



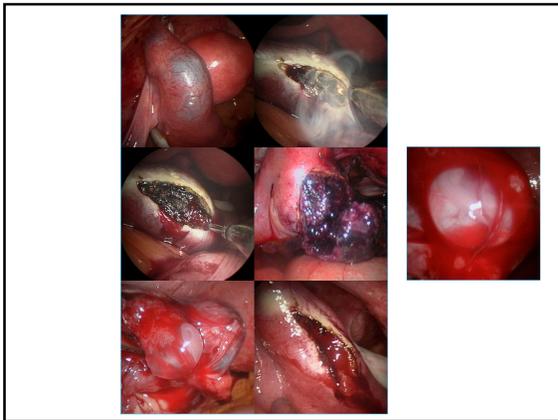
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Ectopic pregnancies

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European
theAcademy of
Gynaecological
Surgery

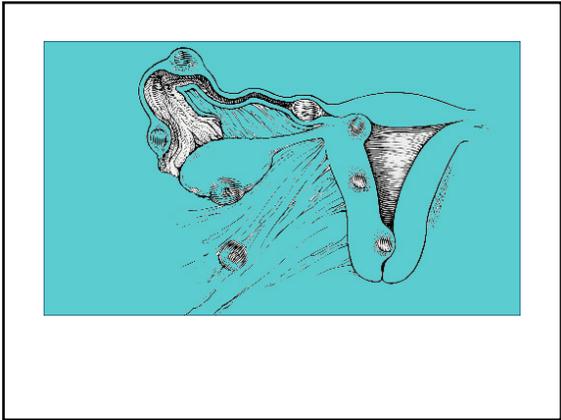


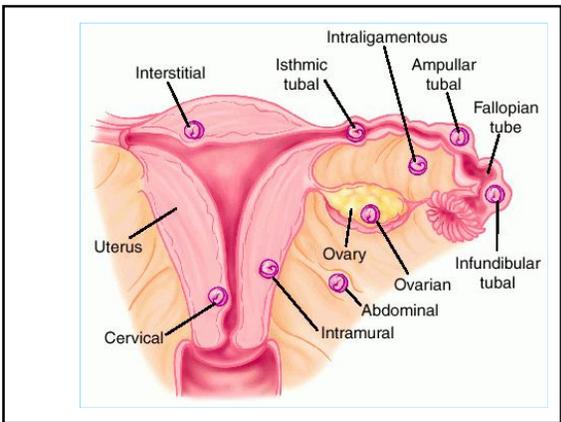


"ectopic" means "out of place"

- Tubal (98,3%)
 - ampullary (80-90%)
 - isthmic (5-12%)
 - fimbrial (5-6%)
- Extratubal (<2%)
 - intramural (within serosal lining of the uterus)
 - **cornual (0,5%)**
 - **in endocervical canal**
 - e.g. in the defect underneath the scar of a previous C-section (n=1:2000)
 - **intramyometrial, e.g. inside an area of adenomyosis**
 - extramural (outside serosal lining of the uterus)
 - **ovarian (0,15%)**
 - **abdominal (1,4%)**

outside the 'eutopic'
endometrial lining
of the uterine cavity
incidence 0,96 – 1,15%
of all spontaneous pregnancies





SIS following SC



Ectopic inside the defect underneath the scar of a previous C-section, colonized with ectopic endometrium

