Early Pregnancies of Unknown Location or Unknown Viability

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No Disclosures

Early First Trimester Ultrasound

- Is the pregnancy intrauterine?
  OR
- Is the pregnancy ectopic?
- Is the pregnancy viable*?
  OR
- Is the pregnancy a miscarriage

*Has potential to result in live born infant

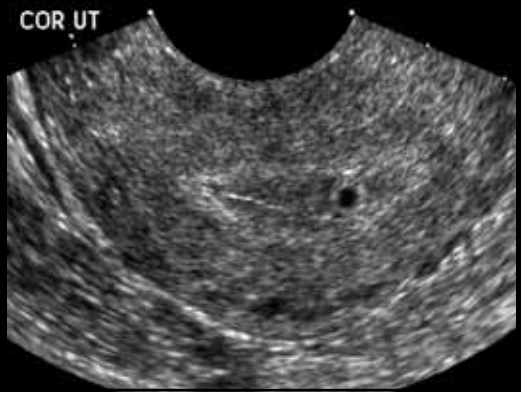
Terminology & Definitions

- Intrauterine Pregnancy of Unknown Viability (IPUV)
  Ultrasound findings:
  Intrauterine gestational sac with no embryonic heartbeat
- Pregnancy of Unknown Location (PUL)
  ⊕hCG & Ultrasound findings:
  No intrauterine gestational sac or adnexal mass
- Early pregnancy failure
  Not: Miscarriage, spontaneous abortion…

Intrauterine Sac-Like Structure 1st Sign of Pregnancy

- Usually seen Transvaginally by 5.0 weeks
- Usually seen Transabdominally by 5.5 weeks
- Usually when hCG > 1000 mIU/ml (1st or 3rd IRP)

Early Pregnancy – Transvaginal Scan

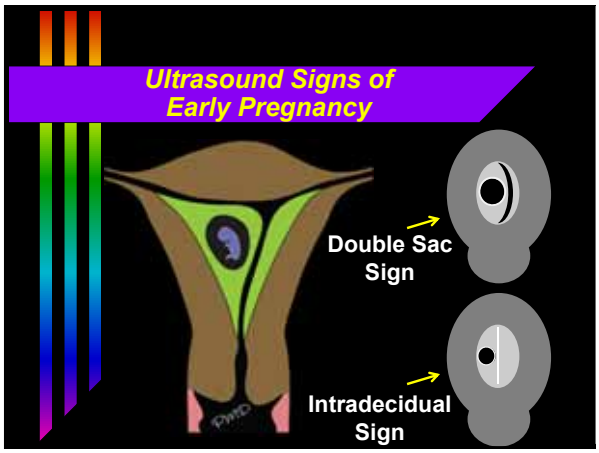


Published Ultrasound Signs of Early Pregnancy

- Double sac sign* (reported 1982)
- Intradecidual sign* (reported 1984)

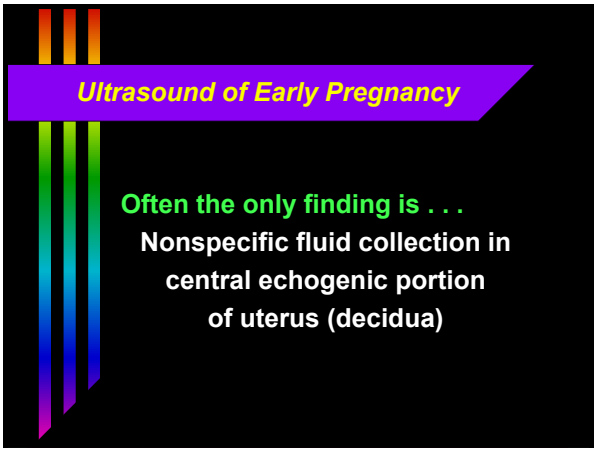
*If present, diagnosis = IUP
*If absent, does not mean no IUP

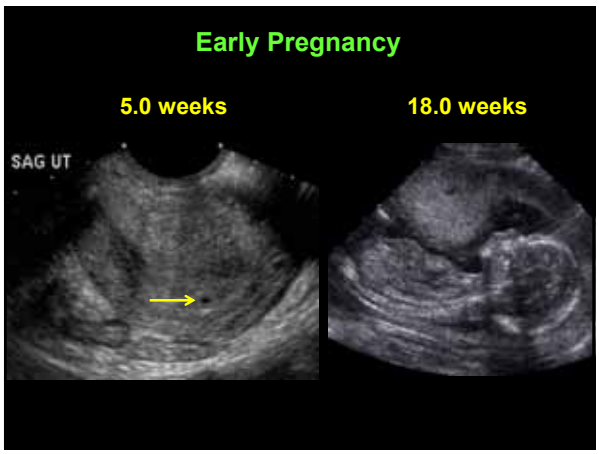
IUP = intrauterine pregnancy

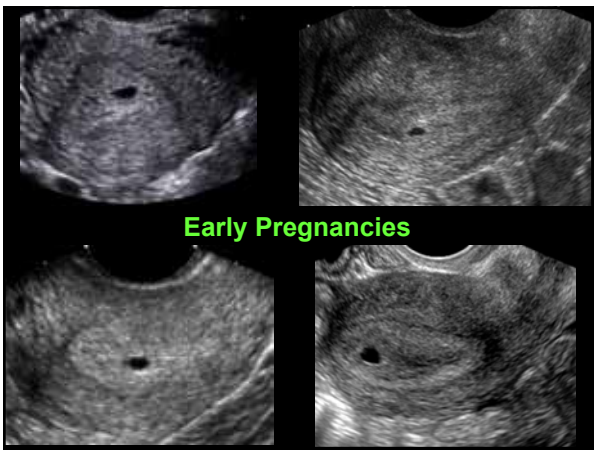

Ultrasound Signs of Early Pregnancy
Double Sac Sign
Intradecidual Sign


Intradecidual sign
SAG UT
SAG UT


Double sac sign


Ultrasound of Early Pregnancy
Often the only finding is . . .
Nonspecific fluid collection in central echogenic portion of uterus (decidua)


