UCL

Clinical Impact of Pregnancies of Unknown location

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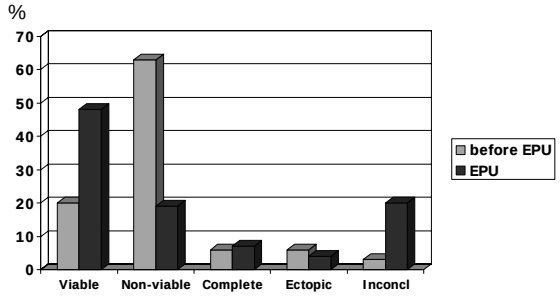
Effect of EPU on pregnancy outcomes



Walker, 1995

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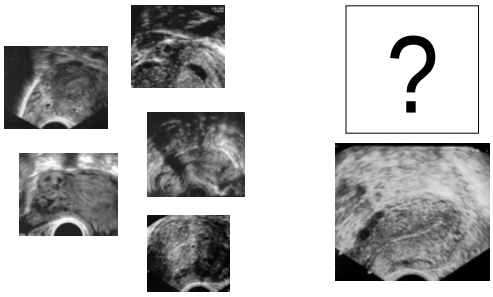
Diagnosis of early pregnancy complications



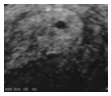
Discriminatory zone

- Prospective study of 383 patients
- Prevalence of ectopic pregnancy 27%
- Absence of an intrauterine sac above 6,500 IU hCG diagnosed ectopic with 100% sensitivity and 96% specificity

Conclusions

- Positive identification of ectopic by ultrasound is rarity
- The visualisation of gestational sac below discriminatory zone is associated with miscarriage in 65% of cases

Green Journal 1985

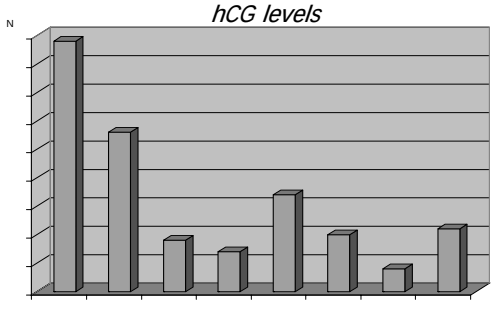


If serum hCG >1500 IU and "empty" uterus = ectopic was true then...

- Ectopic pregnancies with hCG below 1500 IU do not exist
- Following spontaneous miscarriage hCG levels are always below 1500 IU/l
- All normal pregnancies look the same
- Every uterus is normal
- All ultrasound examinations are of same quality

Tubal ectopics

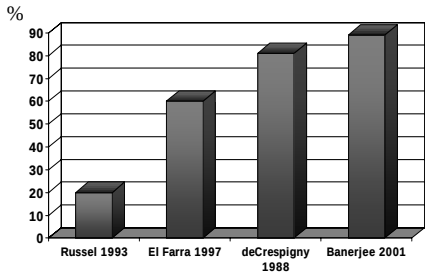
hCG levels



N=144

In 50% of cases hCG below 1000IU/l

Detection of ectopic pregnancy at the initial scan



Results

- Using hCG >1500 IU/l as a cuf off for intervention 35 unnecessary laparoscopies would have been performed and 85% of ectopics requiring intervention would have been missed
- Average unit looking after 5,000 women/year with 20% inconclusive scans rate should expect to perform 100 unnecessary laparoscopies/year

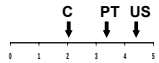
Pregnancies of unknown location (inconclusive ultrasound scan)

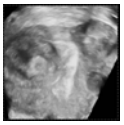
Definition

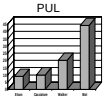
- No evidence of intra-uterine or extra-uterine pregnancy in clinically stable women with a positive pregnancy test
- Concept applicable to early pregnancies where initial assessment is made using transvaginal ultrasound scanning
- Designed as an alternative to “suspected ectopic pregnancy” in order to emphasise relatively low risk of adverse outcomes

Pregnancy of unknown location
Why does it happen?