Maymon et al., HRU 2004
Incidence 1:2000 early preg

Risk factors include a history of

- ≥ 2 C-sections (54%)
- D&C
- placental pathology
- ectopic pregnancy
- IVF



False route in adenomyosis

Images courtesy of Rudy Campo

Intramural pregnancy following embryo transfer

US vs UK

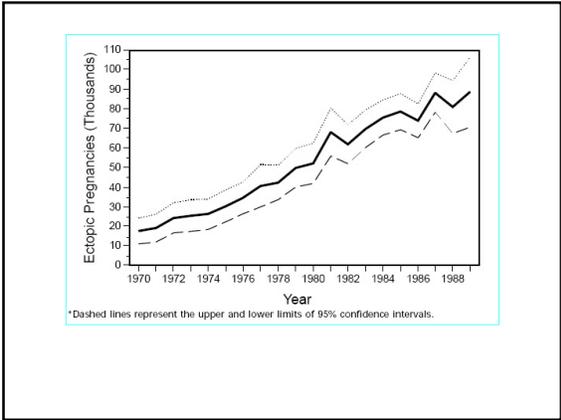
The Centers for Disease Control (CDC) examined ectopic pregnancies occurring during a 19 year period (1970-1989) in the US and noted that:

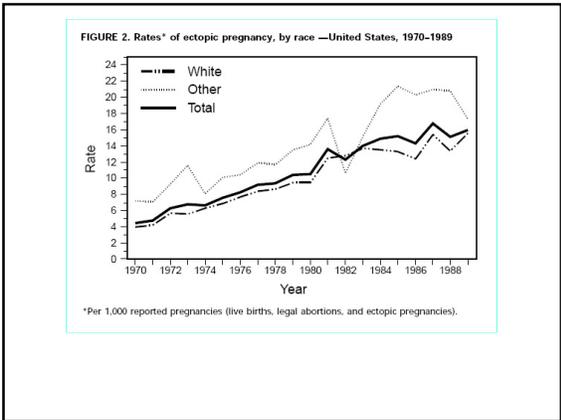
- the ectopic pregnancy rate increased almost 4-fold mainly due to STD (from 4.5 to 16.8 per 1,000 reported pregnancies)
- the fatality rate from ectopic pregnancies dropped by almost 90% (from 35.5 to 3.8 per 10,000 ectopics, 860 deaths in 1970-1989)
- ectopics were still the 2nd leading cause of maternal mortality in the US (accounting for 12% of all maternal deaths in 1987)

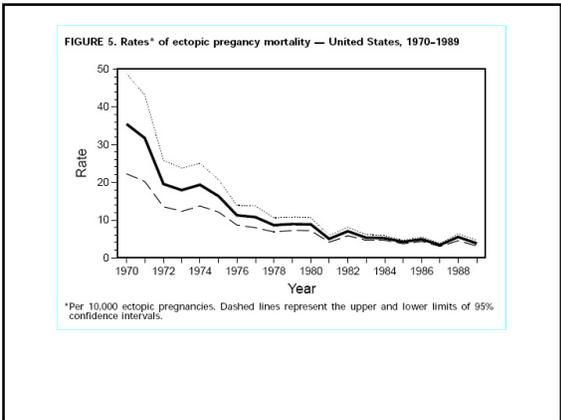
Over more recent years the incidence has remained static in the UK:

- 11.1 per 1,000 pregnancies, i.e. almost 32,000 ectopics annually ~ UK
- still 13 maternal deaths resulting from an ectopic in the UK 1997-1999
- 4th leading cause direct maternal deaths ~ 80% of first trimester deaths

CDC Surveillance Summaries, 17/12/1993, Vol. 42
 Condous et al. 2004, Gynecol Surg, 1, 81-86







Risk factors

- ❑ a prior history of ectopic pregnancy (recurrence rate ~ 15% in case of 1 earlier EUP, ~ 25% in case of 2)
- ❑ a history of surgery on the fallopian tubes or within the pelvis
- ❑ a history of pelvic infection, i.e. salpingo-oophoritis or PID
- ❑ a history of infertility & the use of assisted reproductive technology
- ❑ a history of IUD use (copper >> hormone IUD)
- ❑ a history of destruction of the cavity lining (e.g. Ashermann)
- ❑ a history of DES exposure in utero
- ❑ a history of non-infectious pelvic inflammation (e.g. endometriosis)
- ❑ salpingitis isthmica nodosa

