Miscarriages and recurrent miscarriages

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Problems in early pregnancy

- Pregnancy of unknown location(PUL)
- Ectopic pregnancy
- Miscarriages
- Recurrent miscarriages

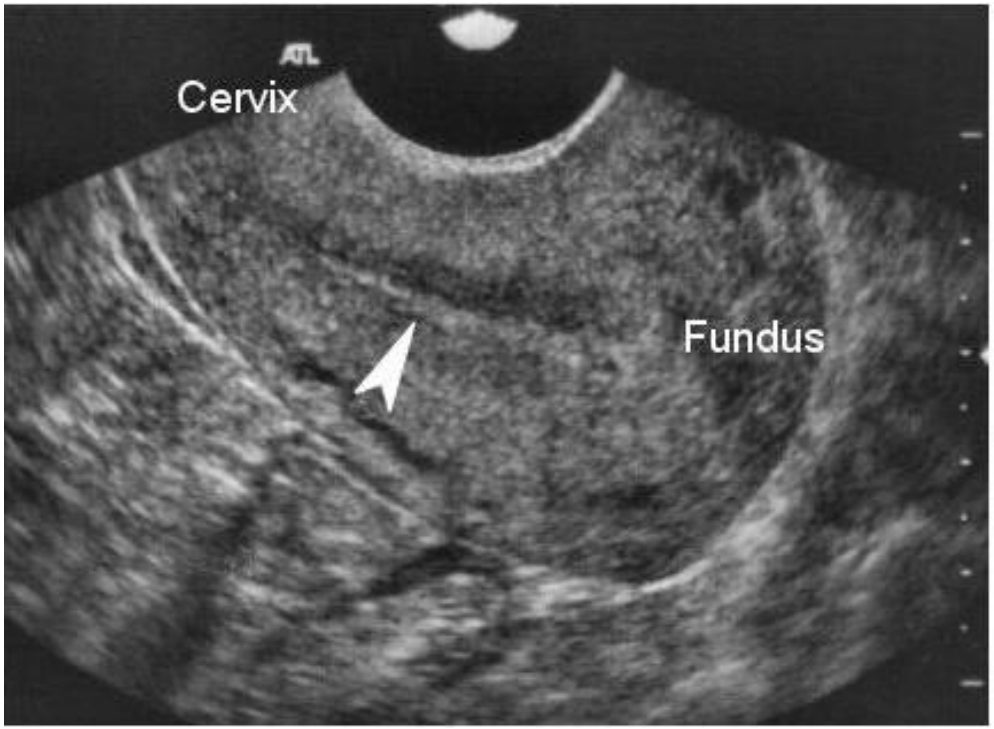
Definitions

Miscarriage :Spontaneous loss of a pregnancy at or before 24 weeks

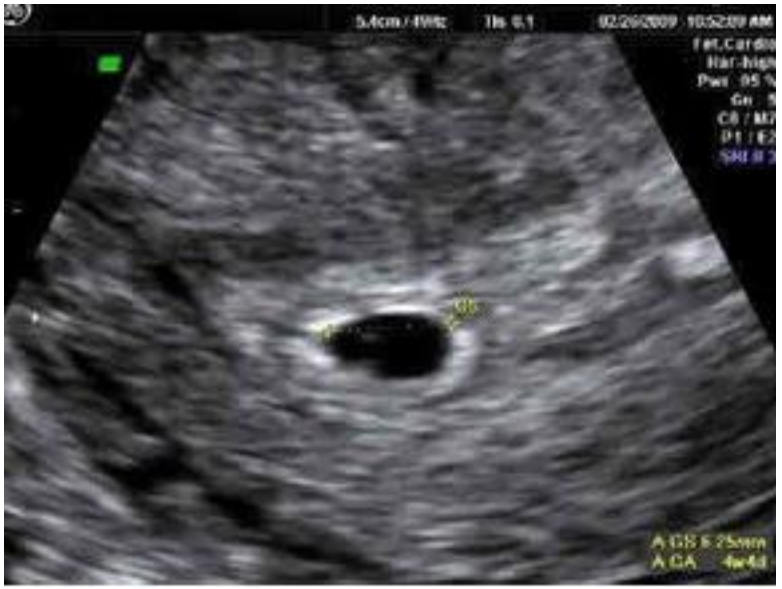
Ectopic pregnancy: Implantation of a pregnancy outside the uterine cavity

