The ultrasound diagnosis of ectopic pregnancy

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Ultrasound Diagnosis of Ectopic Pregnancy

- Transvaginal sonography (TVS) is an accurate diagnostic test for ectopic pregnancy with a high sensitivity (87.0-99.0%) and specificity (94.0-99.9%)
  Braffman et al., 1994, Shalev et al., 1998, Atri et al., 2003, Condous et al., 2005

- Diagnosis based on positive visualisation of an extra-uterine pregnancy, rather than the inability to visualise an intra-uterine pregnancy

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Appearance of an Ectopic Pregnancy on TVS

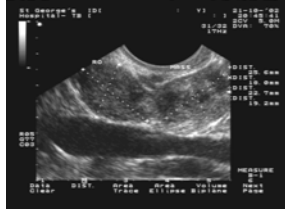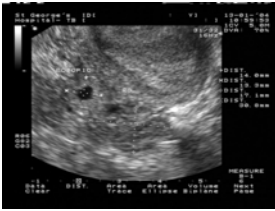### Tubal

Gestational sac and CRL   Visible cardiac activity
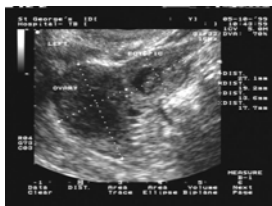
Appearance of an Ectopic Pregnancy on TVS

Tubal

'Bagel Sign'   Inhomogeneous Mass

Appearance of an Ectopic Pregnancy on TVS

Non - Tubal

Cervical

- An empty endometrial cavity, with a gestational sac present below the level of the uterine arteries.
- An absent "sliding sign".
- Visible blood flow around the gestation sac using colour Doppler

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Appearance of an Ectopic Pregnancy on TVS

Non - Tubal

Interstitial

- An empty endometrial cavity with products of conception located outside of the endometrial echo, surrounded by a continuous rim of myometrium, within the interstitial area.

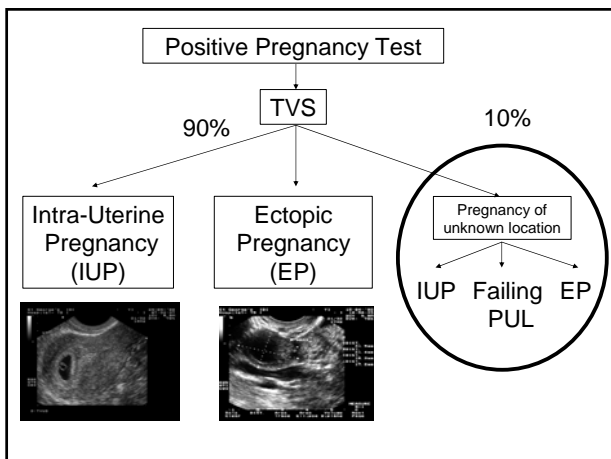## Appearance of an Ectopic Pregnancy on TVS

Non - Tubal

Caesarean Section Scar

- An empty endometrial cavity and cervical canal with a gestational sac implanted within the lower anterior segment of uterine wall
- Evidence of myometrial dehiscence

Diagnosis on the initial TVS examination?

- Studies reporting high sensitivities examined women using TVS immediately prior to laparoscopy, and correlated sonographic features to surgical findings

- Results are therefore possibly misleading as not all ectopic pregnancies would have been visualised on the initial TVS examination

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Positive Pregnancy Test

TVS

90%

10%

Intra-Uterine Pregnancy (IUP)

Ectopic Pregnancy (EP)

Pregnancy of unknown location

IUP   Failing   EP
PUL

Pregnancy of Unknown Location (PUL)

- Positive pregnancy test
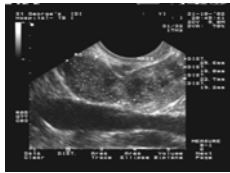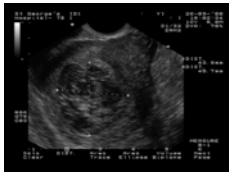- No pregnancy visualised on scan
- Not interchangeable with 'ectopic pregnancy'
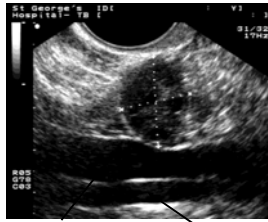
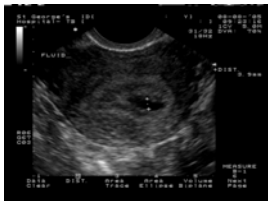Int. Iliac vein   Int. Iliac artery

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X Pregnancy of Unknown Location (PUL)