Symptoms

- ❑ Asymptomatic (± 15%)
- ❑ Amenorrhea
- ❑ Abdominal Pain (30%)
- ❑ Vaginal Bleeding (13%)
- ❑ Pain and bleeding (37%)
- ❑ Syncope
- ❑ Shock
- ❑ Pelvic Mass

β-hCG - Romero et al. 1986

- ❑ β-hCG levels double every 48 hrs
- ❑ < 66% rise/48 hrs consistent with ectopic
 - ⇒ PPV 80.7%, false positive rate 12.5% ←
- ❑ single determination not helpful enough
- ❑ reliable if done within same laboratory
- ❑ never rules out an ectopic

β-hCG - Cacciatore et al. 1990

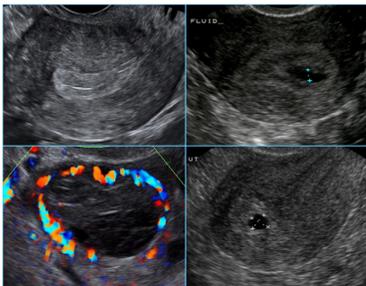
- In patients with an initial β-hCG level exceeding 1000 IU/L, an intrauterine sac was found in all the intrauterine pregnancies but in none of the ectopic pregnancies.
 - PUL + β-hCG ≥1000 IU/L, a normal IUP can be ruled out.
 - The use of this threshold in combination with sonographic detection of an adnexal mass is pathognomonic for an ectopic pregnancy.
- sensitivity 97%, specificity 99%, PPV 98%, NPV 98%**

IUP at TvS

	T _{vag} S	T _{abd} S
Amniotic sac	4 - 5	5 - 6
Yolk sac	5 - 6	6 - 7
Embryo	5 - 6	6 - 7
Heart beat	5 - 6	6 - 7

weeks of pregnancy

IUP at TvS - week 4 (32-34d)



images courtesy of Dirk Timmerman

IUP at TvS - week 5

- Amniotic sac grows 1 mm/day
- CRL 2 mm at the end of the 5th week
- Yolk sac confirms IUP
- positive heart beat



images courtesy of Dirk Timmerman

How good is TvS in the detection of an ectopic pregnancy?

- Cacciatore et al. 1990, Br J Obstet Gynaecol
 - Sensitivity 93%, Specificity 99%, PPV 98%, NPV 96%
- Shalev et al. 1998, Fertil Steril
 - Sensitivity 87%, Specificity 94%, PPV 92,5%, NPV 90%
- Condous et al. 2005, Hum Reprod
 - Sensitivity 90,5%, Specificity 99,8%, PPV 92,1%, NPV 99,8%

Requirements for an early and accurate diagnosis

- a high index of awareness
 - i.e. a high level of suspicion
 - especially in case of assisted reproduction
- a detailed history
 - i.e. know your risk factors!
- a skilful TvS by a skilled operator

Condous et al. 2004, Gynecol Surg

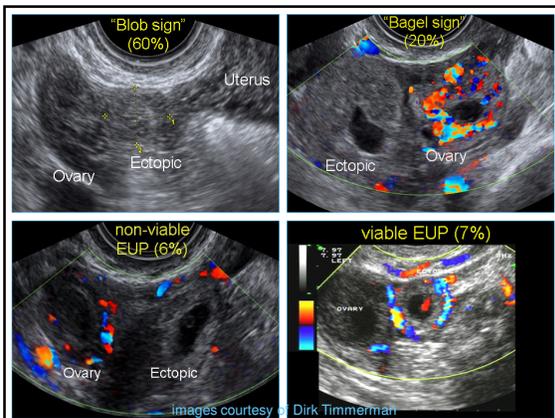
The diagnosis of ectopic pregnancy should not be based on an inability to visualise an IUP, but **on the positive visualization of an adnexal mass using high-resolution probes at TvS**. This should in turn result in a **decrease in the number of false positive laparoscopies**. If a pregnancy cannot be seen using TvS, then it is classified as a PUL, **10% of which are ectopic**. Misdiagnosis should be a rare event with the use of TvS. An EPU standard of care **can be judged by its false-positive and false-negative rates** for the diagnosis of an ectopic

