Short and long term outcomes following 1st trimester threatened miscarriage

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Threatened miscarriage

- Vaginal bleeding before 24 weeks gestation
- 15-20% ongoing pregnancies
- 673 000 births annually in UK
  - 100-135 000 women presenting to healthcare system
    - Increased visits
    - Anxiety
    - **Short and long term outcomes?**

Threatened miscarriage

- Presentation
- Ultrasound findings:

Normal

Haematoma

Viable IUP

Threatened miscarriage

Follow-up?

Rescan 7-10 days Why? | **Antenatal Care? ?hospital led** | **Anti-D?**

'may be prudent to administer anti-D Ig where bleeding is heavy or repeated…associated abdominal pain'
RCOG Green Top Guideline (22) May 20002

Threatened miscarriage

Follow-up?

Rescan 7-10 days Why? | **Antenatal Care? ?hospital led** | **Anti-D?**

Treatment?

Short term outcomes
1st trimester miscarriage

Authors (year)	Study type	Entry criteria	N	Miscarriage rate
Tongsong et al 1995	Prospective case-control	TM/viable IUP	1444	5-7%
Ball et al (1996)	Case-control	TM/viable	520	5.5% RR 2.9
Johns et al (2006)	Prospective case control	TM/viable	428	9.3%

Short term outcomes
1st trimester miscarriage (+IUH)

Authors	Year	Study type	Entry criteria	N	Outcome	Comments
Mantoni & Pedersen	1981	Observational	TM	10	3 patients miscarried	IUH >50mls
Goldstein et al	1983	Prospective observational	TM	10	20% miscarried	IUH only
Joupilla et al	1985	Prospective observational	TM	33	18.7% miscarried	No volume correlation
Sauerbrei & Pham	1986	Prospective observational	TM	30	10% miscarried	
Borlum et al	1989	Case-control	TM	86	22% miscarried	
Stabile et al	1989	Prospective observational	TM	22	No increase in mc	
Pedersen & Mantoni	1991	Prospective observational	TM	23	No increase in mc	IUH >50mls
Pedersen & Mantoni	1990	Prospective observational	TM	62	11% miscarried	No volume correlation
Dickey et al	1992	Retrospective	Routine US	230	No increase in mc	Assisted conception
Kurjak et al	1996	Case-control	IUH on US	59	17% mc rate	Site relevant not size
Ball et al	1996	Retrospective case-control	IUH on US	?	Increased mc rate OR 2.8	Bleeding alone increased mc rate
Bennett et al	1996	Retrospective	IUH on US	516	9.3% miscarried	13.7% if < 8/40
Tower & Regan	2001	Prospective	IUH on US	41	No increase in mc	Recurrent miscarriage
Maso et al	2005	Unclear	IUH on US	182	14.3% miscarried	If IUH < 9 weeks
Johns & Jauniaux	2006	Prospective case-control	TM	428	9.3% miscarried	TM independently associated with mc

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Intrauterine Haematomas (IUH)

IUH = intrauterine haematoma ECC = exocoelomic space

Intrauterine Haematomas (IUH)

- Echo-free area between membranes and uterine wall (Mantoni & Pedersen 1981)
- Incidence 3-18% depending on criteria used (Johns 2007)
- 4-33% miscarriage rate (Pearlstone & Baxi 1993)
- Early reports suggested large (>50mls) IUH significantly increased risk of miscarriage
- Later data suggests no difference (Stabile 1989, Dickey 1992, Johns 2003)

IUH = intrauterine haematoma ECC = exocoelomic space

Long term outcomes

- Increased incidence of:
  - Later fetal loss[1,2]
  - Abruption[3,4,5]
  - Fetal growth restriction
  - Pre-term labour[3,4,5]
  - Pre-term pre-labour ROM[3]
  - Pre-eclampsia[3]
  - Low birth weight[6]

Often retrospective, uncontrolled and reliant upon patient recall

1. Farrell Br J Obstet Gynecol 1996;103:926-28.
2. Strobino Am J Obstet Gynecol 1987;157:1150-54.
3. Weiss. Am J Obstet Gynecol 2004;190:745-50.
4. Mulik J Obstet Gynaecol 2004;24:249-53.
5. Ball Am J Obstet Gynecol 1996;174:996-1002.
6. Baztofin Obstet Gynecol 1984;63:515-18.

Long term outcomes

Johns J & Jauniaux E 2006. Threatened miscarriage as a predictor of obstetrics outcome. Obstet Gynecol 107; 4: 845-850

	Study Group N=214	Control Group N=214
Mean Maternal Age (y)	32	31.5
Median Maternal Age (y)	32	31
Primigravidas	52%	48.6%
Mean Gestation at Presentation (w) Range (w)	8 5-14	11 6-14
Mean Gestation at Delivery (w) Median Gestation at Delivery (w)	38.6 39	39 40
Mean Birth Weight (g)	3215.6	3336
Live Births (*)	182 (95%)	212 (99.5%)
First Trimester Miscarriages	20 (9.3%)	0
Late Miscarriages (14-22+6 weeks)	7 (3.3%)	1 (0.46%)
Stillbirths	3 (1.4%)	0
Termination of Pregnancy	2 (0.9%)	1 (0.46%)

*after exclusion of 1st trimester miscarriages

Characteristics and outcomes in 214 women with threatened miscarriage compared with 214 asymptomatic controls

Long term outcomes

Johns J & Jauniaux E 2006.