Early Pregnancy
5.0 weeks
18.0 weeks
SAG UT


Early Pregnancies

Problem

If nonspecific fluid collection in central echogenic portion of uterus reported as no intrauterine pregnancy or the possibility of a "pseudogestational sac"

↓

Clinician concludes ectopic pregnancy

↓

Patient treated with Methotrexate or dilatation & curettage (D&C)

Problem

When early intrauterine pregnancy is exposed to Methotrexate (MTX)

↓

Follow up: intrauterine pregnancy with heartbeat

↓

Miscarriage or fetal malformations

Study of Ultrasound Signs of Early Pregnancy

Two readers assessed

199 proven intrauterine gestations

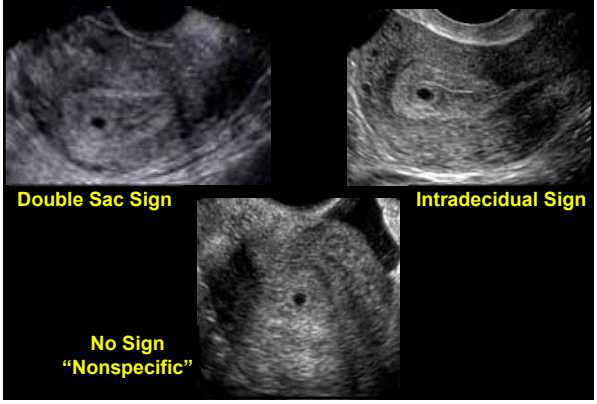
- fluid in uterus, no YS or embryo
- embryonic heartbeat on follow up

First trimester outcome

148 (74.4%) live

51 (25.6%) miscarriage

Signs (or Absence of Signs) of Early Pregnancy



Study of Ultrasound Signs of Early Pregnancy

	Reader 1	Reader 2
DSS present*	32%	30%
IDS present**	23%	39%
Neither sign	57%	48%

Kappa = *0.24 & **0.23 (poor inter-observer agreement)

No relationship between outcome and presence/absence of DSS & IDS ($p > 0.10$, Fisher exact test)

Early Intrauterine Gestation

- Early intrauterine gestations often have a nonspecific appearance (>50% in our study)
- Even in the absence of an intradecidual sign or a double sac sign, it's most likely an early intrauterine gestation

Early Intrauterine Gestation

How should one report an
Intrauterine fluid collection with
no yolk sac or embryo and
normal adnexa?

"Intrauterine sac-like structure that is almost certainly an intrauterine gestational sac"

OR

"Probable early intrauterine gestation. Follow up ultrasound suggested for definitive confirmation"

"Pseudogestational Sac"

Definition:

Fluid in the uterine cavity

mimicking a gestational sac

with ectopic pregnancy

Misuse of Term Pseudogestational Sac

Definition: fluid in uterine cavity
with ectopic pregnancy

Frequency with ectopic pregnancy

1979 report: 20%

1990 reports: 10%

Intrauterine Fluid in Ectopic Pregnancy: A Reappraisal

All proven ectopic pregnancies
July 2008 to August 2011 = 229 cases

Fluid, when present, characterized by

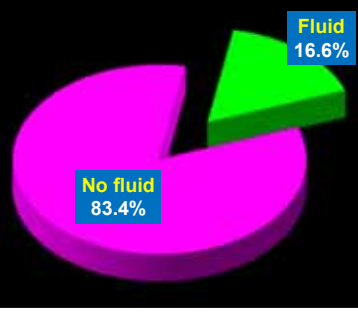
Shape:
pointy-edged or smooth*

Location:
clearly in cavity* or uncertain

Fluid contents:
echoes & debris or anechoic*

*Features of early intrauterine pregnancy

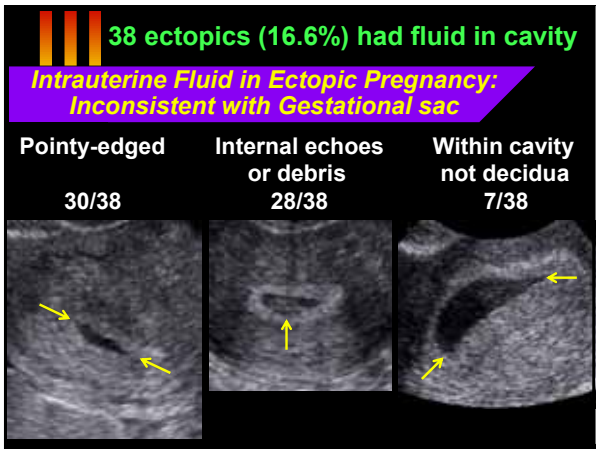
Intrauterine Fluid in Patients With Ectopic Pregnancy