Condous et al. 2005, Hum Reprod

The accuracy of transvaginal ultrasonography for the diagnosis of ectopic pregnancy prior to surgery

George Condous^{1,4}, Emeka Okaro¹, Asma Khalid¹, Chuan Lu², Sabine Van Huffel², D Timmerman³ and Tom Bourne¹

- 6621 consecutive TvS
- 5840 (88,2%) ~ IUP
- 581 (8,8%) ~ PUL
- 200 (3,0%) ~ EUP
- 48 excluded ~ no AP
- leaving n=152 EUP/TvS
- 58% "blob sign"
- 7% viable EUP
- 6% non viable EUP
- 20% "bagel sign"
- i.e. 91% correct TvS
- 7,2% PUL
- 1,3 % IUP



Pregnancies of unknown location:
consensus statement

G. CONDOUS^{1,2}, D. TIMMERMAN¹,
S. GOLDSTEIN³, L. VALENTIN³,
D. JURKOVIC⁴ and T. BOURNE^{5,6}

% of PUL

Quality of TvUS is crucial:

- with experience the # of early IUP & EUP diagnoses will increase significantly
- % of PUL is inversely proportional to the quality of the TvS
- PUL rates must remain below 15%

Culdocentesis ... ? an old slide

- Highly specific if performed and interpreted correctly: presence of free-flowing, NON-clotting blood ...
- A negative tap however is inconclusive ...
- May obviate, i.e. render unnecessary, the use of sonography ...
- Is most helpful in emergent situations to confirm a suspected diagnosis; remains controversial in literature ...

Human Reproduction Vol.21, No.19 pp. 2706-2710, 2005
Advance Access publication June 21, 2005 doi:10.1093/humrep/del223

There is no role for uterine curettage in the contemporary diagnostic workup of women with a pregnancy of unknown location

G.Condous^{1,2}, F.Kirk³, C.Lu², B.Van Calster², S.Van Huffel², D.Timmerman² and T.Bourne¹

Single hormonal markers

Single hormone measurement 0 h	PUL outcome	Area Under ROC Curve	Sensitivity	Specificity
Prog < 20 nmol/L	Failing PUL	0.952	87.2%	89.6%
hCG > 1000 IU/L	Ectopic	0.666	21.6%	87.3%
hCG > 1500 IU/L	Ectopic	0.666	18.9%	93.4%
hCG > 2000 IU/L	Ectopic	0.666	13.5%	95.2%

Condous et al., Hum Reprod 2004
& Ultrasound Obstet Gynecol 2005

Condous et al. 2004, Int J Gynaecol Obstet

- ❑ Serum hCG and progesterone levels at defined times can be used to predict the immediate viability of a PUL, but cannot be used reliably to predict its location.
- ❑ Clinical experience does not significantly improve the ability to assess PUL outcome

Hum. Reprod. Advance Access published April 10, 2009
Human Reproduction, Vol.0, No.0 pp. 1-7, 2009
doi:10.1093/humrep/dgp084

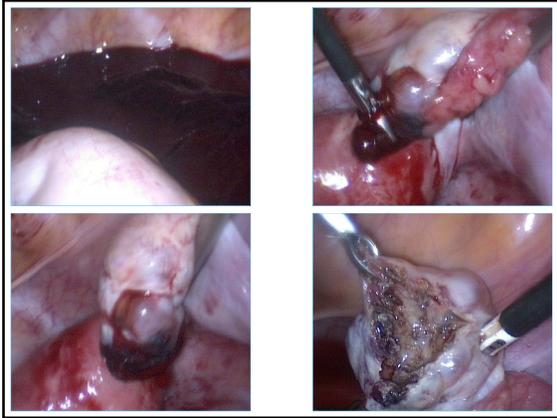
human reproduction

ORIGINAL ARTICLE *Early pregnancy*

The optimal timing of an ultrasound scan to assess the location and viability of an early pregnancy