- Too early
- Too late
- Too difficult
- Too bad

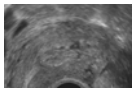


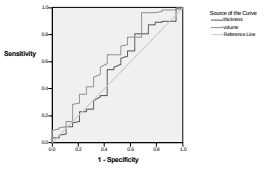




Diagnosis of incomplete miscarriage

Author	*Cut-off*



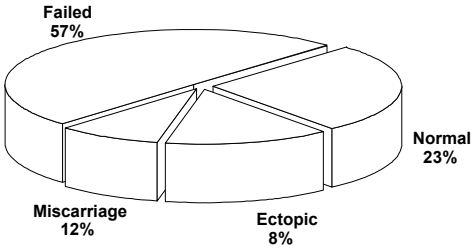


Sawyer 2007

Incomplete miscarriage
Ultrasound diagnosis

Sawyer 2005

Pregnancies of unknown location
Final diagnosis



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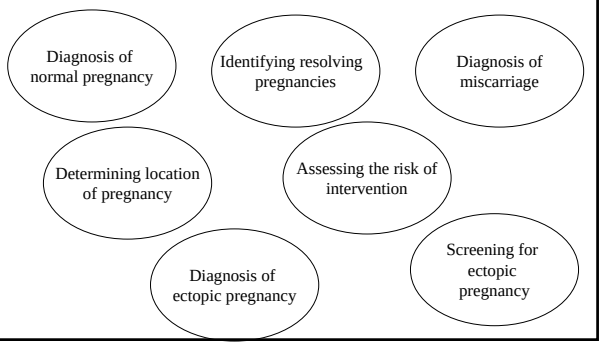
Aims of PUL management



Management of inconclusive scans
Objectives

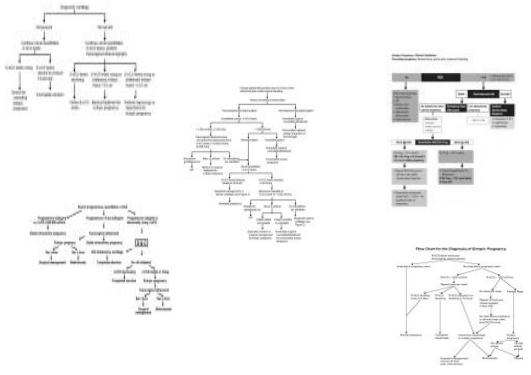
- Minimise need for follow up
- Minimise number of interventions
- Minimise adverse outcomes

Pregnancies of unknown location
ISOUG consensus statement 2006

- The rate of inconclusive scan is determined by the quality of scanning
- Clinically stable women with PUL should be managed expectantly
- The role of biochemistry and mathematical models have to assessed in prospective multicentre trials
- There is no role for D&C in the management
- Single visit is not appropriate

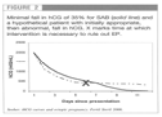
Current concepts
Aims

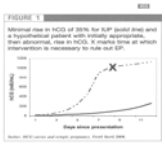
- To diagnose an ectopic pregnancy as early as possible in order to initiate treatment
- To differentiate patients with pathological pregnancy that will resolve spontaneously form those with pathological pregnancy necessitating active therapeutic intervention and those with an early normal intrauterine pregnancy



hCG dynamics

- Abnormal changes in hCG levels are diagnostic of ectopic pregnancy

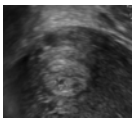


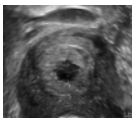


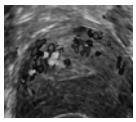
Barnhart 2006

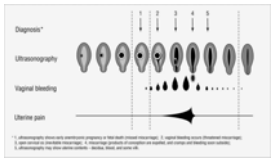
Condous 2007

Natural history of miscarriage





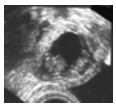


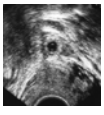


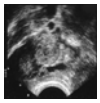
Ankum et al. 2001

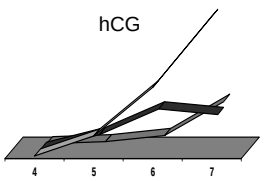
Tubal ectopics

Morphology and hCG



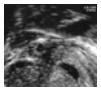


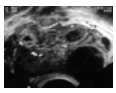


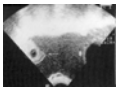


Ectopic pregnancies

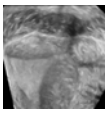
Extrauterine
- Tubal
- Ovarian
- Abdominal

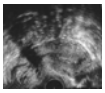


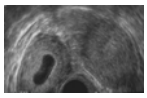


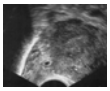


Uterine
- Interstitial
- Cervical
- Caesarean scar
- Intramural
- Cornual



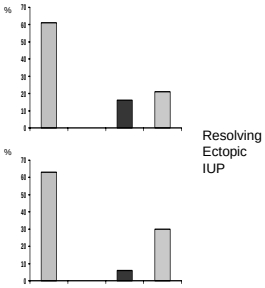




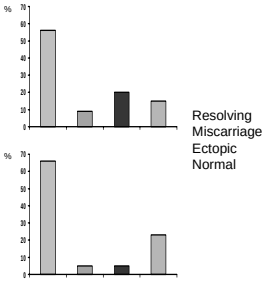


Final outcomes

hCG based management
pregnancy location



Progesterone based management
active intervention



PUL - Logistic models

hCG ratio = hCH 48 hours/hCG 0 hours

Condous 2004

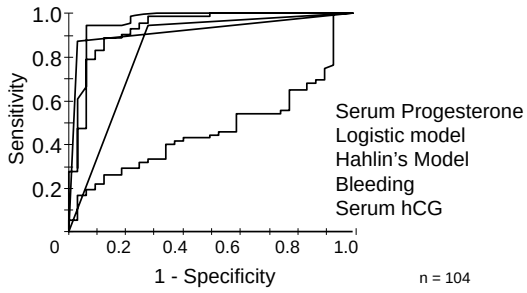
Pregnancies of unknown location
Prediction of spontaneous resolution

