

Sonographic Evaluation of Early Pregnancy Loss

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Disclosures

Relevant Financial Relationships: None

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Learning Objectives

After completing this presentation, the learner will:

Objective 1: understand the limitations of the hCG
"discriminatory level"

Objective 2: know the sonographic criteria for definite pregnancy failure and probable pregnancy failure in early pregnancy

Objective 3: know the sonographic findings that, in the presence of an embryonic heartbeat, indicate a high risk of impending pregnancy loss

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Introduction

- 10-25% of all clinically recognized pregnancies end in pregnancy failure ("miscarriage")
- Ultrasound is the primary method for diagnosing pregnancy failure, using criteria for *definite*, *probable*, and *impending* pregnancy failure
- Sonographic criteria for definite pregnancy failure should be set to virtually eliminate false positives, in order to avoid interventions that could eliminate or damage a normal intrauterine pregnancy

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Lecture Outline

- Normal U/S findings in early pregnancy
- Early pregnancy loss: terminology, incidence, general principles
- Early pregnancy loss: sonographic diagnosis
 - Scenario 1: Ultrasound demonstrates no intrauterine or ectopic pregnancy in a woman with positive pregnancy test
 - Can a single hCG value ("discriminatory level") exclude a viable IUP?
 - Scenario 2: Ultrasound demonstrates an intrauterine gestational sac; no cardiac activity is seen (with or without a visible embryo)
 - What findings indicate definite pregnancy failure?
 - What findings are suspicious for pregnancy failure?
 - Scenario 3: Ultrasound demonstrates an intrauterine pregnancy with cardiac activity
 - What findings suggest impending pregnancy failure?

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- Normal U/S findings in early pregnancy
- Early pregnancy loss: terminology, incidence, general principles
- Early pregnancy loss: sonographic diagnosis

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Normal Sonographic Findings in Early Pregnancy

Gestational Age
(weeks)

- 5.0 — Gestational sac
- 5.5 — Yolk sac
- 6.0 — Embryo with heartbeat
- 6.5 —
- 7.0 — Amnion around embryo

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Normal Sonographic Findings in Early Pregnancy

5.0 Weeks: No Visible Contents
("nonspecific" saclike structure)

5.5 Weeks: Yolk Sac

6.0 Weeks: Embryo with Heartbeat

7.0 Weeks: Amnion around embryo

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- Normal U/S findings in early pregnancy
- Early pregnancy loss: terminology, incidence, general principles
- Early pregnancy loss: sonographic diagnosis

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U/S of Early Pregnancy Loss

- Terminology
 - *Miscarriage* = Spontaneous loss of an intrauterine pregnancy prior to 20 weeks of gestation
 - *Early pregnancy failure*: Often used to describe spontaneous loss of an intrauterine pregnancy in the first trimester
 - Other terms
 - spontaneous abortion
 - blighted ovum

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U/S of Early Pregnancy Loss

- Incidence
 - 10-25% of all clinically recognized pregnancies end in miscarriage
 - Highest rate of miscarriage is at ≤6 weeks of gestation, then progressively declines
- Chromosomal anomalies are thought to be the most common cause of miscarriage

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Society of Radiologists in Ultrasound
Consensus Conference on Early 1st Δ Sonography:
Guidelines for Diagnosing Miscarriage and
Excluding a Viable Intrauterine Pregnancy

Baltimore, MD
October 23-24, 2012



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Society of Radiologists in Ultrasound Consensus Conference on Early 1st Δ Sonography: Guidelines for Diagnosing Miscarriage and Excluding a Viable Intrauterine Pregnancy

Moderator: Peter Doubilet

- ❖ Radiology
 - Beryl Benacerraf
 - Carol Benson
 - Rusty Brown
 - Roy Filly
 - Ted Lyons
 - Dolores Pretorius
- ❖ OB/Gyn
 - Kurt Barnhart
 - Tom Bourne
 - Steven Goldstein
 - Misty Porter
 - Ilan Timor
- ❖ Emergency Medicine
 - Michael Blaivas
 - Chris Fox
 - John Kendall