(PUL)No evidence of pregnancy can be seen either inside or outside the uterus

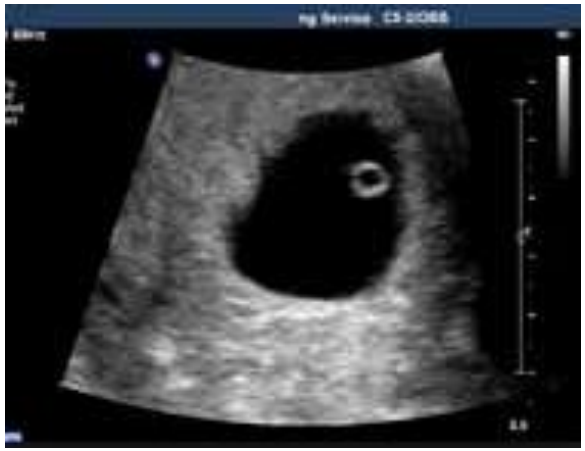
Normal uterus



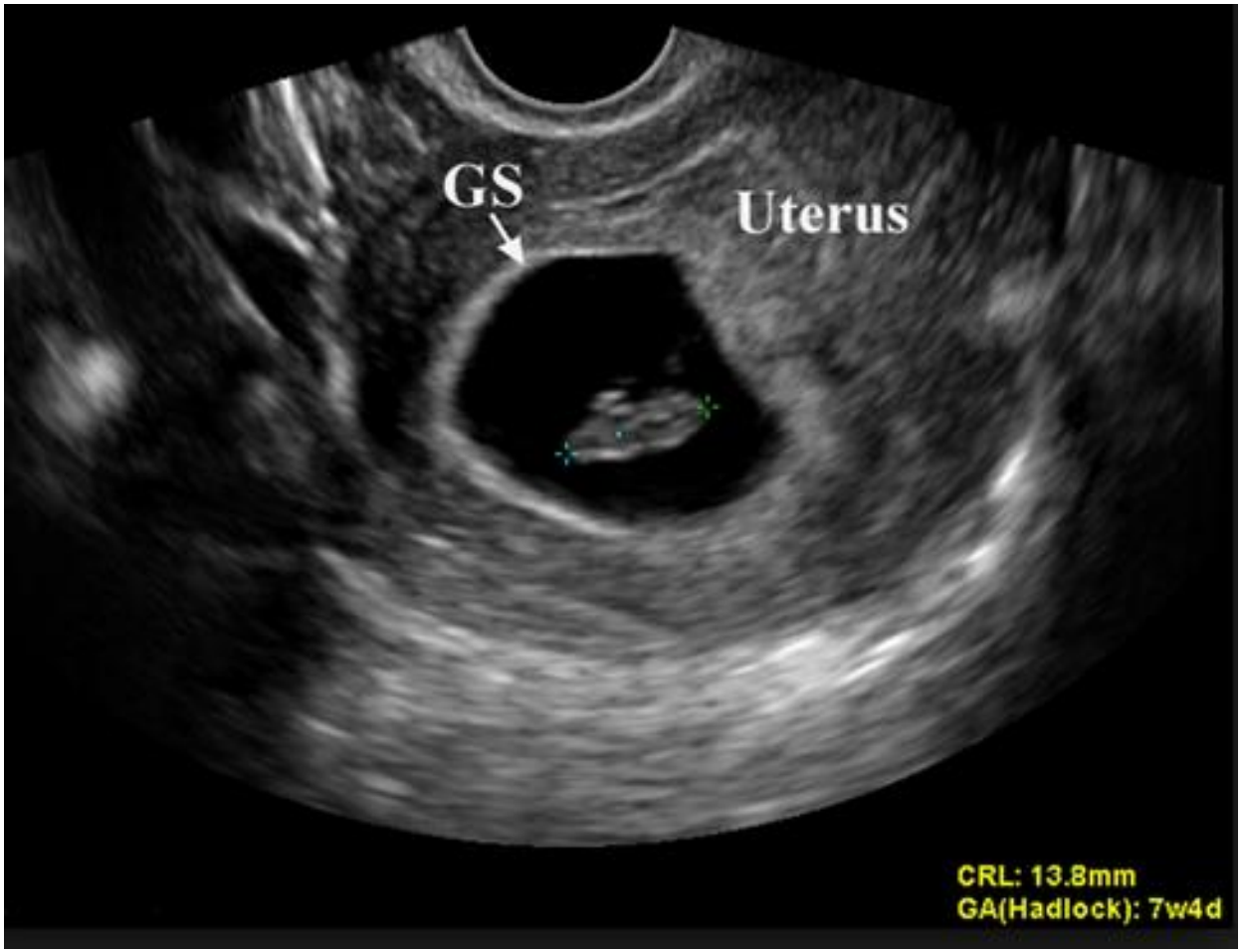
Gestational sac



Yolk sac



Fetal pole



Pregnancy of unknown location

- No evidence of pregnancy can be seen either inside or outside the uterus

Very early IU pregnancy

Ectopic

Failing pregnancy(intra or extra uterine)

- Early scans increase rate of PUL, 49 days of gestation
- Behavior of the HCG

HCG

- Beta HCG,glycoprotien,half life 24 hours
- < 5IU/mL not pregnant
- > 25 IU/mL pregnant
- 85% HCG double every 48 hr
- 1.4 days before 5 weeks , 2.4 days up to 7 weeks

If hCG increases >63% after 48 hours –likely intrauterine, repeat scan in one week

PUL

- HCG ratio

HCG 48 hrs/HCG 0 hrs

<0.8 missed miscarriage

0.8<HCG<1.66 EP or PUL

>1.66 intrauterine pregnancy

Expectant or medical treatment

Miscarriage

- Spontaneous loss of a pregnancy at or before 24 weeks
- 20% of clinical pregnancies
- Could occur during the first or second trimester
- Most common in first trimester

Clinical features

- Pain and bleeding after a positive pregnancy test
- Clinical presentation will aid the choice of investigation and management

Etiology

- Increasing maternal and paternal age
- At age of 20 risk 20%
- 45 years 93%
- Obesity
- Smoking
- Previous miscarriage 40% after three losses

Etiology

- Chromosomal :trisomy,monosomy, triploidy
- Poorly controlled diabetes,APS, thrombophilias
- Alcohol, drugs MTX,antiepileptic drugs
- Infection :varicella, rubella
- Uterine abnormalities, fibroid
- Cervical injury or surgery

classifications

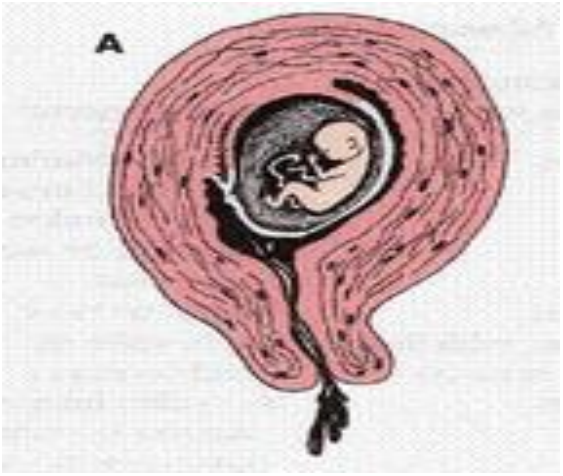
- Threatened miscarriage
- Inevitable miscarriage
- Complete and incomplete miscarriage
- Missed miscarriage

Classification of miscarriage

Threatened miscarriage

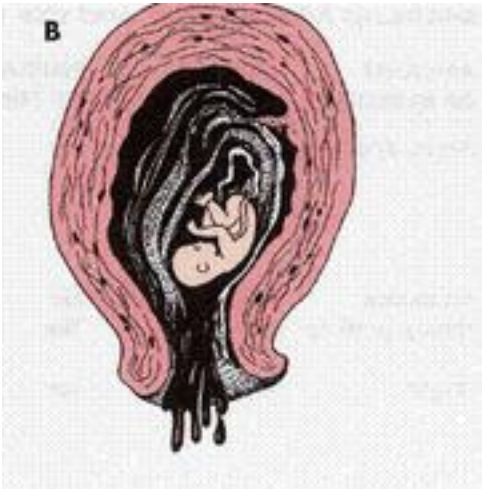
- Vaginal bleeding in the presence of viable pregnancy

Intrauterine pregnancy =gestational sac+ yolk sac+/-fetal pole and cardiac activity

