Sherif A. Shazly
Nashwa Eltaweel
*Editors*

# MRCOG Part 2

## Essential Revision Guide

Springer

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Sherif A. Shazly • Nashwa Eltaweel
Editors

Middle-East Obstetrics and Gynaecology Graduate Education
(MOGGE) Foundation - Practice and Education Office

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ISBN 978-3-030-78047-0 ISBN 978-3-030-78048-7 (eBook)
https://doi.org/10.1007/978-3-030-78048-7



This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

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# PART I

## General obstetrics

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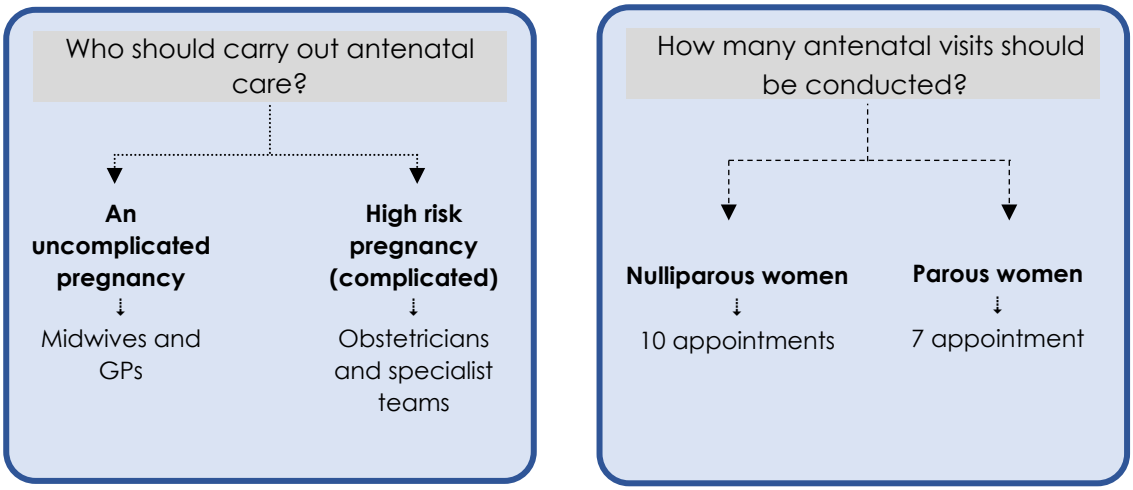
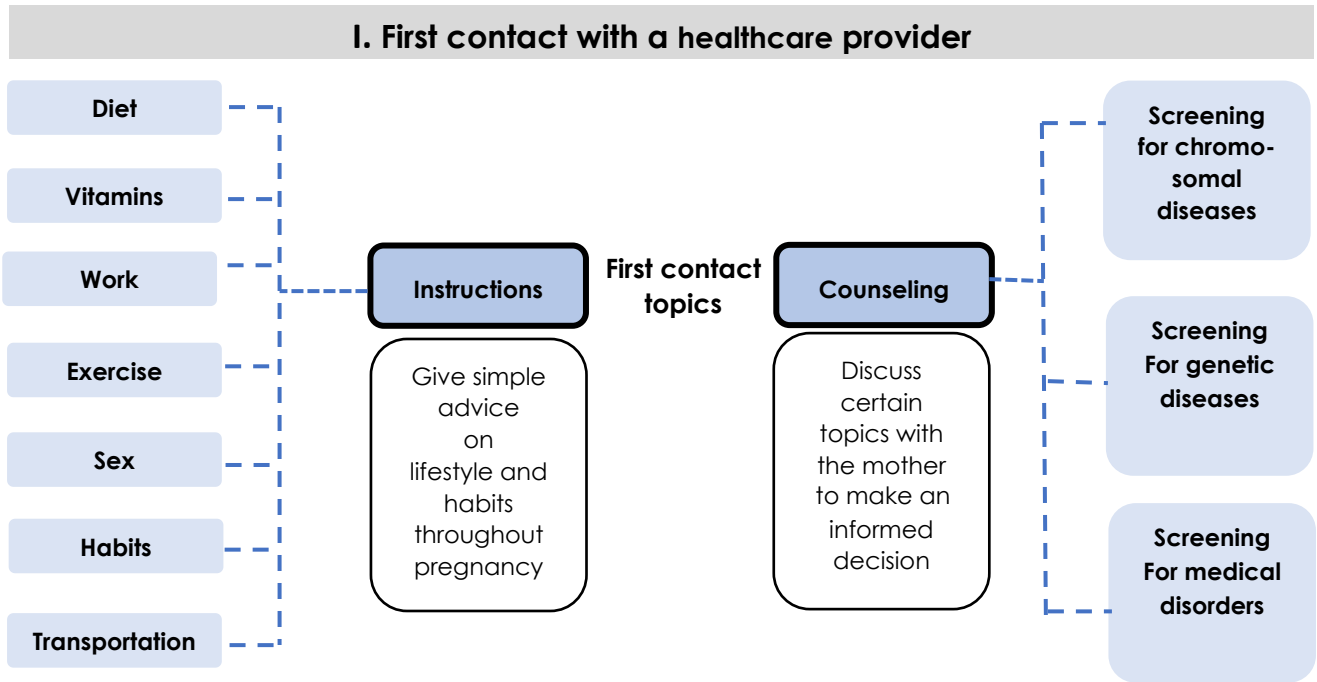
# Antenatal Care

## General Concepts of Antenatal Care




## Contents of appointments







S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_1

## I. Instructions

**Diet**

- Advise on balanced diet
- Advise against ripened soft cheese, uncooked or undercooked meals (risk of listeriosis)
- Advise against raw, partially cooked eggs, mayonnaise, raw or undercooked meat (risk of salmonella)

**Vitamins**

- Folic acid (400 µg/day) preconceptionally and throughout the first trimester
- Vitamin D (10 µg/day) during pregnancy and lactation
- Vitamin A (more than 700 µg/day) should be avoided (teratogenic)
- Routine iron therapy is not indicated

**Work**

- Reassure her that work during pregnancy is safe (unless there is specific job risk)

**Exercise**

- Reassure her that moderate exercise is safe
- Stressful exercise and scuba diving should be avoided in pregnancy

**Sex**

- Reassure her that sex is safe during pregnancy

**Habits**

- Give information about smoking risks. Support cessation decision. Nicotine replacement therapy may be considered in these women.
- Advise on cessation of alcohol intake particularly in the first trimester. If cession cannot be achieved, drinking should be markedly reduced (e.g. one small glass of wine once or twice weekly)
- Cannabis should be avoided during pregnancy

**Travels**

- **Advise that air travel may be allowed with the following precautions:**
  - Medical contraindications to travelling are ruled out e.g. recent sickling crisis
  - No air travelling beyond 36 weeks (33 weeks for dichorionic multiple pregnancy)
  - Compression stockings are worn during travelling if > 4 hours
  - Vaccinations should be considered when travelling to endemic areas
- **Advise that seat belts should be applied above and below the uterine bump**

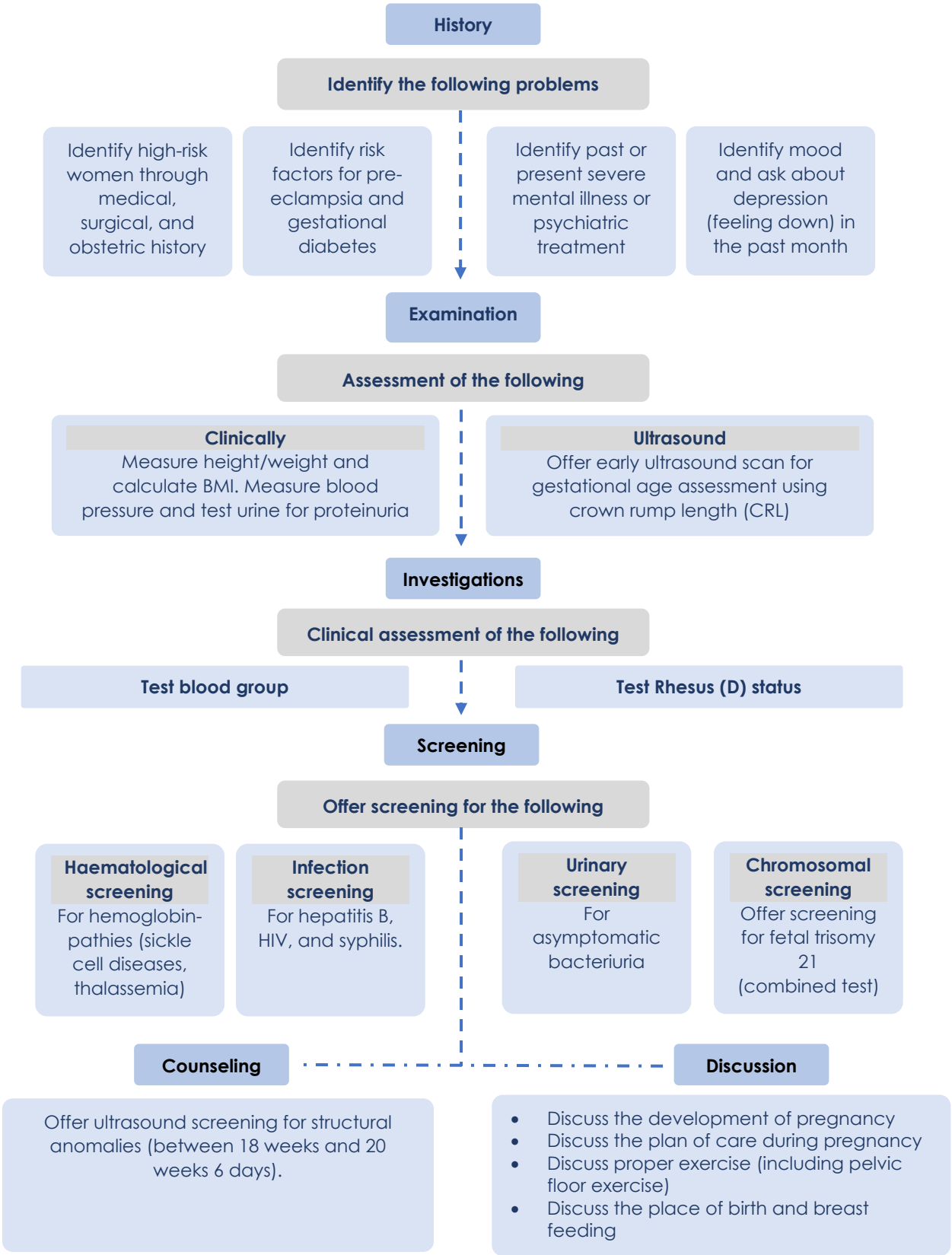
## II. Counseling

**Screening**

**Offer and discuss screening options including their value, nature, benefits, risks, what further management is recommended per results. Reliability of screening test results should also be explained. Antenatal screening tests cover:**

- Genetic diseases (sickle cell diseases and thalassemia): It should be offered for all women at 10 weeks of pregnancy.
- Chromosomal disorders (Trisomy 21): offered at or after 11 weeks.
- Medical disorders:(diabetes mellitus): if maternal risk factors are present
- Infections (Hepatitis B, HIV, and syphilis): at the 10$^{th}$ week of pregnancy

## II. Booking appointment (ideally by 10 weeks)



## III. At 16 weeks

**Interview**

**Discuss results of screening tests**

If the level of hemoglobin is below 11 gm/dl, consider iron therapy

**Examination**

**Assessment of the following**

**Measure blood pressure**

**Test urine for proteinuria**

**Discussion**

**Discuss the next appointment**

**Anomaly scan (for structural anomalies): between 18 to 21 weeks**

**Ultrasound scan for structural anomalies. Fetal echocardiography is considered if cardiac assessment is concerning**

The presence of structural anomaly (confirmed by second opinion) indicates a referral to a fetal medicine specialist.

Some anomalies may not require referral (e.g. anencephaly)

The presence of an isolated soft marker should not be used as an indicator of Down's syndrome.

The presence of increased nuchal fold (≥ 6 mm) or 2 or more soft markers warrants referral to a fetal medicine specialist.

**Ultrasound assessment of the position of the placenta should be considered during examination**

If the placenta is low lying but is not covering the internal os (minor), asymptomatic women should be re-examined on the 36th week of pregnancy to confirm the diagnosis

If the placenta is covering the internal os (major), asymptomatic women should be re-examined on the 32nd week of pregnancy to confirm the diagnosis

## IV. At 25 weeks – for nulliparous women

**Examination**

**Assessment of the following**

- Measure blood pressure
- Test urine for proteinuria

## V. At 28 weeks

**Examination**

**Assessment of the following**

- Measure blood pressure after a period of rest
- Measure and plot symphysis–fundal height (28th week & onwards)
- Test urine for detection of proteinuria

**Screening**

**Offer and discuss the following**

- Offer re-screening for anaemia (hemoglobin level)
- Offer screening for atypical red-cell alloantibodies

**Interference**

**Offer the following treatment options**

- Offer iron therapy for women with hemoglobin level < 11 g/dL
- Offer anti-D prophylaxis to rhesus D-negative women

## VI. At 31 weeks – for nulliparous women

**Examination**

- Measure blood pressure after a period of rest
- Measure and plot symphysis–fundal height
- Test urine for detection of proteinuria

**Discussion**

Discuss and record the results of screening tests in the previous visit (28 weeks) and offer management accordingly.

## VII. At 34 weeks

**Examination**

**Assessment of the following**

- Measure blood pressure after a period of rest
- Measure and plot symphysis–fundal height
- Test urine for detection of proteinuria

**Discussion**

**Discuss the past and future**

- Discuss and record the results of screening tests of the 28th week
- Discuss labor plan, how to recognize active labor and pain management

**Interference**

**Offer the following treatment options**

- Offer a second dose of anti-D prophylaxis to rhesus D-negative women

## VIII. At 36 weeks

**Examination**

**Assessment of the following**

- Measure blood pressure
- Measure and plot symphysis–fundal height
- Test urine for proteinuria
- Check fetal position

**Discussion**

**Discuss these future issues**

- Discuss breast feeding and the good management of breast-feeding practice
- Discuss care of the newborn including vitamin K prophylaxis and newborn screening tests
- Discuss postnatal care with special emphasis on the postnatal blues and depression
- Offer and counsel on external cephalic version if the foetus is breech presented

## IX. At 38 weeks and at 40 weeks (for nulliparous women)

Examination

Assessment of the following

Measure maternal blood pressure

Measure and plot symphysis–fundal height

Test urine for detection of proteinuria

Discussion

Discuss future possibilities

Discuss plan of management of prolonged pregnancy in case it happens

## X. At 41 weeks

Examination

Assessment of the following

Measure maternal blood pressure

Measure and plot symphysis–fundal height

Test urine for detection of proteinuria

Intervention

Offer these options for the postdate

Offer membrane sweeping

Offer induction of labor

If these options are denied

Allow expectancy till the 42nd week of gestation

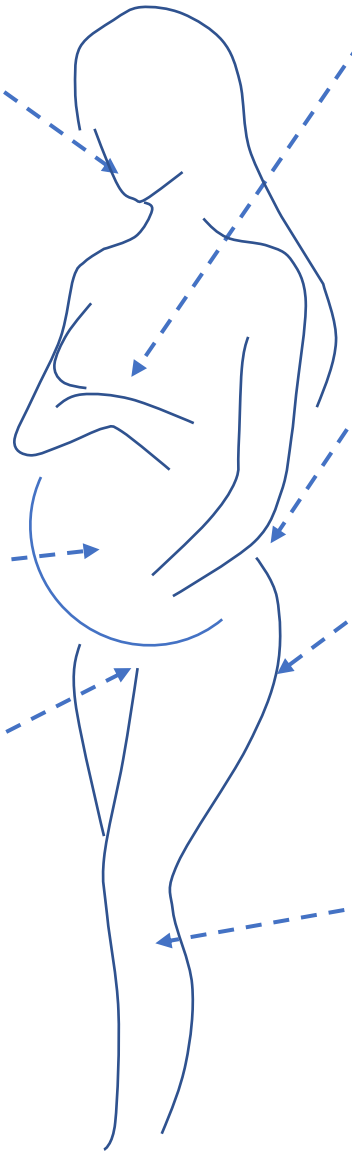
If no labor is achieved by 42 weeks

Offer immediate induction of labor

If denied

Twice-weekly CTG & weekly USS for maximum fluid depth

## Management of common symptoms



### Nausea and vomiting

- Reassurance: Most cases of nausea and vomiting resolve spontaneously within 16 to 20 weeks (no poor pregnancy outcome).
- Treatment: If a woman asks for treatment:
  - *Non-pharmacologic:* ginger - acupressure.
  - *Pharmacological:* antihistamines.

### Heart burn

- Advice: regarding lifestyle and diet modification.
- Antacids: may be given if heartburn remains.

### Backache

Exercising in water, massage therapy and back care classes

### Constipation

Diet modification including bran or wheat fiber is usually sufficient

### Hemorrhoids

- Advice: on diet modification
- Hemorrhoid creams are considered if there is no improvement.

### Vaginal discharge

- Reassurance: Women should be informed that an increase in vaginal discharge is normal during pregnancy.
  It should be investigated only if it is associated with itch, soreness, offensive smell or pain on passing urine.
- For vaginal candidiasis: Topical imidazole is given for 1 week (no oral treatment).

### varicose veins

- Reassurance: varicose veins are a common symptom of pregnancy that will not cause harm.
- Compression stockings: can improve the symptoms.

## Malpractice during antenatal care

| During maternal assessment | During fetal assessment |
|---|---|
| ▪ Repeated weighing<br>▪ Undue breast or pelvic examination.<br>▪ Routine screening for chlamydia, cytomegalovirus, hepatitis C virus, group B streptococci, toxoplasmosis, bacterial vaginosis<br>▪ Routine screening for preterm labor.<br>▪ Gestational diabetes screening using fasting plasma glucose, random blood glucose, glucose challenge test or urinalysis for glucose<br>▪ Routine ultrasound scanning after 24 weeks. | ▪ Routine Doppler ultrasound in low-risk pregnancies.<br>▪ Ultrasound estimation for suspected large-for-gestational-age fetuses.<br>▪ Routine fetal movement counting<br>▪ Routine auscultation of fetal heart<br>▪ Routine antenatal electronic cardiotocography |

**Appendix - I** **RCOG recommendations for special situations**

## Air travel during pregnancy

### Health hazards

As an obstetrician, you should understand the hazards of air travel during pregnancy and be able to respond to woman's inquires. Although there is no direct risk on pregnancy, the following are possible risks related to air travel:

- Ear troubles especially in the presence of nasal congestion (aggravated by physiologic vasodilation of pregnancy).
- Motion sickness that may aggravate morning sickness of pregnancy.
- Lower limb oedema and deep venous thrombosis (DVT) with prolonged travel (pregnancy is a hyper-coagulable state).

### Travelling rules

- Many airlines do not allow women to fly after 36 completed weeks of gestation because of the risk of labor. Women should not fly after 33 completed weeks of gestation If there are any risk factor for preterm labour (e.g, dichorionic multiple pregnancy).
- A letter from a midwife or doctor confirming that there are no pregnancy complications and confirmation of the expected date of delivery is usually required.