C. Bottomley^{1,5}, V. Van Belle², F. Mukri¹, E. Kirk³, S. Van Huffel², D. Timmerman⁴, and T. Bourne^{1,3,4}

- ❑ The ability to confirm viability or non-viability is significantly related to gestational age.
- ❑ In asymptomatic women with no previous ectopic pregnancy TvS should be delayed ~ 49 days.
- ❑ Their data suggest that this would reduce the number of inconclusive scans, without an associated increase in morbidity from missed ectopic pregnancies.



**Management of ectopic pregnancy
either ... or ... (1)**

<p>strict follow-up of evidence based guidelines</p> <ul style="list-style-type: none"> □ Dutch Society 2001 □ RCOG 2004 □ Cochrane 2007 □ ACOG 2008 	versus	<p>individualized patient care based on personal clinical experience & the clinical experience of our peers</p>
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**Management of ectopic pregnancy
either ... or ... (2)**

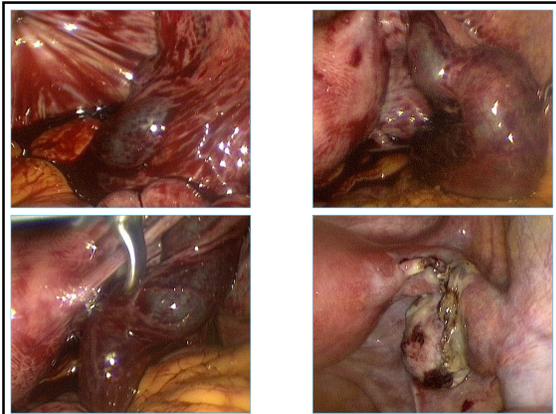
<p>What is the best guarantee of a complete removal of all trophoblast, a "blood"proof hemostasis and a recurrence rate at least at that site of 0% ?</p>	versus	<p>What is the best guarantee of an intact tubal integrity, a preserved fertility potential despite the risk of persistent bleeding and/or trophoblast ?</p>
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Management of ectopic pregnancy

- β -hCG monitored expected management unless CV unstable, moderate/severe pelvic pain, +HR inside ectopic, or hemoperitoneum: 95% success if β -hCG is < 175 vs. 66% if β -hCG 176 to 1500
- Methotrexate (MTX) is a folic acid antagonist. It inhibits DNA synthesis and cell reproduction, primarily in actively proliferating cells such as trophoblast ~ ACOG but what about fertility patients ?
- Surgical management: laparoscopy is superior to and cheaper than laparotomy and salpingotomy is preferred over salpingectomy
- Salpingectomy indicated if uncontrolled bleeding from implantation site, recurrent ectopic in the same tube, severely damaged tube, large tubal pregnancy (>5cm) or if completed childbearing.
- Persistent trophoblast can occur in 4-15% of women after a salpingotomy: β -hCG should be followed weekly until it is negative.

Expectant management

Date	β -hCG	E_2	Prog
07/09/2009	36	165	26,61
11/09/2009	31	148	25,49
16/09/2009	116	< 30	1,30
21/09/2009	96	65	0,96
24/09/2009	165	92	1,68
28/09/2009	171	120	5,16
01/10/2009	251	136	9,47



- If the patient is in shock or hemodynamically compromised, treatment should be immediate resuscitation and laparotomy without delay, even before blood and fluid losses have been completely replaced.
- However, in some emergency situations if prompt haemostasis and a clear surgical field of view can be achieved, and provided the surgeon is skilled and experienced, laparoscopic treatment may still be considered the first line.

Persistent trophoblast ... ?

