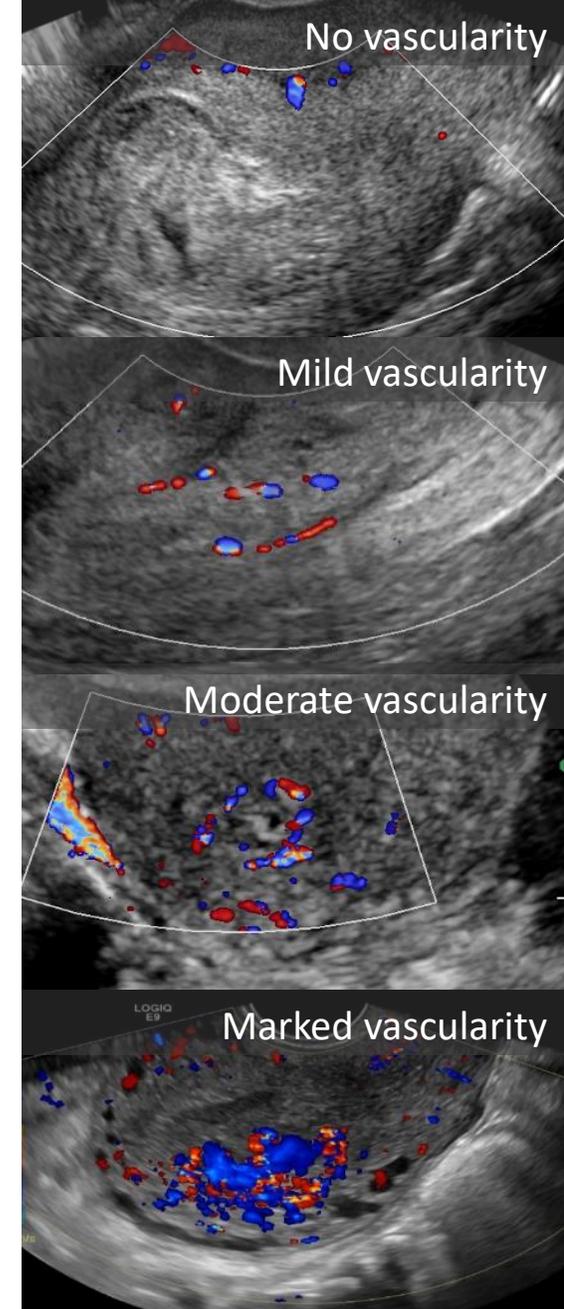
This is seen on both transverse and longitudinal images, confirming the masslike nature of the structure.

RPOC

Color Doppler US findings:

- Presence of flow in a thickened endometrium or endometrial mass is highly predictive (PPV, 96%)²⁵
- Absence of flow does not exclude products of conception (POC; can represent clot or avascular POC)²⁶
- Avascular POC will probably pass without intervention²⁵
- Markedly vascular POC has a risk of severe bleeding during dilation and curettage, which may be secondary to mistakenly unroofing a large vessel. As such, the obstetrician should be notified.²⁵

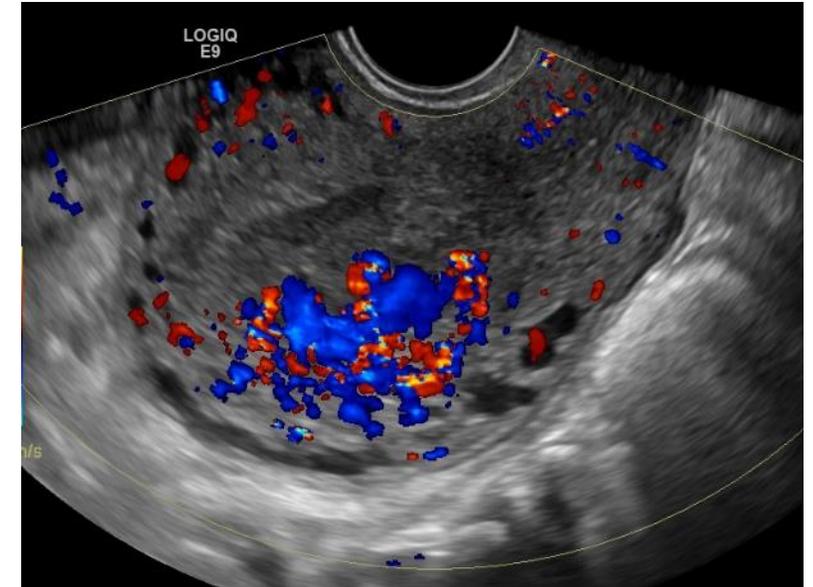
No RPOC	RPOC
EEC < 10 mm (NPV 63%–80%)	EEC > 10 mm Sensitive (80%), not specific (20%)
No endometrial mass NPV 85%–95%	Endometrial mass Less sensitive (29%–79%), more specific PPV 80%
No vascularity NPV 88%–95% Absence of all findings (PPV 100%)	Vascularity Combination of vascularity with thickened stripe or endometrial mass (PPV 96%)



RPOC

Differential diagnosis:

- Arteriovenous malformation (AVM)
 - Usually post-traumatic (dilation and curettage)
 - AVM: vascularity centered in the myometrium at US
 - RPOC: vascularity centered in the endometrium at US
- Subinvolution of the placental implantation site
 - Rare
 - Uterine vessels fail to involute after delivery
 - May appear as dilated myometrial vessels at US²⁵
- Nonobstetric condition (polyps, fibroids)
- GTD
 - β -hCG levels remain elevated (β -hCG levels should decline with RPOC)