### Contraindications

Medical complications that contraindicate air travel include:

- Severe anemia (haemoglobin less than 7.5 g/dl)
- Unstable fractures, where significant leg swelling can occur during air flight (particularly hazardous if a cast is in place)
- Recent haemorrhage
- Otitis media and sinusitis
- Serious respiratory disease, particularly with marked breathlessness
- Recent sickling crisis
- Recent gastrointestinal surgery, where suture lines taken in the intestine could come under stress due to the reduction in pressure and gaseous expansion during air flight.

### Instructions

- Avoid air travel from 37 weeks of gestation (uncomplicated pregnancy) or beyond 34 weeks of gestation (uncomplicated dichorionic pregnancy).

### Instructions (cont.)

- Recommended immunization and antimalarial medication should be considered according to the destination area.
- The seat belt is tightly fastened under the abdomen and across the top of the thighs.
- The following instructions are followed to minimize the risk of DVT:
  - Take regular walks every 30 minutes on a medium or long-haul flight.
  - Maintain a good fluid intake.
  - Minimize caffeine and alcohol intake (to avoid dehydration).
  - Further measures depend on the duration of air travel and the individual risks of the woman:
    - *For short journeys:* no specific measures are required.
    - *For medium to long flights (> 4 hours):* properly fitted graduated elastic compression stockings are advised for all pregnant women.
    - *If there are additional risk factors of DVT:* low-molecular-weight heparin (LMWH) is considered on the day of travel and several days thereafter, if the woman is not already on LMWH.

    Aspirin is not recommended for thromboprophylaxis in these women.
- A letter confirming that there are no pregnancy complications and confirmation of the expected date of delivery is usually required (and if she is carrying a supply of LMWH injections).

## Exercise during pregnancy

### Risks

- Musculoskeletal alterations (increased joint laxity and hypermobility) increase the risk of injury during exercise (contact sports and weight-bearing exercise should be avoided).
- Hyperthermia (from exercise and higher metabolic rate during pregnancy) is potentially teratogenic in the first trimester (if core temperatures are in excess of 39.2°).

### Benefits

- Exercise reduces many common complaints of pregnancy (fatigue, varicosities and swelling of extremities).
- Exercise reduces insomnia, stress, anxiety and depression.
- Exercise improves glycaemic control in women with gestational diabetes mellitus and may even prevent the development of gestational diabetes mellitus.
- Weight-bearing exercise reduces the length of labor and decreases delivery complications.
- Evidence has suggested fetuses of exercising women may tolerate labour better.

**Benefits (cont.)**

- Fetal/neonatal stress is less frequent in women who exercise at 50% of preconception level during pregnancy, compared with athletes who discontinued exercise before the end of the first trimester.
- Generally, exercise reduces the risk of coronary heart disease, osteoporosis, hypertension, colon cancer, perhaps breast cancer, and reduces body fat.

**Exercise program**

This should be individualized according to woman's age and pre-conceptional activity:

- *Based on heart rate:* consider a maximal heart rate of 60–70% for women who were sedentary prior to pregnancy (60–90% for women wishing to maintain fitness during pregnancy):
  - If aged <20, the target heart rate is 140–155 beats/minute.
  - If aged 20–29, the target heart rate is 135–150 beats/minute.
  - If aged 30–39, the target heart rate is 130–145 beats/minute.
  - If aged >40, the target heart rate is 125–140 beats/minute.
- *Based on the talk test:* the woman should be able to maintain a conversation with comfort during exercise.
- *Based on Borg's rating of perceived exertion:* it is a self-paced scale of intensity of exertion. It is scaled from 6 (no exercise) to 20 (maximum exertion). A woman should maintain a moderate exercise (12-14).
- *Based on the duration of exercise:* sedentary women should begin with 15 minutes of continuous exercise three times a week, increasing gradually to 30-minute sessions 4 times a week then to daily.
- *Based on previous activity and gestational age:* regular exercisers before pregnancy should be able to perform activities like jogging and aerobics (high intensity exercise). However, activity and fitness are expected to diminish as pregnancy advances.

**Precautions:**

- Contact sports and weight-bearing exercise should be avoided (due to joint laxity changes).
- Maintain adequate hydration and avoid exercising in hot, humid wheather (hyperthermia is teratogenic).
- Avoid hypoglycemia by adequate caloric consumption and limited exercise time (< 45 minutes).
- Avoid exercise in the supine position (it is associated with lower cardiac output due to vena caval compression after 16 weeks of gestation).
- Avoid overexertion in altitudes over 2500 meters until after 4–5 days of accommodation to this high attitude (blood shifts from the uteroplacental unit to the exercising muscles).

**Precaution (cont.)**

- Avoid scuba dive in pregnancy (risk of fetal decompression sickness and gas embolism).
- Avoid horseback riding, downhill skiing, ice hockey, gymnastics and cycling during pregnancy (risk of fall and fetal trauma).
- Generally, water exercise is more beneficial. However, water temperature should not exceed 32° (35° while using a hydrotherapy pool).
- Warning signs to terminate exercise and to seek medical advice should be clearly taught to the pregnant women:
  - Excessive shortness of breath
  - Chest pain or palpitations
  - Presyncope or dizziness
  - Painful uterine contractions or preterm labor
  - Leakage of amniotic fluid
  - Vaginal bleeding
  - Excessive fatigue
  - Abdominal pain, particularly in back or pubic area
  - Pelvic girdle pain
  - Reduced fetal movement
  - Dyspnea before exertion
  - Headache
  - Muscle weakness
  - Calf pain or swelling.
- These conditions need extra-cautions for exercising women:
  - Cardiac disease and restrictive lung disease
  - Persistent bleeding in the second and third trimesters
  - Pre-eclampsia or pregnancy-induced hypertension
  - Preterm labor (previous/present) and preterm pre-labor rupture of membranes
  - Intrauterine growth restriction
  - cervical weakness/cerclage
  - Placenta previa after 26 weeks
  - Heavy smoker (more than 20 cigarettes a day)
  - Poorly controlled hypertension
  - Extremely sedentary lifestyle and morbid obesity (body mass index > 40)
  - Unevaluated maternal cardiac arrhythmia
  - Chronic bronchitis
  - Multiple gestation (individualized and medically supervised)
  - Poorly controlled thyroid disease
  - Malnutrition or eating disorder
  - Poorly controlled diabetes mellitus
  - Poorly controlled seizures
  - Anaemia (haemoglobin less than 100 g/l).

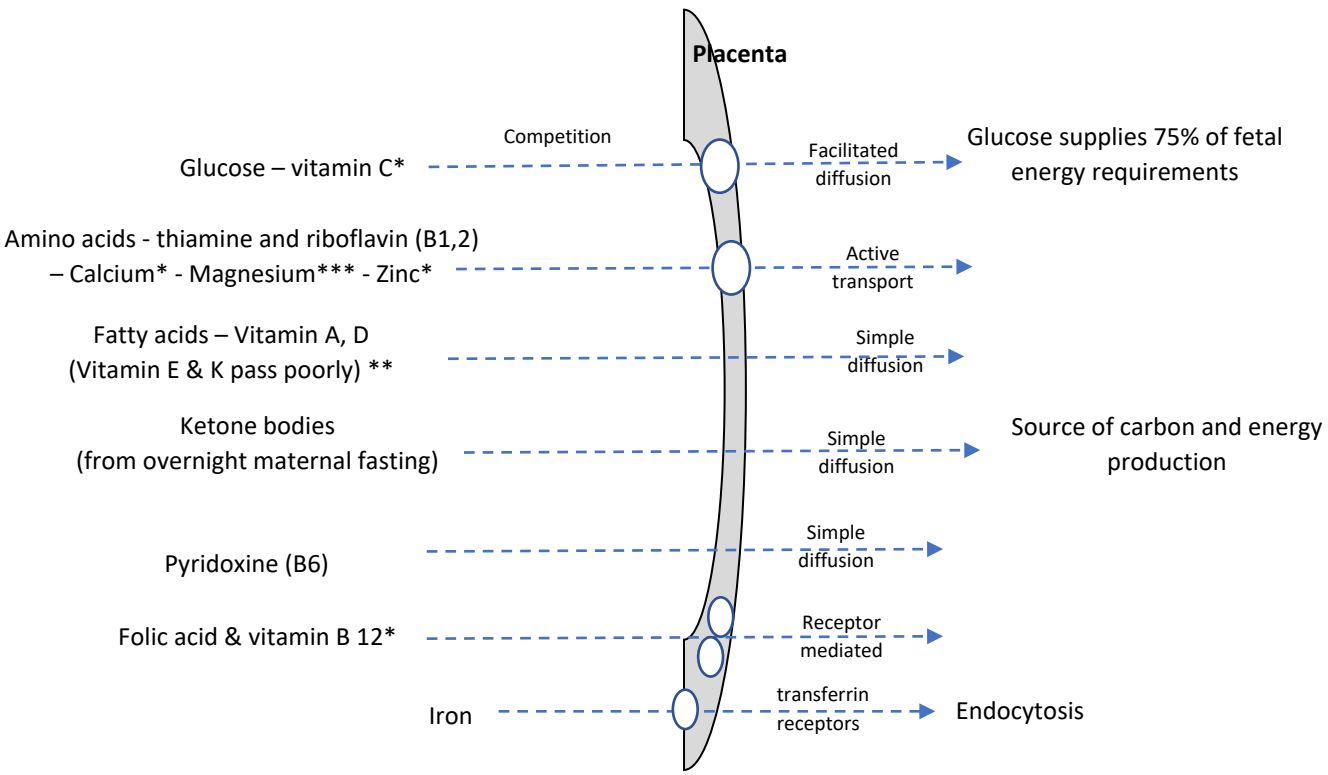
## Postpartum exercise

- *If pregnancy and delivery are uncomplicated:* a mild exercise program (walking, pelvic floor exercises and stretching) is recommended immediately postpartum. This reduces anxiety and depression and adjusts body weight.
- *If delivery was complicated or by caesarean section:* Resuming pre-pregnancy activity should be postponed (after 6–8 weeks). Resuming activity should be gradual.

## Nutrition during pregnancy

### Pre-pregnancy diet

- Pre-pregnancy counselling should include BMI adjustment through dietary modifications.
- Pre-pregnancy folic acid is advised (400 micrograms/day). Folate deficiency is present in 5% of the general population.




* Fetal > maternal concentration
** Maternal > fetal concentration
*** No certain relation

## Pregnancy regimen

### How much to eat?

Pregnant women vary greatly in their energy consumption from 13 000 kcal reduction in energy expenditure in energy sparing group, to an additional 80 000 kcal increase in energy expenditure in energy profligate group. Accordingly, the rule is to 'eat to appetite'.

### What is needed in diet?

| Energy | Protein | Thiamine | Riboflavin |
|---|---|---|---|
| 1940 + 200* kcal | 45 gm + 6 gm** | 0.8 mg + 0.1 mg* | 1.1.mg + 0.3 mg** |
| **Niacin** | **Vitamin B6** | **Vitamin B12** | **Folate** |
| 13 mg | 1.2 mg | 1.5 g | 200 µg + 100 µg** |
| **Vitamin C** | **Vitamin A** | **Vitamin D** | **Calcium** |
| 40 mg + 10 mg** | 600 µg + 100 µg** | 0 + 10 µg** | 700 mg |
| **Phosphorus** | **Magnesium** | **Sodium** | **Potassium** |
| 550 mg | 270 mg | 1600 mg | 3500 mg |
| **Chloride** | **Iron** | **Zinc** | **Copper** |
| 2500 mg | 14.8 mg | 7 mg | 1.2 mg |
| | **Selenium** | **Iodine** | |
| | 60 µg | 140 µg | |

* (+) in the third trimester only
** (+) during the whole pregnancy

### How to supply these needs?

**Group I: Bread, cereals & potatoes**

Eat plenty of this group

**Group II: Fruits and vegetables**

Eat a variety (at least five portions/day).

**Group III: Milk & dairy food**

Use moderate amounts, low-fat versions

**Group IV: Meat, fish & others (beans, eggs)**

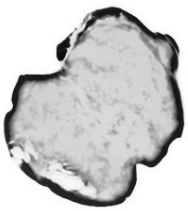
Eat moderate amounts and choose lower fat meat.

**Group V: High fat/sugar foods and drinks**

Avoid high sugar contents (tooth decay), Eat food with high amount of fat sparingly (use low fat alternatives).

## Diet precautions

### Liver products



Avoid liver and liver products as they contain high concentrations of pre-formed vitamin A (retinol) which is teratogenic.

### Soft cheeses

Avoid mould-ripened soft cheeses, unpasteurized milk, or pates (risk of food-borne listeriosis).

### Undercooked meat

Avoid undercooked meat or salad vegetables contaminated with soil (risk of toxoplasmosis).

### Caffeine

Avoid caffeine consumption over 200 mg/day (2 mugs of instant coffee). A high caffeine intake is associated with small-for-gestational-age babies and miscarriage.

### Oily fish (omega 3 fatty acids)

This is controversial (the benefit of omega 3 fatty acids versus the risk of contamination by methyl mercury and polychlorinated biphenyls on the fetus).

Consume two portions of fish a week (one of them should be oily but no more than two portions of oily fish should be consumed).

Avoid eating shark, swordfish and marlin.

Limit the amount of tuna (no more than two steaks a week or four medium-sized cans a week).

**Appendix - II** **Weight management during pregnancy**

**What does it mean?**

Weight management means to:

- Evaluate and follow body weight.
- Prevent overweight (BMI 25–29.9 kg/m$^2$) or obesity (BMI ≥ 30 kg/m$^2$)
- Achieve and maintain a healthy weight before, during and after pregnancy.

**Elements of weight management**

**Behavior modification**

- **Inform** about the short, medium and longer-term consequences of behavior on maternal health.
- **Encourage** women about the benefits of healthy behaviors.
- **Consider** women's social contexts and relationships that may influence their behavior and plan for possible situations that may influence your plan. Consider the "if-then" coping strategy.
- **Help** easy changes in behavior over time.

**Diet control**

**I. Weight loss programs**

- Identify individual barriers to weight loss
- Identify individual needs, options and concerns
- Consider a balanced, healthy diet
- Consider regular physical activity
- Limit weight loss to no more than 0.5–1 kg a week

**II. Achievement of ideal weight**

**Diet modification**

- Starchy base meals (e.g. potatoes, bread). Consider wholegrain.
- Eat fiber-rich foods e.g. beans, fruit, and vegetables.
- Eat at least 5 portions of a variety of fruit and vegetables each day. Avoid increasing fat and/or calorie intake.
- Eat a low-fat diet and
- Minimize fried food; drinks and foods high in added sugars (e.g. pastries) and fat (e.g. fast foods)

**Exercise**

- Consider activities e.g. walking, cycling, swimming, aerobics everyday
- Change activity pattern e.g. taking the stairs instead of the lift, walking instead of motorcars.
- Minimize sedentary activities e.g. watching television, computers

# Vaccination in Pregnancy

## Types of vaccines

| | |
|---|---|
| **Live attenuated vaccines** | They should be avoided in pregnancy because of theoretical risk of activation due to maternal immunodeficient status |
| **killed vaccines** | Safe in pregnancy, less effective than live attenuated vaccines |
| **Purified macromolecules; subunits** | Examples include hepatitis B vaccines |
| **Inactivated toxins; toxoid vaccines** | Examples include tetanus and diphtheria toxoid vaccines |
| **Conjugated polysaccharide vaccines** | Examples include Haemophilus influenzae, Streptococcus pneumoniae, and Neisseria meningitis |

## Vaccines and pregnancy

| | |
|---|---|
| **Vaccines indicated in pregnancy** | • Influenza vaccine: it can be given at any trimester when it is due. It is ideally given before the influenza season (October to January)<br>• Pertussis, tetanus and diphtheria vaccine: (dTaP) it is given in second trimester to provide immunity to the baby up to 2 months of age<br>• Inactivated polio vaccine: it is given along with dTaP vaccine between 28 and 38 weeks of gestation (ideally 28 to 32 weeks)<br>• Covid-19 vaccines are generally safe |
| **Vaccines allowed in pregnancy if indicated (safe)** | • Hepatitis A<br>• Hepatitis B<br>• Pneumococcal vaccine<br>• Meningococcal vaccine<br>• Yellow fever vaccine<br>• Rabies vaccine<br>• Typhoid vaccine |
| **Vaccines contraindicated in pregnancy** | • Measles, mumps, rubella vaccine (MMR): if given, pregnancy should be avoided for 28 days after vaccination<br>• Varicella vaccine<br>• Vaccinia vaccine<br>• BCG vaccine(theoretical)<br>• HPV vaccine (if the series of shots was started and a woman becomes pregnant, the rest of the doses should be delayed to after pregnancy) |

## Vaccines and breastfeeding

- All inactivated, recombinant, subunit, or polysaccharide vaccines are safe in breastfeeding
- Yellow vaccine should be avoided with breastfeeding unless highly necessary

# Obesity with Pregnancy

## Risks

Risks of obesity during pregnancy include:

- Gestational diabetes
- Hypertensive disorders
- Venous thromboembolism
- Slower labour progress 4 – 10cm
- Emergency caesarean
- Postpartum haemorrhage
- Wound infection
- Birth defects
- Prematurity
- Macrosomia
- Shoulder dystocia
- Admission to neonatal care unit
- Stillbirth
- Neonatal death

## Management

**I. Pre-conception care**

**Primary care service**

- For all women during the childbearing period, advice on weight and lifestyle should be given during family planning consultations to encourage optimization of body weight.
- Women are followed-up regularly by weight, body mass index and waist circumference

**Women with BMI > 30?**

Discuss risks of obesity during pregnancy
Support weight loss before pregnancy

Advise 5mg folic acid daily, starting at least one month before conception

**II. Antenatal care**

**Booking visit**

Measure weight, height and BMI. Report data in handheld notes and electronic patient information system

**Women with BMI > 30?**

- Discuss obesity in pregnancy and how to minimize it.
- Assess thromboembolism risk and give thromboprophylaxis if indicated (repeat throughout pregnancy).
- Refer to consultant obstetrician to discuss delivery plan
- Use appropriate size cuff for BP measurement at booking visit and follow-up
- Continue folic acid till 12 weeks, give 10 mcg vitamin D during pregnancy and lactation, give 75mg aspirin if there is additional moderate risk of re-eclampsia (first pregnancy, age > 40 years, family history of pre-eclampsia, multiple pregnancy)

**Further management**

**BMI 30 - 35**

No additional care required at booking visit

**BMI > 35 - 40**

**No additional risk of pre-eclampsia**

Community monitoring every 3 weeks between 24-32 weeks and every 2 weeks till delivery

**Additional risk of pre-eclampsia**

Referral to specialist input to care

**BMI > 40**

Antenatal consultation & review by an obstetric anesthetist to identify potential difficulties with venous access, regional or general anaesthesia and future delivery plan

**Additional risk**

**No additional risk of pre-eclampsia**

**24-28 weeks**

Screen all women for gestational diabetes by 75g oral glucose tolerance test

**Third trimester**

Re-measure weight
Risk assessment for manual handling requirements*

*Manual handling requirements include consideration of appropriate loads of beds and theatre tables, lateral transfer equipment, and appropriately sized thromboembolic deterrent stockings.