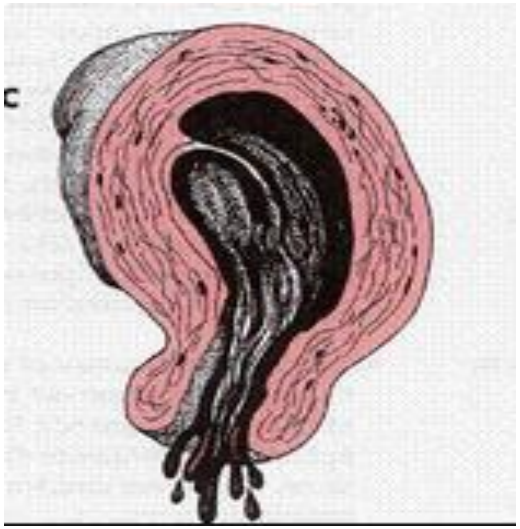


Inevitable pregnancy

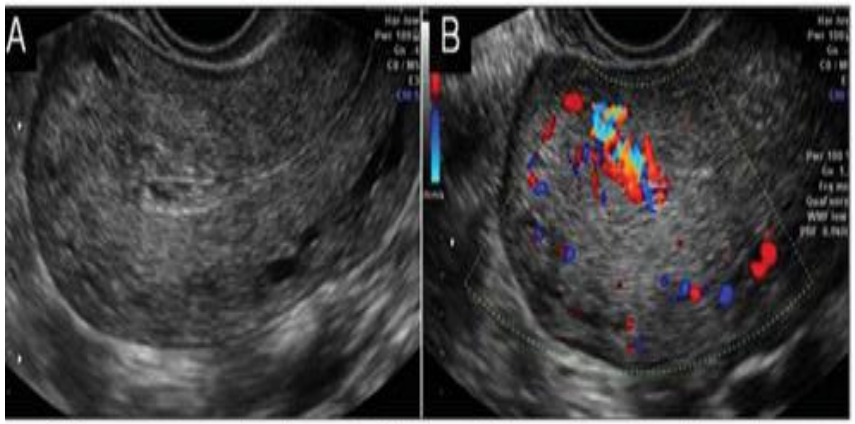
- Vaginal bleeding in the presence of open cervical os and pregnancy associated tissue still present



- Incomplete miscarriage
- Vaginal bleeding that is ongoing where pregnancy tissue has already been passed but ultrasound showed retained product of conception >15 mm in diameter (with or without gestational sac)

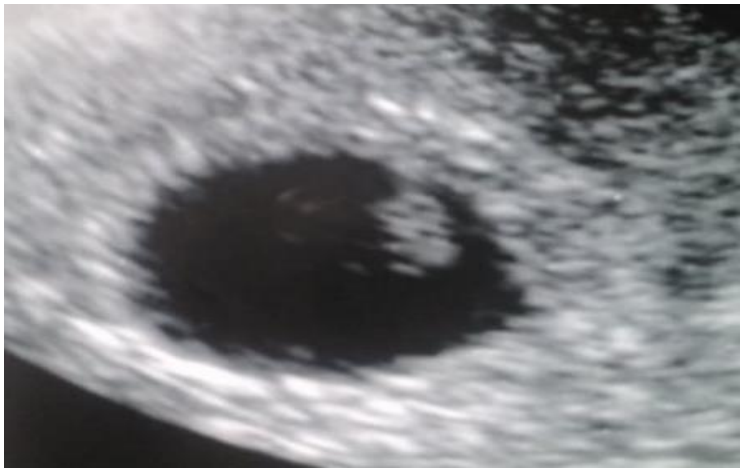


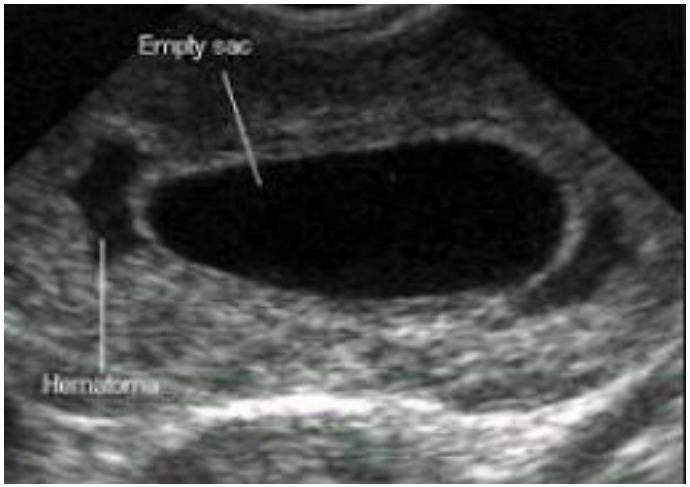
- Complete miscarriage
- Cessation of bleeding and a closed cervix following miscarriage
- Empty uterus or retained products of conception< 15 mm in diameter, falling HCG,where an intrauterine pregnancy was previously confirmed



igure 3. Absence of retained products of conception. **A:** Endometrial thickness of 5 mm with small intracavitary contents orresponding to coagula. **B:** Focally increased vascularization represented by a small group of vessels extending deeply nto the myometrium, site of previous connection.

- Missed miscarriage or early fetal demise
- Minimal or no symptoms
- Mean gestational sac diameter >25 mm with no obvious yolk sac or fetal pole
- With CRL > 7 mm with no fetal heart activity





Diagnosis

- Its important to differentiate between

Ectopic pregnancy

Intrauterine pregnancy of uncertain viability

PUL

- History taking
- Examination

History taking

- LMP (regular, length, contraception)ovulation might be affected
- Pregnancy testing: HCG quantity, ultrasound
- Symptoms:vaginal bleeding , pain, diarrhea, urinary symptoms, passage of tissues or vesicles
- past obstetric and gynecology history(risk factors)
- Past medical history:diabetes
- medications:

Examination

- General examination: vital signs, level of consciousness
- Abdominal palpation: masses,distention, pain
- Vaginal examination:

Cervix

Tissue→histopathology

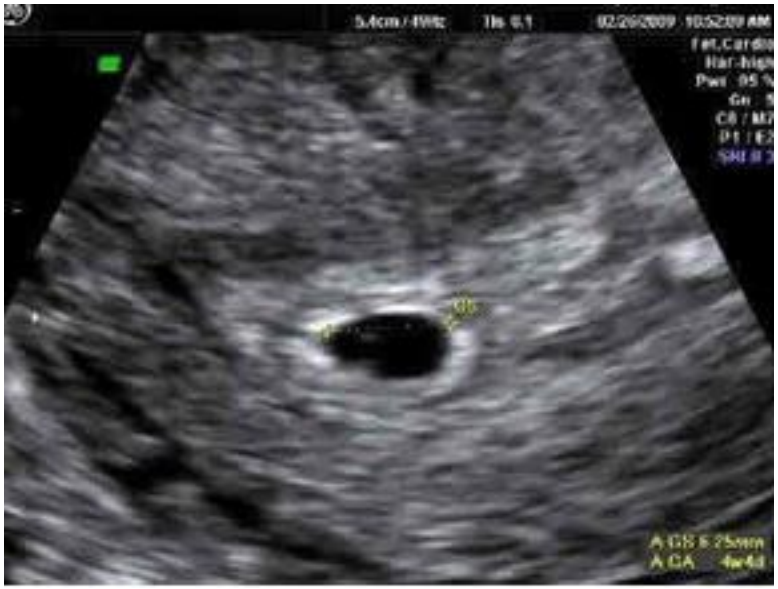
Diagnosis

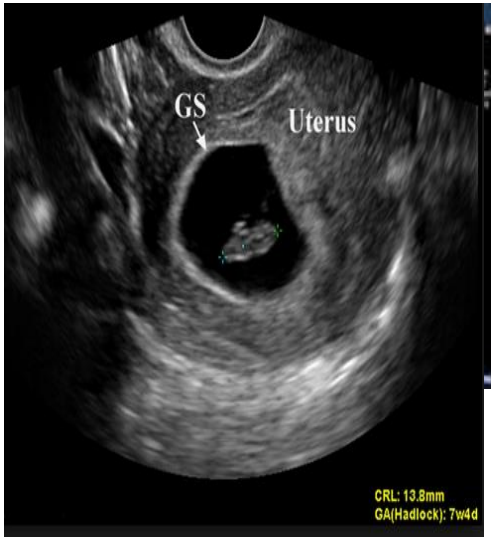
If pelvic os is open, no passage of tissues → the miscarriage is inevitable

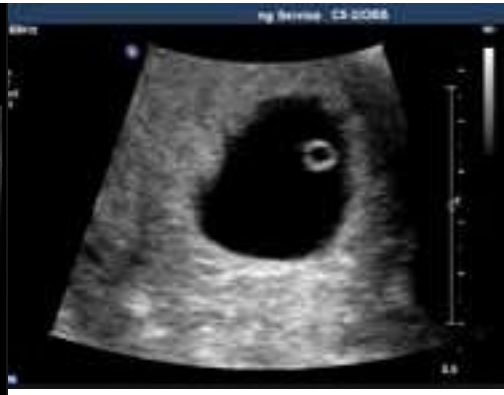
- If products of conception are seen , the miscarriage either is ongoing or complete
- Diagnosis is by TVS
- Additional testing serial hCG
- Serum progesterone <25 nmol/L ass. With non viable pregnancy

Diagnostic tools

- Ultrasound:
- Week 5: visible gestational sac
- Week 6: yolk sac
- Week 6: embryo
- Week 7: visible amnion
- Discrepancy between us and GA we have to rescan in 7 days







Management

- Expectant
- Medical
- surgical

Expectant

- Nature to take its course
- Rate of spontaneous resolution at 2 weeks
- 70% for incomplete miscarriage
- 53% blighted ovum
- 35% missed miscarriage
- The rate is lower if the gestational sac is intact

Medical management

- Misoprostol: prostaglandin analogue that is equally effective orally or vaginally
- Vaginally carries less GIT side effects
- Binds to the myometrial cells causes strong myometrial contractions leading to expulsion of tissues
- Causes ripening and dilatation of the cervix

Medical treatment

- After antiprogesterone priming (mifepristone)
- Encourage trophoblast separation
- Incomplete miscarriage misoprostol
- Missed miscarriage: higher and repeated doses in addition to mifepristone

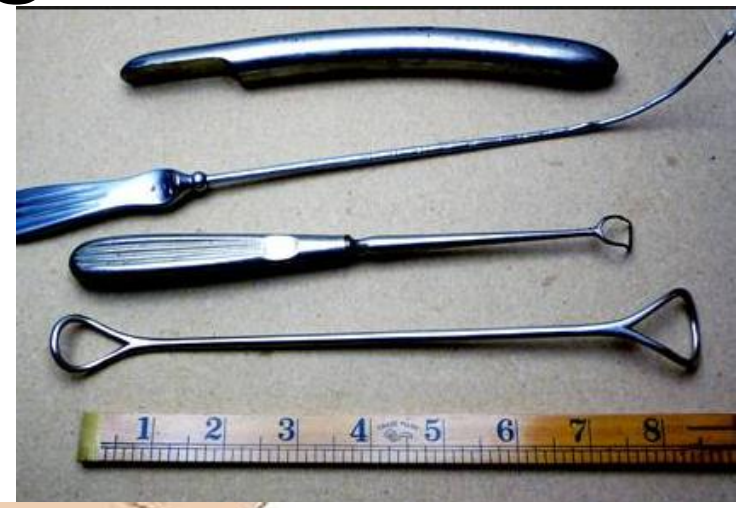
Medical management

- Bleeding after medical management can take 3 weeks to subside
- Outpatient management

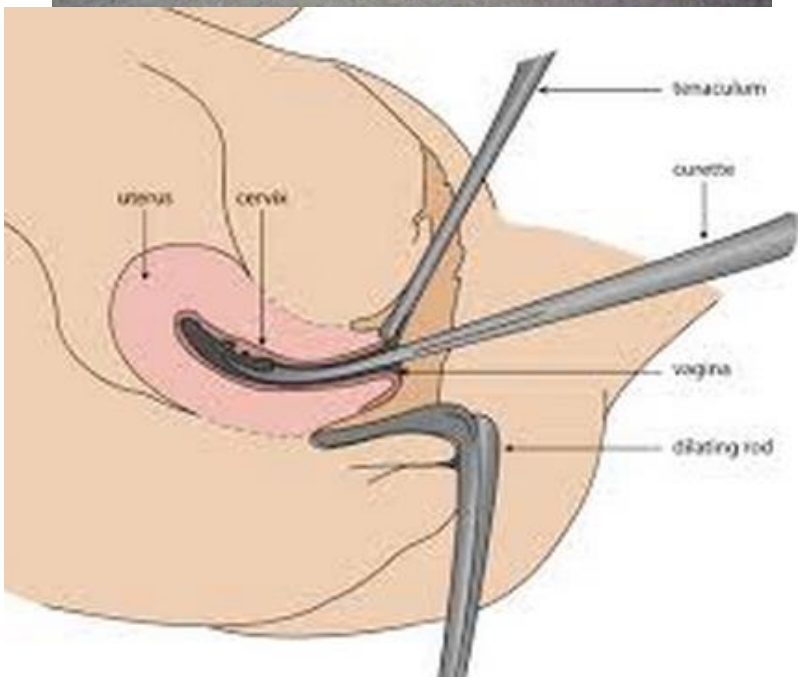
Surgical management

- ERPC
- Persistent ,
- excessive bleeding
- haemodynamic compromise
- Infected retained products
- Suspicion of gestational trophoblastic disease
- Patient prefers it