Progesterone < 20 nmol/l
& daily hCG decrease > -5%

Sensitivity 73%
Specificity 97%
PPV 97%

Hahlin et al. 1995

Pregnancies of unknown location
Performance of various parameters



n = 104

Pregnancies of unknown location
Prediction of spontaneous resolution

Parameter	*Sensitivity (%)*	*Specificity (%)*	*PPV (%)*

n = 104

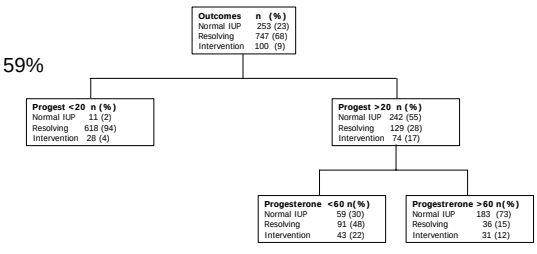
Management of inconclusive scans

Progesterone (nmol/l)	*β-hCG (IU/l)*	*Likely diagnosis*	*Follow up*

Follow up of non-diagnostic scans

	June-07	Patients N= 31		June-08	Patients N = 30
	Total Number	Mean/pt		Total Number	Mean
Visits	107	3.45		88	2.9
Scans	56	1.8		57	1.9
Length of follow up (days)	362	11.6		480	16
β-hCG	91	2.93		48	1.6
Progesterone	40	1.29		34	1.1
Urinary pregnancy tests	1	0.03		16	0.53

Pregnancy of unknown location
Intervention rates



N=1100

PUL
Outcomes

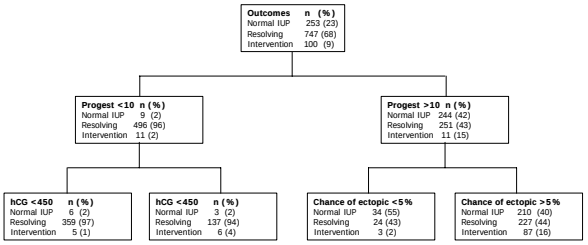
Final diagnosis	*Intervention rate N (%)*
Ectopic	50/87 (57)
Miscarriage	50/127 (39)
Molar pregnancy	2/2 (100)

Expectant management of ectopics

- Type 1 ectopics (74%) - sustained hCG decline from day 0 at a mean half time of 3.6 days
- Type 2 ectopics (26%) - hCG plateaus for average of 9.6 days (range 2-26) before starting to decline at the same rate as in Type 1

N=116

Pregnancy of unknown location
Single visit strategy



N=1100

Pregnancy of unknown location
Single visit strategy

Criteria	*Population (%)*	*False negatives (%)*

Rationalizing follow up of PULs using hCG ratio

- 220/363 (60.6%) classified as resolving pregnancies after second blood test
- 6/23 (26%) ectopics misclassified on 48 follow up visit but only 2(9%) would have been discharged as resolving pregnancies
- There were no interventions in women with miscarriages
- Only women with hCG <10000 included
- All women with initial hCG >1000 were re-scanned within 24 hours to rule out an ectopic

Kirk 2007

Outcome of initially non-diagnostic scans

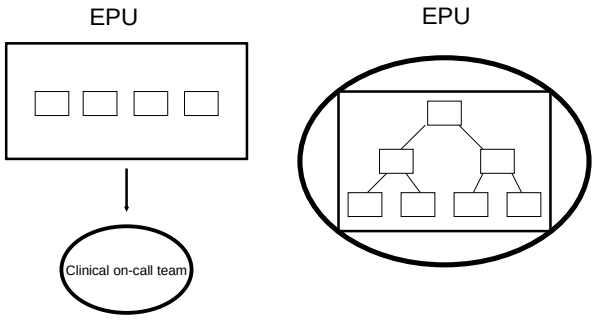
	June-07		**June-08**	
IUP	4	12.9%	6	19.9%
Spontaneous Resolution	20	64.5%	20	66.6%
Ectopic	3	9.6%	2	6.6%
Miscarriage	1	3.2%	1	3.3%
DNA	3	9.67%	1	3.3%
Total	31		30	

PUL puzzle
Solutions

Hahling principles

- Avoid preforming interventions which are not necessary and can be harmful
- Diagnosis should be certain before treatment is initiated

Unit organisation



PUL puzzle
Solutions

- Invest in ultrasound training and equipment
- Use serum progesterone to minimise the need for follow up
- Clinical and ultrasound findings should determine the need for intervention rather than the measurements of serum hCG
- If the diagnosis is not clear than D&C should be performed rather than laparoscopy

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PUL puzzle

The most valuable diagnostic instrument
is the passage of time

HG Miller 1968