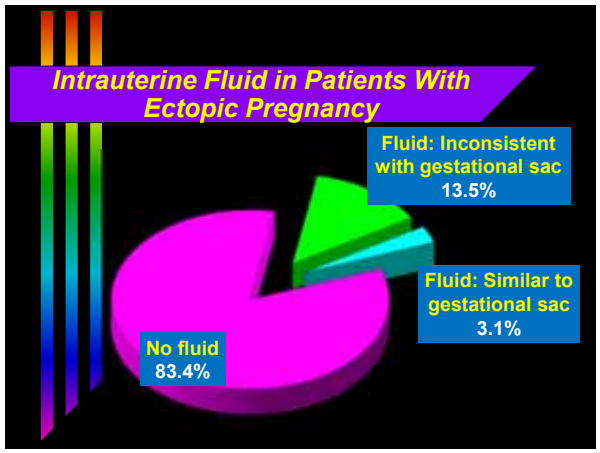


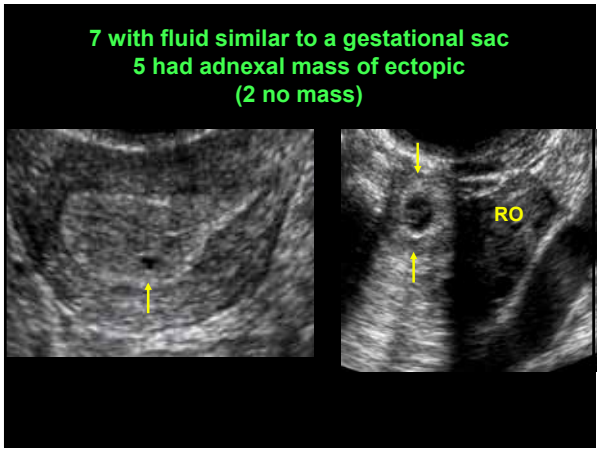
Intrauterine Fluid in Ectopic Pregnancy: Fluid Characterization

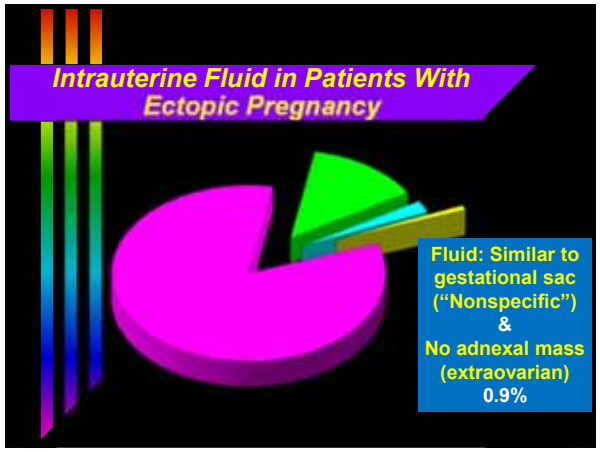
Fluid inconsistent with gestational sac
pointy-edged
clearly within uterine cavity
(not the decidua)
containing echoes or debris

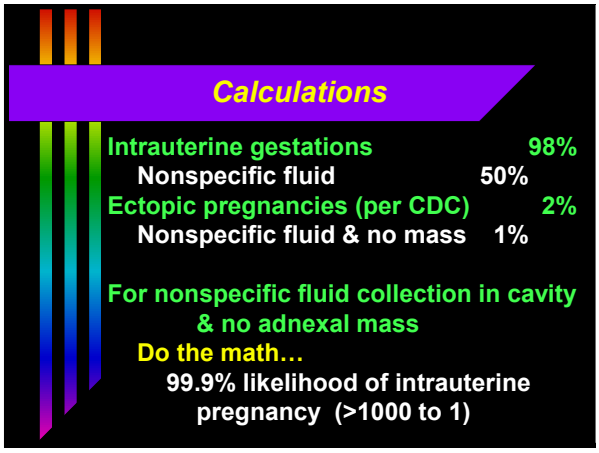
Fluid similar to a gestational sac
smooth margins
not clearly within uterine cavity
anechoic

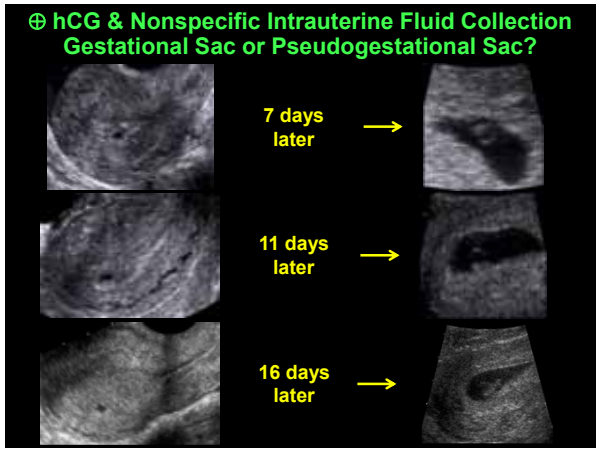

38 ectopics (16.6%) had fluid in cavity
Intrauterine Fluid in Ectopic Pregnancy: Inconsistent with Gestational sac
Pointy-edged
30/38
Internal echoes or debris
28/38
Within cavity not decidua
7/38


Intrauterine Fluid in Patients With Ectopic Pregnancy
Fluid: Inconsistent with gestational sac
13.5%
Fluid: Similar to gestational sac
3.1%
No fluid
83.4%


7 with fluid similar to a gestational sac
5 had adnexal mass of ectopic
(2 no mass)
RO


Intrauterine Fluid in Patients With Ectopic Pregnancy
Fluid: Similar to gestational sac ("Nonspecific")
&
No adnexal mass (extraovarian)
0.9%


Calculations
Intrauterine gestations 98%
Nonspecific fluid 50%
Ectopic pregnancies (per CDC) 2%
Nonspecific fluid & no mass 1%
For nonspecific fluid collection in cavity & no adnexal mass
Do the math…
99.9% likelihood of intrauterine pregnancy (>1000 to 1)