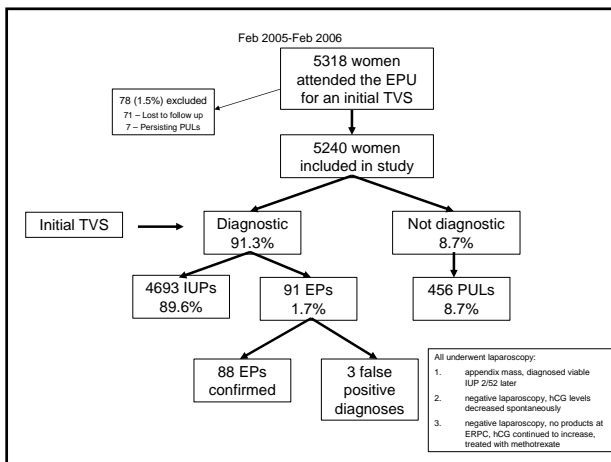Early Intra-uterine Gestational Sac
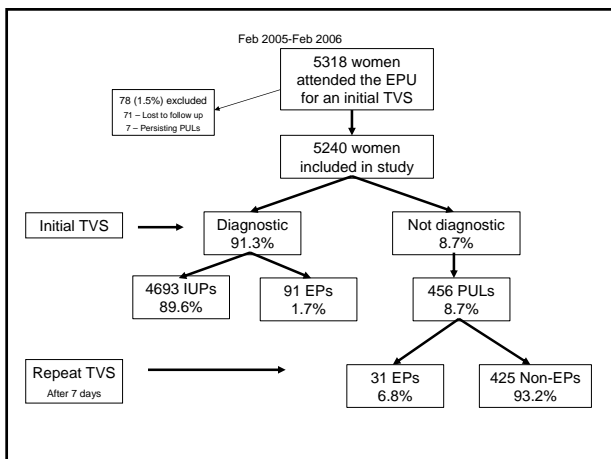
Fluid in the endometrial cavity

Diagnostic effectiveness of the initial TVS to diagnose ectopic pregnancy

▪ A prospective observational study including all women attending the Early Pregnancy Unit with a positive pregnancy test over a one-year period

▪ Outcome measure = ectopic pregnancy

▪ The sensitivity, specificity, PPV, NPV and likelihood ratio with 95% confidence intervals (CI) for the initial USS to diagnose ectopic pregnancy were calculated

Kirk et al, Hum Reprod 2007

Feb 2005-Feb 2006

5318 women attended the EPU for an initial TVS

78 (1.5%) excluded
71 – Lost to follow up
7 – Persisting PULs

5240 women included in study

Initial TVS → Diagnostic 91.3%   Not diagnostic 8.7%

4693 IUPs 89.6%   91 EPs 1.7%   456 PULs 8.7%

88 EPs confirmed   3 false positive diagnoses

All underwent laparoscopy:
1. appendix mass, diagnosed viable IUP 2/52 later
2. negative laparoscopy, hCG levels decreased spontaneously
3. negative laparoscopy, no products at ERPC, hCG continued to increase, treated with methotrexate

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Repeat TVS
After 7 days

31 EPs 6.8%   425 Non-EPs 93.2%

Sensitivity of TVS to detect ectopic pregnancy

- Initial TVS:
  - Sensitivity 73.9% (95% CI: 55.7 – 81.2%)
  - Specificity 99.9% (99.8-100.0%)
  - PPV 96.7% (91.6 – 99.2%)
  - NPV 99.4% (99.1 – 99.6%)

- Overall (including follow-up scans):
  - Sensitivity 98.3% (95% CI: 94.1 - 99.8%)
  - Specificity 99.9% (99.8 - 100.0%)
  - PPV 97.5% (92.9 - 99.5%)
  - NPV 100% (99.9 - 100.0%)

Why are some ectopic pregnancies missed on the initial scan?

	Initial TVS result		
	Ectopic Pregnancy	PUL	p-value
n	353	58	-
Maternal age (years) Mean (SD)	30.4 (5.9)	32.0 (6.3)	0.0551
Bleeding n (%)	216 (61.2)	39 (67.2)	0.4657
Pain n (%)	233 (66.0)	34 (58.6)	0.2997
ET mm Mean (SD)	10.1 (5.7)	11.1 (5.3)	0.098

Why are some ectopic pregnancies missed on the initial scan?