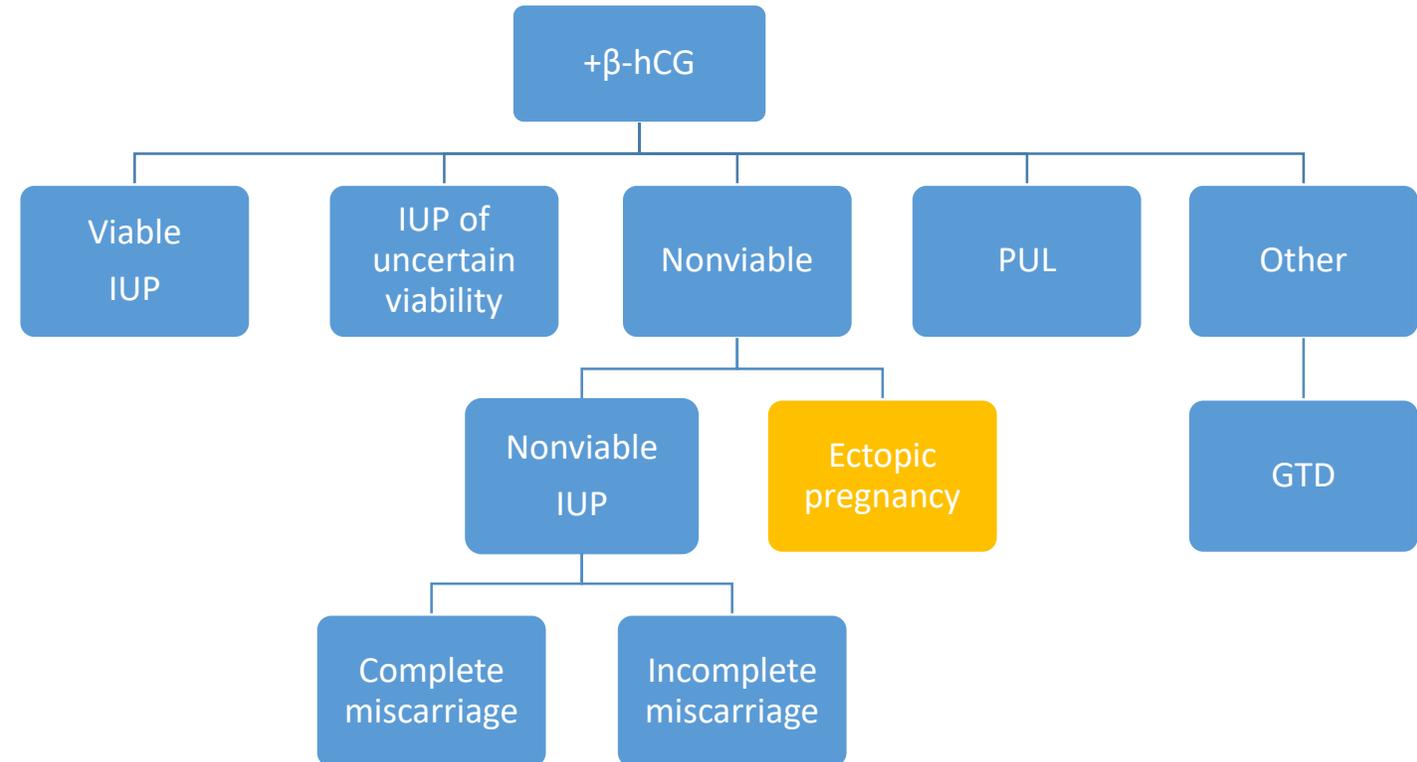
Color Doppler US image of a postpartum patient shows marked vascularity extending from the myometrium to the endometrium, suggesting RPOC.

Ectopic Pregnancy

Ectopic pregnancy is the most common cause of pregnancy-related maternal mortality in the first trimester.²⁷

Initial evaluation consists of performing hormonal assays and pelvic US.

Pelvic pain with an abnormal β -hCG level should trigger evaluation for an ectopic pregnancy.



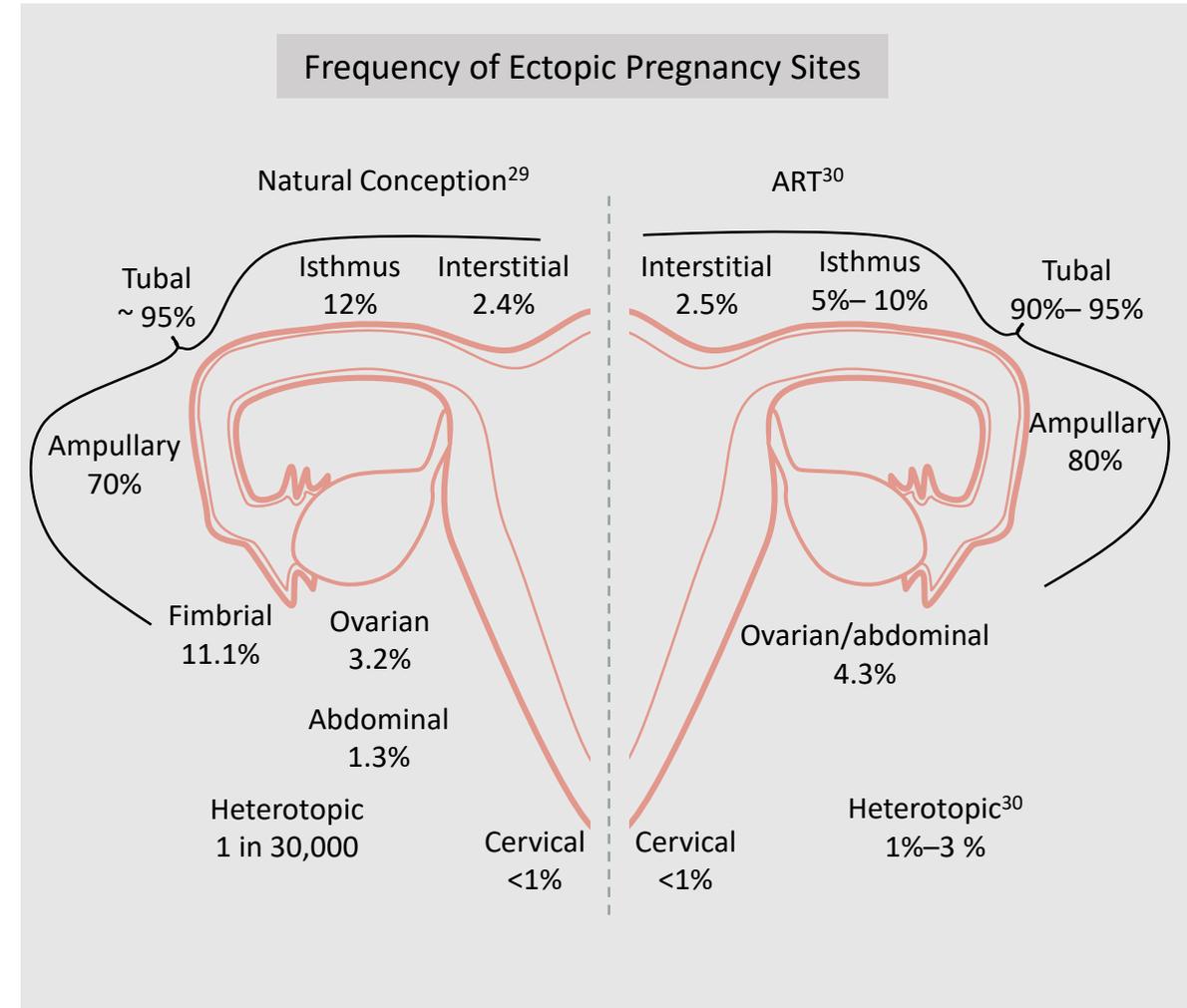
Ectopic Pregnancy

Overall incidence: 1%–2% of pregnancies²⁷

Prevalence was thought to be increasing owing to the use of assisted reproductive technology (ART), although it is currently declining, possibly from evolving ART techniques.²⁸