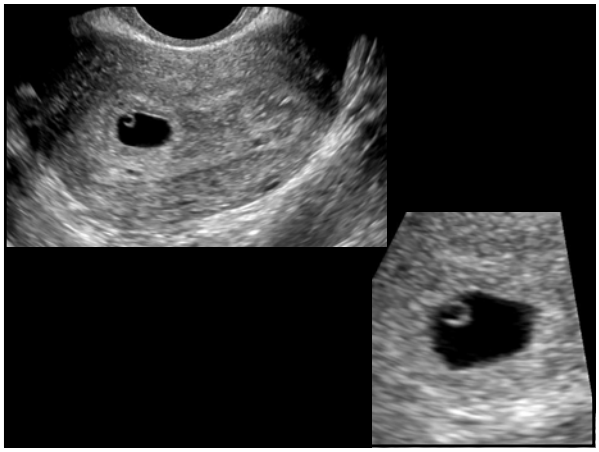

⊕ hCG & Nonspecific Intrauterine Fluid Collection
Gestational Sac or Pseudogestational Sac?
7 days later
11 days later
16 days later

Pseudogestational Sac

- Little or no value, avoid the term
- If definite ectopic pregnancy term has no value
- Otherwise, odds are strongly in favor of intrauterine gestation (99.9%)
- Report nonspecific fluid collection in uterus as "almost certainly an intrauterine gestational sac"

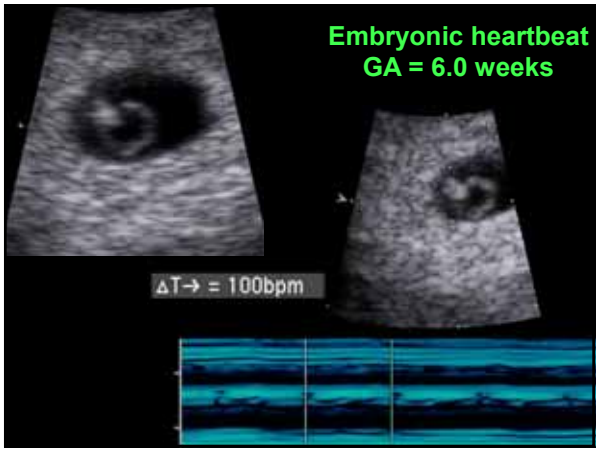
Yolk Sac

- Usually seen on transvaginal ultrasound by 5.5 weeks
- Usually seen when mean sac diameter > 10 mm
- Visualization of yolk sac confirms gestational sac is a pregnancy



Fetal Cardiac Activity

- Usually seen on transvaginal ultrasound by 6.0 weeks
- Visualization of embryonic heartbeat confirms viability



Pregnancy Failure

Most frequent early in pregnancy:

- 6 - 8 weeks with heartbeat 10 - 17% will be lost
- After 8 weeks with heartbeat < 4% will be lost

Pregnancy Failure

Increased loss rates
Existing conditions

- Prior miscarriages
- Uterine duplication anomalies
- Fibroids
- Advanced maternal age

Pregnancy Failure

Increased loss rates
Once pregnant

- Bleeding
- Slow fetal heart rate
- Subchorionic hematoma

Pregnancy Failure

Definitive diagnosis

- Embryo ≥ 7 mm* with no heartbeat
- Mean sac diameter ≥ 25 mm* with no heartbeat
- No heartbeat & gestational age 2 wks after gestational sac seen* (GA >7 wks by prior ultrasound)
- Sliding sac

*SRU Consensus Panel on Dx of Early Pregnancy Failure 2012

Pregnancy Failure

Findings on follow up ultrasound

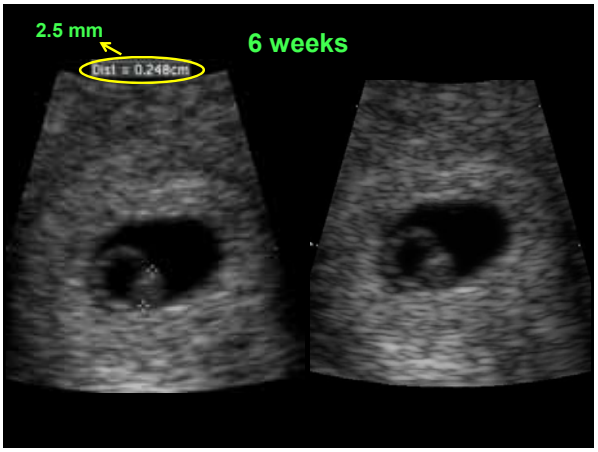
Current U/S Finding	Definite failed pregnancy if:	Suspicious for failed pregnancy if:
Gestational sac with no embryo	≥2 wks since GS without YS	7-13 days since GS without YS
Gestational sac with no embryo	≥11 days since GS with YS	7-10 days since GS with YS

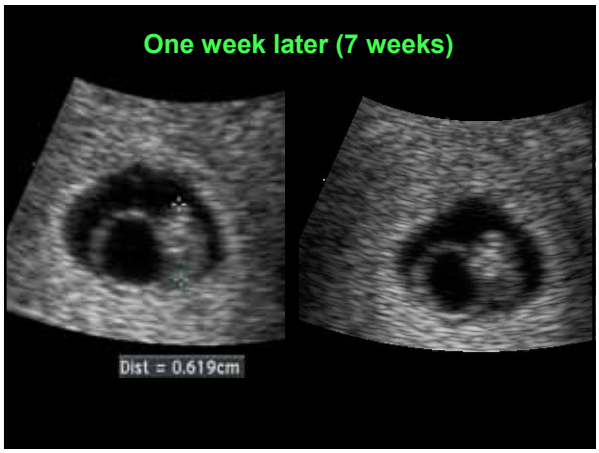
*SRU Consensus Panel on Dx of Early Pregnancy Failure 2012
GS = gestational sac; YS = yolk sac