Surgical management



- Day case
- GA
- Preoperative cervical priming reduce the risk of uterine and cervical trauma
- Lithotomy position
- EUA done
- Cervix grasped by vulsella and dilated by Hegar up to(8-10 mm)
- Suction curette (reduce blood loss)
- Oxytocin (encourage haemostasis and decrease the median blood loss)
- Septic abortion: delay surgical intervention for 12 hours to administer intravenous antibiotics first



Surgical management

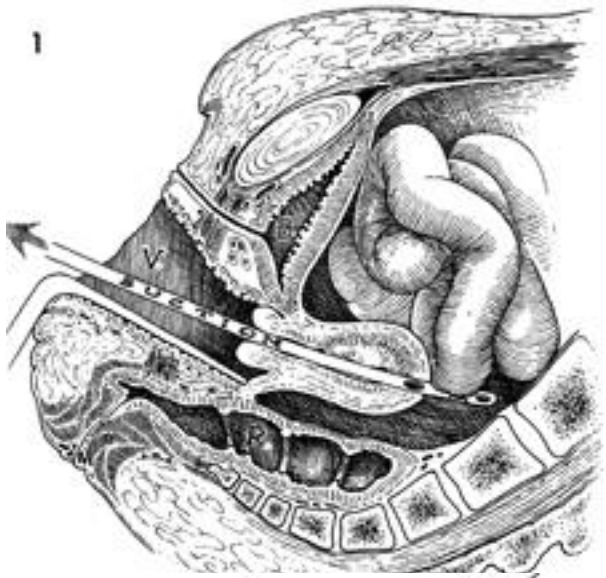
Counseled about risks

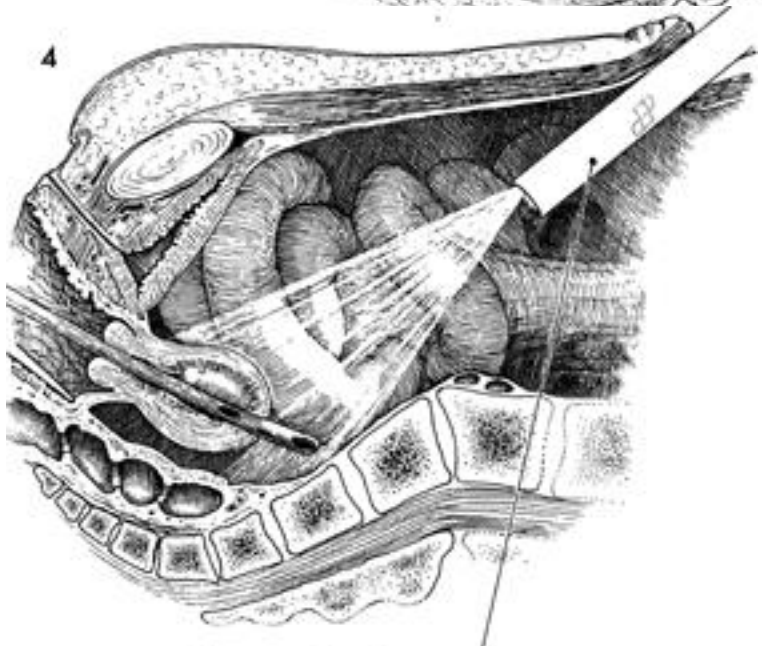
- Uterine perforation 5/1000

If suspected uterine perforation

Hysteroscopy and laparoscopy to assess the injury , and assess visceral damage

Admitted for observation, IV antibiotics 24-48 hrs





Surgical management

- Blood transfusion 1-2 per 1000
- Repeated evacuation 4%
- Infection 3%
- Cervical trauma(rare)

- Products should be sent for histopathology to exclude EP and GTD
- Psychological support

Rhesus status

- Despite the absence of antigen on the surface of embryonic red blood cells until 12 weeks gestation , there is concern regarding the possibility of sensitization of rhesus-negative women from early pregnancy events
- RCOG

Spontaneous miscarriage

- > 12 weeks, Anti-D should be given to all non-sensitized RhD-negative women
- < 12 weeks , FMT only occurs after curretage

If no instumentation→ no need for Anti-D

In curettage→Anti –D should be given

Threatened miscarriage

- > 12 weeks , Anti-D should be given to all non sensitized RhD-negative
- If bleeding continues→ Anti –D should be given in 6 weeks intervals
- Sensitization below 12 weeks is rare

Give Anti- D where bleeding is heavy , repeated or associated with abdominal pain

Anti-D

- 250 units before 20 weeks
- 500 units after 20 weeks
- Kleihauer test may be performed to assess the quantity of feto-maternal haemorrhage after 20 weeks

Recurrent miscarriage

- loss of three or more consecutive pregnancies and affect up to 1% of couples

Etiology

- Parental age
- Maternal age ass. With decline in no. and quality of oocytes
- 20-45 years increase risk of miscarriage 11%-93%

Etiology

- Increasing number of previous miscarriage

40% if three previous miscarriages

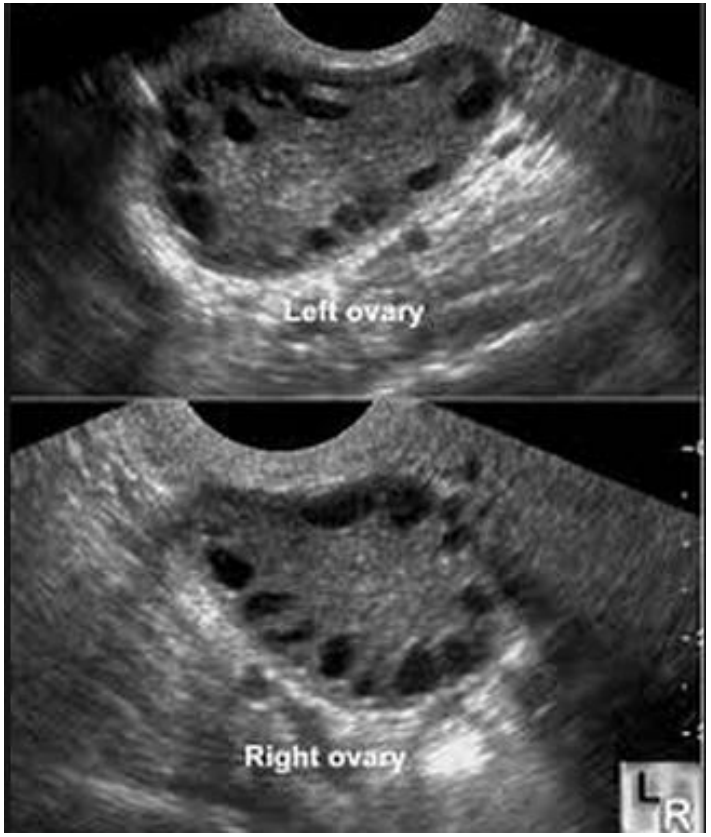
- Maternal cigarette smoking, caffeine consumption, heavy alcohol consumption, maternal obesity(BMI>30 kg/m2)
- Endocrinology
- Genetic
- Immunological
- Uterine anomalies, cervical weakness
- Infection
- APL and thrombophilias