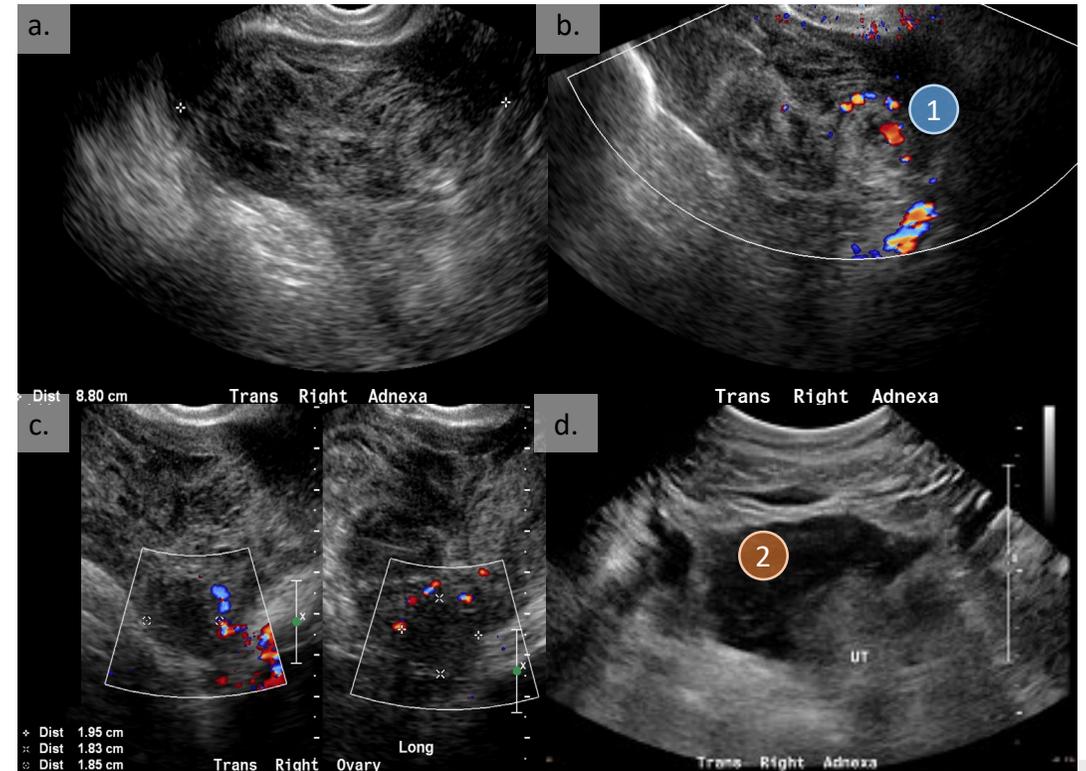
Risk factors

- Prior ectopic pregnancy
- Tubal injury
- Pelvic inflammatory disease
- Salpingitis isthmica nodosa
- Endometrial injury or congenital anomalies
- Intrauterine device (IUD) use



Ectopic Pregnancy: Tubal Ectopic Pregnancy

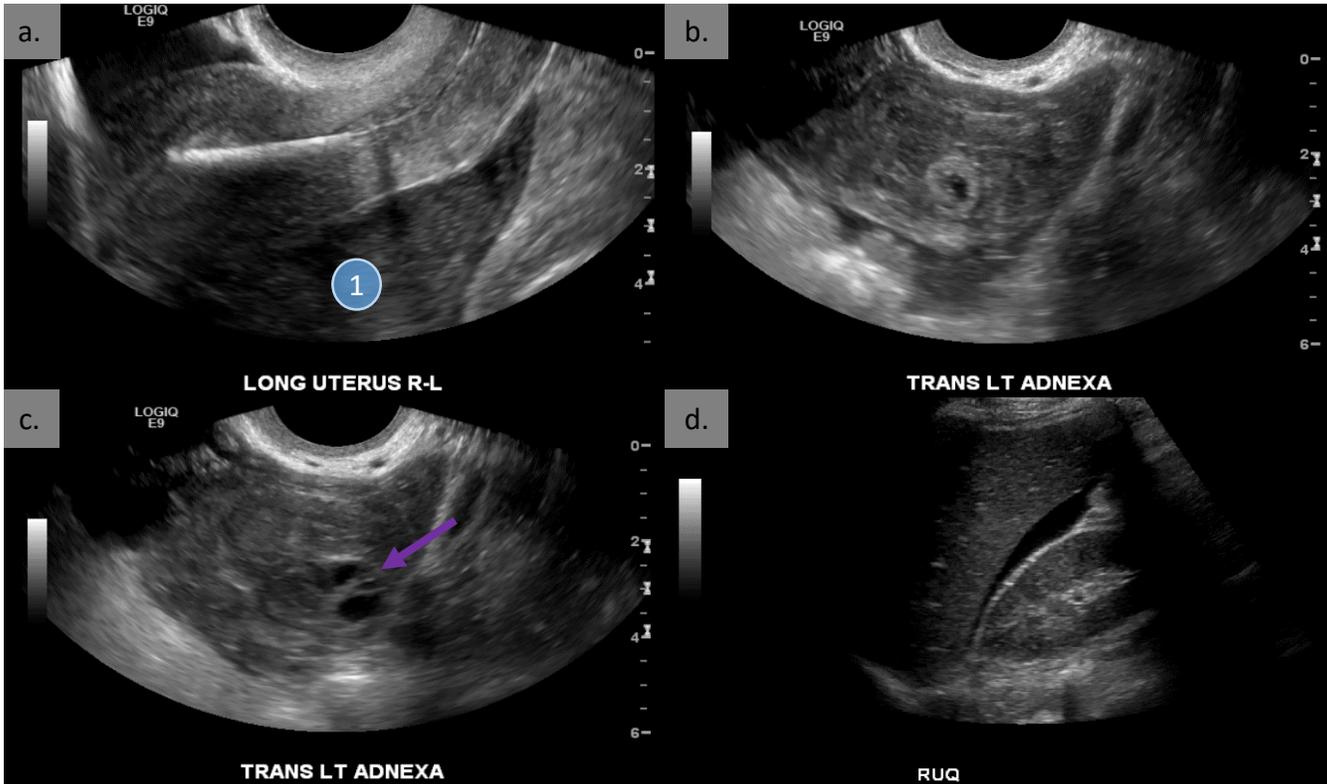
- 95% of ectopic pregnancies are located in the fallopian tube.²⁷
- Most common finding is an adnexal mass, which is separate from the ovary (seen in 89%–100% of patients). An adnexal mass may not be detected at transvaginal US in 15%–35% of patients.²⁷
- Second most common finding is a “ring of fire” sign, which is seen as peripheral hypervascularity on color Doppler US images. This is a nonspecific finding and can be seen with corpus luteal cysts. Thus, the sign is useful after confirming the ring of fire in an adnexal mass outside of the ovary.²⁷
- Echogenic fluid within the Morrison pouch and the cul-de-sac should raise concern for a ruptured ectopic pregnancy. In a patient with positive β -hCG levels, echogenic fluid is predictive for ectopic pregnancy, with an 86%–93% ppv.³¹
- Absence or presence of free fluid is not a reliable indicator to exclude a tubal rupture, according to one study.³²
 - 21% of cases of tubal rupture were found to have no fluid or trace free fluid
 - 37% of patients with free fluid in the right upper quadrant were found to have intact fallopian tubes



US (a) and color Doppler US (b–d) images show a large complex mass in the right adnexum. Within this mass is an area of peripheral vascularity, representing the ring of fire sign (1 in b), which helps confirm an ectopic pregnancy. The ring of fire sign is surrounded by an avascular area that represents a clot that extruded from the fallopian tube during surgery.