## III. Intrapartum care

**BMI 30 - 35**

Individual risk assessment to decide the plan of birth

**BMI > 35**

Advise birth in consultant-led obstetric unit

**BMI > 40**

Inform duty anesthetist at delivery or intervention

**Delivery**

Normal birth is encouraged (induction of labour may be associated with failure and Cesarean section which is risky) → Alert staff if weight > 120 and needs operative intervention

**No obstetric contraindication to vaginal birth**

**Vaginal delivery**

**If the BMI > 40:**

- Offer continuous midwifery care.
- Establish early venous access and consider early epidural analgesia
- Inform senior obstetrician and anesthetist (at least ST6). They should attend in case of operative delivery

**If there is any obstetric indication**

**Cesarean section**

- A single dose of prophylactic antibiotics is given at Caesarean section.
- A subcutaneous fat > 2 cm needs to be suture-closed.
- Inform senior obstetrician and anesthetist (at least ST6). They should attend Caesarean section

## IV. Postpartum care

**BMI 30 - 35**

**BMI > 35**

- Encourage mobilization as early as possible.
- Encourage and support breastfeeding. Give information about benefits, initiation and maintenance of breastfeeding (less adherence to breastfeeding is recognized in obese mothers).
- Refer for future diet and lifestyle advice

**If gestational diabetes was diagnosed**

Test of glucose tolerance 6 weeks after delivery

Offer lifestyle and weight management advice

Annual screening for type 2 diabetes and cardio-metabolic risk factors (Refer to GP)

**BMI > 40**

Beside other measures, give thromboprophylaxis for 10 days regardless of mode of delivery

**Thrombo-prophylaxis**

If ≥ 1 additional risk factors for thromboembolism, give postnatal thrombo-prophylaxis for 7 days

If ≥ 2 additional risk factors for thromboembolism, Provide compression stockings

# Obstetric Analgesia

## Types of pain medications

| | |
|---|---|
| **Paracetamol** | • Oral formulation works within 40 min<br>• IV formulation works within 5 min |
| **Non-steroidal anti-inflammatory drugs (NSAIDs)** | • They are COX inhibitors.<br>• They prevent synthesis of prostaglandins (which promote inflammation, pain, and fever) |
| **Codeine** | • It is a prodrug that is converted to morphine (through cytochrome P450 pathway)<br>• Ultrarapid metabolizers (5% of Caucasians) have 50% higher serum plasma level. Therefore, they are more liable to toxicity |
| **Dihydrocodeine** | • Unlike Codeine, it is not a prodrug. Therefore, it is not influenced by liver metabolism<br>• Only a small amount is converted to dihydromorphine |
| **Tramadol** | • It is a prodrug that is suitable for mild to moderate pain<br>• It has fewer side effects compared to opioids (respiratory depression, constipation)<br>• It may be associated with psychiatric side effects. More than 10% of patients stop the medication due to these side effects |
| **Morphine** | • It is a potent opioid that is used for moderate to severe pain<br>• Peak plasma level is reached in:<br>▪ 15-20 min with parenteral administration (intramuscular)<br>▪ 30-90 min with oral administration<br>• Compared to parenteral route, oral route is half potent due to first pass metabolism) |

| Antenatal analgesia | Postnatal analgesia |
|---|---|
| • **Non-pharmacologic options (1st line):**<br>▪ Rest<br>▪ Hot and cold compresses<br>▪ Massage, acupuncture<br>▪ Physical therapy and exercise | |
| • **Paracetamol:**<br>▪ First choice<br>▪ Suitable for mild to moderate pain<br>▪ Safe in pregnancy in all trimesters | • **Paracetamol:**<br>▪ Safe in breastfeeding<br>▪ A small amount passes in breast milk, which is within neonatal therapeutic range |
| • **NSAIDs:**<br>▪ Data on increased risk of miscarriage in is conflicting<br>▪ It is generally better avoided in pregnancy. If its use is necessary, the lowest possible dose should be used for the shortest duration<br>▪ It is contraindicated after 30 weeks of gestation because of foetal risk of:<br>① Premature closure of ductus arteriosus<br>② Pulmonary hypertension<br>③ Oligohydramnios | • **NSAIDs:**<br>▪ Ibuprofen is preferred (long-term use of diclofenac is associated with increased cardiovascular risks)<br>▪ Safe in breastfeeding (very small amount passes in breast milk)<br>▪ Contraindications:<br>① Hypersensitive patients<br>② Significant haemorrhage, risk of bleeding, hypovolemia<br>③ Impaired renal function<br>④ Pre-eclampsia<br>⑤ Severe asthma, or asthma known to be exacerbated by NSAIDs "10%"<br>⑥ History of gastric ulceration |
| • **Opioids:**<br>▪ Can be used in pregnancy and breastfeeding for short-term as a second line (if paracetamol is not effective)<br>▪ If used in the 1st trimester, they may increase risk of neural tube defects (limited evidence)<br>▪ There is no increased risk of foetal toxicity. However, there is risk of: | • **Opioids:**<br>① Codeine:<br>▪ It should be avoided in breastfeeding (ultra-rapid metabolizers will have increased serum levels with subsequent risk of neonatal toxicity). Tramadol or dihydrocodeine should be used instead |

| | |
|---|---|
| ◻ Neonatal respiratory depression, if given around time of delivery<br>◻ Neonatal withdrawal if given for a long term in pregnancy | ▪ If used, the lowest effective dose should be used for the shortest duration. Breastfeeding should be stopped, and medical advice requested if side effects develop<br>▪ If regular use extends beyond 3 days, medical supervision is necessary<br>② Morphine:<br>▪ 10-20mg may be given every 2 hours for moderate to severe pain.<br>▪ Double route should be avoided. Therefore, Post-caesarean morphine intrathecal injection should be reviewed before administering morphine for pain control<br>③ Tramadol:<br>It is another option that should be used with caution (a prodrug) |
| • **Gabapentin:**<br>▪ It does not increase risk of miscarriage<br>▪ It is not associated with increased risk of birth defects (However, folic acid should be given preconceptionally and in the 1st trimester)<br>▪ If it is given around time of delivery, observe for signs of neonatal withdrawal (and notify paediatric team) | |

| Post-discharge pain control (after delivery) |
|---|
| Paracetamol and ibuprofen ± dihydrocodeine (if the patient still needs morphine for pain control immediately before discharge), maximum 4 doses per day (tramadol is an alternative if dihydrocodeine is not tolerable) |

# External Cephalic Version

## Timing

- External cephalic version (ECV) should be offered at:
  - 37 weeks of gestation in multipara
  - 36 weeks of gestation in nullipara (reversion is less common)
- Intrapartum ECV may be considered if there are no contraindications and membranes are still intact. Informed consent should be obtained

## The procedure

- Electronic foetal monitoring, ultrasound and facilities of emergency caesarean delivery should be available
- Regional analgesia should not be offered as a routine and should be limited to cases where women cannot tolerate the procedure due to pain
- Although facilities for emergency caesarean delivery should be available, preoperative preparation is not indicated, and maternal fasting is not required
- During the procedure, abdominal ultrasound should be performed intermittently to assess foetal heart rate, and should be repeated at the end of the procedure
- Transient foetal bradycardia (for up to 3 minutes) is common. In these cases, management includes:
  - Placing the patient in a left lateral position
  - Electronic foetal monitoring

  If resolution does not occur in 6 minutes, category I caesarean delivery should be performed
- Electronic foetal monitoring is recommended after completion of the procedure regardless of outcome

- The procedure should stop after 4 attempts with a maximum of 10 minutes
- Rh negative women should be offered anti-D and be tested for fetomaternal haemorrhage

## Outcomes

- ECV is associated with 50% success rate (60% in multipara vs. 40% in nullipara) compared to 8% chance of spontaneous version if no intervention is done
- Tocolysis increases the chance of procedure success e.g.
  - Terbutaline 250 mcg subcutaneously
  - Salbutamol 250 mcg in 25ml of normal saline by slow intravenous infusion

Betamimetics are contraindicated in women with considerable cardiac disease and hypertension. If women are using beta-blockers, they will reduce effectiveness of beta-mimetics

- If the procedure is unsuccessful at 36 weeks, the chance of spontaneous version is low (3-7%)
- If the procedure is successful at 36 weeks, the chance of reversion to breech is low (3%)
- Compared to spontaneous version, successful ECV is associated with:
  ① Higher risk of instrumental delivery
  ② Higher risk of caesarean delivery

### Predictors of ECV success

- Multiparity
- Non-engagement of the breech
- Palpable foetal head
- Use of tocolysis
- Maternal weight < 65 kgs
- Posterior placenta

## Complications

Complications of ECV are generally very rare:

- Emergency caesarean section (0.5%). The most common causes are vaginal bleeding and abnormal cardiotocography
- Placental abruption and fetomaternal haemorrhage (very rare)
- High pain scores (5%)

## Contraindications

- Multiple pregnancy
- Placental abruption
- Vaginal bleeding (ongoing or recent, within the last week)
- Severe preeclampsia
- Rupture of membranes
- Abnormal cardiotocography
- Rh isoimmunization
- Obstetric contraindications to vaginal delivery

ECV in a woman with previous 1 caesarean delivery is not associated with higher risk compared to baseline

# Anti-D Administration in Pregnancy

## Administration of anti-D

- **Routine administration:**

  Rh negative women who are not sensitized should receive anti-D routinely during pregnancy, regardless of anti-D given for any specific event:

  - **During pregnancy:**
    - A single dose at 28 weeks of gestation (screen for maternal antibodies before administration) OR
    - Two doses at 28 and 34 weeks of gestation
  - **After delivery:**
    - Neonatal cord blood should be tested for ABO and Rh type
    - If neonatal Rh is positive, 500 IU of anti-D is given, and feto-maternal bleed is tested to determine if further doses are required

- **Event-specific administration:**

  Anti-D is given after any potential feto-maternal bleed. It should be given optimally within 72 hours of these events. However, it still provides some benefit up to 10 days of administration

| | |
|---|---|
| **Pregnancy < 12 weeks** | Anti-D 250 IU is given without testing for fetomaternal haemorrhage (FMH) |
| **12 – 20 weeks** | Anti-D 250 IU is given without FMH testing |
| **Pregnancy > 20 weeks** | Anti-D 500 IU is given. Further dosage is determined by testing for FMH |

| Special circumstances | |
|---|---|
| **Continuous bleeding** | • 500 IU is given every 6 weeks if bleeding is ongoing<br>• If there are further intermittent bleeding episodes, FMH should be tested every 2 weeks<br>• If there are any new episodes of bleeding or pain, treat as a new sensitizing event<br>• An alternative is to test foetal blood type using non-invasive foetal blood typing. Incidence of false negative results is 0.1% |
| **Intrauterine foetal death** | If it is diagnosed, anti-D should be given within 72 hours of diagnosis regardless of delivery time |
| **Intraoperative cell salvage** | 1500 IU are given, followed by FMH testing after 30-45 minutes |
| **Platelet transfusion** | Rh negative women should receive Rh negative platelets. If not possible, 250 IU of anti-D are given (cover 5 platelet units)<br>Avoid intramuscular injections if platelet count is < 30,000 |
| **Blood transfusion** | If Rh positive blood is transfused to Rh negative women:<br>• If less than 15 mL, give intramuscular anti-D as appropriate<br>• If more than 15 mL, give 1500-2500 IU intravenously and perform FMH testing 48 hours after intravenous injection, 72 hours after intramuscular injection and give further anti-D accordingly<br>• If more than 1 litre is given, red cell exchange transfusion is indicated:<br>▪ Single blood volume exchange transfusion causes 65-70% reduction in red blood cell load<br>▪ Double blood volume exchange transfusion causes 85-90% reduction in red blood cell load<br>This should be followed by flow cytometry to test for FMH |

## Role of FMH testing

If FMH is tested, IV anti-D is given and FMH testing should be repeated after 72 hours (if intramuscular anti-D is given) or 48 hours (if intravenous anti-D is given) to confirm clearance of Rh-positive red blood cells

## Abstract

Antenatal care is the essence of obstetric practice. Despite being practiced by almost all obstetricians, antenatal care practice is always critical since risk factors may evolve at any stage of pregnancy and failure to recognize these risks may result in unfortunate sequences. In this chapter, we will discuss current recommendations on antenatal care of uncomplicated pregnancy.

## Keywords

Antenatal care, vaccination, anti-D, obesity, external cephalic version

## Further readings

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# Preterm Labour

## Definitions of preterm labour

| Suspected preterm labour | Diagnosed preterm labour | Established preterm labour |
|---|---|---|
| Symptoms of preterm labour **PLUS** clinical assessment (including a speculum or digital vaginal examination) that confirms the possibility of preterm labour but rules out established labour | Suspected preterm labour PLUS a positive diagnostic test | If she has progressive cervical dilatation (4 cm or more) with regular contractions |

## Prevention of preterm labour

**Women at increased risk of preterm labour**

Patient and family may be anxious

Give information (oral and written)

Care discussed and offered

Describe symptoms and signs of preterm labour

Information includes

- Likelihood of neonatal survival
- Short/long term outcomes of the baby
- Neonatal care including location of care
- Immediate problems to the baby that are associated with preterm labour
- Wishes about resuscitation

Offer the opportunity to tour the neonatal unit, opportunity to speak to a neonatologist or paediatrician




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_2

**Offer prophylactic vaginal progesterone or prophylactic cervical cerclage to women with**

- History of spontaneous preterm labour (up to 34 weeks) or mid-trimester loss (after 16 weeks)
- Transvaginal ultrasound (TVUS) between 16-24 weeks of pregnancy that show a cervical length of 25 mm or less

**Consider prophylactic vaginal progesterone if**

1. History of spontaneous preterm labour (up to 34 weeks) or midtrimester loss (from 16 weeks) OR
2. TVUS between 16-24 weeks of pregnancy that show a cervical length of 25 mm or less

Start vaginal progesterone between 16-24 weeks until at least 34 weeks

**Consider prophylactic cervical cerclage**

1. TVUS between 16-24 weeks, CL ≤ 25 mm AND
2. Preterm prelabour rupture of membranes (PPROM) in previous pregnancy OR history of cervical trauma

**'Rescue' cervical cerclage**

| Contraindications | Indication | Explain to women |
|---|---|---|
| • Signs of infection or<br>• Active vaginal bleeding or<br>• Uterine contractions | For women between 16 - $27^{+6}$ weeks with dilated cervix and exposed unruptured membranes | • Risks of the procedure<br>• Goal of delaying birth (increase likelihood of the baby surviving and of reducing serious neonatal morbidity) |

- Take into account gestational age (benefits are greater at earlier gestations) and extent of dilatation
- Consultant obstetrician and consultant paediatrician should be involved

## Diagnosis of PPROM

In woman with symptoms suggestive of PPROM

Offer speculum exam to look for pooling

If positive → No further testing

If negative → Perform ILGF-binding protein-1 test or placental alpha-microglobulin-1 test of vaginal fluid

| If positive | If negative with no pooling |
|---|---|
| Do not use test results alone. Consider the following before making decision regarding management:<br>1. Clinical condition<br>2. Medical and pregnancy history<br>3. Gestational age. Then either:<br>• Offer PPROM care or<br>• Reassess diagnosis at a later time point | No prophylactic antibiotics. PPROM is unlikely. She should return if symptoms occur<br>★<br>• Do not use nitrazine to diagnose PPROM.<br>• No tests are required if labour is established and women has symptoms of PPROM |

**Antenatal prophylactic antibiotics for women with PPROM**

| Oral Erythromycin | Oral Penicillin | Co-amoxiclav ⃠ |
|---|---|---|
| 250 mg 4 times a day for 10 days or until labour is established | If erythromycin is not tolerable | Do not offer |

**Detection of infection in women with PPROM**

| Combination of clinical assessment and tests as: | Do not use any one of the following in isolation: ⃠ | If results of clinical assessment or any of the tests are not consistent with each other |
|---|---|---|
| CRP, WBC count and cardiotocography (CTG) | Isolated results of CRP or WBC, CTG | Continue to observe the woman and consider repeating the tests |

## Diagnosis of Preterm labour

### Diagnosing preterm labour with intact membranes

**Explain to symptomatic women:**

1. Clinical assessment and diagnostic tests and how we perform them
2. Benefits, risks and possible consequences of assessment and tests (sequences of false results) taking into account gestational age

**Offer clinical assessment to symptomatic women:**

1- Clinical history taking and initial assessment

2- Speculum examination (digital examination if extent of cervical dilatation cannot be assessed)

If clinical assessment indicates suspected preterm labour ≤ $29^{+6}$ weeks

Advise treatment for preterm labour

If clinical assessment indicates suspected preterm labour ≥ 30 weeks

Consider TVUS of cervical length (CL) to determine risk of birth within 48 hours

If CL > 15 mm

Explain that:

- Labour is unlikely and alternative diagnoses should be assessed
- Discuss benefits and risks of going home compared with close monitoring/treatment in hospital

If CL ≤ 15 mm

Diagnosed preterm labour - offer treatment

If she is ≥ 30 weeks and TVUS is declined or not available

Consider fetal fibronectin (FFN) to determine risk of birth within 48 hours

If FFN is negative (≤ 50 ng/ml)

Explain that:

- Labour is unlikely and alternative diagnoses should be ruled out
- Discuss benefits and risks of going home compared with close monitoring/treatment in hospital

Advise her that if she does decide to go home, she should return if symptoms suggestive of preterm labour persist or recur

If FFN is positive (> 50 ng/ml)

This is "diagnosed preterm labour". Treatment should be offered

If suspected preterm labour, ≥ 30 weeks with no available TVUS or FFN

Offer treatment consistent with diagnosed preterm labour

⃠ *Do not use both TVUS and FFN in combination to diagnose preterm* labour

## Treatment of preterm labour

### ❶ Tocolysis

Decision depends on:

1. Suspected or diagnosed preterm labour
2. Other clinical features as bleeding or infection (contraindications to tocolysis)
3. Gestational age at presentation - benefits of maternal corticosteroids
4. Need to transfer (unavailable NICU)
5. Preference of the woman

**Consider nifedipine for tocolysis**

- Between 24-25$^{+6}$ weeks +
- Intact membranes +
- Suspected preterm labour

**Offer nifedipine for tocolysis**

- Between 26-33$^{+6}$ weeks +
- Intact membranes +
- Suspected or diagnosed PTL

**If nifedipine is contraindicated**

- Offer oxytocin receptor antagonists

- Do not offer betamimetics for tocolysis ⃠

NICU = Neonatal intensive care unit

### ❷ Maternal corticosteroids

Discuss the use of maternal corticosteroids (individual circumstances) for women:

1. Between 23 and 23$^{+6}$ weeks +
2. Suspected or established preterm labour or planned preterm labour or PPROM

**Offer steroids between 24 - 33$^{+6}$ weeks**

If suspected, diagnosed or established preterm labour or planned preterm labour or PPROM

**Consider steroids between 34 - 35$^{+6}$**

- If suspected, diagnosed or established preterm labour or planned preterm labour or PPROM

- When offering or considering steroids, discuss: how steroids may help, potential risks