Diagnostic Criteria for Nonviable Pregnancy Early in the First Trimester

Peter M. Doubilet, M.D., Ph.D., Carol B. Benson, M.D.,
Tom Bourne, M.B., B.S., Ph.D., and Michael Blaivas, M.D., for the Society of
Radiologists in Ultrasound Multispecialty Consensus Panel on Early First Trimester
Diagnosis of Miscarriage and Exclusion of a Viable Intrauterine Pregnancy*
N Engl J Med 2013;369:1443-51

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U/S of Early Pregnancy Loss Consequences of False ⊕ & ⊖ Dx

False ⊕: Erroneous
diagnosis of failed
pregnancy

Consequence: Uterine
evacuation when there is a
potentially normal IUP

False ⊖: Missed
diagnosis of failed
pregnancy

Consequence: Delayed
intervention for
failed IUP

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U/S of Early Pregnancy Loss Key Principle

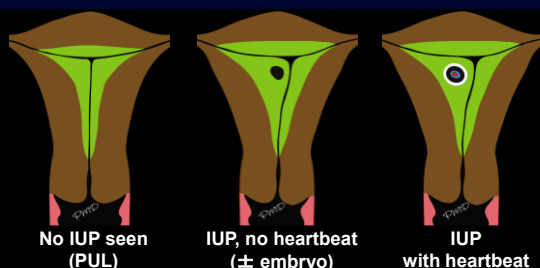
- Criteria for pregnancy failure should be set to:
 - eliminate false positives
 - apply to a broad range of U/S facilities that meet at least minimum quality criteria, not solely to experts in early OB U/S

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- Normal U/S findings in early pregnancy
- Early pregnancy loss: terminology, incidence, general principles
- Early pregnancy loss: sonographic diagnosis

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U/S of Early Pregnancy Loss Three Scenarios*



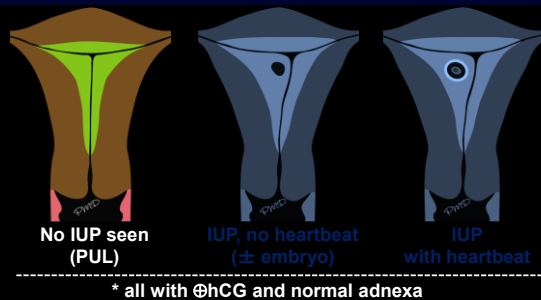
* all with ⊕hCG and normal adnexa

U/S of Early Pregnancy Loss Three Scenarios*

U/S Finding	Key Questions
No IUP seen	Can a single hCG value ("discriminatory level") exclude viable IUP?
IUP, no heartbeat (± embryo)	What findings indicate <i>definite</i> pregnancy failure? What findings are <i>suspicious</i> for pregnancy failure?
IUP with heartbeat	What findings suggest <i>impending</i> pregnancy failure?

* all with ⊕hCG and normal adnexa

U/S of Early Pregnancy Loss Three Scenarios*



U/S of Early Pregnancy Loss Three Scenarios*

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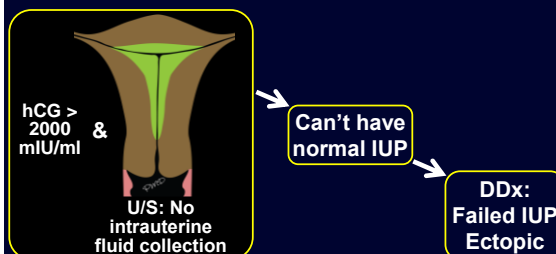
* all with \oplus hCG and normal adnexa

hCG "Discriminatory Level"

- Concept Originated by Kadar in 1981
- Definition
 - hCG level at which normal IUP is consistently seen
- Improved U/S Technology \rightarrow ↓ Discrim Level
 - 1981: 6500 mIU/ml
 - 1985: 3600 mIU/ml
 - 1990 & beyond (TV U/S): 1000-2000 mIU/ml

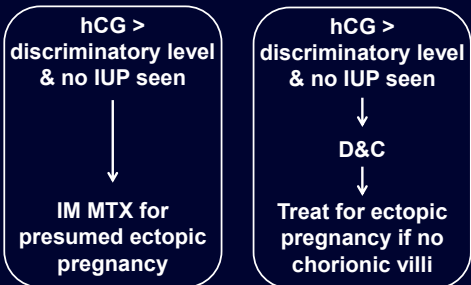
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hCG "Discriminatory Level" Rationale