The mass is adjacent to the right ovary (c), which also contains a corpus luteal cyst that shows peripheral vascularity. A small amount of complex fluid that contains internal echoes is noted adjacent to the right adnexal mass (2 in d), concerning for ruptured ectopic pregnancy.

Ectopic Pregnancy: Tubal Ectopic Pregnancy



(a) Longitudinal US image of the uterus (a) shows complex fluid within the posterior cul-de-sac (1), as well as an IUD within the endometrial cavity.

(b, c) US images show a thick walled cystic structure in the left adnexum, which appears separate from the left ovary (arrow in c).

Overall, the findings are highly concerning for a ruptured ectopic pregnancy with hemoperitoneum.

Whenever hemoperitoneum is present, additional views should be obtained in the right and left upper quadrants to evaluate the extent of hemorrhage.

(d) US image from an additional evaluation of the right upper quadrant shows fluid in the hepatorenal recess, concerning for a large volume of hemoperitoneum.

Ectopic Pregnancy: Differentiating Ovarian from Adnexal

If it is unclear if the mass is separate from the ovary, consider a technique that uses a combination of US transducer pressure with stomach palpation to evaluate the movement of the two structures.

Movement of the structure in question as one with the ovary

→ suggests mass is within the ovary

Movement of the structure in question separate from the ovary

→ suggests mass is outside the ovary

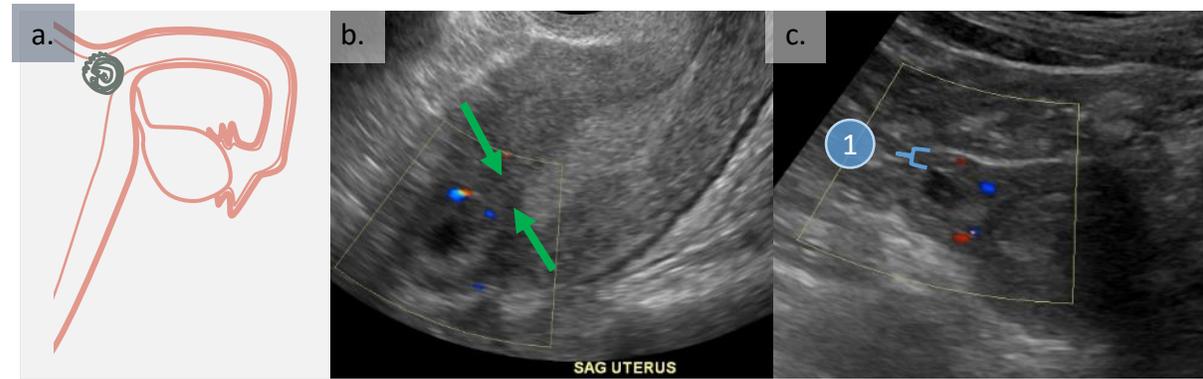


US cine clip shows the right adnexum with a combination of US transducer pressure and palpation of the stomach.

A complex mass was shown to move as one with the ovary, suggesting the lesion was ovarian in origin and likely a hemorrhagic corpus luteum rather than an ectopic pregnancy.

Ectopic Pregnancy: Interstitial Ectopic Pregnancy

- Uncommon
- Occurs when implantation takes place within the intramyometrial segment of the fallopian tube
- Can manifest later (up to 16 weeks GA) owing to distensibility of this segment³³
- Accounts for almost 20% of deaths caused by hemorrhage in ectopic pregnancies, despite an incidence of 2%–6% of ectopic pregnancies
- Sometimes used interchangeably with the term *cornual ectopic pregnancy*, which technically refers to implantation within the cornua of a bicornuate or septate uterus
- Findings:
 - Eccentrically located sac surrounded by thin myometrium (< 5 mm)²⁷
 - Interstitial line sign (a thin echogenic line connecting the endometrium to the gestational sac, representing the interstitial portion of fallopian tube) (80% sensitive, 98% specific)³⁴



(a) Illustration shows the gestational sac within the intramyometrial portion of the fallopian tube.

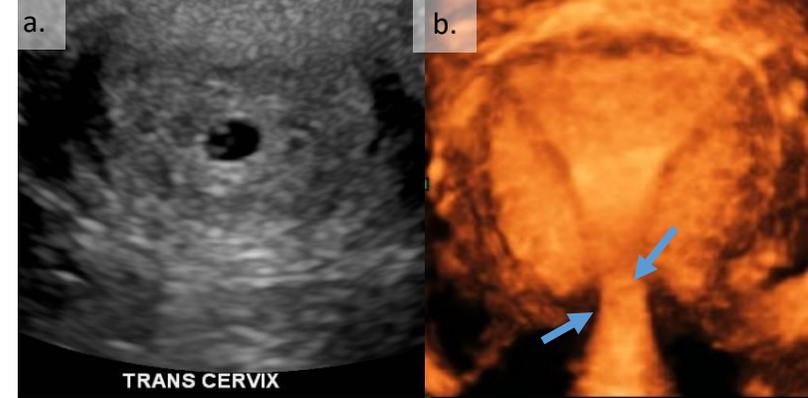
(b, c) Longitudinal (b) and transverse (c) color Doppler US images of the uterus show a gestational sac that appears separate from the fundal endometrium. Both appear connected by an echogenic line (arrows in b), representing the interstitial line sign. The gestational sac appears eccentric and surrounded by a thin layer of myometrium (1 in c).



US cine clip of an interstitial pregnancy shows a round gestational sac that appears separate from the endometrium. There is associated fluid within the endometrial cavity.

Ectopic Pregnancy: Cervical Ectopic Pregnancy

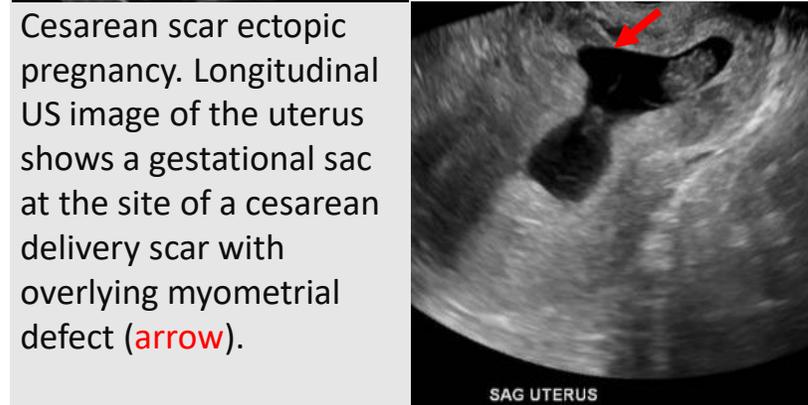
- Uncommon
- Must be distinguished from a miscarriage in progress
- US findings:
 - Hourglass appearance of uterus as fetus expands the cervix³⁵
 - Cardiac activity below the internal os³⁵
- Differential diagnosis:
 - Miscarriage in progress
 - Gestational sac may be noted to change shape or location during or between US examinations
 - Sliding sign: if US transducer can manipulate the gestational sac, it suggests nonadherence to the cervix³⁶
 - Cesarean scar ectopic pregnancy
 - Gestational sac in anterior myometrium, with overlying myometrial defect²⁷
 - May also rupture from myometrial thinning along the cesarean scar



Cervical ectopic pregnancy. (a) Transverse US image of the cervix shows a gestational sac with a yolk sac. (b) Three-dimensional US image shows the gestational sac below the internal os (arrows).