- Do not routinely offer repeat courses
- Decision to give a second course depends on:
  1. Interval since the end of last course
  2. Gestational age
  3. Likelihood of birth within 48 hours

**❸ Magnesium sulfate [for neuroprotection]**

| Between 23-23$^{+6}$ weeks | Between 24-29$^{+6}$ weeks | Between 30-33$^{+6}$ weeks |
|---|---|---|
| AND | AND | AND |
| Established or planned preterm labour within 24 hours | Established preterm labour or planned preterm labour within 24 hours | Established preterm labour or planned preterm labour within 24 hours |
| Discuss with the woman (IV magnesium sulphate) for neuroprotection | Offer IV magnesium sulphate for neuroprotection | Consider IV magnesium sulphate for neuroprotection |

Regimen consists of 4 g of IV bolus over 15 min, followed by IV infusion of 1 g/hour until birth or for 24 hours (whatever is sooner)

Monitor for clinical signs of magnesium sulphate toxicity every 4 hours:

- Pulse
- Blood pressure
- Respiratory rate
- Deep tendon (patellar) reflexes

Monitor urine output. Since magnesium sulphate is excreted in urine, low urine output may be associated with magnesium sulphate toxicity

★

*If a woman has or develops oliguria or other signs of renal failure: monitor more frequently and reduce the dose of magnesium sulphate*

## Foetal monitoring

### ❶ Cardiotocography and intermittent auscultation

- It should be discussed with women in suspected, diagnosed or established preterm labour:
  1. Purpose of foetal monitoring
  2. Impact on clinical decision at different gestational ages. Foetuses at the threshold of viability may not be monitored if this will not lead to intervention
- Senior obstetricians are involved in discussions about whether and how to monitor foetal heart rate between 23-25$^{+6}$ weeks
- Explain to women that:
  1. There is limited evidence on usefulness of specific features to suggest hypoxia or acidosis in preterm babies. Available evidence is based on babies at term
  2. Normal cardiotocography is reassuring that the baby is coping well with labour
  3. Abnormal findings do not necessarily indicate foetal hypoxia or acidosis
  4. There is no evidence that using cardiotocography improves preterm labour outcomes compared to intermittent auscultation
- If there is established preterm labour with no other risk factors, offer a choice of foetal monitoring using either cardiotocography or intermittent auscultation

### ❷ Foetal scalp electrode

- Foetal scalp electrode if < 34 weeks unless:
  1. It is not possible to monitor foetal heart rate using cardiotocography or intermittent auscultation
  2. Benefits outweigh risks
  3. Alternatives (immediate birth, intermittent ultrasound, no monitoring) are unacceptable

  The decision should be discussed with senior obstetrician
- The use of foetal scalp electrode between 34-36$^{+6}$ weeks should be discussed with the patient if it is not possible to monitor externally and benefits outweigh risks
- If a blood sample cannot be obtained, caesarean section should be considered

## Mode of birth

- Highlight difficulties associated with performing caesarean section for preterm labour, especially increasing likelihood of vertical uterine incision and the implications of this for future pregnancies
- Explain that in preterm labour, there are no known benefits or harms for the baby from caesarean section
- Consider caesarean section if suspected, diagnosed, established preterm labour between 26-$36^{+6}$ weeks with breech presentation

## Timing of cord clamping

- If a preterm baby needs to be moved immediately for resuscitation, or there is significant maternal bleeding, delayed cord clamping is not appropriate. Therefore, cord milking and immediate clamping should be performed
- If there is no indication of immediate cord clamping and the mother and baby are stable, delayed cord clamping at least 30 seconds, no longer than 3 minutes, should be considered
- The baby should be positioned at or below the level of the placenta before the cord is clamped

# Management of Normal Labour

## Birth setting

| Birth setting | | |
|---|---|---|
| **Home and midwifery unit** | **Alongside midwifery unit** | **Obstetric unit** |
| Home and freestanding midwifery unit are suitable for low risk multipara | Alongside midwifery unit is suitable for low risk primiparous women | Obstetric unit is assigned to higher risk women |

- There are no differences in neonatal outcomes with planning birth at any birth setting
- Birth in an obstetric unit is associated with a higher rate of interventions, such as instrumental vaginal birth, caesarean section, compared to other settings

- **Most common reasons of transfer to obstetric unit:** (in order)
  - Pain control (regional analgesia)
  - Episiotomy
  - Caesarean birth
  - Instrumental birth
  - Blood transfusion

- **Indications of felivery in Obstetric unit:** (Registrar or consultant led)
  - **Cardiovascular disease:** e.g. cardiac disease, hypertensive disorders, history of thromboembolic disorders
  - **Respiratory disorders:** e.g. asthma requiring an increase in treatment or hospital treatment

- **Haematologic disorders:** e.g. haemoglobinopathies, bleeding disorders, platelet disorders (platelet count below $100 \times 10^9$/litre), Von Willebrand's disease, atypical antibodies (risk of haemolytic disease of the newborn)
- **Endocrine disorders:** e.g. hyperthyroidism, diabetes
- **Infections:** e.g. group B streptococci (GBS), hepatitis B/C with abnormal liver function, HIV, active TORCH infection, tuberculosis under treatment
- **Immune disorders:** e.g. systemic lupus erythematosus, scleroderma
- **Renal disorders:** e.g. abnormal renal function, renal disease
- **Neurologic disorders:** e.g. epilepsy, myasthenia gravis, previous cerebrovascular accident
- **Psychiatric disorder** requiring current inpatient care
- **Obstetric history:** e.g. previous stillbirth or neonatal death, neonatal encephalopathy, preeclampsia requiring preterm birth, placental abruption, eclampsia, uterine rupture, primary postpartum haemorrhage with blood transfusion, shoulder dystocia
- **Current Pregnancy complications:** e.g. multiple birth, preterm labour, preterm prelabour rupture of membranes (PPROM), placental abruption, haemoglobin < 85 g/litre, intrauterine foetal death, induction of labour, substance misuse, malpresentation, body mass index at booking > 35 kg/m$^2$, recurrent antepartum haemorrhage, foetal growth restriction, oligo-/polyhydramnios

## First stage of labour

- **Phases of the first stage of labour:**

| | |
|---|---|
| **Latent first stage** | This is a period, not necessarily continuous, when:<br>• There are painful contractions and<br>• There is some cervical change, including cervical effacement and dilatation up to 4 cm |
| **Established first stage** | • There are regular painful contractions and<br>• There is progressive cervical dilatation starting at 4 cm |

- **Routine management of the first stage:**
  - **Pain control:**
    - Breathing exercises, immersion in water and massage may reduce pain and may be considered during latent phase

- Epidural analgesia is performed in an obstetric Unit, if requested by the patient (even in latent phase)
  - Once diagnosis of full dilatation in a woman with regional analgesia is made, discuss plan of care with the woman which ensures that birth is achieved within 4 hours regardless of parity
  - Do not routinely use oxytocin in women with epidural analgesia unless indicated

- **Auscultation of foetal heart rate:**
  - Auscultation should continue for a minimum of 1 minute immediately after a contraction
  - Intermittent auscultation is suitable for low risk women. Continuous cardiotocography (CTG) is indicated in high risk women (listed above)
  - if intermittent auscultation is suspicious, CTG should be offered for 20 minutes. If CTG is normal, return to intermittent auscultation
  - If foetal death is suspected despite the presence of an apparently recorded foetal heart rate, offer ultrasound assessment to check cardiac activity

**Meconium stained amniotic fluid**

- If there is significant meconium: No foetal blood sampling (FBS) could be done in labour. Significant meconium indicated continuous CTG and transfer to obstetric unit
- If there is insignificant meconium, midwifery unit management and intermittent auscultation is suitable

- **Management of abnormal first stage:**
  - If delayed first stage of labour is a concern:
    - Transfer women to obstetric-led care
    - Vaginal examination 2 hours later. If progress is less than 1 cm, delayed first stage is diagnosed
    - Amniotomy if membranes are intact. Examination should be performed 2 hours later
    - Consider oxytocin

- If oxytocin is used:
  - Start at a low rate (2 mIU/min).Increment infusion rate every 30 minutes till 4–5 contractions in 10 minutes are achieved
  - vaginal examination 4 hours after starting oxytocin in established labour
    - If cervical dilatation has increased by less than 2 cm after 4 hours of oxytocin, further obstetric review is required to determine caesarean section decision
    - If cervical dilatation has increased by 2 cm or more, advise 4-hourly vaginal examinations

- **Prelabour rupture of membranes at term:**
  - **Risks:**

    the risk of serious neonatal infection is 1% (compared to 0.5% in women with intact membranes)
  - **Diagnosis:**
    - There is no need for speculum examination if there is definite clinical evidence that the membranes have ruptured. Otherwise, speculum examination should be considered
    - Avoid digital vaginal examination in the absence of contractions (risk of infection)
  - **Management:**
    - 60% of women with prelabour rupture of the membranes will go into labour within 24 hours
    - Induction of labour is appropriate approximately 24 hours after rupture of the membranes.
    - Until the induction is started or if expectant management beyond 24 hours is chosen by the woman:
      - Do not offer lower vaginal swabs or assessment of C-reactive protein
      - To detect any infection that may be developing, advise the woman to track her temperature every 4 hours during waking hours and to report any change in the colour or smell of her vaginal loss immediately
      - Inform the woman that bathing or showering is not associated with an increase in infection, but that sexual intercourse may increase risk and is better avoided

    - First labours last 8 hours on average and are unlikely to last over 18 hours
    - Second and subsequent labours last 5 hours on average and are unlikely to last over 12 hours
  - Offer a vaginal examination 4-hourly or if there is concern about progress or in response to the woman's wishes (after abdominal palpation and assessment of vaginal loss)

## Second stage of labour

- **Phases of the second stage of labour:**

| | |
|---|---|
| **Passive second stage** | It starts with full dilatation of the cervix before or in the absence of involuntary expulsive contractions |
| **Established first stage** | Onset of the active second stage of labour is considered when:<br>▪ The baby is visible<br>▪ Expulsive contractions with full dilatation of the cervix or other signs of full dilatation of the cervix<br>▪ Active maternal effort after full dilatation of the cervix in the absence of expulsive contractions |

- **Duration of the second stage of labour:**

| | **Normal duration** | **Diagnosis of delay** | **Management of delay** |
|---|---|---|---|
| **Nulliparous women** | Birth would be expected to take place within 3 hours of the start of the active second stage in most women | Diagnosis of delay of the active second stage is made when it has lasted 2 hours | Refer the woman to a healthcare professional trained to perform operative vaginal delivery if birth is not imminent |
| **Multiparous women** | Birth would be expected within 2 hours of the start of the active second stage of labour in most women | Diagnosis of delay of the active second stage is made when it lasts for 1 hour | |

- **Routine management of the second stage of labour:**
  - **Vaginal examination:**
    - If full dilatation of the cervix is confirmed in a woman without regional analgesia, but she does not feel the urge to push, perform next assessment after 1 hour
    - Offer vaginal examination hourly in the active second stage, or earlier if maternally requested

- **Auscultation of foetal heart rate:**
  Perform intermittent auscultation immediately after a contraction for at least 1 minute, and every 5 minutes
- **Perineal management:**
  Perineal massage in the second stage of labour is not recommended
  Lidocaine spray for pain control in the second stage of labour is not recommended
  Routine episiotomy during spontaneous vaginal birth or after previous third- or fourth-degree perineal tear is not recommended

**Episiotomy**

- Perform episiotomy only if there is a clinical indication e.g. instrumental birth or suspected foetal compromise
- If episiotomy is performed, the recommended technique is a mediolateral episiotomy
- The angle to the vertical axis should be between 45 and 60 degrees at the time of the episiotomy

- **Management of abnormal second stage:**
  - If there is delay in the second stage of labour, or if the woman is significantly distressed, support, encouragement and pain management are crucial in management
  - Offer amniotomy if the membranes are intact
  - Women should be transferred to obstetric-led care
  - An obstetrician should assess a woman with delay in the second stage before decision of oxytocin administration is considered. After initial obstetric assessment, maintain ongoing obstetric review every 15–30 minutes afterwards
  - Consider operative vaginal delivery

## Third stage of labour

| | Active management the third Stage | Physiological management of the third stage |
|---|---|---|
| **Method** | • Routine use of uterotonic drugs<br>• Deferred clamping and cutting of the cord<br>• Controlled cord traction after separation of the placenta | • No routine use of uterotonic drugs<br>• No clamping of the cord until cord pulsation stops<br>• Delivery of the placenta by maternal effort |
| **Nausea and vomiting** | 100 in 1000 women | 50 in 1,000 women |
| **Bleeding > 1 litre** | 13 in 1,000 women | 29 in 1,000 women |
| **Blood transfusion** | 14 in 1,000 women | 40 in 1,000 women |

Active management shortens the third stage compared with physiological management

**Diagnosis of prolonged third stage**

if the third stage is not completed within 30 minutes of the birth with active management or within 60 minutes of the birth with physiological management

### Intrapartum transfer the woman to obstetric-led care

Intrapartum transfer the woman to obstetric-led care is indicated if any of the following are observed:

- Maternal pulse > 120 beats/minute on 2 occasions 30 minutes apart
- A single reading of either raised diastolic blood pressure of 110 mmHg or more or raised systolic blood pressure of 160 mmHg or more OR raised diastolic blood pressure of 90 mmHg or more or raised systolic blood pressure of 140 mmHg or more on 2 consecutive readings taken 30 minutes apart
- 2+ proteinuria on urinalysis and a single reading of either raised diastolic blood pressure (90 mmHg or more) or raised systolic blood pressure (140 mmHg or more)

- Temperature of 38°C or above on a single reading, or 37.5°C or above on 2 consecutive readings 1 hour apart
- Any vaginal blood loss (other than a show)
- PPROM more than 24 hours before the onset of established labour
- Significant meconium
- Pain that differs from the pain associated with contractions
- Any abnormal presentation
- high (4/5–5/5 palpable) or free-floating head in a nulliparous woman
- Suspected foetal growth restriction or macrosomia
- Suspected anhydramnios or polyhydramnios
- Foetal heart rate < 110 or > 160 beats/minute
- A deceleration in foetal heart rate on intermittent auscultation
- Reduced foetal movements in the last 24 hours reported by the woman.
- Confirmed delay in the first or second stage of labour
- Request by the woman for regional analgesia
- Obstetric emergency e.g. antepartum haemorrhage, cord prolapse, postpartum haemorrhage, or need for advanced neonatal resuscitation
- Retained placenta
- Third-degree or fourth-degree tear or other complicated perineal trauma

If none of these are observed, continue with midwifery-led care unless the woman requests transfer

## Intrapartum CTG

- **Principles of CTG interpretation:**
  - Assessment of CTG trace should include contractions and foetal heart rate features (baseline; variability; decelerations ± concerning features, accelerations)
  - The presence of foetal heart rate accelerations, even in the presence of reduced baseline variability, is a reassuring sign that indicated the baby is healthy

| Features | Normal | Non Reassuring | Abnormal |
|---|---|---|---|
| **Baseline** | 110 – 160 | 100 - 109† OR 161 - 180 | < 100 OR >180 |
| **Variability** | 5 -25 | < 5 for 30 - 50 minutes > 25 for 15 -25 minutes | < 5 for more than 50 minutes OR > 25 for more than 25 minutes OR Sinusoidal |
| **Decelerations** | • None or early<br>• Variable decelerations with no concerning characteristics* for < 90 minutes | • Variable decelerations with no concerning characteristics* for 90 minutes or more<br>• Variable decelerations with any **concerning characteristics** in up to 50% of contractions for 30 minutes or more<br>• Variable decelerations with any **concerning characteristics** in > 50% of contractions for < 30 minutes<br>• Late decelerations in > 50% of contractions < 30 minutes (without risks e.g. thick meconium) | • Variable decelerations and **concerning characteristics** with > 50% of contractions for 30 minutes<br>• Late decelerations for 30 minutes<br>• Acute bradycardia, or a single prolonged deceleration lasting 3 minutes or more |
| **Management** | Continue Care | • Correct cause e.g.: hypotension or uterine hyperstimulation<br>• full set of maternal observations<br>• conservative measures* | • Exclude acute events clinically (e.g., cord prolapse, suspected placental abruption or suspected uterine rupture)<br>• Correct any underlying causes, such as hypotension or uterine hyperstimulation<br>• Start 1 or more conservative measures.<br>• If CTG is still pathological after implementing conservative measures:<br>▪ offer digital foetal scalp stimulation<br>▪ If CTG after foetal scalp stimulation:<br>▪ consider foetal blood sampling<br>▪ consider expediting the birth |

**Concerning features**

- lasting more than 60 seconds
- reduced baseline variability within the deceleration
- failure to return to baseline
- biphasic (W) shape
- No shouldering

- **CTG Categories:**
  - **Normal CTG:** all features are reassuring
  - **suspicious CTG**:
    1 non-reassuring feature and 2 reassuring features (but if accelerations are present, foetal acidosis is unlikely)
  - **pathological CTG:**
    1 abnormal feature or 2 non-reassuring features

- **Need for urgent intervention:**
  - **Indications:**
    - Acute bradycardia
    - Single prolonged deceleration for 3 minutes or more
  - **Interventions:**
    - Urgently seek obstetric help
    - If there is an acute event (e.g., cord prolapse, suspected placental abruption or suspected uterine rupture), expedite delivery
    - Correct any underlying causes, such as hypotension or uterine hyperstimulation
    - Start 1 or more conservative measures as listed
    - Prepare for an urgent birth (Category 1 CS) if clinically indicated
    - Expedite delivery if the acute bradycardia persists for 9 minutes (Remember the rule of 3 = 3 min help, 3 Min transfer to theatre, 3 min delivery)

**Conservative management**

- Mobilisation
- Lateral position to avoid being supine (release aortocaval compression)
- IV fluids if hypotensive.
- stopping oxytocin if it is being used
- tocolytic drug (subcutaneous terbutaline 0.25 mg) if contracting > 4-5 / 10 (hyperstimulation)

- If the foetal heart rate recovers any time within the 9 minutes, reassess and review decision to expedite the birth with the patient
- If the non-reassurign feature is a baseline fatal heart rate between 100 and 109 beats/ minute while there is normal baseline variability and no variable or late decelerations, continue usual care

- **Foetal scalp stimulation:**
  - if CTG is pathological, offer digital foetal scalp stimulation
  - If scalp stimulation results in an acceleration, foetal blood sampling is only indicated if the cardiotocograph trace is still pathological
  - If digital foetal scalp stimulation (during vaginal examination) yields an acceleration, interpret this findings as a sign of a healthy foetus
  - Take this into account when reviewing the whole clinical picture

- **Foetal blood sampling:**
  - **Contraindications:**
    - There is an acute event (cord prolapse, suspected placental abruption or suspected uterine rupture)
    - Risk of maternal-to-foetal transmission of infection or
    - Risk of foetal bleeding disorders.
    - During or immediately after a prolonged deceleration.