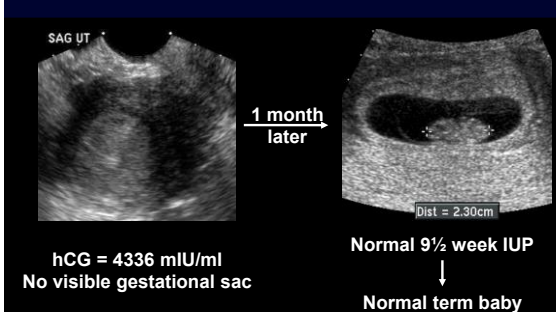
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hCG "Discriminatory Level" Proposed Management Algorithms

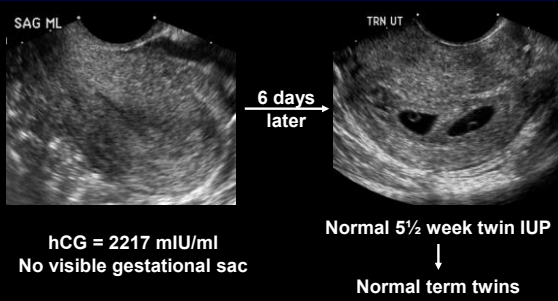


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hCG "Discriminatory Level" Reality



hCG "Discriminatory Level" Reality



hCG > 2000 mIU/ml & No Intrauterine Fluid
Collection → ⊕ FH on F/U U/S
BWH Experience 1/1/2000 – 12/31/2010

hCG at 1st U/S	# of ⊕ FH's on F/U U/S	Pregnancy Outcome
2215	1	1 normal liveborn
2217	2	2 normal liveborns
2374	1	1 normal liveborn
2530	1	Demise at 21 weeks
2539	1	1 normal liveborn
2993	1	1 normal liveborn
4336	1	1 normal liveborn
4476	1	Demise at 8 weeks
6567	1	Demise at 8 weeks

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hCG ↔ Pregnancy of Unknown Location (PUL)

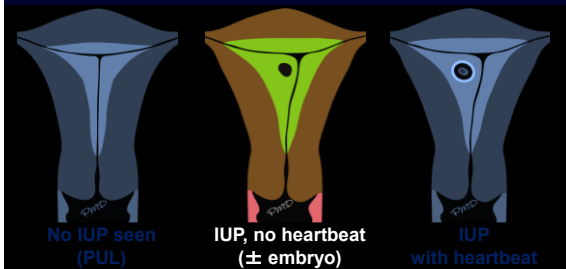
- hCG levels in normal IUPs, abnormal IUPs, and ectopic pregnancies have considerable overlap
- If U/S shows no evidence of intrauterine or ectopic pregnancy, don't intervene based on a single hCG measurement
 - Get at least one F/U U/S & hCG, in order to avoid:
 - damaging a potentially normal IUP
 - giving MTX to a woman with failed IUP



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Consensus
Panel

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U/S of Early Pregnancy Loss Three Scenarios*



* all with ⊕hCG and normal adnexa

U/S of Early Pregnancy Loss Three Scenarios*

U/S Finding	Key Questions
No IUP seen	Can a single hCG value ("discriminatory level") exclude viable IUP?
IUP, no heartbeat (± embryo)	What findings indicate <i>definite</i> pregnancy failure? What findings are <i>suspicious</i> for pregnancy failure?
IUP with heartbeat	What findings suggest impending pregnancy failure?

* all with ⊕hCG and normal adnexa

Diagnosis of Pregnancy Failure Criteria

- Non-visualization of a heartbeat by a certain embryonic size
 - Crown-rump length (CRL) without heartbeat
- Non-visualization of an embryo by a certain gestational sac size
 - Mean sac diameter (MSD) without embryo
- Non-visualization of an embryo by a certain point in time
 - No embryo seen after a time interval since 1st scan

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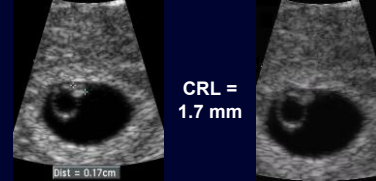
Diagnosis of Pregnancy Failure Criteria: Up to ~2012

- Non-visualization of a heartbeat by a certain embryonic size
 - Crown-rump length ≥ 5 mm without heartbeat
- Non-visualization of an embryo by a certain gestational sac size
 - Mean sac diameter ≥ 16 mm without embryo
- Non-visualization of an embryo by a certain point in time
 - Not well established

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Crown-Rump Length

- ❖ Heartbeat is *usually* seen as soon as the embryo is visible



- ❖ At what CRL is the heartbeat *always* seen in a normal pregnancy?