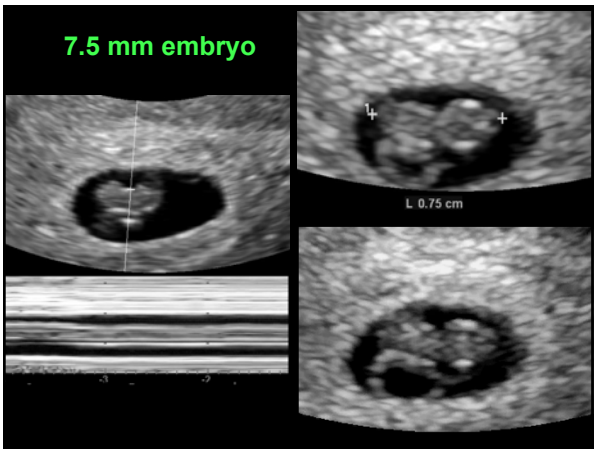
Pregnancy Failure by Crown-Rump Length (CRL)

Rationale for ≥ 7 mm cutoff

- Set value to virtually eliminate any false positive diagnoses **(100% specificity)**
- Prior criteria not stringent enough Based on small numbers of cases
- Need to account for interobserver variability **(± 15%)**



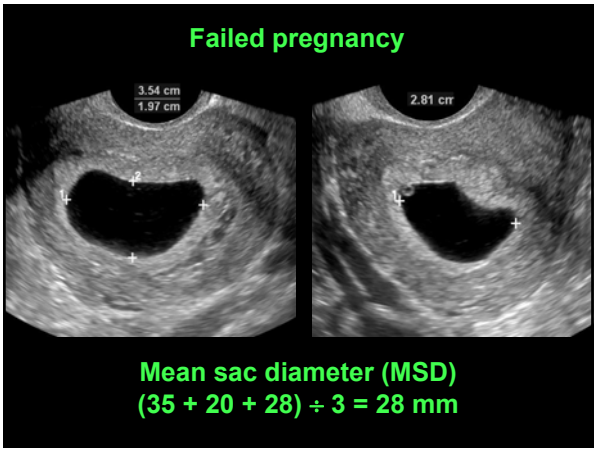




Pregnancy Failure by Mean Sac Diameter (MSD)

Rationale for ≥ 25 mm cutoff

- Set value to virtually eliminate any false positive diagnoses **(100% specificity)**
- Prior criteria not stringent enough Based on small numbers of cases
- Need to account for interobserver variability **(± 19%)**



Sliding Intrauterine Gestational Sac

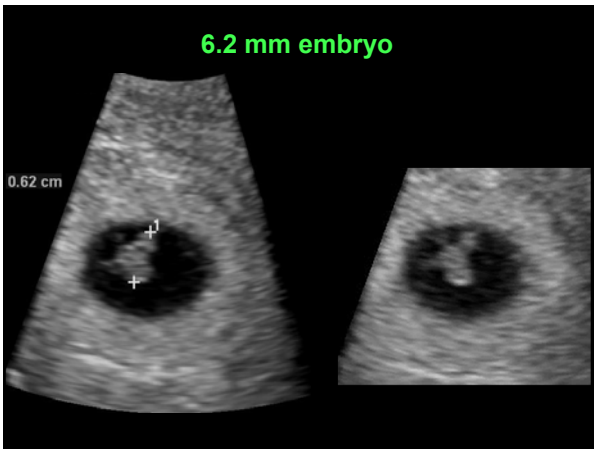
- Gestational sac within uterine cavity, not embedded in decidua
- Shifts position within uterine cavity on realtime scanning

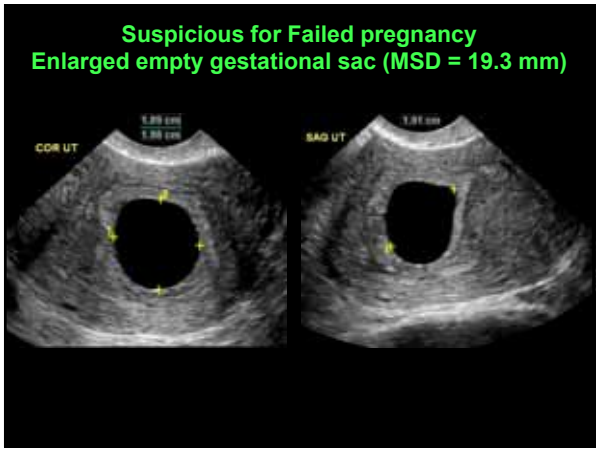


Pregnancy Failure

Suspicious but not definitive

- Embryo < 7 mm with no heartbeat
  larger the embryo, higher the risk
- Mean sac diameter 16 - 24 mm
  with no heartbeat
- > 6 weeks gestation by LMP with
  gestational sac, but no embryo