    Be aware that for women with sepsis or significant meconium, foetal blood sample results may be falsely reassuring

  - **Results interpretation**

| | Normal | Borderline | Abnormal |
|---|---|---|---|
| **PH** | 7.25 or above | borderline: 7.21 to 7.24 | abnormal: 7.20 or below |
| **Lactate** | 4.1 mmol/l or below | 4.2 to 4.8 mmol/l | 4.9 mmol/l or above |
| **Management** | If no accelerations in response to foetal scalp stimulation | If no accelerations in response to foetal scalp stimulation | expedite the birth |

| | | | |
|---|---|---|---|
| | 2nd foetal blood sample no more than 60 minutes later | 2nd foetal blood sample no more than 30 minutes later if pathological CTG | |

If a foetal blood sample cannot be obtained and the CTG has not improved, expedite delivery (caesarean section or operative vaginal delivery)

- **CTG storage:**
  - Store cardiotocograph traces for 25 years
  - If there is any concern that the baby may have developmental delay or any possible adverse effects, photocopy CTG and store them indefinitely

# Breech Presentation

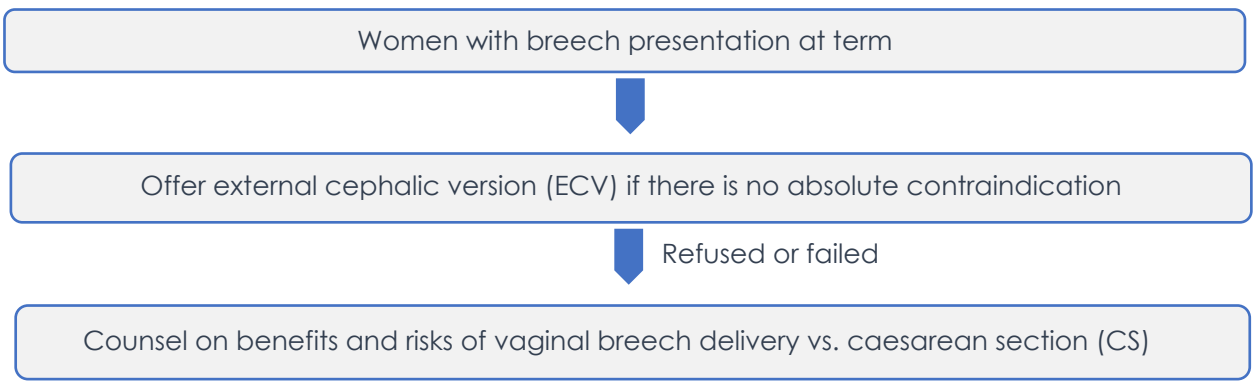
## Epidemiology

- Breech presentation accounts for 3-4% of term deliveries
- Incidence is more common in nulliparous women with high recurrence rate
- Recurrence rate of breech presentation is 10%

## Diagnosis

- By abdominal examination, the presenting part is irregular, soft and not ballotable. The head is felt in the fundus and is hard, circular, and ballotable. Diagnosis is confirmed by ultrasound
- During labour, failure to feel foetal head and head sutures during pelvic examination and the presence of thick meconium after rupture of membranes may indicate undiagnosed breech presentation (25% of cases are diagnosed in labour)

## Antenatal management



**Women should be counselled thoroughly on different delivery approaches**

- **Perinatal mortality:**
  - Incidence is 0.5:1000 with planned CS, 1:1000 with planned vaginal cephalic delivery, and 2:1000 with planned breech delivery

**Causes of better neonatal outcomes with CS vs. vaginal breech delivery**

① Avoidance of stillbirth that may occur beyond 39 weeks of gestation
② Avoidance of intrapartum risks of vaginal delivery
③ Avoidance of intrapartum complications of vaginal breech delivery

  - Appropriate patient selection and intrapartum care can reduce the gap in perinatal mortality between breech and cephalic vaginal delivery

- **Maternal outcomes:**
  - Compared to CS, breech vaginal delivery is associated with:
    - Smaller risk of immediate maternal complications (small difference)
    - Smaller risk of long-term pregnancy complications

**Long-term complications of CS**

- Incidence of repeat CS is > 50%
- 3-fold increase in uterine scarring
- Risk of endometritis, transfusion, hysterectomy and maternal death is higher in future pregnancies (regardless of mode of delivery)
- Placenta praevia and accreta (risk is higher with elective compared to emergency CS) e.g. incidence of accreta is 0.3% after 1 CS and 2.3% after 4 CS
- Uterine rupture in future deliveries (delivery-related perinatal mortality is 13:10.000)

- Planned breech vaginal delivery is associated with 40% risk of emergency CS, which carries the highest maternal risk compared to planned CS (intermediate risks), and successful vaginal delivery (low risk)

- **Neonatal outcomes:**
  - Compared to CS, breech vaginal delivery is associated with:
    - Lower APGAR score
    - Higher risk of short-term serious complications
    - No increase in long-term morbidity
  - CS is associated with slight increase in the incidence of stillbirths in subsequent pregnancies (1.5 times, the relation may not be causal and may be related to the indication)

**Patient selection**

- Breech vaginal delivery should be contraindicated in the presence of the following factors:
  ① Hyper-extended neck on (by ultrasound)
  ② High estimated foetal weight (> 3.8 Kg)
  ③ Low estimated birth weight (< 10$^{th}$ centile)
  ④ Footling or kneeling presentation
  ⑤ Foetal compromise
  ⑥ Foeto-pelvic disproportion
- If there is no available expertise in breech vaginal delivery, women should be counselled that this may increase perinatal risks and they should be offered referral

## Intrapartum management

### Management of unplanned breech vaginal delivery

- If women present in labour with no prior plan of vaginal delivery, management depends on the following factors:

① Stage of labour
② Risk factors of poor vaginal delivery outcomes (contraindications)
③ Availability of expertise and informed consent

- In women presenting in established labour close to or in the second stage of labour:

CS should not be offered routinely

Assess risk factors by ultrasound, if possible

Counsel women on vaginal delivery

## Management of planned breech vaginal delivery

**Adherence to management protocol reduces perinatal complications**

- **Delivery setting:**
  Delivery should be conducted in well-equipped hospitals that facilitates CS, if needed
- **Induction of labour:**
  It is generally not recommended and should not be routinely offered
- **Augmentation of labour:**
  It is generally not recommended. However, it may be offered if there is slow labour progression that associated with:
  ① Infrequent contractions (< 4 contractions/10 minutes) AND
  ② Epidural analgesia
- **Epidural analgesia:**
  Epidural analgesia increases the risk of interventions. Its impact on success of vaginal delivery is not clear
- **Continuous electronic foetal heart rate monitoring (EFM):**
  EFM is recommended as it may improve outcomes (robust evidence is lacking):
  - If EFM is declined, intermittent auscultation is performed. If any abnormalities are detected, EFM should be used
  - If EFM is abnormal, CS should be performed unless feotal buttocks are visible at the perineum or labour progress is rapid. Foetal blood sampling is not recommended

| | |
|---|---|
| **First stage of labour** | • Management of labour is generally similar to standard care in normal vaginal delivery<br>• The most preferred position is dorsal or lithotomy position<br>• Amniotomy should be avoided unless there is definite clinical indication |
| **Second stage of labour** | • Active second stage is encouraged only if passive second stage shows adequate descent<br>• Passive second stage is allowed for 2 hours only. If the buttocks are visible at the perineum, active second stage (pushing) is allowed. Otherwise, CS should be performed<br>• Positions of delivery are all –fours or semi recumbent positions depending on patient and provider preference<br>• Assisted breech delivery, rather than breech extraction, is allowed<br>• During active second stage, assistance to expedite delivery (WITHOUT traction) is required if there is:<br>▪ Prolonged second stage:<br>□ Delay > 5 minutes from buttocks to head OR<br>□ Delay > 3 minutes from umbilicus to head)<br>▪ Poor foetal status<br>• The foetus should be grasped from the pelvic girdle (not foetal soft tissues)<br>• Episiotomy is not a routine |

| **Second stage manoeuvres to facilitate delivery of the foetus after delivery to the umbilicus** |
|---|
| • Anterior rotation of the shoulder |
| • Hocking down the arms after the anterior scapula is visible at the perineum |
| • Lovset manoeuvre to delivery through a nuchal arm |
| • Delivery of the head using Mauriceau-Smellie-Veit manoeuvre or using forceps (Burns-Marshall method is not recommended). Suprapubic pressure may be used |
| • Bracht manoeuvre, which includes grasping the body with both hands, keeping the legs flexed to the abdomen bringing it up against maternal symphysis with suprapubic pressure |

## Management of preterm breech delivery

- **Spontaneous labour:**
  - If women present with preterm breech presentation in labour, CS is not offered as a routine and they are manged in the same manner as term breech
  - Mode of delivery should be selected based on:
    - Stage of labour
    - Foetal well-being
    - Type of breech presentation
    - Skilled operator in breech vaginal delivery
  - Risk of head entrapment is 14%
- **Planned labour:**

  CS is recommended for labour is planned due to maternal or foetal indications

Head entrapment during vaginal delivery and CS is manged by cervical incision (2, 6, and 10 o'clock) or vertical uterine incision extension, respectively

CS is not routinely recommended in women between 22-25+6 weeks of gestation

## Management of twins with breech presentation

**First twin is breech**

**Planned**

CS is recommended

**In labour**

Decision depends on intrapartum factors:

- Cervix dilatation
- Station
- Type of breech pentation
- Foetal status
- Availability of expertise

**Second twin is breech**

CS should not be offered regardless of gestational age

Second twin is non-vertex in 40% df case

# Shoulder Dystocia

## Background

**Definitions**

It is a complication of vaginal cephalic delivery, which requires specific obstetric manoeuvres to deliver the foetus after delivery of the head when gentle traction has failed to deliver the shoulders of the foetus

**Risk factors**

**Antepartum risks**

- Diabetes mellitus
- Body mass index > 30kg/m$^2$
- Previous shoulder dystocia
- Macrosomia (more than 4.5kg)

**Intrapartum risks**

- Induction of labour
- Oxytocin augmentation
- Assisted vaginal delivery
- Prolonged first stage of labour
- Secondary arrest
- Prolonged second stage

**Complications**

**Maternal complications**

- Postpartum haemorrhage (11%)
- Third and fourth-degree perineal tears (3.8%)

Maternal complications are not related to the number and nature of manoeuvres that are made to deliver the foetus

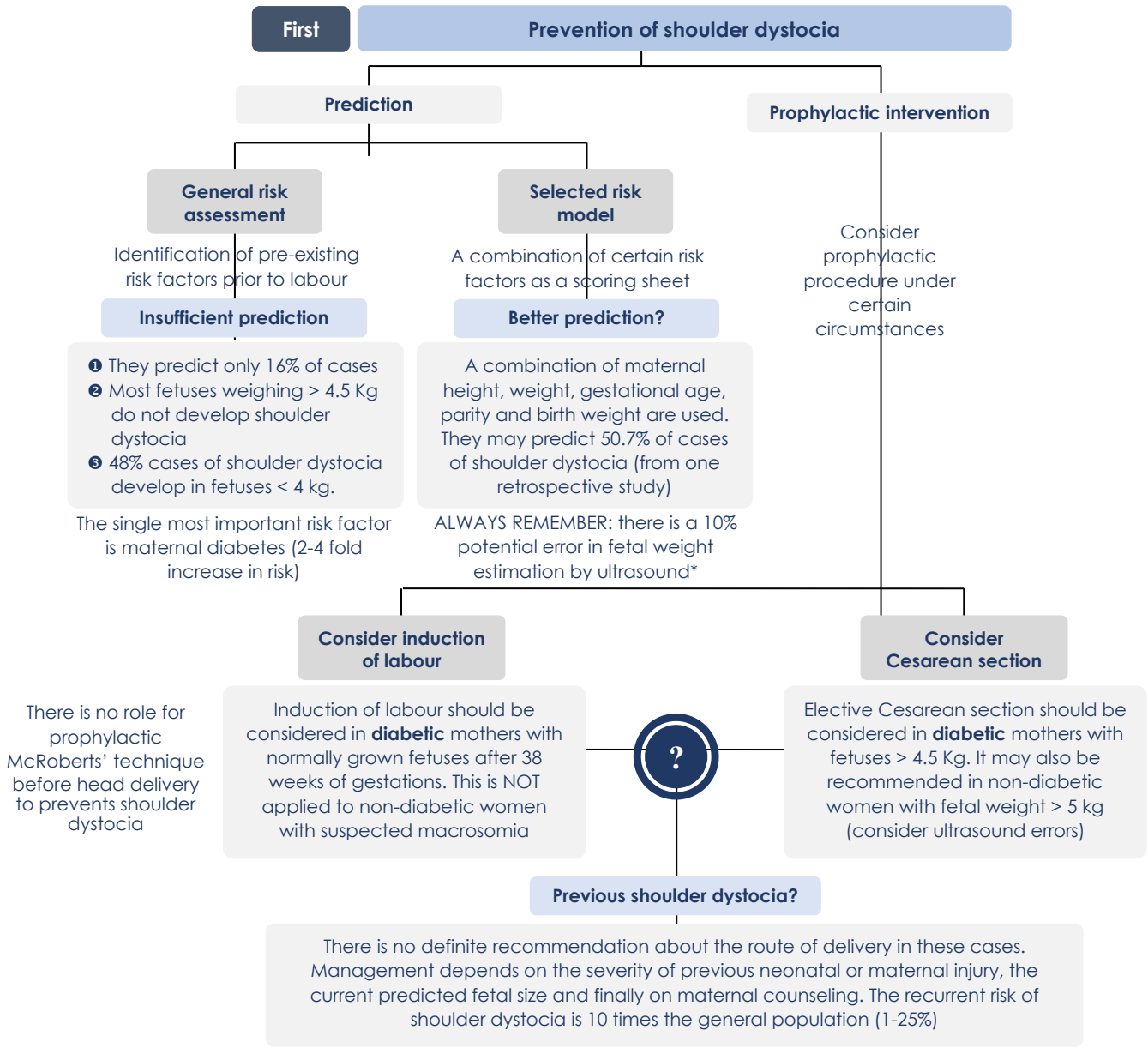
**Fetal complications**

- Brachial plexus injury (BPI) in 2.3% to 16%

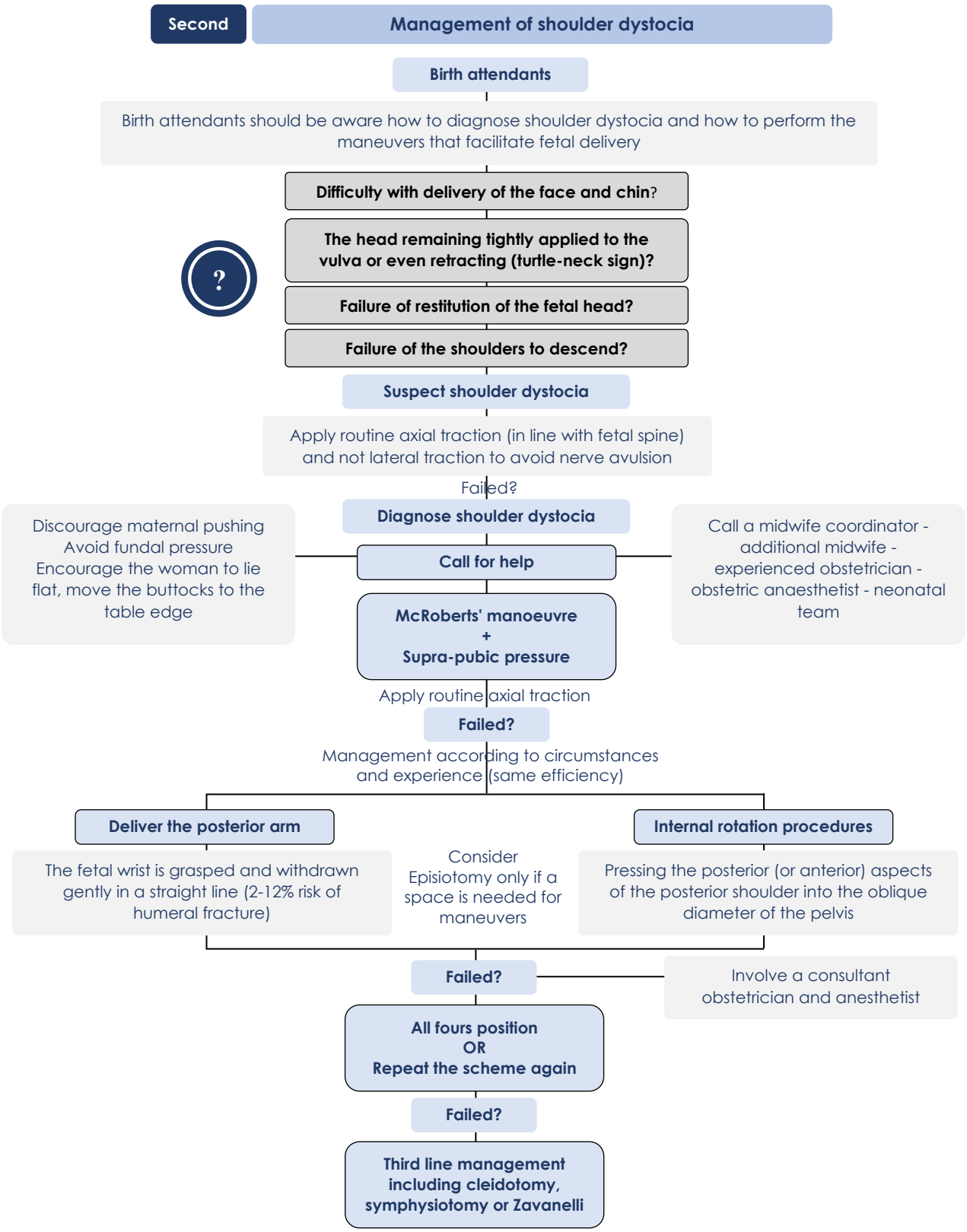
BPI is the most common cause of litigation in cases of shoulder dystocia. The following facts about shoulder dystocia should be well known:

- Most cases of BPI resolve without permanent disability. Only < 10% of cases may suffer permanent problems (more with large infants)
- BPI is not always associated with malpractice. Only 46% of cases may be associated with substandard care
- About 4-12 % of BPI injuries were reported after uncomplicated caesarean section.
- As a medico-legal issue, the shoulder that was affected at the time of birth should be reported clearly because BPIs in the posterior shoulder are unlikely to be caused by the obstetrician

## Clinical approach




*This risk model depends on actual rather than estimated fetal weight


Second
Management of shoulder dystocia
Birth attendants
Birth attendants should be aware how to diagnose shoulder dystocia and how to perform the maneuvers that facilitate fetal delivery
?
Difficulty with delivery of the face and chin?
The head remaining tightly applied to the vulva or even retracting (turtle-neck sign)?
Failure of restitution of the fetal head?
Failure of the shoulders to descend?
Suspect shoulder dystocia
Apply routine axial traction (in line with fetal spine) and not lateral traction to avoid nerve avulsion
Failed?
Diagnose shoulder dystocia
Discourage maternal pushing
Avoid fundal pressure
Encourage the woman to lie flat, move the buttocks to the table edge
Call for help
Call a midwife coordinator - additional midwife - experienced obstetrician - obstetric anaesthetist - neonatal team
McRoberts' manoeuvre
+
Supra-pubic pressure
Apply routine axial traction
Failed?
Management according to circumstances and experience (same efficiency)
Deliver the posterior arm
The fetal wrist is grasped and withdrawn gently in a straight line (2-12% risk of humeral fracture)
Consider Episiotomy only if a space is needed for maneuvers
Internal rotation procedures
Pressing the posterior (or anterior) aspects of the posterior shoulder into the oblique diameter of the pelvis
Failed?
Involve a consultant obstetrician and anesthetist
All fours position
OR
Repeat the scheme again
Failed?
Third line management including cleidotomy, symphysiotomy or Zavanelli

### ❶ The McRoberts' manoeuvre

- **The manoeuvre:**
  This manoeuvre involves flexion and abduction of the maternal hips to place the thighs on the abdomen.
- **Mechanism (rationale):**
  - This manoeuvre straightens the lumbosacral angle.
  - It also rotates the maternal pelvis upwards.
  - It also increases the anterior-posterior diameter of the pelvis.
- **Steps:**
  - The woman is placed flat.
  - The woman's legs are removed from the supports (if any).
  - The woman's legs are hyperflexed with the aid of 2 assistants on each side.
  - Routine axial traction is then applied to the fetal head to assess release of the shoulders from the maternal pelvis.
- **Success rate:**
  It reaches up to 90%.
- **Complications:**
  It has a low rate of complications because it does not involve internal manoeuvres.