Endocrinology

- Diabetes and thyroid disease

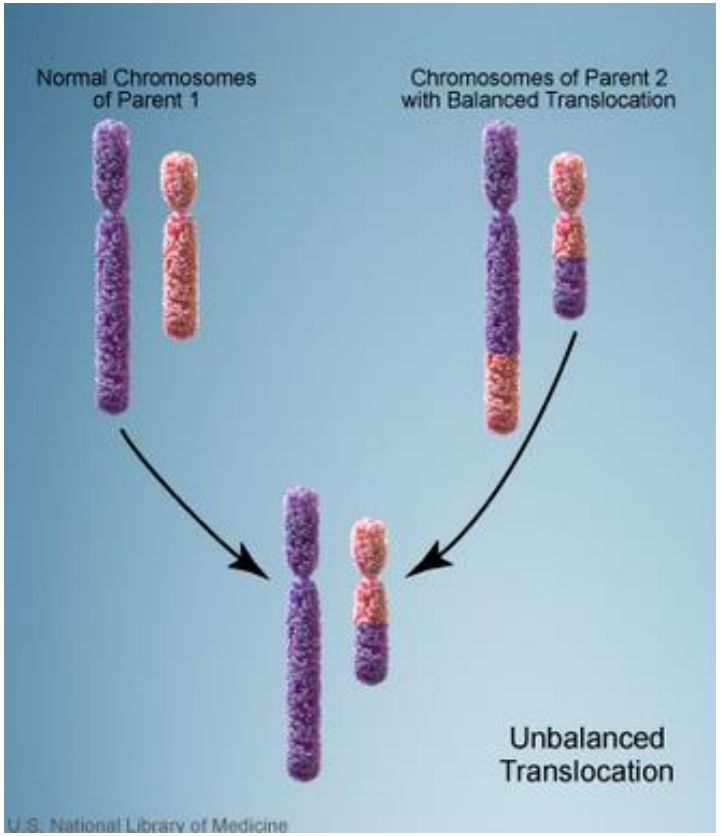
PCOS

- PCOS related to insulin resistance and hyperandrogenaemia
- Simple and safe way to reduce risk of miscarriage is Weight loss
- Metformin



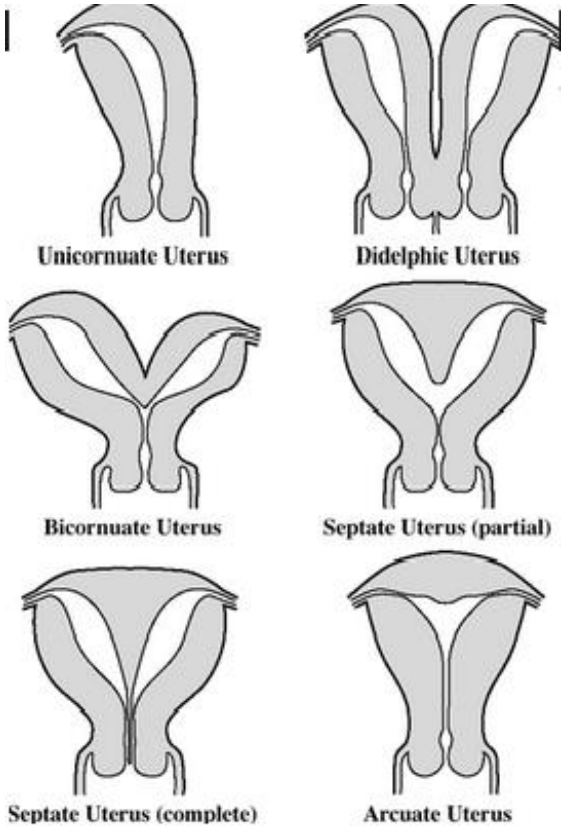
Genetic causes

- 2-5%
- Balanced translocation of one partner→unbalanced translocation and result in miscarriage
- 30-60% trisomies which increase with advanced maternal age