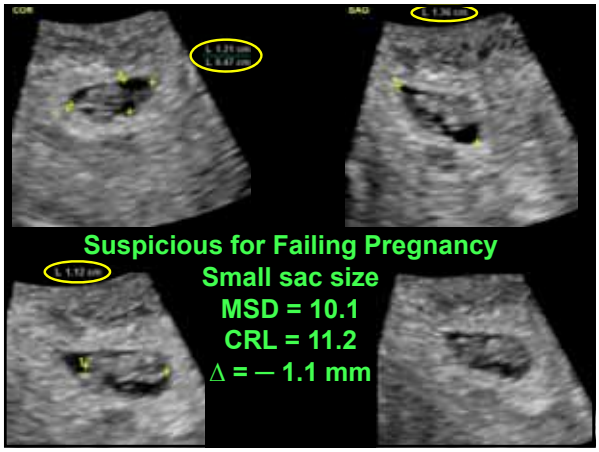


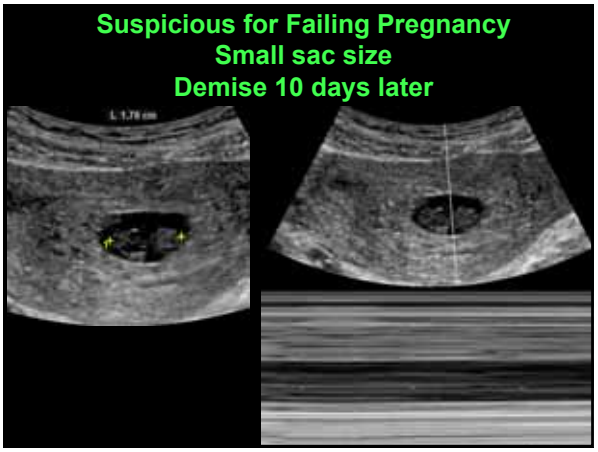


Pregnancy Failure

High likelihood of subsequent
pregnancy failure

- Small sac size (MSD – CRL < 5 mm)
  even with heartbeat
- Embryonic bradycardia
  (the slower the rate,
  the greater the risk)
- Large subchorionic hematoma
  size > 50% gestational sac size

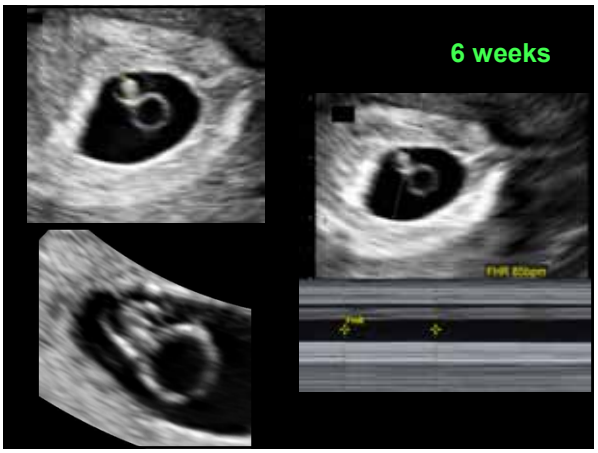




Slow Fetal Heart Rate

Associated with first trimester pregnancy loss

Especially for FHR < 90 bpm



Subchorionic Hematoma & Live Embryo

Prognosis (risk of failed pregnancy)*

- Hematoma size
- Gestational age at diagnosis
- Maternal age

	Gestational Age (Weeks)		
	6.0-7.0	7.1-8.0	8.1-11.0
Demise %	19.6%	14.6%	3.6%

	Maternal Age (Years)	
	<35	≥35
Demise %	9.6%	19.6%

*n=434; demise by end of 1st trimester

Subchorionic Hematoma & Live Embryo

Which method is best for assessing hematoma size?

- Subjective: small, moderate, large?
- Size compared to gestational sac? (%): ≤10; 10-25; 25-50; >50
- Fraction of gestational sac surrounded by hematoma? (%): ≤10; 10-25; 25-50; >50
- 3 orthogonal measurements to calculate "volume"?

Subchorionic hematoma – 5.5 weeks



- Subjective size: Moderate
- Hematoma size >50% size of gestational sac
- Surrounds 25-50% of gestational sac
- Measured 19 x 16 x 10 mm

Subchorionic Hematoma & Live Embryo

434 pregnancies 6-11 weeks

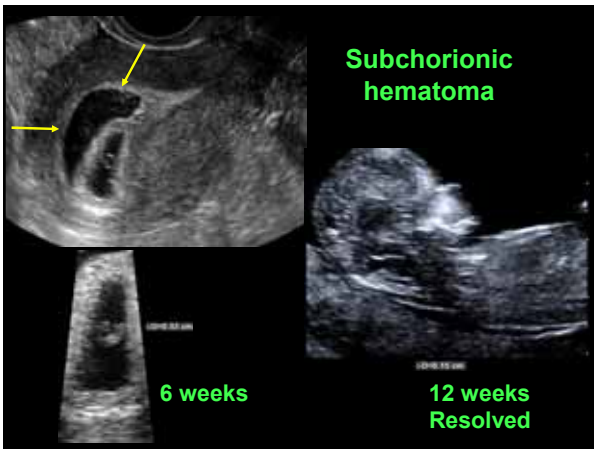
- Size compared to gestational sac (%): ≤10; 10-25; 25-50; >50
  Correlated best with outcome (p<0.001)
- X Subjective: small, moderate, large (p=0.142)
- X Fraction of gestational sac surrounded (%): ≤10; 10-25; 25-50; >50 (p=0.085)
- X 3 orthogonal measurements calculate "volume" (poor correlation, spurious results)

Subchorionic Hematoma & Live Embryo

434 pregnancies 6-11 weeks*

	Hematoma Size as Fraction of Gestational Sac Size (p<0.001)			
	≤10%	10-25%	25-50%	>50%
Live*	114	112	66	89
Demise	7	11	8	27
Demise %	5.8%	8.9%	10.8%	23.3%