**Suprapubic pressure**

- **The manoeuvre:**
  Suprapubic pressure may be applied along with the McRoberts' manoeuvre to increase the chance of success.
- **Mechanism (rationale):**
  - This manoeuvre minimizes the descending fetal bisacromial diameter through the pelvis (pushing the anterior shoulder towards the pelvis).
  - It also rotates the anterior shoulder into the oblique pelvic diameter.
- **Steps:**
  - An assistant applies pressure just above the maternal symphysis pubis from the side of the fetal back. The direction of pressure is downward and lateral.
  - The pressure may be continuous or intermittent (rocking). No method is superior to the other.

### ❷ Rotational manoeuvres

- **The manoeuvre: (Woods and Rubin)**
  Gaining access through the vagina is made to press on the posterior shoulder (either on the anterior or posterior aspect).
- **Mechanism:**
  - This manoeuvre brings the shoulders into the wider oblique diameter.
  - If the posterior aspect of the posterior shoulder is pressed, this also adducts the shoulders and reduces the shoulder diameter.
- **Steps:**
  - Pressure is best applied on the posterior aspect of the posterior shoulder.
  - If this fails, an attempt to apply pressure on the posterior aspect of the anterior shoulder should be made.

**❸ Posterior arm delivery**

- **The manoeuvre:**
  Gaining access through the vagina is made to bring the posterior arm through the pelvis into the vagina.
- **Mechanism:**
  The manoeuvre brings the width of the arm below the pelvic inlet and thus reduces the diameter of the fetal shoulders.
- **Steps:**
  - The hand of the operator is inserted through the vagina and the fetal wrist is grasped.
  - The posterior arm is gently withdrawn following a straight line.
- **Complications:**
  - Humeral fractures (2% - 12%). However, this is controversial. It may be attributed to the procedure or to the condition itself.
  - Generally, it was reported that the incidence of both BPI and humeral fractures is higher than in those who were managed by rotational methods.

**Episiotomy**

- There is no rule of episiotomy to facilitate shoulder delivery because it involves soft tissues rather than pelvic bone, which prevents shoulder descent. Accordingly, episiotomy does not decrease the incidence of shoulder dystocia or its complications including BPI.
- Episiotomy is only indicated if it is going to help the operator to perform internal procedures by allowing more space for these manoeuvres.

**❹ All fours position**

The All fours position is suitable in certain circumstances. If the woman is slim, mobile and without epidural anaesthesia specially with a single attending midwife, this position may be attended. Otherwise, internal manoeuvres are more appropriate.

**❺ Third line procedures**

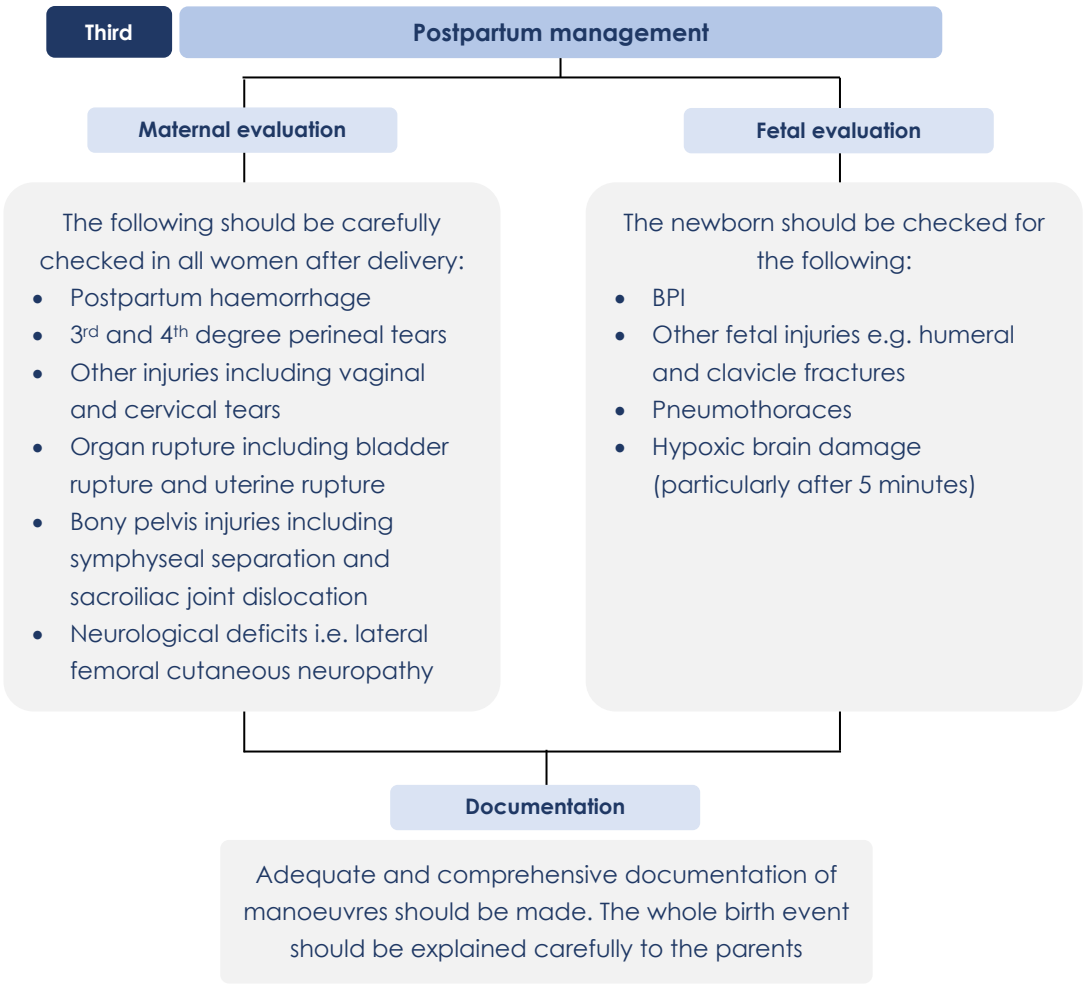
① **Cleidotomy:** surgically induced clavicle fracture or bending of the clavicle with a finger).

② **Symphysiotomy:** dividing the anterior fibres of symphyseal ligament to widen the pelvis.

This procedure is helpful. However, it may cause serious maternal morbidity. Furthermore, the neonatal outcome is generally poor.

③ **Zavanelli manoeuvre (rare):** pushing the head through the vagina then caesarean section to deliver the fetus.

- ***Advantages:***
  This procedure is best resorted to bilateral shoulder dystocia (one shoulder above the symphysis pubis and the other above the sacral promontory).
- ***Disadvantages:***
  The procedure is difficult and time consuming; the risk of hypoxic ischaemic injury is low within 5 minutes but becomes significant thereafter.


Third
Postpartum management
Maternal evaluation
Fetal evaluation
The following should be carefully checked in all women after delivery:
Postpartum haemorrhage
3rd and 4th degree perineal tears
Other injuries including vaginal and cervical tears
Organ rupture including bladder rupture and uterine rupture
Bony pelvis injuries including symphyseal separation and sacroiliac joint dislocation
Neurological deficits i.e. lateral femoral cutaneous neuropathy
The newborn should be checked for the following:
BPI
Other fetal injuries e.g. humeral and clavicle fractures
Pneumothoraces
Hypoxic brain damage (particularly after 5 minutes)
Documentation
Adequate and comprehensive documentation of manoeuvres should be made. The whole birth event should be explained carefully to the parents

# Operative Vaginal Delivery

## Prevention of operative vaginal delivery

The following factors are associated with reduced risk of operative vaginal delivery:

- Continuous support
- Upright/lateral position in the second stage
- No epidural anaesthesia (However, it should not be discouraged or discontinued for this indication)
- Delayed pushing in primigravida (reduces use of rotational and midcavitary forceps) Delayed pushing starts after 1-2 hours or till there is an urge to push) is recommended

- Oxytocin should not be used routinely in the second stage. It does not lead to reduction in operative vaginal delivery.
- There is no difference between patient controlled epidural and continuous infusion, or epidural and combined epidural/spinal analgesia

## indications

Incidence of operative vaginal delivery is 10-13%

| | |
|---|---|
| **Foetal indications** | • Foetal compromise |
| **Maternal indications** | • Medical conditions e.g. hypertensive crisis, proliferative retinopathy, cardiac disease, spinal injury, autonomic dysreflexia, myasthenia gravis<br>• Maternal exhaustion. |
| **Labour progress** | • Second stage longer than 3 hours (or 2 hours without epidural) in nullipara<br>• Second stage longer than 2 hours (or 1 hours without epidural) in multipara |

It is not indicated in women with dural puncture unless she has severe headache that worsens with pushing

## classification

| | Abdominal examination | Vaginal examination | Notes |
|---|---|---|---|
| **High** | The head is 2/5 or more palpable abdominally | The head is above the level of the ischial spine | It is not recommended and should not be performed |
| **Mid** | No more than 1/5 palpable abdominally | Head station between 0 and +2 | 2 subtypes:<br>Rotation ≤ 45° from OA position<br>Rotation >45° including OP position |
| **Low** | The head is not palpable abdominally | Head station is +2 or more but skull is not at pelvic floor | 2 subtypes:<br>Rotation ≤ 45° from OA position<br>Rotation >45° including OP position |
| **Outlet** | The head is not palpable abdominally | The head is at the perineum, the scalp is externally visible | Rotation does not exceed 45° |

OA = occiptoanterior, OP = occiptoposterior

## Contraindications

| Absolute contraindications | Relative contraindications |
|---|---|
| • Face presentation (Vacuum)<br>• Incomplete cervical dilatation | • Foetal bleeding disorders (autoimmune thrombocytopenia)<br>• Predisposition to fractures (osteogenesis imperfecta) |

- Vacuum extraction should be avoided prior to 34 weeks because of higher risk of subglial haemorrhage, cephalohematoma and intracranial haemorrhage
- Maternal viral infection is not a contraindication. However, operative vaginal delivery should be used with caution

## Prerequisites

- **A**dequate pelvis
- **A**naelgesia: pudendal nerve block or epidural anaesthesia
- **A**mniotomy (membranes are ruptured)
- **B**ladder is empty and the catheter is removed
- **C**onsent: verbal consent is appropriate if written consent is not possible. Prenatal consent is recommended specially with the first pregnancy
- **D**ilation of the cervix is dull
- **E**xamination of the abdomen reveals less than 1/5 of foetal head is palpable
- **F**oetal presentation is vertex

## Vacuum vs. forceps

**Vacuum**

- Higher risk of failure (1.7 times), Kiwi soft cup is less successful than conventional cup (13% failure rate).
- Higher risk of cephalohematoma (2.4 times)
- Higher risk of retinal haemorrhage (2.0 times)
- Higher maternal anxiety on the baby (2.2 times)

Rapid or stepwise wise increment in cup pressure are comparable in terms of outcomes

**Forceps**

- Higher risk of maternal perineal and vaginal trauma
- Risk is significant with sequential delivery (vacuum and forceps trial)

- No difference between vacuum and forceps in caesarean section rate, 5min APGAR or need for neonatal phototherapy
- No difference in long term outcomes

- **Setting:**
  - Operative delivery is usually performed in labour room
  - Operative delivery is conducted in the theatre if there is high risk of failure:
    - Mid cavity
    - Occiptoposterior position
    - Estimated foetal weight beyond 4000 grams
    - Maternal bod mass index > 30
  - Decision-to-delivery should not exceed 30 minutes

- **Method:**
  - Choosing between vacuum and forceps delivery is determined by provider's preference, experience, and judgement of clinical circumstances
  - Vacuum delivery is generally safe beyond 36 weeks of gestation. It should be used with caution between 34-36 weeks only if indicated, and should be avoided prior to 34 weeks of gestation
  - If rotational delivery is required, the following options may be used:
    - Kielland forceps (associated with higher risk, requires expertise)
    - Manual rotation followed by direct forceps traction
    - Rotational vacuum
  - Sequential operative delivery is associated with higher risk of complications and should not be routinely performed. The provider should weigh risks of sequential operative delivery against risks of caesarean section after unsuccessful operative delivery before a decision is made. If sequential operative delivery is attempted, the neonatologist should be informed

**Second stage caesarean section vs. successful operative delivery**

- Higher risk of major obstetric haemorrhage
- Prolonged hospital stay
- Higher incidence of neonatal admission to special care unit

- **Episiotomy**

  It is not indicated as a routine and the decision should be individualized

- **Termination:**
  - Operative delivery should be terminated if:

    ① Delivery is not imminent after 3 pulls

    ② There is no progress with moderate traction after each contraction
  - Any operative delivery should be followed by reporting of paired cord blood samples
  - Incident report is indicated in the following situations:
    - Unsuccessful operative delivery
    - Birth trauma
    - Cord arterial blood pH < 7.1
    - APGAR score < 7 after 5 minutes
    - Admission of a term baby to neonatal intensive care unit

- **Antibiotics:**

  The procedure should be done under aseptic conditions. Otherwise, there is no need for prophylactic antibiotics

## Postpartum care

- **pain control:**

  Regular paracetamol and diclofenac

- **Bladder care:**
  - Timing and volume of the first void should be checked, and post voiding residual urine should be measured if there is concern on urinary retention
  - Risk of urinary retention is higher in women who had spinal anaesthesia or epidural anaesthesia that was topped up to cover operative delivery. Therefore, an indwelling catheter may be left for 12 hours to reduce risk of urinary retention and bladder overfilling
  - Heavy regional anaesthesia, prolonged labour and operative delivery present risk factors for urinary retention, which may be complicated by long-term dysfunction

- **Physiotherapy:**

  It should be offered to women after delivery to reduce the risk of urinary incontinence

- **Thromboprophylaxis:**

  It should be determined according to presence of risk factors per standard protocols

- **Debriefing:**
  - Circumstances of operative delivery are highly stressful to mothers and it may be associated with psychological morbidity. Midwife-led debriefing does not seem to improve or prevent these sequalae. Therefore, women should have a discussion with the obstetrician who conducted operative delivery regarding the indications, complications, and sequences of operative delivery including future pregnancies
  - The discussion should emphasize on the high likelihood of spontaneous vaginal delivery in next pregnancies (80%). However, women who had 3$^{rd}$ or 4$^{th}$ perineal laceration should be counselled on the risk of recurrence in future pregnancies

# Umbilical Cord Prolapse

## Definition

- **Umbilical cord prolapse:**
  It is defined as descent of the umbilical cord below the presenting part into or beyond the cervix after rupture of membranes:
  - **Occult cord prolapse:** the cord descents alongside the cervix
  - **Overt cord prolapse:** the cord descents beyond the cervix
- **Umbilical cord presentation:**
  It is defined as presence of the cord between the cervix and the presenting part with or without rupture of membranes

## Incidence

- Incidence of umbilical cord prolapse is 0.1 – 0.6%
- The incidence is higher with breech presentation (1%)

## Risk factors

- Maternal factors: Multiparity
- Foetal factors:
- Foetal congenital anomalies
  - Low birthweight (< 2.5 kg) and preterm labour
  - Malpresentation, abnormal lies including unstable lie
  - Non-engagement of the presenting part
  - Second twin
- Amniotic fluid: Polyhydramnios

- Cord: Cord abnormalities
- Placenta: Low lying placenta
- Interventions:
  - External cephalic version or internal podalic version
  - Amniotomy with high presenting part
  - Vaginal manipulations in the presence of ruptured membranes
  - Insertion of intrauterine pressure transducer
  - Induction of labour using a large balloon catheter

## Screening

| Routine ultrasound | Selective screening |
|---|---|
| Routine screening of cord presentation is not recommended. It yields poor sensitivity and specificity (13% detection rate) | Selective screening of cord presentation is considered in term breech presentation when vaginal delivery is opted |

## Prevention

| | |
|---|---|
| **Transverse, oblique presentation and unstable lie** | Admission to hospital at 37 weeks of gestation (risk of persistent transverse lie in labour is 17%) Alternatively, women may be advised to present immediately to hospital if labour pains start |
| **Preterm prelabour rupture of membranes (PPROM) n in the presence of non-cephalic presentation** | Immediate admission |
| **Mobile or high presenting part in labour** | Amniotomy should be avoided. Otherwise, immediate caesarean section (CS) should be prepared |
| **Rupture of membranes during labour** | Upward pushing of the presenting part with each examination should be avoided |
| **If the cord is palpable during examination** | Amniotomy should be avoided. CS should be performed for cord presentation |

## Early diagnosis (suspicion)

- Women with risk factors of cord prolapse, who had rupture of membranes, should be checked for cord prolapse with each examination
- Foetal heart rate auscultation is recommended after rupture of membranes and after each vaginal examination
- Cord prolapse should be excluded (by speculum or digital examination) if there are foetal heart rate changes after rupture of membranes. Cord prolapse may be associated with variable decelerations, prolonged decelerations, or persistent bradycardia
- If rupture of membranes occurs in absence of risk factors or foetal heart rate changes, no additional examination is required

## Management

### I. If the cervix is not fully dilated

- **Immediate intervention:**

  While preparing for CS, the following interventions are made while moving to the theatre:

  - **Minimal handling of prolapsed cord loops:** loops prolapsing outside the vagina should be minimally handled to avoid the risk of vasospasm

    Manual replacement of the cord back to the uterus above the presenting part to permit vaginal delivery is **NOT** recommended

  - **Elevating the presenting part:**

    The presenting part can be elevated to prevent cord compression by the presenting part either by:

    - Continuous manual elevation through the vagina or
    - Manual elevation followed by suprapubic application of upward pressure
    - Filling the bladder with a Foley catheter (using 500-750 ml of fluid)

- **Positioning:**
  Patients should be positioned either in a knee chest position OR left lateral position with head down and a pillow placed below the left hip
- **Tocolysis:**
  Subcutaneous terbutaline 0.25 mg may be considered if foetal heart rate changes persist despite the above measures
  In community setting, the same interventions are recommended while transferring to the nearest consultant-led labour service unless delivery is imminent