Pre-term labour and PPROM

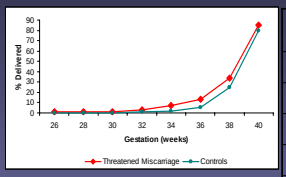
Outcome	Study Group	Control Group	Relative Risk (95% CI)	Fishers Exact Test
Pre-term Labour	22 (11.9%)	11 (5.6%)	2.29 (1.4-4.6)	p=0.018
Mid-Trimester Miscarriage	7 (3.3%)	1 (0.5%)	6.9 (0.86-56)	p=0.068
PPROM	13 (7%)	4 (1.9%)	3.72 (1.2-11.2)	p=0.01
PPROM total	17 (7.9%)	4 (1.8%)	4.2 (1.4-12.3)	p=0.006

Relative risks of an adverse obstetric outcome in women with threatened miscarriage compared with controls
PPROM=pre-term pre-labour rupture of the membranes

Long term outcomes

Johns J & Jauniaux E 2006.

Pre-term labour



Distribution of gestational age at delivery.

Cumulative percentage is calculated from the number of women delivered by each gestational age group as a percentage of the total number for each group.

Gestation	Study Group (%)	Control Group (%)	Fishers Exact Test	Relative Risk (95% CI)
≤ 32 weeks	6 (3.2%)	3 (1.4%)	p=0.31	-
≤ 33 weeks	9 (4.9%)	3 (1.4%)	**p=0.07**	-
≤ 34 weeks	13 (7%)	4 (1.9%)	**p=0.01**	3.72 (1.2-11.2)
≤ 35 weeks	18 (9.7%)	5 (2.4%)	**p=0.002**	4.1 (1.6-10.9)
≤ 36 weeks	24 (13%)	11 (5.2%)	**p=0.008**	2.5 (1.3-5.0)
≤ 37 weeks	31 (16.8%)	20 (9.4%)	**p=0.04**	1.78 (1.0-3.0)
≤ 38 weeks	63 (34%)	52 (24.5%)	p=0.05	1.4 (1.0-1.9)

Long term outcomes

Johns J & Jauniaux E 2006.

Other outcomes

- Birth weight
- Fetal growth restriction
- PET
- Abruption
- Placenta previa

No significant difference

- Ultrasound parameters
  - Earlier gestation IUH detected = higher risk of miscarriage
  - No difference between adverse outcomes and volume of IUH

Long term outcomes

Weiss et al 2004. Threatened abortion: A risk factor for poor pregnancy outcome, a population based study. AJOG 190: 745-750

- Large prospective multi-centre study
- 16506 patients recruited at ***10-14*** weeks
  - Recall of bleeding (none, light, heavy)

Pregnancy loss before 24 weeks

	Rate	Odds Ratio
No bleeding	0.4%	
Light bleeding	1.0%	2.5 (1.5-4.3)
Heavy bleeding	2.0%	4.2 (1.6-10.9)

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	Light bleeding v controls		Heavy bleeding v controls	
Outcome	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
IUGR	1.4 (0.9-2.1)	0.09	2.6 (1.2-5.6)	0.02
Gestational hypertension	1.0 (0.9-1.3)	0.67	1.5 (0.9-2.4)	0.09
Pre-eclampsia	**1.4 (1.1-1.8)**	**0.009**	1.1 (0.5-2.4)	0.8
Pre-term delivery	**1.3 (1.1-1.7)**	**0.01**	3.0 (1.9-4.5)	<0.01
PPROM	1.3 (0.9-1.9)	0.06	3.2 (1.8-5.7)	0.01
Placental abruption	**1.6 (1.1-2.6)**	**0.03**	3.6 (1.6-7.9)	<0.01
Placenta previa	0.9 (0.5-1.8)	0.89	2.5 (0.9-6.9)	0.08
Caesarean delivery	**1.1 (1.01-1.3)**	**0.03**	1.4 (1.04-1.8)	0.02

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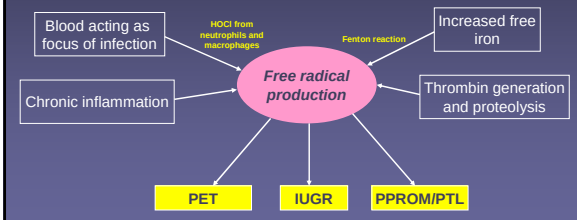
Mechanism?

? 1st trimester bleeding indicates underlying placental dysfunction

?disruption of chorionic – amniotic plate makes membrane more susceptible to rupture



Management?

- Antioxidants
  - Vitamin C supplementation?
  - Large RCT's required
  - Recent data on use of vitamin E in pregnancy
- Progesterone
- Bed rest?

Management?

- Surveillance
  - High risk hospital led antenatal care?
  - Cervical length measurements
  - Fetal fibronectin + cervical length
  - Infection screening – PREMET study

Aid in decision making in high risk women regarding mode/timing of delivery, antibiotics and steroids