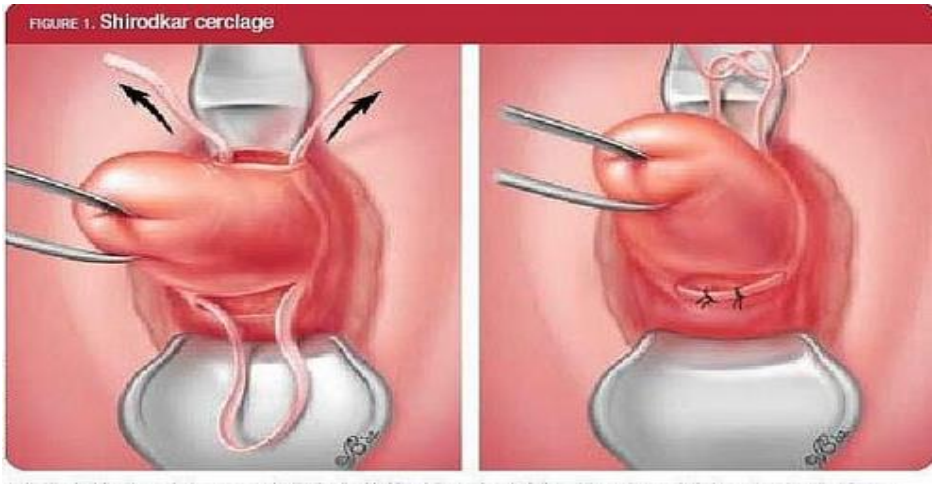
Congenital uterine anomalies

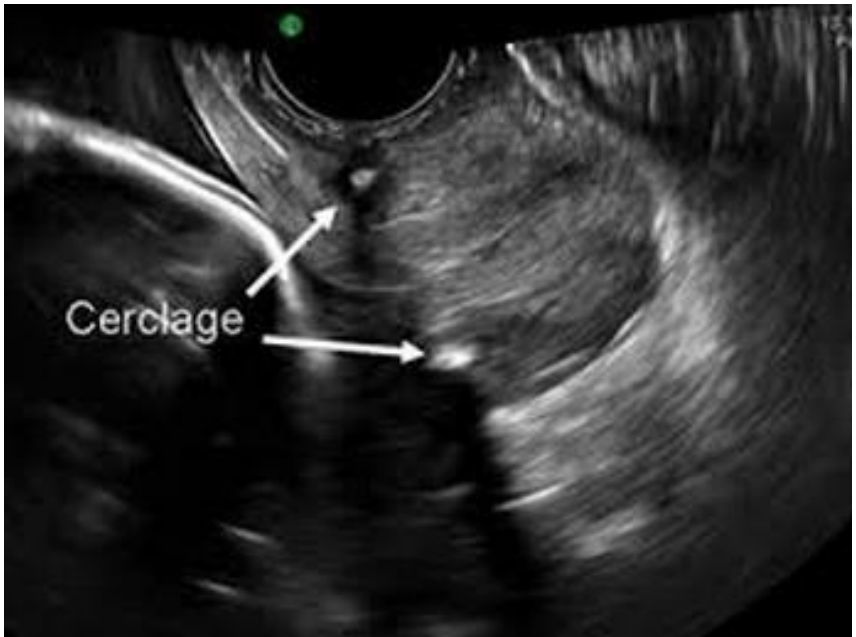
- Uterus didelphys
- Bicornuate uterus
- 1.8-37 %
- Recurrent second trimester miscarriages



Cervical weakness

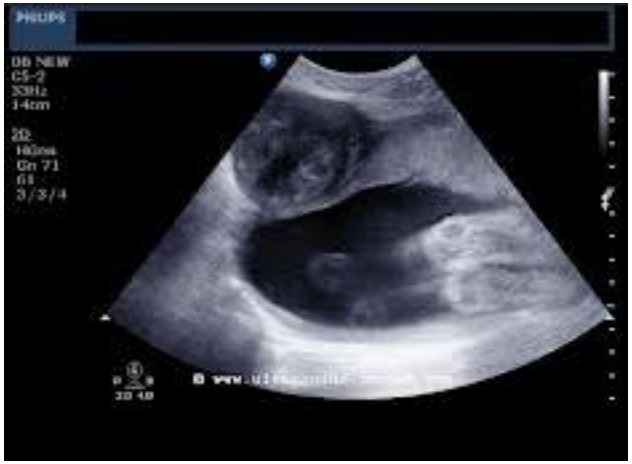
- Second trimester miscarriage
- Diagnosed following a history of second trimester miscarriage preceded by spontaneous rupture of membrane or painless cervical dilatation
- Cervical cerclage end of first trimester

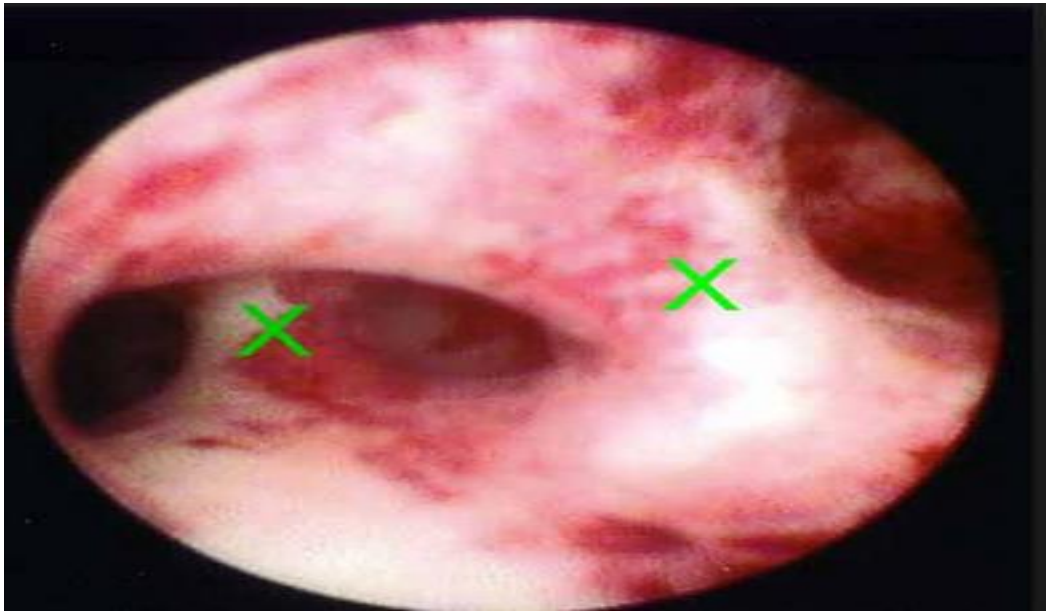




Acquired uterine anomaly

- Fibroid
- Intrauterine adhesions





Antiphospholipid syndrome

- Adverse pregnancy outcome
- Lupus anticoagulant
- Anticardiolipin
- Anti b2 glycoprotein -1 antibodies
- Thrombosis of uteroplacental vasculature
- Activated protein c , antithrombin III and prothrombin (cause late pregnancy loss)

Table 1.

Updated antiphospholipid syndrome classification criteria [Miyakis *et al.* 2006].