- **Delivery:**
  - **Category I CS (delivery within 30 minutes):**
    It is indicated if there is suspicious or pathological foetal heart rate pattern. Verbal consent is appropriate
  - **Category II CS (delivery within 30-75 minutes):**
    It is indicated in the presence of normal foetal heart rate pattern. Regional anaesthesia may be considered

  Paired cord sampling is indicated

**Periviable delivery (23 – 25 weeks)**

Given the poor neonatal outcome at this gestational age, women are counselled on expectant management vs. termination of pregnancy. There is no role of replacing the cord. Feticide may be offered at 22 weeks and beyond

### II. If the cervix is fully dilated

- **Cephalic presentation:** operative vaginal delivery may be considered
- **Breech presentation:** breech extraction may be appropriate

Delayed cord clamping may be considered depending of baby's status

Cord prolapse is an indication of incident reporting

## Prognosis

- Umbilical cord prolapse is associated with 9% mortality rate
- Most of these cases are attributed to prematurity and congenital anomalies
- Neonatal asphyxia may be caused by cord compression or vasospasm
- The risk of perinatal mortality with home delivery is 10 times higher than hospital delivery

- Cord prolapse is associated with higher incidence of neonatal resuscitation; incidences of low APGAR scores at 1 and 5 minutes are 21% and 7%, respectively

# Vaginal Birth After Ceasrean

## Antenatal care

- **Goals of antenatal counselling:**

① A final decision on mode of birth is made

② The date for elective repeat caesarean section (ERCS) is scheduled

③ A plan is made in case labour starts before the scheduled date

④ Informed consent and shared decision making in women undergoing vaginal birth after caesarean (VBAC) should be confirmed

All these points should be clearly documented in the notes

| VBAC candidates | Contraindications of VBAC |
|---|---|
| Offer VBAC to women at 37+0 weeks or beyond who have:<br>① Singleton pregnancy<br>② Cephalic presentation<br>③ Single previous lower segment caesarean delivery | ① Prior classic caesarean section<br>② Prior uterine rupture<br>③ Absolute contraindication to vaginal delivery<br>Complicated uterine scars should be reviewed by a senior obstetrician |

| | |
|---|---|
| **Two or more previous cesarean sections (CS)** | VBAC may be offered after counselling by a senior obstetrician. Success rate is comparable to 1 previous CS (71%), risk of rupture is higher (1.4%), and risks of hysterectomy and transfusion are higher |
| **VBAC success** | Success rate of planned VBAC is 72–75%. Success rate is the highest rate if there is history of previous successful VBAC (85-90%) |

- **Elements of antenatal counselling:**

| Risk and benefits of planned VBAC (Counselling information) |
|---|
| • Best delivery outcome and least complication are achieved if VBAC is successful<br>• Worst outcomes including highest risk of complications occur if VBAC fails with subsequent emergency caesarean delivery<br>• Risk of uterine rupture with planned VBAC is 1 in 200 (0.5%) versus 0.02% as a baseline<br>• Risk of perinatal death with VBAC is similar to risk among nulliparous women<br>• ERCS is associated with future risks including risk of placenta Previa and/or accreta in subsequent pregnancies, and risk of pelvic adhesions<br>• ERCP performed before 39 weeks of gestation is associated with slight increase in neonatal respiratory morbidity A preoperative course of antenatal corticosteroids |

- **Antenatal care schedule:**

| | |
|---|---|
| 12 weeks | Written information on delivery options |
| 18-21+6 weeks | Mid trimester ultrasound including assessment of placental site and placental abnormalities. If a low-lying placenta is present, ultrasound is repeated at 32-34 weeks |
| 32-34 weeks | **Obstetrician visit:** it is indicated if ultrasound confirms low laying placenta. The visit will focus on possibility of placenta accreta spectrum and management plan<br>**Midwifery visit:** if there is no concern on placental site, midwives can discuss mode of delivery and establish patient's preference if VBAC is not contraindicated |
| **36 weeks** | **Obstetrician visit:** Discuss mode of delivery in women who decide to undergo ERCS, women who remain indecisive, or women with obstetric complications e.g. foetal macrosomia, foetal growth restriction<br>**Midwifery visit:** Confirm patient decision and eligibility |
| 39 weeks | elective repeat caesarean section |
| 41 weeks | Women who opt for VBAC should be counselled on available options including labour induction, expectant management, and ERCS<br>Induction of labour reduces risk of perinatal mortality without increasing the incidence of caesarean section |

## Intrapartum management of VBAC

**Delivery setting**

- Available resources for immediate caesarean delivery and advanced neonatal resuscitation
- Epidural analgesia should be offered as with all vaginal deliveries (not contraindicated). However, if pain relief becomes an issue with increased requirements to control pain, impending uterine rupture should be considered
- The following should be available:
  - One to one observation
  - Intravenous access
  - Blood type, screen and save
  - continuous electronic foetal monitoring
  - Regular monitoring of maternal symptoms and signs and labour progress

**Induction and augmentation**

- Labour induction, method of induction, frequency of vaginal examination and decision of discontinuing VBAC should all be discussed with a senior obstetrician
- Induction/augmentation of labor increases risk of uterine rupture 2-3 times and increase risk of emergency caesarean section by 1.5-fold
- Higher dose of oxytocin above 20 mIU/min results in 4-fold increase in risk of uterine rupture
- Prostaglandins, if used, should be administered in the lowest possible dose as it increases risk of uterine rupture and neonatal death I the standard dose
- Induction of labour using mechanical methods (amniotomy or Foley catheter) has a lower risk of scar rupture compared with labour induction using prostaglandins
- Planned preterm VBAC has similar success rate to planned term

In case of emergency caesarean section, cefuroxime and metronidazole should be used

## Risk factors of uterine rupture

- Short inter-delivery interval less than 12 months
- Postdate
- Maternal age more than 40 years
- Obesity
- Macrosomia
- Low Bishop score
- Lower uterine segment thickness
- Term pregnancy (vs. preterm)

## Signs of uterine rupture

- Abnormal CTG
- Intense pain
- Acute scar tenderness
- Abnormal vaginal bleeding
- Haematuria
- Cessation of contractions
- Loss of station
- Abnormal abdominal contour
- Loss of Foetal tone

**Time of diagnosis**

- > 90% of cases are diagnosed in labour (most commonly at 4-5 cm)
- 18% of cases are diagnosed in second stage
- 8% are diagnosed after delivery

- Abnormal CTG: 70% of cases or uterine rupture
- Abnormal CTG and pain: 50% of cases
- Abnormal CTG, pain, and bleeding: 10%

50% of patients with uterine dehiscence are asymptomatic

## Probability of VBAC success

| | |
|---|---|
| **General probability** | 72-75% |
| **History of prior successful VBAC** | 85-90% |
| **Induction of labour** | 40% |
| **Body mass index more than 30** | 40% |
| **Prior CS for malpresentations** | 85% |
| **Prior CS for foetal distress** | 70-75% |
| **Prior CS for labour dystocia** | 60-65% |
| **Prior CS for unsuccessful instrumental delivery** | 60% |

## Comparison between VBAC and ERCS

| | VBAC | ERCS* |
|---|---|---|
| **Pelvic injury and complications** | Incidence of sphincter injury is 5%. Possibility of instrumental delivery is 40% | It may reduce risk of pelvic organ prolapse and urinary incontinence |
| **Transient respiratory morbidity** | 2.3 % | 4-5% (6% if performed at 38 weeks, 11% if performed at 37 weeks) |
| **Maternal mortality** | 4:100000 | 13:100000 |
| **hypoxic ischemic encephalopathy** | 0.08% (60% are caused by uterine rupture) | 0.01% |
| **Respiratory distress syndrome** | 0.05% | 0.5% |
| **Perinatal death** | 4:10000 | 1:10000 |
| **Future complications** | None | • Cumulative increase in risk of placenta praevia (PP):<br>▪ 1% after 1 CS<br>▪ 1.7% after 2 CS<br>▪ 2.8% after 3 CS<br>• Cumulative increase in risk of placenta accreta:<br>▪ Prior 1 CS and PP: 10-15%<br>▪ Prior 2 CSs and PP: 20-40%<br>▪ Prior 5 CSs and PP: 70% |

* If sterilization is considered at time of ERCS, women should be counselled and consented at least 2 weeks prior to delivery to reduce risk of regret

## Special situations

| condition | consideration |
|---|---|
| Twins | • Success of VBAC may be comparable to singleton |
| Foetal macrosomia (> 4 kg) | • Probability of VBAC success is below 50%<br>• Risk of uterine rupture is 4% |
| Stillbirth | • Probability of VBAC success is 87%<br>• Risk of uterine rupture is 2-5% |
| Maternal age above 40 | • Timing of delivery 39-40 week may risk of still birth |
| Preterm VBAC | • VBAC success is comparable to term pregnancy<br>• Rate of uterine dehiscence is lower than uterine dehiscence in term pregnancy |

# Induction of Labour

## Epidemiology

Induction of labour (IOL) accounts for 1:5 (20%) of deliveries

IOL ends in vaginal delivery without intervention in 2/3 of deliveries

15% of women may eventually have instrumental delivery after IOL

22% of women end up in an emergency cesarean section after IOL

## Decision-making

- At 38 weeks' visit, women with uncomplicated pregnancy should be informed about risks of pregnancy prolongation beyond 42 weeks, and their options which include:

| | |
|---|---|
| Membrane sweeping | • It makes spontaneous labour more likely<br>• It reduces the need for IOL by 20%<br>• It may cause discomfort and vaginal bleeding |
| IOL between 41+0 and 42+0 weeks | |
| Expectant management | • Only if other options are declined<br>• Patients should be offered twice weekly cardiotocography and amniotic fluid assessment |

- When offering IOL to a patient, you should explain:

Indication | Timing | Setting | Approach | Risks | Support and pain relief

Alternative options | Benefits of IOL | Induction methods | Failure of IOL

**Preterm prelabour rupture of the membrane after 34 weeks**

The maternity team should discuss whether to induce IOL with vaginal PGE2 regarding:

| ① Risks to the mother | ② Risks to the baby | ③ Local availability of NICU |
|---|---|---|
| • Sepsis<br>• Possible need for caesarean section | • Sepsis<br>• Complications of preterm birth | |

| **Vaginal PGE2** | The preferred method of IOL unless the risk of uterine hyperstimulation |
|---|---|
| **Forms** | • Gel<br>• Tablet<br>• Controlled-release pessary |
| **Regimens** | • *One cycle of vaginal PGE2 tablets or gel:* one dose, followed by a second dose after 6 hours if labour is not established (2 doses only)<br>• *One cycle of vaginal PGE2 controlled-release pessary:* one pessary is placed over 24 hours |

- Vaginal prostaglandin (PG) E2 is not recommended or should be used with caution in preterm rupture of membranes. A consent should be obtained and documented

## Special indications

| IOL in specific circumstances | |
|---|---|
| **Uncomplicated pregnancy** | • Standard care of uncomplicated pregnancy is to anticipate spontaneous labour<br>• After 42 weeks, women should be counselled on the increased risk of foetal loss if IOL is declined |
| **Prelabor rupture of labour at term** | • After 37 weeks, IOL is offered using vaginal PGE2<br>• Expectant management for 24 hours after rupture of membranes (expecting spontaneous labour) is reasonable before IOL is initiated |
| **Previous caesarean section** | • If delivery is indicated, IOL may be offered to these patients using vaginal PGE2,<br>• Compared to spontaneous labour, IOL may be associated with:<br>① Higher risk of emergency caesarean section<br>② Higher risk of uterine rupture |
| **Maternal request** | • IOL should be limited to exceptional circumstances and should be allowed before 40 weeks |
| **Breech presentation** | • IOL is generally not recommended<br>• IOL is only considered if external cephalic version failed and elective caesarean section is declined. Patients should be extensively counselled regarding risks |
| **Foetal growth restriction** | • IOL should not be offered if severe GFR is associated with proved foetal compromise |
| **History of precipitate labour** | • IOL should **NOT** be routinely recommended for this indication |
| **Intrauterine foetal death** | • Both IOL and expectant management can be offered if patients are physically well, with intact membranes, and no evidence of infection or bleeding<br>• Immediate IOL is indicated if there is rupture of membranes, evidence of infection, or bleeding<br>• IOL is performed using oral mifepristone followed by vaginal PGE2 or vaginal misoprostol<br>• If there is previous CS, risk of uterine rupture is higher. Therefore, the dose of vaginal prostaglandins should be decreased in the 3rd trimester |
| **Suspected foetal macrosomia** | • IOL is **NOT** recommended solely for this indication |

## Methods of IOL

### Recommended methods for IOL

#### Membrane sweeping

- It is an adjunct to IOL rather than an actual method of IOL and should not substitute pharmacological IOL
- It aims at mechanically separating the membranes from the lower segment. If the cervix cannot admit a finger, massage is applied around the cervix in the vaginal fornices
- It is offered before formal IOL, at 40-41 weeks in nulliparous women, and 41 weeks in parous women
- Repeated sweeping may be offered

#### Pharmacological methods

- **Vaginal PGE2:**
  When offered, women should be informed about the associated risks of uterine hyperstimulation
- **PGE1 (Misoprostol):**
  It should be limited to women with Intrauterine foetal death only

#### Surgical methods

- Amniotomy with or without oxytocin should not be used as the first method of IOL
- It may be used only if PGE2 is not recommended for fear of uterine hyperstimulation

### Methods not recommended for IOL

#### Pharmacological

- Oral, intravenous, extra-amniotic or intracervical PGE2
- IV oxytocin alone
- Hyaluronidase
- Steroids or oestrogen

#### Non-pharmacological

- Herbal supplements
- Acupuncture
- Homeopathy
- Castor oil
- Hot baths
- Enemas
- Sexual intercourse

#### Mechanical methods

- Balloon catheters.
- Laminaria.

Mechanical methods should not be used routinely for IOL

## Setting

**Outpatient setting**

- IOL should only be offered if safety and support procedures are made
- Continuous audit is required

**Inpatient setting**

- IOL with vaginal PGE2 should be started in the morning. This is associated with higher maternal satisfaction

Wherever IOL is considered, facilities should be available and accessible for continuous electronic foetal heart monitoring and uterine contraction monitoring.

## Management of IOL

- Before IOL is initiated, providers should:
  ① Determine the Bishop score
  A bishop score of 8 or more indicates a favourable cervix, which is associated with high opportunity of spontaneous labour and good response to IOL
  ② Ensure normal foetal heart rate pattern before starting IOL
- After vaginal PGE2 is placed, foetal status should be monitored using continuous electronic foetal monitoring once contractions start
- If continuous electronic foetal monitoring is normal, intermittent auscultation can be used thereafter
- Pain control:
  - Women should be aware that induced labour may be more painful than spontaneous labour
  - Pain control options range from oral analgesics to epidural analgesia. Labour in water is an option
- Bishop score should be assessed 6 hours after vaginal PGE2 tablet or gel, or 24 hours after pessary to monitor progress
- If a woman goes home after insertion of a vaginal PGE2 tablet or gel, she should contact her obstetrician or midwife if:
  ① Contractions starts
  ② There are no contractions after 6 hours

## Failed induction

Failed induction means that labour has not started after one cycle of pharmacological induction

**Immediate action**

- Reassess maternal wellbeing and foetal status using electronic foetal monitoring
- Discuss diagnosis, offer support and counsel on future management

**Management options**

① Further attempt to induce labour depending on maternal status, feotal status, and patient preference

② Caesarean section

## Complications

| Complication | Prevention and management |
|---|---|
| **Uterine hyper-stimulation** | If uterine hyperstimulation develops, tocolysis should be immediately administrated |
| **Cord prolapse** | • **To reduce risk of cord prolapse at amniotomy, you should:**<br>① Assess engagement of the presenting part<br>② Rule out umbilical cord presentation by palpation<br>③ Avoid dislodgment of foetal head during amniotomy<br>④ Avoid amniotomy if feotal head station is high<br>• **A low-lying placenta should be always checked before membrane sweeping and before IOL using ultrasound** |
| **Uterine rupture** | If clinically suspected, emergency caesarean section is indicated |

# Third and Fourth Degree Perineal Tears

## Epidemiology

Incidence in the UK is 3% (2% in multipara and 6% in nullipara)

## Classification

| | |
|---|---|
| **First degree** | Vaginal mucosa and/or perineal skin |
| **Second degree** | Perineal muscles but not anal sphincters |
| **Third degree** | 3A: < 50% of the external anal sphincter<br>3B: > 50% of the external anal sphincter<br>3C: external and internal anal sphincters |
| **Fourth degree** | Anal mucosa |

## Risk factors

- Asian race
- Nulliparity (7-fold increase)
- Birth weight > 4 kg
- Shoulder dystocia
- Occipto-posterior position
- Prolonged second stage (1.5 times after 2-3 hours, 2 times after 4 hours)
- Operative vaginal delivery:
  - Risk is halved if vacuum use is combined with episiotomy, doubled if no episiotomy is performed compared to baseline

- Risk is 1.5 times higher with forceps if episiotomy is performed, 6 times higher without episiotomy

## Prevention

- **Episiotomy:**
  - Role of episiotomy in preventing perineal tears is controversial
  - It is indicated with instrumental delivery
  - Mediolateral episiotomy is superior to other types of episiotomy
  - A correct mediolateral episiotomy should be performed at angle of 60 degrees from the midline during perineal distension
- **Perineal protection:**

  Perineal protection should be considered at crowning to reduce the risk of perineal tears
- **Warm compresses:**

  Application of warm compresses to the perineum during the second stage is recommended to reduce risk of perineal tears

## Management

- **Principles of repair:**
  - Adequate lighting
  - Adequate anaesthesia (regional or general)
  - Repair is performed in the operating theatre (or the delivery room if decided by a senior obstetrician)
  - Repair should be performed by a trained obstetrician or by a trainee under direct supervision
  - Figure-of-eight sutures should not be used to avoid tissue ischemia
  - A rectal examination should be performed after repair to rule out mucosal involvement by the stitches

- **Surgical technique:**

| | |
|---|---|
| **Anorectal mucosa** | Polyglactin 3-0 continuous or interrupted sutures |
| **Internal anal sphincter** | • Interrupted or mattress sutures |

| | |
|---|---|
| | • Polyglactin 2-0 or PDS 3-0 is used<br>• It should be repaired separately without overlap |
| **External anal sphincter** | • Full thickness (3C): overlapping or end to end repair<br>• Partial thickness (3A and 3B): end to end repair only<br>• Polyglactin 2-0 or PDS 3-0 is used |

Sutures used to repair sphincters should be buried beneath the superficial perineal muscles (risk of suture migration is 7%)

- **Postoperative management:**
  - **Broad spectrum antibiotics:** they should be used to reduce risk of infection and wound dehiscence
  - **Laxatives:** they should be used to reduce the risk of wound dehiscence. Bulking agents are not indicated e.g. 10 days of lactulose
  - **Physical therapy:** may be beneficial
  - **Follow-up:** a postpartum visit at 6-12 weeks should be scheduled to assess symptoms and healing. Women should be referred to a specialist if there is persistent pain or incontinence