	Initial TVS result		
	Ectopic Pregnancy	PUL	p-value
Gestational age (days) Mean (SD)	45.6 (14.5)	41.4 (13.5)	0.0317
hCG IU/L Median (IQR)	1286 (3384, 478-3826)	635 (1796, 234-2030)	0.0010
Prog nmol/L Median (IQR)	19 (27, 9-36)	30 (26, 19-45)	0.0095

Why are some ectopic pregnancies missed on the initial scan?

	TVS to visualise ectopic pregnancy		
	Initial TVS	Subsequent TVS	p-value
hCG IU/L Median (IQR)	1286 (3384, 473-3826)	1259 (2657, 340-2997)	0.2431
Prog nmol/L Median (IQR)	19 (27, 9-36)	20 (17, 11-28)	0.7334
Appearance on TVS: Inhomogeneous mass n (%)	222 (62.9)	25 (71.4)	0.1029
Empty gestational sac n (%)	77 (21.8)	9 (25.7)	
Gestational sac with yolk sac/fetal pole n (%)	54 (15.3)	1 (2.9)	
Mean size of ectopic mass mm (SD)	22.2 (9.3)	15.4 (5.3)	<0.0001

Why are some ectopic pregnancies missed on the initial scan?

- Compared to ectopic pregnancies visualised on the initial TVS, ectopic pregnancies initially classified as PULs had:
  - Lower mean gestational age
  - Lower mean initial hCG,
  - Higher mean progesterone level at presentation

- However, at the time of visualization: serum hCG, serum progesterone levels and the appearance were not significantly different between the two groups
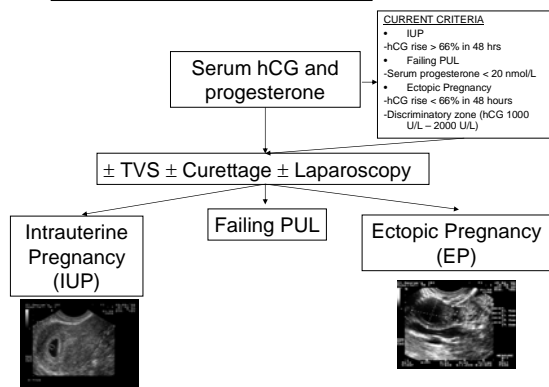

Why are some ectopic pregnancies missed on the initial scan?

- Failure of visualization of the ectopic pregnancy on the initial TVS may be due to the fact that they are too small and probably too early in the disease process

Diagnosis of ectopic pregnancies in PUL population

1. Hormones

2. Surgical intervention

3. Mathematical models

PUL Management

Serum hCG and progesterone

CURRENT CRITERIA
- IUP
  -hCG rise > 66% in 48 hrs
- Failing PUL
  -Serum progesterone < 20 nmol/L
- Ectopic Pregnancy
  -hCG rise < 66% in 48 hours
  -Discriminatory zone (hCG 1000 U/L – 2000 U/L)

± TVS ± Curettage ± Laparoscopy

Intrauterine Pregnancy (IUP)

Failing PUL

Ectopic Pregnancy (EP)

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1. Hormones

- Human chorionic gonadotrophin (hCG)
- Progesterone
- Other:
  - CA 125
  - Creatine kinase
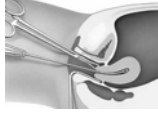 - Activin A
  - Inhibin A

2. Surgical Intervention

▪ Laparoscopy

▪ Curettage

▪ The combination of a positive pregnancy test and the absence of an IUP on TVS is an accepted indication for laparoscopy

▪ Serial measurements of hCG and progesterone, TVS and uterine curettage have been combined into various diagnostic algorithms when a pregnancy cannot be seen on TVS

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3. Use of mathematical models

- Mathematical models have been developed to predict the outcome of PULs

- They do not require any understanding of the behaviour of serum biochemistry in early pregnancy and could possibly lead to more standardised management protocols

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Summary

- TVS has a high sensitivity for the detection of ectopic pregnancy:

  - Diagnosis is based on positive visualisation of an ectopic mass
  - ~75% of ectopic pregnancies can be visualised on the initial TVS examination
  - Those missed on the initial TVS should be classified as pregnancies of unknown location
  - Overall >90% can be visualised on TVS prior to treatment

Summary

- Detecting ectopic pregnancy in the PUL population:

  - The majority of PULs are not ectopic pregnancies
  - Expectant management is safe
  - There is no role for the routine use of uterine curettage or laparoscopy in the management of PULs

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Summary

- Detecting ectopic pregnancy in the PUL population:

  - A discriminatory zone level of serum hCG is not helpful in a PUL population where ectopic pregnancy diagnosis is TVS based
  - Mathematical models do allow prediction of PUL outcome
  - There is the possibility to rationalise the follow-up of PULs

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