*Live at end of 1st trimester



Pregnancy Failure

Recommended follow up of suspicious but not definitive findings (IPUV*)

- Ultrasound, not hCG
- 7-10 days (in most cases)

*Intrauterine pregnancy of unknown viability

⊕hCG & No Intrauterine Gestational Sac

Ultrasound diagnosis

- Pregnancy of Unknown Location (PUL)
  ⊕hCG & Ultrasound findings:
  No intrauterine gestational sac or adnexal mass
- Ectopic Pregnancy
  No intrauterine gestational sac & findings of ectopic pregnancy

Ectopic Pregnancy

Transvaginal Ultrasound Findings

No intrauterine gestation

Adnexal mass separate from ovary

- Tubal ring
- Internal yolk sac
- Embryo with heartbeat

Free fluid

hCG Discriminatory Level

Rationale for setting this:

If hCG > discriminatory level

and

No intrauterine gestation (IUP) seen

↓

Safe to treat suspected ectopic

Will not damage a normal pregnancy

hCG Discriminatory Level

Levels proposed (mIU/ml):

- 6,500 (1981)
- 3,600 (1985)
- 1,000-2,000 (1990 and beyond)

Improved equipment and transvaginal probes

Our Study

Methods:

Transvaginal sonograms 2000-2010

Positive pregnancy test and

No intrauterine fluid collection

Subsequent live intrauterine gestation

hCG at time of no IUP recorded

Pregnancy outcomes collected

hCG levels

hCG	N	Live at 14w*
< 1000	162	89.9%
1000-1499	19	88.6%
1500-1999	12	86.6%
≥ 2000	9	80.6%

*No difference in miscarriage rates among hCG groups (p>0.05)

9 Cases with hCG ≥2000

hCG	Pregnancy outcome
2215	Term singleton
2217	Term twins
2374	Term singleton
2530	Live at 21w, loss from chorio
2539	Term singleton
2993	Term singleton
4336	Term singleton
4476	Live at 7.6w, loss before 14w
6567	Live at 7.1w, slow FH, 8w demise

hCG levels

- 6567 = Highest hCG with subsequent live IUP
- 4336 = Highest hCG with subsequent live born

hCG & Ectopic Pregnancy*

US Finding	Key Points
No intrauterine fluid collection Normal adnexa	• A ***single hCG*** in a woman with an "empty" uterus on U/S: • **DOES NOT** reliably distinguish between ectopic and intrauterine pregnancy • **DOES NOT** definitively exclude a potentially normal IUP (though normal IUP is unlikely if >3000 mIU/ml) • **DOES NOT** exclude an ectopic pregnancy (even if <1000 mIU/ml) • **DOES NOT** justify presumptive treatment for ectopic pregnancy, using methotrexate or other medical/surgical means • The concept of a "discriminatory" hCG level – an hCG value for ruling in or ruling out ectopic pregnancy at a single point in time – should not be used to guide management decisions

*SRU Consensus Panel on Dx of Early Pregnancy Failure 2012

Safe Rule

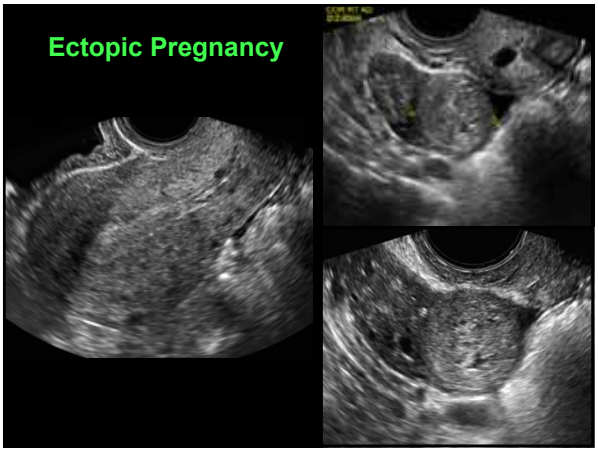
- No matter what the hCG, definitive interventions, like D&C or MTX, should be avoided in suspected but unproven ectopic pregnancy
- Unless patient is unstable, get f/u ultrasound and/or hCG before intervention

Ectopic Pregnancy

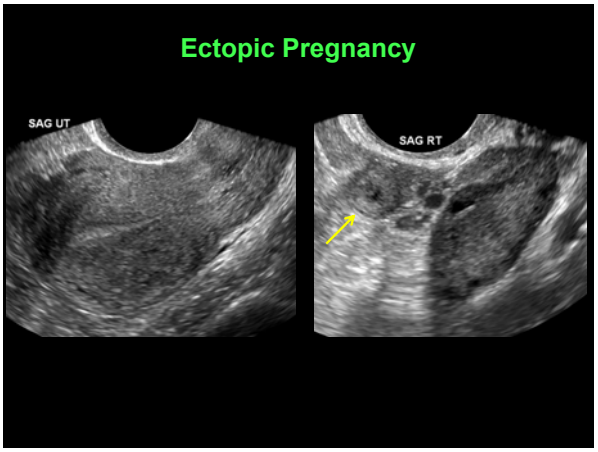
Transvaginal Ultrasound Findings

- No intrauterine gestation
- Adnexal mass separate from ovary
  - Tubal ring
  - Internal yolk sac
  - Embryo with heartbeat
- Free fluid