Miscarriage in progress. Longitudinal US image of the uterus shows a flattened irregular gestational sac (arrow).



Cesarean scar ectopic pregnancy. Longitudinal US image of the uterus shows a gestational sac at the site of a cesarean delivery scar with overlying myometrial defect (arrow).

Ectopic Pregnancy:

Additional Types³⁷

- Ovarian ectopic pregnancy
 - Accounts for 3% of ectopic pregnancies
 - May be a part of a heterotopic pregnancy
 - Strongly associated with use of an IUD
 - May be suggested by the presence of a gestational sac, chorionic villi, or an atypical cyst with hyperechoic ring with a normal fallopian tube
- Abdominal ectopic pregnancy
 - Accounts for 1.3% of ectopic pregnancies
 - Occurs within the intraperitoneal cavity
 - Significant risk of hemorrhage with maternal mortality is 7.7 times greater than other ectopic pregnancy locations
- Heterotopic pregnancy
 - Rare in the general population (1 in 30,000)
 - Represents coexistence of an IUP and ectopic pregnancy
 - Not uncommon in patients undergoing in vitro fertilization (IVF) (1%–3% of all pregnancies)
 - Note that the rate of heterotopic pregnancies in the IVF population (1%–3%) is similar to that of all ectopic pregnancies in the general population (1%–2%). Thus, careful examination should occur in the IVF population to evaluate for heterotopic pregnancies.

Pregnancy of Unknown Location

Classification of US Findings³⁸

Definite Ectopic Pregnancy	Probable Ectopic Pregnancy	PUL	Probable IUP	Definite IUP
Extrauterine gestational sac + yolk sac and/or embryo	Inhomogeneous adnexal mass or extrauterine saclike structure	No signs of intrauterine or extrauterine gestation at transvaginal US	Intrauterine echogenic saclike structure	Intrauterine gestational sac + yolk sac and/or embryo

One proposed classification scheme for uniformity in categorizing the location of pregnancy is listed above.

PUL

Classification of US Findings³⁸

Definite Ectopic Pregnancy	Probable Ectopic Pregnancy	PUL	Probable IUP	Definite IUP
Extrauterine gestational sac + yolk sac and/or embryo	Inhomogeneous adnexal mass or extrauterine saclike structure	No signs of intrauterine or extrauterine gestation at transvaginal US	Intrauterine echogenic saclike structure	Intrauterine gestational sac + yolk sac and/or embryo

When the location of a pregnancy cannot be determined (no intrauterine fluid collection and normal/near-normal adnexa), this is considered a PUL. Near-normal adnexa includes the corpus luteum, small amount of pelvic free fluid, and a paratubal cyst.³

When pregnancy location cannot be established, it is important to understand the role of β -hCG in determining management.

Review of β -hCG

- β -hCG levels peak at 9–11 weeks, after which they decline (Table 1)
- The average doubling time of β -hCG levels in a normal viable IUP is approximately 48 hours (range 1.2 – 2.2 days) (Table 2)
- A less than 50% rise in 48 hours is almost always a nonviable pregnancy (intrauterine or extrauterine)³⁹
- Ectopic pregnancies may manifest with abnormal rise, fall, or early plateau of β -hCG levels
- β -hCG level is not always reliable
 - 1% with viable IUP show slower doubling time⁴⁰
 - 21% of ectopic pregnancies show normal doubling times⁴¹
 - Thus, evaluation is made with a combination of β -hCG levels and US

Table 1. β -hCG Levels during Pregnancy

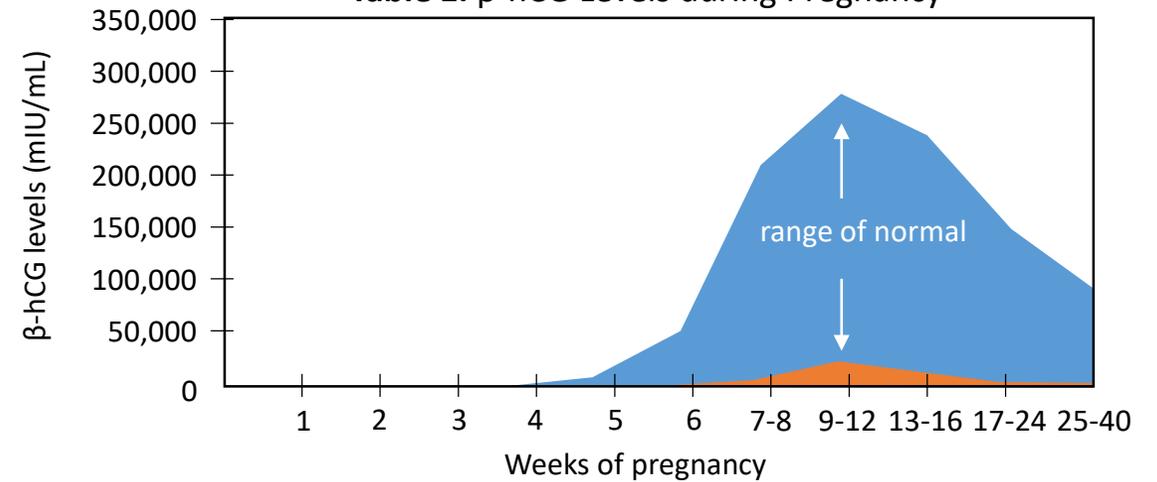


Table 2. Serial β -hCG levels

Level of β -hCG	Indication
Rising	
Normal (> 50% in 48 hours)	Supports diagnosis of viable IUP 21% of ectopic pregnancies show normal doubling times
Abnormal (< 50% in 48 hours)	Almost certainly a nonviable pregnancy (intrauterine or extrauterine)
Early plateau	Highly suggestive of ectopic pregnancy
Decreasing	Most consistent with failed pregnancy (including miscarriage, spontaneously resolving ectopic pregnancy)

Review of β -hCG

- The use of a discriminatory zone (orange in Table 1), a defined single β -hCG level in which a gestational sac should be visualized at US, has been widely investigated. Some define this value up to 3500 mIU/mL.⁴²
- Because of considerable overlap of β -hCG values among viable IUP, non-viable IUP, and ectopic pregnancies, a single β -hCG measurement cannot reliably establish the location of a pregnancy.³
- For example, in a patient with a β -hCG level of 2000–3000 mIU with no gestational sac at US, an ectopic pregnancy is 19 times more likely than an IUP. However, there is a 2% chance of viable IUP.³
- The use of a single β -hCG and discriminatory zone may be used as an aid to guide management in terms of follow-up but should not be used as an indication for initiating treatment for ectopic pregnancy.