Clinical criteria

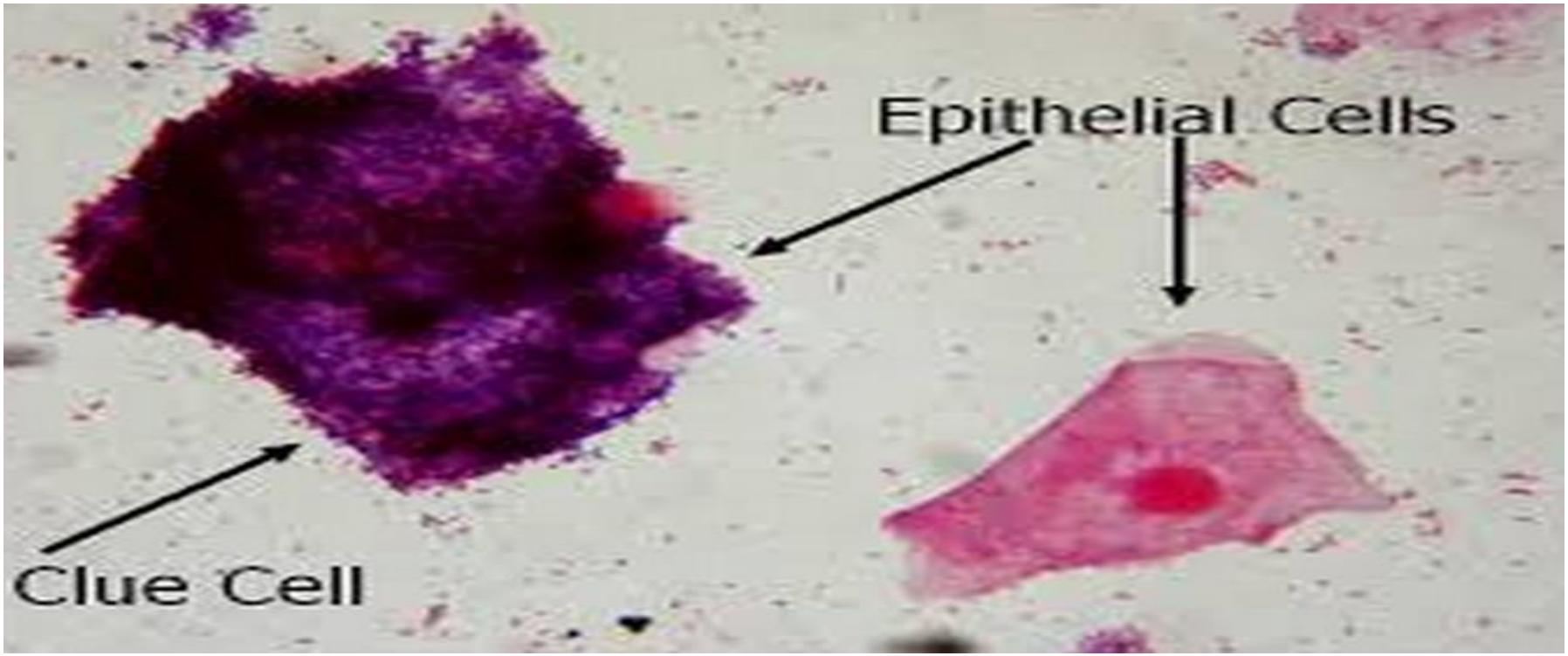
1. Vascular thrombosis:
   ≥ 1 clinical episodes of arterial, venous, or small vessel thrombosis, in any tissue or organ
2. Pregnancy morbidity:
   (a) ≥ 1 unexplained deaths of a morphologically normal fetus at or beyond the 10th week o
   (b) ≥ 1 premature births of a morphologically normal neonate before the 34th week of ge
severe preeclampsia, or recognized features of placental insufficiency, or
   (c) ≥ 3 unexplained consecutive spontaneous abortions before the 10th week of gestation,
hormonal abnormalities and paternal and maternal chromosomal causes excluded.

Laboratory criteria

1. Lupus anticoagulant present in plasma, on ≥ 2 occasions at least 12 weeks apart
2. Anticardiolipin antibody of IgG and/or IgM isotype, in medium or high titer (>40 GPL or MP
≥ 2 occasions, at least 12 weeks apart.
3. Anti-β_2-glycoprotein-I antibody of IgG and/or IgM isotype, in medium or high titer (> the 9
occasions, at least 12 weeks apart

infection

- Bacterial vaginosis in the first trimester is associated with increase risk of miscarriage in second trimester



Immune factors

- Antithyroid antibody

Mechanism autoimmune or thyroid insufficiency

? Levothyroxine treatment even with normal thyroid function

- Natural killer cells (peripheral and uterine)
- No significant benefits of immunotherapies
- Pateranl cell immunization
- Third party donor cell immunization

Diagnosis

- Cytogenetic analysis of product conception

If abnormal -→parental karyotyping

- Uterine abnormality
- Ultrasound
- HSG
- Insulin resistence
- TFT
- NKC??

Management

- APS→Low dose Aspirin and LMWH

Reduction of miscarriage by 45%

At risk of preterm labour, preeclampsia,FGR

- Genetic counseling if structural abnormalities

PGD and IVF

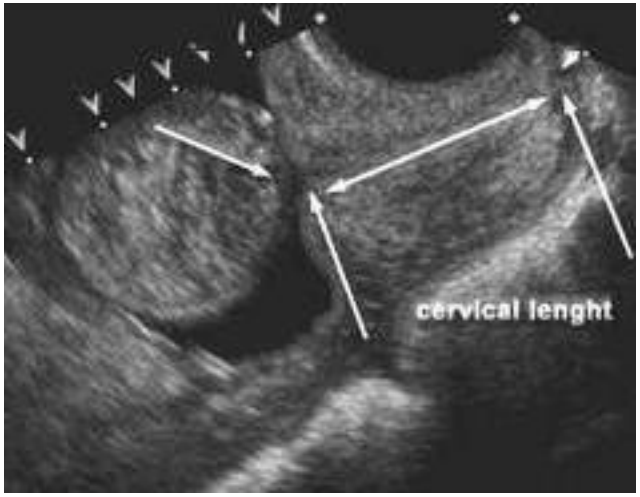
CVS and amniocentesis

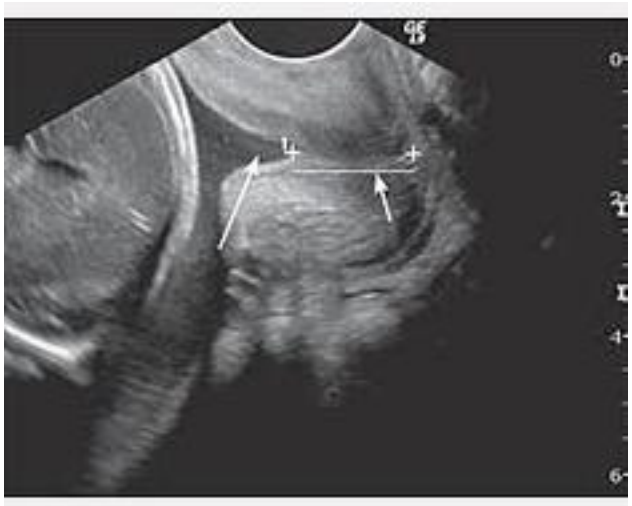
Management

- Uterine abnormalities (uterine septate)
- Open surgery might lead to postoperative infertility
- Hysteroscopic approach

Management

- Cervical incompetence
- Singleton, history of one second trimester miscarriage attributed to cervical incompetence
- if cervical length before 24 weeks 25 mm or less





Management

- Use of progesterone supplementation
- Evidence is insufficient

Cochrane review suggests that use of progesterone is effective in treatment of threatened miscarriage

Management

- hCG
- Metformin
- Immunotherapies(paternal cell immunization, IVIG)
- Not proven to improve live births

Thank you