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Crown-Rump Length

Cutoff value above which cardiac activity is consistently visible on TV U/S in a normal pregnancy

- Early studies
 - Levi 1990: 4 mm
 - Goldstein 1992: 4 mm
 - Brown 1990: 5 mm
 - Pennell 1991: 5 mm
- 5 mm became the generally accepted cutoff

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Crown-Rump Length

- Concerns With the Early Data
 - Small study populations \rightarrow 95% confidence range of specificity = 0.90-1.0
 - Several cases of embryos with CRL of 5-6 mm and no cardiac activity that subsequently proved to be normal have been reported (Abdallah 2011; Hamilton 2011)
 - Interobserver variability of CRL measurement has been found to be $\pm 15\%$ (Pexsters 2011)
 - One practitioner's 6 mm CRL may be 15% higher, or 6.9 mm, when measured by others

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Crown-Rump Length

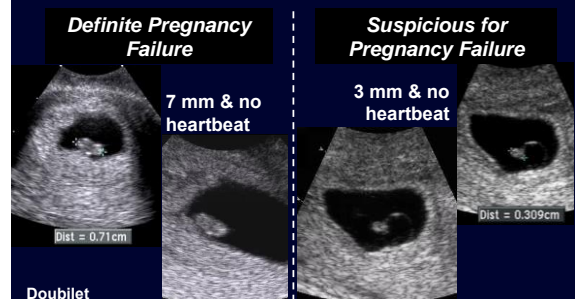
- CRL ≥ 7 mm & no heartbeat: *definitive* for failed pregnancy
- CRL < 7 mm & no heartbeat: *suspicious* for failed pregnancy



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Crown-Rump Length



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Mean Sac Diameter

Cutoff value above which an embryo is consistently visible on TV U/S in a normal pregnancy

- Early studies
 - Levi 1988: 16 mm
 - Tongsong 1994: 17 mm
- 16 mm became the generally accepted cutoff

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Mean Sac Diameter

- Concerns With the Early Data
 - Small study populations → 95% confidence range of specificity = 0.88-1.0
 - Several cases of embryos with MSD of 17-21 mm and no cardiac activity that subsequently proved to be normal have been reported (Abdallah 2011; Rowling 1997)
 - Interobserver variability of MSD measurement has been found to be $\pm 19\%$ (Pexsters 2011)
 - One practitioner's 21 mm MSD may be 19% higher, or 25.0 mm, when measured by others

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Mean Sac Diameter

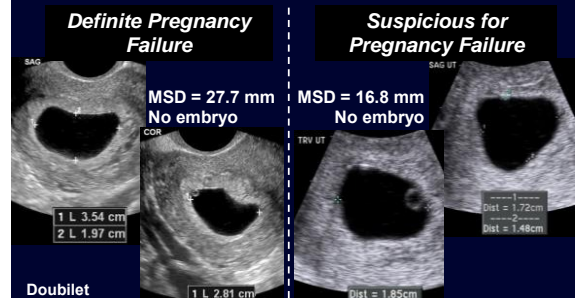
- MSD ≥ 25 mm & no embryo: *definitive* for failed pregnancy
- MSD 16-24 mm & no embryo: *suspicious* for failed pregnancy



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Mean Sac Diameter



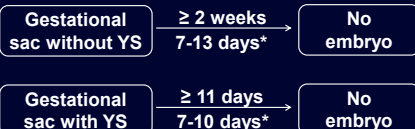
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Time-Based Criteria for Pregnancy Failure