Table 1. β -hCG Levels during Pregnancy

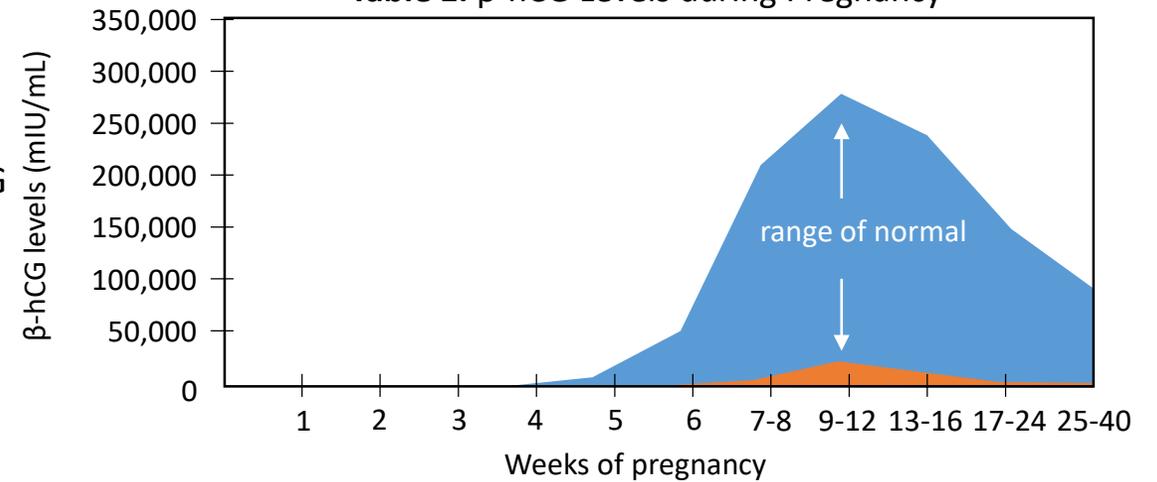
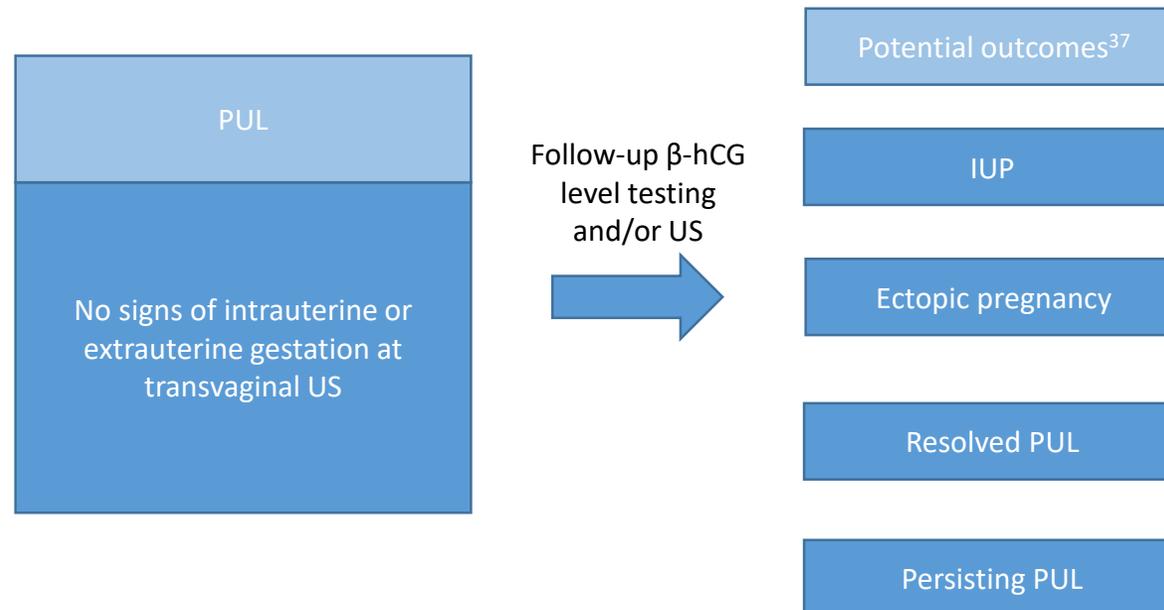


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Abnormal (< 50% in 48 hours)	Almost certainly a nonviable pregnancy (intrauterine or extrauterine)
Early plateau	Highly suggestive of ectopic pregnancy
Decreasing	Most consistent with failed pregnancy (including miscarriage, spontaneously resolving ectopic pregnancy)

PUL

- Differential diagnosis of PUL includes an early IUP, failed pregnancy, or ectopic pregnancy.
- Management of PUL varies considerably.
- Follow-up β -hCG level tests and/or US are recommended in a stable patient who desires the pregnancy.⁴²
- Other tests include progesterone levels, biomarker levels, the use of mathematical models, and endometrial aspiration in certain situations to guide management.