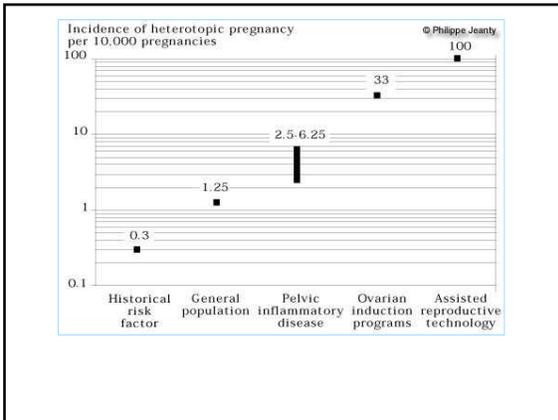
Hajenius et al. 1995, Hum Reprod 10, 683-687

Clearance curves of serum human chorionic gonadotrophin for the diagnosis of persistent trophoblast

- There was no difference in the post-operative clearance of serum hCG after successful conservative surgery compared to radical surgery.
- However, persistent trophoblast occurred in 8 pts (29%) after laparoscopic salpingotomy and in only 1 pt (6.3%) who had a salpingotomy by open surgery.
- Serum HCG clearance curves allow early identification of patients with persistent trophoblast after conservative surgical treatment.
- Moreover, monitoring of post-operative serum HCG until it becomes undetectable is mandatory in order to reveal late-onset types of persistent trophoblast

"ectopic" as part of "heterotopic"

- Simultaneous development of a gestation inside AND outside the uterine cavity (heterotopic = eutopic + ectopic).
- Prevalence: historically 0,3/10.000 pregnancies, now 1,25-2,50/10.000 spt. pregnancies, 0.1% in assisted conceptions
- Aetiological factors:
 - increase in the incidence of PID;
 - prevalent use of copper IUCD's;
 - increase in tubal surgery, notably microsurgery;
 - ovulation induction & superovulation;
 - assisted reproductive technologies like IVF & GIFT
- Risk factors: delayed diagnosis, hemoperitoneum, acute abdomen, tubal rupture



!!!

- 2,8 - 5,7 % of all pregnancies following assisted reproductive technology are indeed ectopic ...
- 0,7 - 1,3 % of all pregnancies following assisted reproductive technology are indeed heterotopic ...

Diagnosis of heterotopic pregnancy

- a high index of suspicion, esp. following ART !!!
- despite normal hCG/prog values (due to the normal IUP)
- at TvS the presence of an intrauterine gestational sac lowers the suspicion of another (i.e. ectopic) pregnancy
- the visualization of an IUP may result in less rigorous sonographic evaluation of the adnexae and a delayed or missed diagnosis of a heterotopic gestation
- an adnexal mass is seen sonographically in 80% of ectopic pregnancies; this also means that potentially the diagnosis of an heterotopic pregnancy can be made in 80% of the cases with rigorous sonographic evaluation of the adnexae

Management of heterotopic pregnancy

- ❑ Surgical removal of the ectopic gestation by salpingotomy or salpingectomy is the treatment of choice, except when in interstitial sites.
- ❑ In patients in whom the diagnosis of ectopic pregnancy can be made without laparoscopy and who sonographically demonstrate an unruptured gestation and a persistent downward trend of the β -hCG, expectant management has been successfully applied.
- ❑ Fine needle aspiration with the injection of methotrexate or KCl (potassium chloride) into the gestational sac is still investigational at this time.

Doppler & trophoblast ?

- ❑ Taylor et al. (1989, Radiology 173:93) have described a high velocity, low resistance Doppler signal that is associated with the developing trophoblast
- ❑ Transvaginal identification of this type of flow pattern in an adnexal mass raised the sensitivity for the diagnosis of an ectopic pregnancy to 96% and a specificity of 93% using transvaginal color Doppler
- ❑ These encouraging results however were not confirmed by other authors