Scan 1

Scan 2

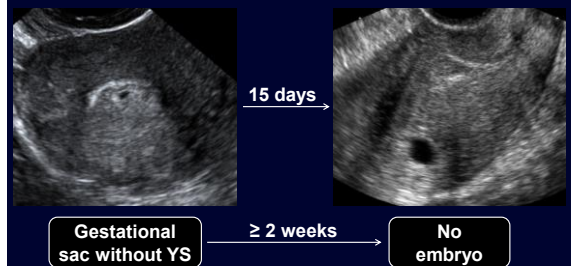


No embryo >6 weeks after LMP*

* suspicious for pregnancy failure

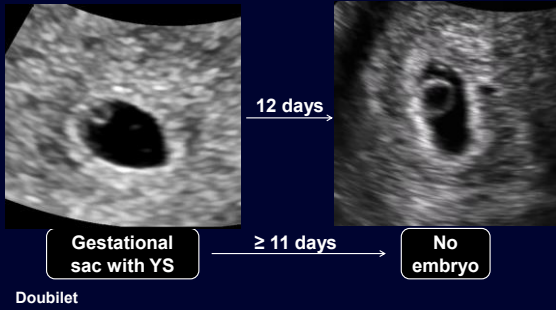
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Time-Based Criteria Definite Pregnancy Failure

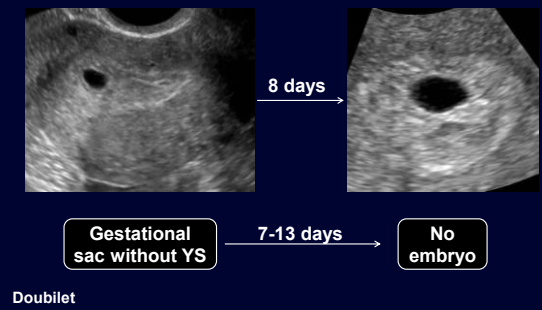


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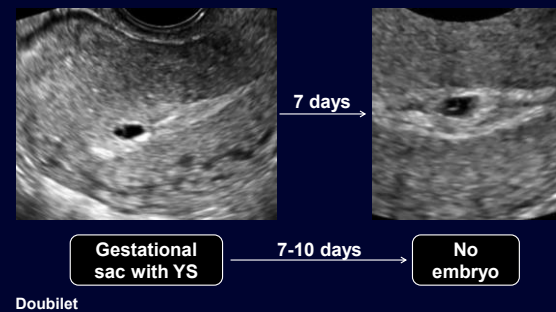
Time-Based Criteria *Definite Pregnancy Failure*



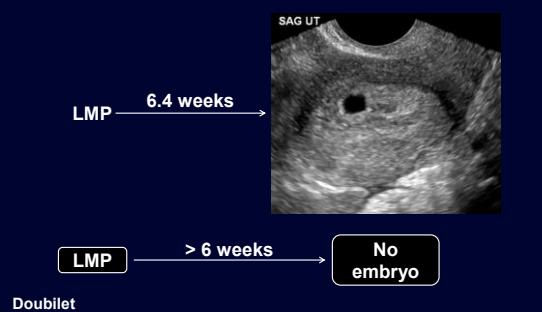
Time-Based Criteria *Suspicious for Pregnancy Failure*



Time-Based Criteria *Suspicious for Pregnancy Failure*



Time-Based Criteria *Suspicious for Pregnancy Failure*



Other Criteria Suspicious for Pregnancy Failure

- “Empty amnion”
 - Amnion adjacent to yolk sac, no embryo
- Large yolk sac ($>6-7$ mm)

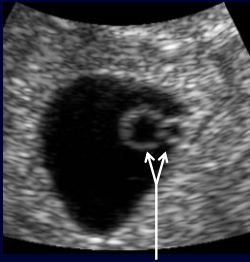
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“Empty Amnion” *Suspicious for Pregnancy Failure*

- Embryo normally appears earlier than amnion
 - Embryo at 6 weeks, amnion at 7 weeks
- Identification of the amnion with no visible embryo is abnormal

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“Empty Amnion” Suspicious for Pregnancy Failure



Yolk sac + amnion, no embryo

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Large Yolk Sac (> 6-7 mm) Suspicious for Pregnancy Failure



Dist = 0.72cm



Distance = 0.91 cm

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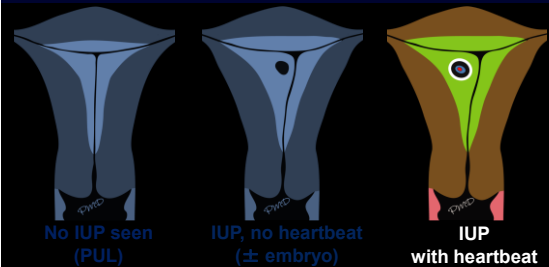
Failed Intrauterine Pregnancy (Miscarriage) Diagnostic Criteria