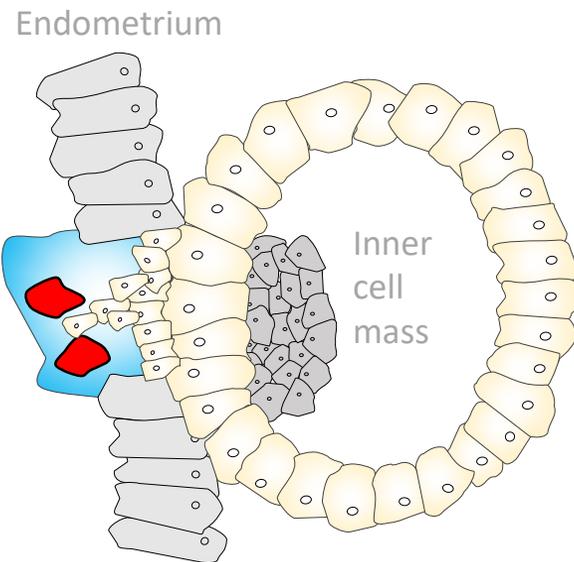
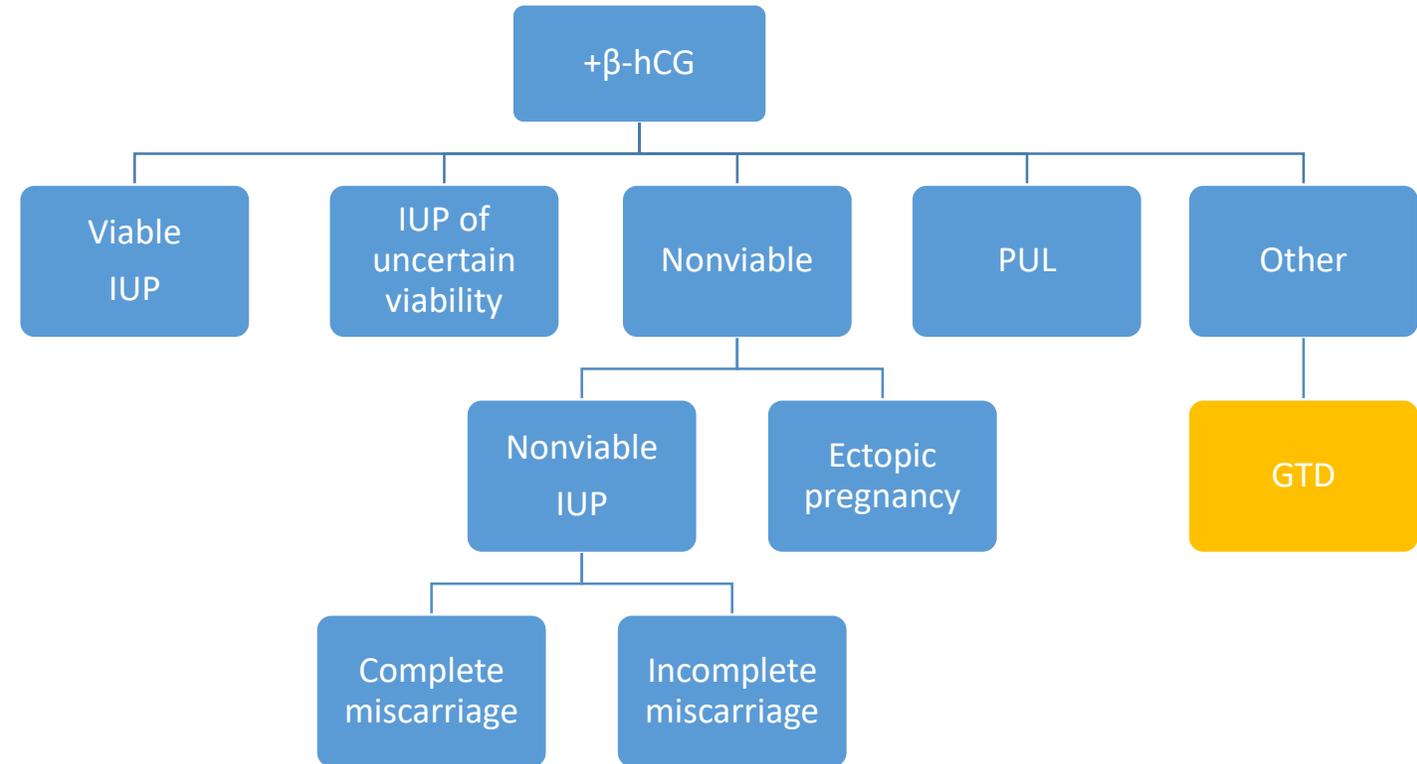


GTD

GTD encompasses benign and malignant forms.

All GTDs arise from the placenta.⁴³

Hydatidiform moles and choriocarcinoma arise from cellular (villous) trophoblasts.⁴³