Ectopic Pregnancy



Ectopic Pregnancy



231 Ectopic Pregnancies

Ultrasound findings present in 94.8%

Adnexal mass	94.4%
Nonspecific mass	54.1%
Tubal ring (no YS or heartbeat)	24.7%
Yolk sac (no heartbeat)	8.3%
Live embryo	7.4%
Free fluid: Moderate – large (no adnexal mass)	0.4%

Frates et al. J Ultrasound Med 2014

Ectopic Pregnancy

Ultrasound findings	Likelihood of ectopic
Intrauterine pregnancy (IUP)	~0%
No IUP, normal pelvis/simple cyst	1%
No IUP, complex mass	92%
No IUP, tubal ring	95%
Live embryo outside uterus	100%

Doppler for Ectopic Pregnancy

Ultrasound findings
Adnexal mass

Color Doppler findings
Rim of color around mass

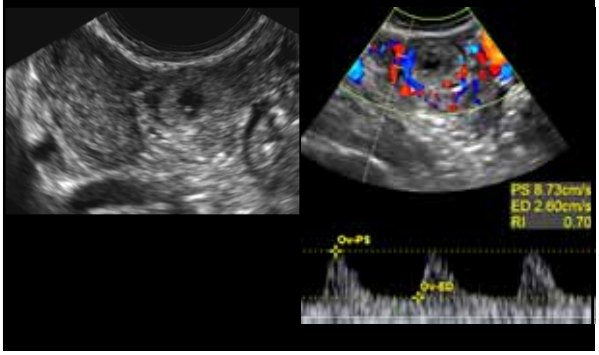
Spectral Doppler findings
Low resistance waveform

Caution
Intraovarian lesion with rim of color is likely corpus luteum

Doppler for Ectopic Pregnancy

- Doppler has limited use over and above ultrasound.
- If there is an adnexal mass, Doppler does **not** assist the diagnosis, because the interpretation should already be **probable ectopic**.

Ectopic Pregnancy



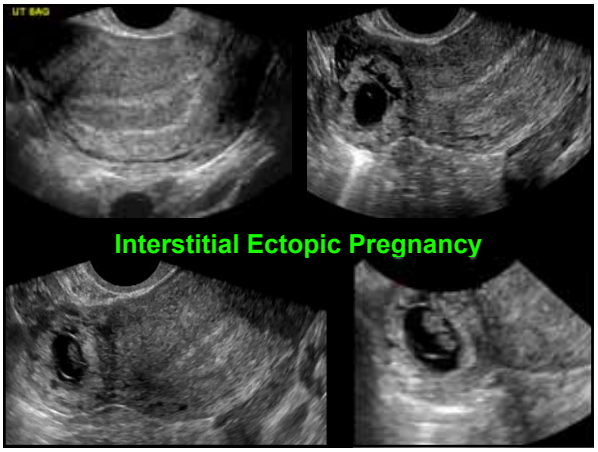
Unusual Ectopic Pregnancies

- Abdominal
- Interstitial (Cornual)
- Cervical
- Ovarian
- Heterotopic (IUP & ectopic)

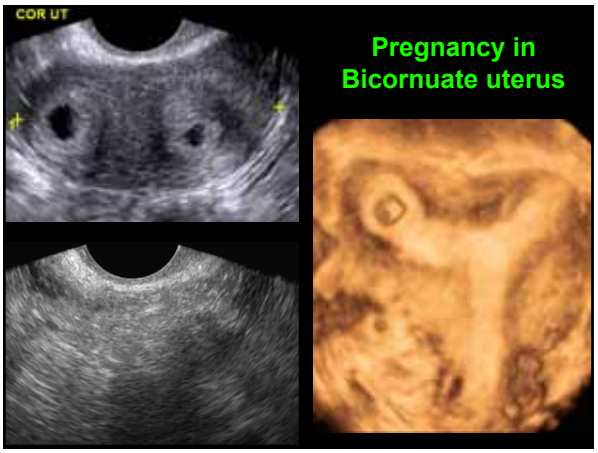
- Cesarean section scar/defect implantation

Interstitial Ectopic Pregnancy

- Embedded in interstitial portion of tube
- Gestational sac upper outer edge of uterus
- Gestational sac outside uterine cavity
- Thin layer or no myometrium around outer gestational sac
- 3D imaging often helpful







Heterotopic Pregnancy

Intrauterine & ectopic pregnancies coexistant

Incidence

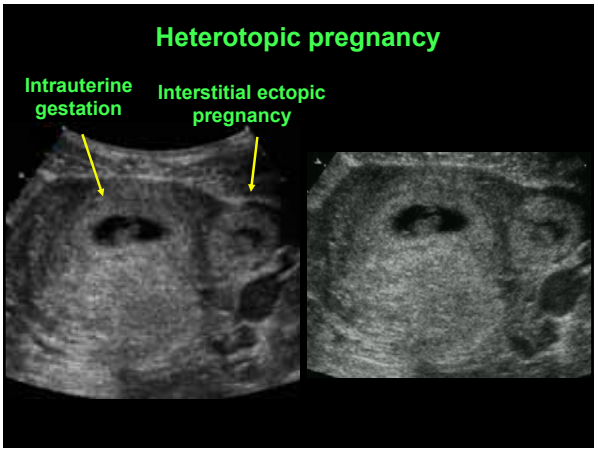
~ 1 / 4,000 - 8,000 (natural)

10x – 20x higher (Rx infertility)

Ultrasound findings

Intrauterine gestation

Ectopic pregnancy



Cervical Ectopic Pregnancy

- Gestational sac implanted in the cervix
- Differential diagnosis includes miscarriage in progress if no embryo with heartbeat
  - May slide within cervical canal
  - May pass on short-term follow up