Parameter	Definite Pregnancy Failure	Suspicious for Failure (F/U in 7-10 Days)
CRL	≥7 mm and no heartbeat	<7 mm and no heartbeat
MSD	≥25 mm and no embryo	16-24 mm and no embryo
Time	- - Absence of embryo ≥2 weeks after a scan that showed a gestational sac without yolk sac Absence of embryo ≥11 days after a scan that showed a gestational sac with yolk sac	No embryo ≥6 weeks after LMP Absence of embryo 7-13 days after a scan that showed a gestational sac without yolk sac Absence of embryo 7-10 days after a scan that showed a gestational sac with yolk sac
Other		Empty amnion Enlarged yolk sac (>6-7 mm)

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U/S of Early Pregnancy Loss Three Scenarios*



No IUP seen
(PUL)

IUP, no heartbeat
(± embryo)

IUP
with heartbeat

* all with \oplus hCG and normal adnexa

U/S of Early Pregnancy Loss Three Scenarios*

U/S Finding	Key Questions
No IUP seen	Can a single hCG value ("discriminatory level") exclude viable IUP?
IUP, no heartbeat (± embryo)	What findings indicate definite pregnancy failure? What findings are suspicious for pregnancy failure?
IUP with heartbeat	What findings suggest <i>impending</i> pregnancy failure?

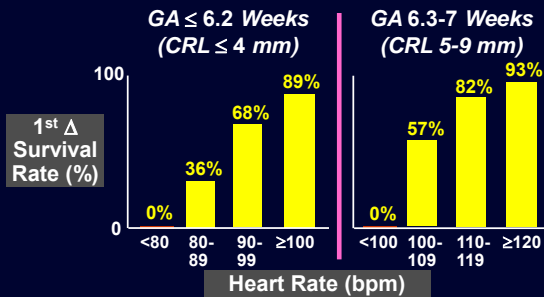
* all with \oplus hCG and normal adnexa

U/S Demonstrates IUP with Heartbeat Risk Indicators of Impending Pregnancy Failure

- Slow or irregular embryonic heartbeat
- Large subchorionic hematoma
- Small gestational sac size in relation to embryo
- Expanded amnion
- Large yolk sac (> 6-7 mm)
- Sliding gestational sac

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Embryonic Heart Rate (6-7 Weeks) Relationship to 1st Δ Survival Rate



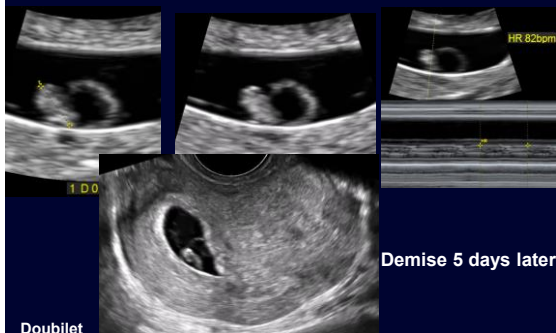
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Early Heart Rate Classification

Classification	≤6.2 Wks CRL ≤ 4 mm	6.3-7.0 Wks CRL 5-9 mm
Slow	<90 bpm	<110 bpm
Borderline	90-99 bpm	110-119 bpm
Normal	≥100 bpm	≥120 bpm

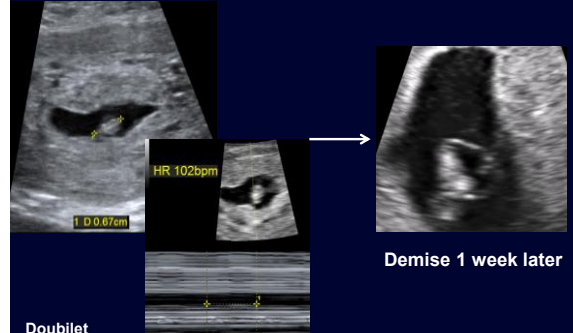
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Slow Embryonic Heart Rate Suspicious for Impending Pregnancy Failure