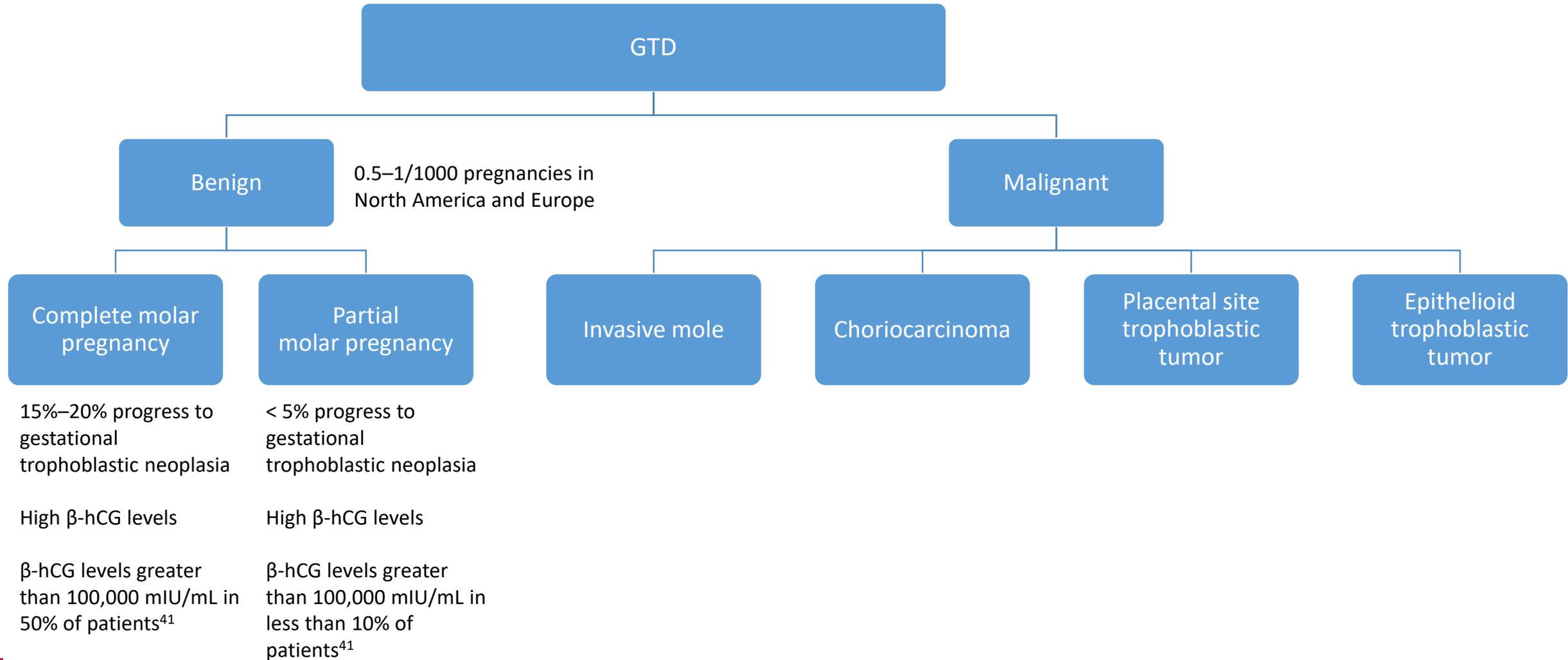
Cellular trophoblasts

- Form chorionic villi

Syncytiotrophoblasts

- Digest the endometrium to form lacunae
- Produce β-hCG

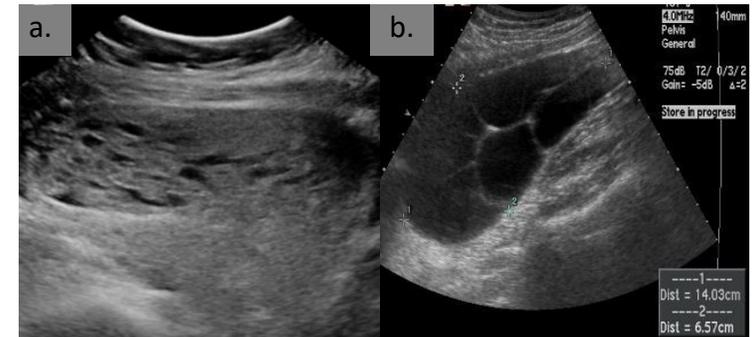
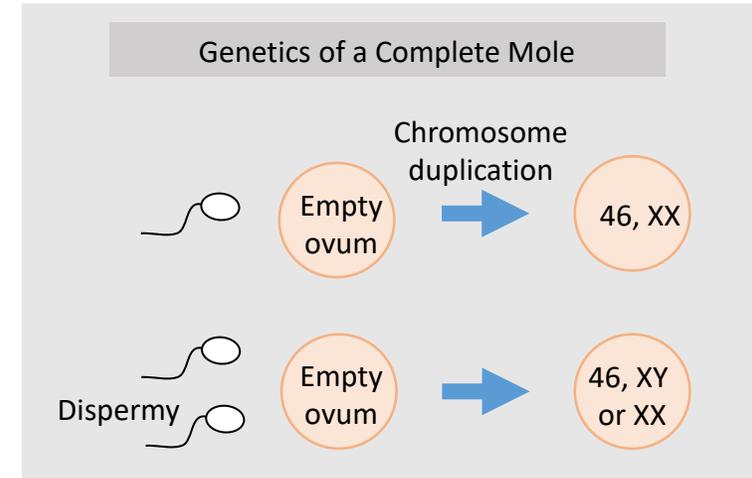
GTD



GTD:

Complete Molar Pregnancy

- Often diagnosed early because of routine US and β -hCG testing
- 58%–95% detection at US⁴⁴
- US findings:
 - Large-for-date uterine size
 - Snowstorm appearance of the endometrium (echogenic mass with hypoechoic foci)
 - Small (1–30 mm) cysts of varying sizes in the endometrium (representing hydropic chorionic villi and described as a “cluster of grapes”)
 - Theca lutein cysts (in 20%), representing large functional ovarian cysts that enlarge the ovaries, may occur secondary to exaggerated ovarian stimulation by the high levels of β -hCG.

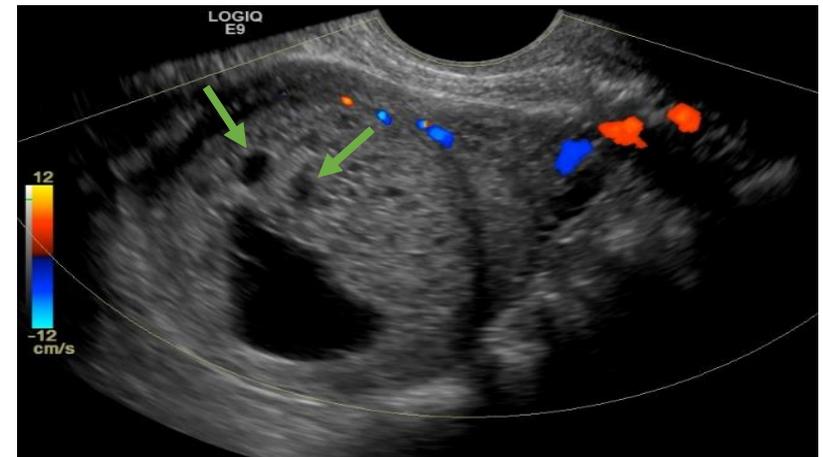
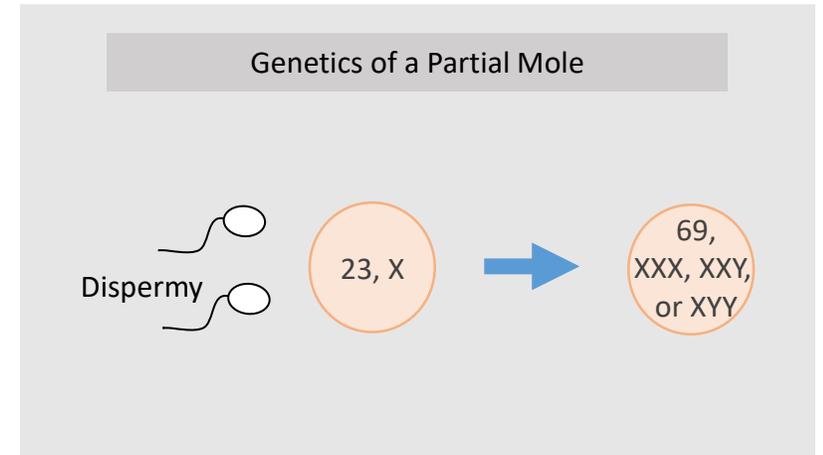


(a) Longitudinal US image of the endometrium shows a thick endometrial mass with cystic spaces representing a complete mole. (b) Longitudinal US image of an ovary shows an enlarged ovary with large cysts compatible with theca lutein cyst.

GTD:

Partial Molar Pregnancy

- False-negative results are common (17%–29% detection at US)⁴⁴
- Can mimic anembryonic pregnancy, miscarriage, or RPOC
- Given the difficulty in detection, correlation with quantitative β -hCG levels is key
- US findings:
 - Gestational sac may appear empty, elongated, or ovoid or contain amorphous echoes (fetal parts)
 - Fetal demise, anomalies, growth restriction
 - Oligohydramnios
 - Enlarged placenta relative to size of the uterus with cystic change (“Swiss cheese” appearance)



Longitudinal color Doppler US image of the uterus shows an enlarged placenta with cystic changes (arrows), giving a Swiss cheese appearance.

Summary

- In early pregnancy, US is important to confirm location of a pregnancy.
- Once an IUP has been confirmed, fetal viability must be determined.
- For IUPs, it is important to distinguish between sonographic findings that are definitive for pregnancy failure and those that are suspicious for but not definitive of pregnancy failure, which require follow-up testing to establish a definitive diagnosis.
- If an IUP has not been confirmed and an ectopic pregnancy is suspected on the basis of the results of laboratory examinations, then an extended search must be performed.
- Most ectopic pregnancies occur in the fallopian tube and most commonly manifest as an adnexal mass.
- PUL is considered when there are no signs of intrauterine or extrauterine gestation.
- β -hCG level is used to help determine fetal viability. A greater than 50% rise over 48 hours suggests a viable IUP. A less than 50% rise over 48 hours suggests a nonviable pregnancy (either intrauterine or extrauterine).
- In miscarriages, the presence of RPOC differentiates a complete miscarriage (RPOC absent) and an incomplete miscarriage (RPOC present).
- A combination of endometrial thickening, an endometrial mass, and vascularity is highly predictive for RPOC.
- A complete mole may be seen as an intrauterine mass with cystic spaces without any associated fetal parts. In comparison, a partial mole may manifest as a gestational sac containing amorphous echoes representing fetal parts.
- Less than 50% of all hydatidiform moles are detected at US, mostly owing to difficulty in detecting partial moles, which can be mistaken for anembryonic pregnancy, miscarriage, or RPOC. Correlation with β -hCG levels is key.

Suggested Readings

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