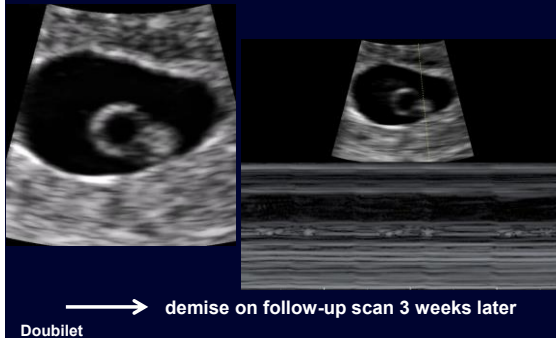
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Slow Embryonic Heart Rate Suspicious for Impending Pregnancy Failure



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Irregular Embryonic Heart Rate Suspicious for Impending Pregnancy Failure



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Subchorionic Hematoma in Conjunction with Heartbeat Clinical Significance

- Subchorionic hematomas have been classified as small, medium, large based on:
 - Subjective assessment
 - Fraction of gestational sac surrounded by hematoma
 - Estimated volume of hematoma

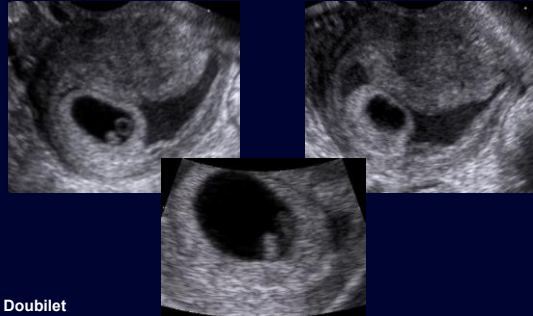
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Subchorionic Hematoma in Conjunction with Heartbeat *Clinical Significance*

- Most studies of subchorionic hematoma in the presence of an embryonic heartbeat find that:
 - Large SCH carries an elevated risk of subsequent pregnancy failure
 - likelihood of failure is ~20-40%
 - Small-moderate SCH carries little-no added risk of subsequent pregnancy failure

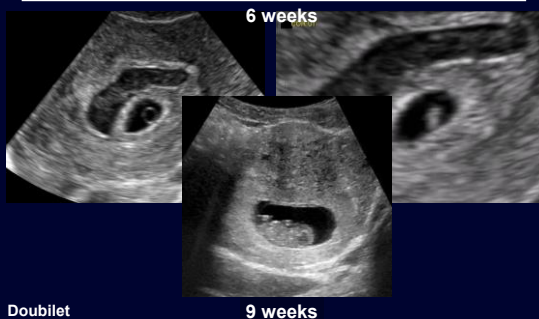
Doubilet

Large Subchorionic Hematoma in Conjunction with Heartbeat *Suspicious for Impending Pregnancy Failure*



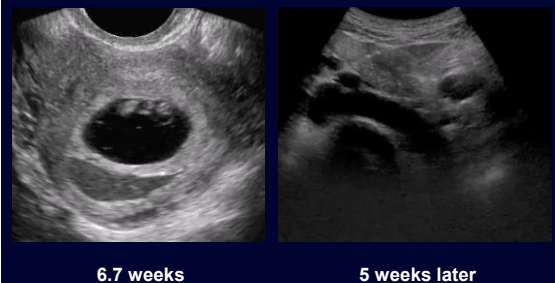
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Large Subchorionic Hematoma in Conjunction with Heartbeat *Suspicious for Impending Pregnancy Failure*



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Small Subchorionic Hematoma in Conjunction with Heartbeat *Little-No Risk*



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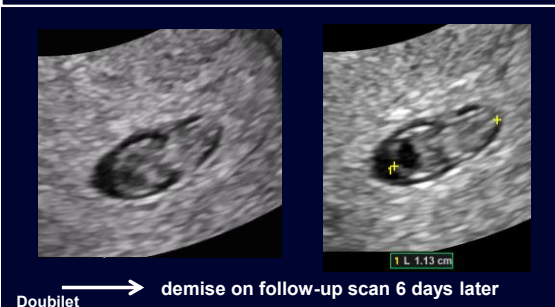
Small Gestational Sac Size in Conjunction with Heartbeat *Suspicious for Impending Pregnancy Failure*

- Small sac size in relation to the embryo can be diagnosed by:
 - Quantitative criterion: MSD-CRL < 5 mm*
 - Subjective assessment
- 16 early 1st Δ pregnancies with normal embryonic heart rates and small sac size
→ 15 (94%) ended in pregnancy loss*

* Bromley 1991

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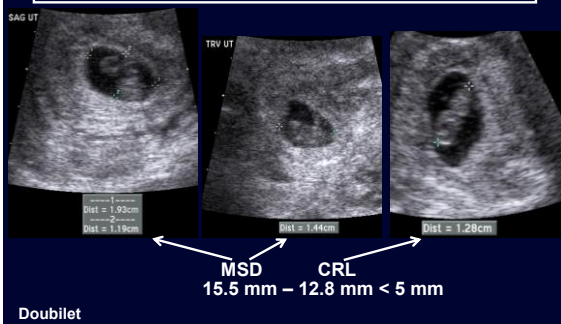
Small Gestational Sac Size in Conjunction with Heartbeat *Suspicious for Impending Pregnancy Failure*



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→ demise on follow-up scan 6 days later

Small Gestational Sac Size in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

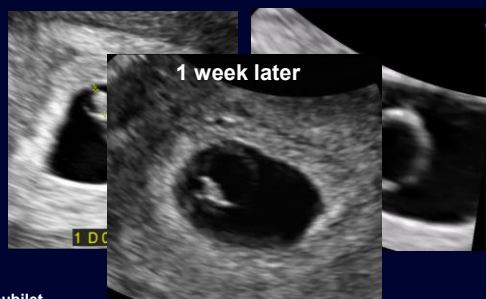


“Expanded Amnion” in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure

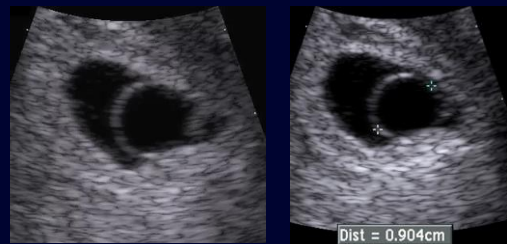
- Amnion normally appears at 6.5-7 weeks (CRL 6-10 mm)
- Identification of the amnion with CRL ≤ 5 mm carries an elevated risk of subsequent pregnancy failure

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“Expanded Amnion” in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure



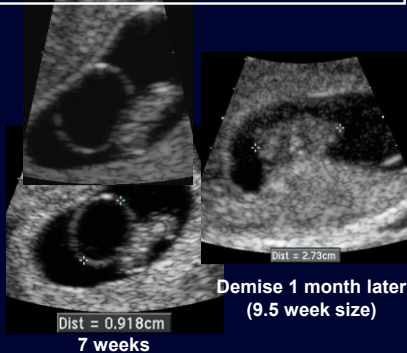
Enlarged Yolk Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure



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Demise 1 week later

Enlarged Yolk Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure



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Sliding Sac in Conjunction with Heartbeat
Suspicious for Impending Pregnancy Failure



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6 weeks

Conclusions

- **Criteria for *definite* pregnancy failure include:**
 - Crown rump length ≥ 7 mm and no heartbeat
 - Mean sac diameter ≥ 25 mm and no embryo
 - Absence of embryo ≥ 2 weeks after a scan that showed a gestational sac without yolk sac
 - Absence of embryo ≥ 11 days after a scan that showed a gestational sac with yolk sac
- **When U/S demonstrates an embryo with heartbeat, signs of *impending* pregnancy failure include:**
 - Slow or irregular embryonic heartbeat
 - Large subchorionic hematoma
 - Small gestational sac size in relation to embryo
 - Expanded amnion
 - Large yolk sac (> 6 -7 mm)
 - Sliding gestational sac

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Key References

Doubilet PM, Benson CB. Further evidence against the reliability of the hCG discriminatory level. J Ultrasound Med 2011; 30: 1637-1642

Doubilet PM, Benson CB, Bourne T et al. Early first trimester diagnostic criteria for nonviable pregnancy. N Engl J Med 2013; 369: 1443-1451

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Benson CB, Doubilet PM. Doubilet PM, Benson CB. Embryonic heart rate in the early first trimester: what rate is normal? J Ultrasound Med 1995; 14:431-434

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