## Prognosis

- 60-80% of women are asymptomatic after 12 months
- Women should be counselled regarding future deliveries. There is generally no role for prophylactic episiotomy. However, caesarean section is indicated if:
  ① There are symptoms related to an old perineal tear
  ② anorectal ultrasound (external anal sphincter defect is > 30 degrees) or manometry (squeeze pressure < 20 mmHg) is abnormal
- Risk of recurrence is 5-7%
- Risk of worsening of faecal symptoms is 17% particularly in women who had persistent incontinence more than 3 months but less than 6 months of the first delivery

# Caesarean Delivery

## Indications

- **Indications of planned caesarean section (CS):**

  The following are examples of these indications:

  - **Placenta Previa:**

    CS should be performed in the presence of a consultant obstetrician and anaesthetist, an experienced paediatrician, and a senior haematologist. Cross-matched blood and critical care bed should be available

  - **Maternal infection:**
    - **HIV Infection:**
      - CS should be offered to women with HIV infection if not receiving antiretroviral therapy (ART) or if viral load is 400 or more
      - C.S is not indicated in women with HIV infection who receive highly Active Antiretroviral Therapy (HAART) with a viral load less than 400 or any anti-retroviral with viral load less than 50
      - If viral load is 50 – 400 and the patient is not receiving HAART, there is insufficient evidence that CS reduces risk of transmission and the patient should be counselled on delivery plan
    - **Hepatitis B:**

      CS is not indicated as it does not decrease risk of transmission
    - **Hepatitis C:**

      CS is not indicated as it does not decrease risk of transmission unless the patient is infected with both HIV and Hepatitis C. In this case, planned C.S is indicated as it reduces risk of transmission of both infections

- **Primary genital herpes simplex virus (HSV) infection**:
  - CS is indicated in women with primary genital HSV in the third trimester to reduce risk of transmission through the birth canal
  - CS is not routinely offered to women with recurrent HSV at birth

- **Body mass index:**

  The value of body mass index itself is not an indication of CS and vaginal delivery remains superior to surgery if clinically appropriate

- **Preterm labour:**

  C.S should not be offered routinely in cases of preterm labour unless associated with breech presentation

- **Foetal malpresentation:**

  If external cephalic version is unsuccessful or contraindicated, planned CS should be offered to decrease perinatal morbidity and mortality

- **Maternal request:**
  - Women should be offered perinatal mental health support if this request is related to anxiety
  - Women are offered planned CS if they continue to decline vaginal delivery. However, it should be offered at 39 weeks of gestation or beyond since there is increased risk of neonatal respiratory morbidity if CS is done before 39 weeks

- **Indications of unplanned CS:**

- **Breech presentation:**

  If women present with breech presentation in labour, CS is indicated unless delivery is imminent

- **Cephalopelvic disproportion (CPD):**

  There is no good method to predict failure to progress and CPD and the diagnosis is made intrapartum based on clinical assessment and progress of labour

- **Abnormal foetal heart rate pattern:**

  Abnormal foetal heart rate pattern, particularly if associated with abnormal scalp blood parameters, is indicative of unplanned CS unless delivery is imminent

## Prevention

Since CS is associated with short term, long term adverse outcomes and financial burden compared to vaginal delivery. Efforts are made to reduce the need for CS whenever possible

| Factors that reduce the probability of CS | Factors that do not change the probability of CS |
|---|---|
| • Continuous support during labour<br>• Offering induction of labour to women with uncomplicated pregnancy at 41 weeks<br>• Using a 4-hour- partograph<br>• Using foetal blood sampling if foetal heart rate pattern is abnormal<br>• Decision of CS should be taken after consulting an obstetrician | • Walking<br>• Taking non-supine positions during labour<br>• Immersion in water during labour<br>• Epidural anaesthesia during labour<br>• Active management of labour<br>• Early amniotomy<br>• Use of raspberry leaves |

## Preoperative preparation

### Blood transfusion

- Risk of blood loss > 1000 cc is 4-10%
- Haemoglobin assessment, blood typing, cross match, and coagulation screening are considered only in complicated pregnancy or high-risk women but not routinely
- On-site blood transfusion service should be available for high-risk women e.g. antepartum haemorrhage, vaginal birth after CS

### Anesthesia

- Regional anesthesia is superior to general anesthesia whenever feasible (less maternal and neonatal morbidity)
- Before regional anaesthesia, volume preload and IV ephedrine or phenylephrine should be given to decrease the risk of hypotension
  With regional anesthesia, an indwelling catheter should be placed to prevent bladder overdistension
- With general anaesthesia, pre-oxygenation, cricoid pressure, and rapid sequence induction are considered to decrease risk of aspiration

### Medications

- Antacids, proton pump inhibitors, and H2 blockers: to decrease the risk of aspiration
  Antiemetics during CS
- Prophylactic antibiotic: CS Infection risk is 8%
- Administration of antibiotics before (rather than after) incision decreases the risk of infection
- Antibiotics should be broad to cover endometritis, urinary tract infections, and wound infection
- Do not use co-amoxiclav

### Positioning

Women are positioned at a lateral tilt of 15 degrees

### Double gloving

Surgeons should double glove in women with HIV

- **Antenatal steroids:**
  They should be offered to women undergoing planned CS between 37 and 38+6 weeks. Women are counselled on uncertain benefits of reducing neonatal respiratory distress and admission to neonatal intensive care unit versus possible risk of neonatal hypoglycaemia and developmental delay

## CS procedure

| | |
|---|---|
| **Incision** | ▪ Transverse abdominal incision is made (Joel Cohen incision)<br>▪ The incision is straight, 3cm above the symphysis pubis<br>▪ Subsequent layers are opened bluntly (shorter operative time and less postoperative febrile morbidity)<br>▪ If sharp dissection is required, scissors are superior to scalpels. There is no need to change the scalpel after the skin is incised<br>▪ A blunt extension of uterine incision is superior to sharp extension (less blood loss, less postpartum haemorrhage, and need for blood transfusion)<br>▪ Risk of urinary tract injury is 1:1000<br>▪ Oxytocin 5 IU slow IV infusion is given |
| **Delivery** | ▪ Forceps may be used to assist head delivery if indicated<br>▪ The placenta should be removed by controlled cord traction rather than manual removal (lower risk of endometritis)<br>▪ Risk of foetal laceration during CS is 2% |
| **Closure** | ▪ Uterine intraperitoneal repair is recommended compared to exteriorization of the uterus (less pain, no difference in bleeding or infection risk)<br>▪ The uterus is sutured in 2 layers<br>▪ The peritoneum (visceral or parietal) should not be closed (less operative time and need for postoperative analgesia)<br>▪ Subcutaneous closure is only indicated if subcutaneous layer thickness is greater than 2 cm<br>▪ Mass closure is offered to midline incisions using slowly absorbable continuous sutures (lower risk of incisional hernia and dehiscence)<br>▪ Superficial drains are not beneficial and should be avoided |

## Second stage CS (CS at full dilation)

| Maternal risk | Neonatal risks |
|---|---|
| • Maternal intraoperative trauma (Bladder injury, bowel injury, and extension of uterine incision) is twice that of first stage CS (10-27%)<br>• Extension of uterine incision occurs in 25% of cases (risk of 3rd-degree tears with operative delivery is 8%)<br>• Incidence of maternal hemorrhage > 1000 cc is 5-10% compared to 3% with first stage CS or operative delivery<br>• One third of women prefer not to get pregnant again due to psychological trauma (comparable to forceps delivery) | • Risk of severe neonatal trauma is 0.2% vs 0% with first stage CS<br>• Risk of minor trauma is more with operative delivery (22% vs 9% with CS)<br>• Risk of fractured clavicle, brachial plexus injury, and neonatal Intracranial Hemorrhage (ICH) is higher with operative delivery<br>• CS is associated with more admissions to the Special Care Baby Unit (SCBU) due to low APGAR and umbilical pH (11% vs. 6% with operative vaginal deliveries)<br>• Risk of perinatal asphyxia is 11% vs. 8% with first stage CS |

60% of CSs are emergency. Of those, 5% are second stage CSs

| Technique |
|---|
| • Oxytocin should be stopped once the decision is taken. There is no role for muscle relaxants<br>• Joel-Cohen incision with blunt opening of underlying layers<br>• A higher incision in the uterus is preferred<br>• Impacted head delivery can be achieved by:<br>  ▪ Push method: push from below and pull from above while applying equal pressure over the head and flex the head (higher risk of head injury, theoretical risk of infection)<br>  ▪ Pull method: reverse breech extraction by grasping one or 2 feet (risk of extensions, trauma to baby's limbs)<br>  ▪ Patwardhan's method: delivery of shoulders, trunk, breech then the head |

Operative delivery trial that ends in CS is not associated with additional risk of maternal morbidity than immediate CS. However, babies tend to have lower arterial pH

## Postoperative care

- **Neonatal care:**
  - **A skilled provider in resuscitation:** should be available for delivery if general anaesthesia is used or if there is foetal compromise
  - **Thermal care:** as babies delivered by CS tend to have a lower temperature
  - **Early skin-to-skin contact:** should be encouraged
  - **Immediate breastfeeding:** should be supported
  - **Umbilical artery pH:** in all CSs indicated for suspected foetal compromise

- **Observation:**
  - Women should be closely observed by skilled personnel till they regain breathing control, cardiovascular stability, and full consciousness. Need for admission to the intensive care unit is low (> 1%)
  - Following CS, women should be observed for vital signs, pain, and sedation every 30 minutes for 1 hour and then hourly if they are stable
  - Hourly observation of sedation, respiration and pain is indicated in women who received intrathecal opioids. Observation should continue for 12 hours (with diamorphine) or 24 hours (with morphine)
  - Hourly observation of sedation, respiration and pain for 2 hours after discontinuation of epidural opioids or patient controlled analgesia (PCA), if any was used

- **Medications:**
  - Intrathecal diamorphine should be offered to all women intra- or postoperatively to reduce the need for postpartum pain medications
  - Non-steroidal anti-inflammatory drugs should be routinely offered to all women to reduce the need for postpartum opioids

- **Nutrition:**

  Postoperative eating and drinking should be resumed once a woman feels hungry or thirsty

- **Foley's catheter:**

  Remove Foley's catheter once women can ambulate, not less than 12 hours after her last epidural top-up dose

- **Wound care:**
  - Wound dressing can be removed after 24 hours. It can be gently cleaned and dried daily thereafter
  - Women should look for signs of wound infection or dehiscence
  - Loose clothes and cotton underwear are encouraged

- **Hospital stay:**
  - Hospital discharge is typically allowed after 3-4 days following CS (compared to 1-2 days after vaginal delivery). However, early dismissal is allowed if women continue to have to symptoms or complaints after 24 hours
  - During hospital stay, it is recommended that the causes and circumstances of any unplanned CS be explained to women. Also, they should be advised regarding trial of vaginal delivery in the future including the need for continuous electronic fetal monitoring (cEFM) and on-site blood transfusion facilities.
  - Discuss with the patient that CS is not associated with higher risk of difficulty in breastfeeding, depression, dyspareunia, or faecal incontinence

- **Postoperative concerns:**
  - Risk of stress urinary incontinence (4%)
  - Risk of deep venous thrombosis
  - Risk of endometritis (should be considered the most likely cause of post-CS heavy or irregular bleeding)

# Postpartum Haemorrhage

## Definitions

- Primary postpartum haemorrhage (PPH) refers to loss of 500 ml of more of blood from the genital tract within 24 hours of delivery:
  - Minor PPH: loss of 500–1000 ml
  - Major PPH: more than 1000 ml, which is either:
    - moderate PPH: 1001–2000 ml
    - severe PPH: more than 2000 ml

Women with low weight (< 60 kg) or body mass index may be significantly affected by a lower threshold of blood loss

- Secondary PPH refers to abnormal or excessive genital bleeding between 24 hours and 12 weeks postpartum

## Risk factors

| Antenatal risk factors | Intrapartum risk factors |
|---|---|
| Multiple pregnancy | Failure to progress in second stage |
| Previous PPH | Prolonged third stage of labour |
| Pre-eclampsia | Retained placenta |
| Fetal macrosomia | Episiotomy |
| Placenta accreta | Perineal laceration |
| Antenatal anaemia | General anaesthesia |

## Prevention

- **Correction of anaemia:**

  Haemoglobin (Hb) < 110 g/l at first antenatal contact and 105 g/l at 28 weeks should be managed either oral iron (or parenteral iron if not responsive to oral route)

- **Intrapartum measurements:**
  - Uterine massage is not beneficial for prevention of bleeding
  - Prophylactic uterotonics for prevention of PPH:

| | Medications after vaginal delivery | Medications after caesarean section |
|---|---|---|
| **Average risk of PPH** | oxytocin (10 iu intramuscular) | oxytocin (5 iu intravenous) |
| **Higher risk of PPH** | Ergometrine–oxytocin (if there is no history of hypertension) | Tranexamic acid + oxytocin |

## Treatment

- **Management outlines:**

| Minor PPH (500-1000 mL without shock) | Major PPH (> 1000 mL, shock, continuous bleed) |
|---|---|
| ▪ Intravenous access<br>▪ Urgent venepuncture (20 ml) for:<br>□ Group and screen<br>□ Full blood count<br>□ Coagulation screen<br>▪ Clinical assessment every 15 minutes (pulse, respiratory rate and blood pressure)<br>▪ Warmed crystalloid infusion. | ▪ Assess airway and breathing and circulation (A, B, C)<br>▪ Keep the patient warm, and in a flat position<br>▪ Immediate blood transfusion<br>▪ Intravenous transfusion of up to 3.5 litres of warmed clear fluids (Crystalloid: Up to 2 L isotonic crystalloid, colloids: up to 1.5 L colloid) until blood arrives<br>▪ Avoid blood filters and hydroxyethyl starch |

- **Replacement therapy:**
  - **Blood Transfusion:**
    - **Indication:**

      Decision of transfusion is made based on clinical and haematological assessment
    - **Type of transfused blood:**

      If need for blood is urgent, immediate transfusion of group O, rhesus D (RhD)-negative and K-negative units should be conducted. Switch to the group-specific blood as soon as feasible

      Intraoperative cell salvage is a valid option particularly in women who refuse blood transfusion

  - **Fresh frozen plasma (FFP):**
    - **Indications:**
      - Clinical indications (if no haemostatic results are available):

        ① after 4 units of packed RBCs (12–15 ml/kg of FFP)

        ② Suspected coagulopathy, such as placental abruption or amniotic fluid embolism

        ③ Delayed detection of PPH
      - Haematological indication:

        If PT/aPTT is more than 1.5 times the normal with ongoing bleeding
    - **Transfused volume:**

      12-15 ml/kg

  - **Fibrinogen**
    - Cryoprecipitate is given to replace fibrinogen
    - Replacement should maintain fibrinogen level ≥ 2 g/l

  - **Platelets:**
    - Platelet transfusion is indicated if platelet count ≤ 75 x$10^9$/l
    - Consider Tranexamic acid

- **Medical management of atonic PPH:**
  - Uterine massage
  - Empty the bladder (with a Foley catheter)

- Oxytocin 5 iu by slow intravenous injection (repeat dose)
- Ergometrine 0.5 mg by slow intravenous or intramuscular injection (unless there is history of hypertension)
- Oxytocin infusion (40 iu in 500 ml isotonic crystalloids at 125 ml/hour)
- Carboprost 0.25 mg by intramuscular injection max 8 doses 15 min apart (contraindicated in patients with asthma)
- Misoprostol 800 micrograms sublingually.

- **Surgical management:**
  - Intrauterine balloon tamponade (1st line in women with atonic PPH)
  - Conservative surgical methods (brace sutures e.g., B-Lynch sutures)
  - hysterectomy sooner rather than later (Two seniors' decision)

**Management of major PPH**

- Multidisciplinary team management (laboratory specialists, consultant obstetrician and consultant anaesthetists, an experienced midwife, the obstetric middle grade, the anaesthetic middle grade)
- Cross-matched blood (4 units minimum)
- Labs (full blood count, coagulation screen, including fibrinogen
- renal and liver function for baseline)
- Clinical monitoring (temperature every 15 minutes, continuous pulse, blood pressure recording and respiratory rate using oximeter)
- Electrocardiogram and automated blood pressure recording
- Foley catheter to monitor urine output
- Two peripheral cannulae, 14 gauge
- Arterial line monitoring.
- Fluid chart recording

## Secondary PPH

- The most common causes are endometritis, retained products of conception and subinvolution of the placental implantation site
- Management includes:
  - Endocervical swab
  - Consider antibiotics if endometritis is suspected (gentamycin and clindamycin)
  - A pelvic ultrasound to exclude retained products of conception
  - Surgical evacuation of retained placental (by a senior obstetrician)

# Maternal Collapse

## Epidemiology

- Incidence of maternal mortality is 7/100.000 (0.07/1000)
- Incidence of maternal morbidity rate is 6/1000

## Causes

| | |
|---|---|
| **Haemorrhage** | • The most common cause of maternal collapse (6:1000)<br>• Common causes of maternal haemorrhage include antepartum haemorrhage, postpartum haemorrhage, and ruptured ectopic pregnancy |
| **Thromboembolism** | • The most common cause of of direct maternal death e.g. pulmonary embolism, cerebral vein thrombosis |
| **Amniotic fluid embolism** | • **Incidence:** it is approximately 2:100.000, may occur during labor, birth or within 30 minutes postpartum<br>• **Clinical presentation:** It presents with acute hypotension, respiratory distress, acute hypoxia, seizures and cardiac arrest (diagnosis is mainly clinical)<br>• **Complications:** disseminated intravascular coagulopathy (DIC), left ventricular failure, and foetal distress if not delivered<br>• **Maternal outcomes:** survival rate is 80%, neurological morbidity is common<br>• **Perinatal mortality:** 6.7% |
| **Cardiac disease** | • The most common cause of indirect maternal deaths. Incidence of Primary cardiac arrest is 1:30.000 |

| | |
|---|---|
| | • The most common causes of death are myocardial infarction, arrhythmias, aortic dissection and cardiomyopathy<br>• Clinical presentation includes chest pain, interscapular pain, wide pulse pressure and new cardiac murmurs |
| **Sepsis** | • The most common causative organisms are group A streptococci (GAS), group A streptococci (GBS), enterococci, pneumococci and E. Coli |
| **Drug toxicity** | • Examples include illicit drug overdose, magnesium sulphate toxicity, accidental intravenous injection of anesthetic agents, total/high spinal block(rare)<br>• Clinical presentation includes sudden loss of consciousness, cardio-vascular collapse, and seizures |
| **Eclampsia** | • Convulsions should be accompanied by features or known diagnosis of preeclampsia |
| **Intracranial haemorrhage** | • It is characterized by severe headache followed by collapse<br>• Common causes include severe hypertension, ruptured aneurysms and arteriovenous malformation |
| **Anaphylaxis** | • Incidence is (0.01 to 0.35/1000<br>• Mortality rate is 1%<br>• It is characterized by sudden and rapid progression, airway, breathing and/or circulatory symptoms, and skin changes e.g. flushing, angioedema, urticaria.<br>• Mast cell tryptase may help diagnosis in unclear cases |

Other causes of collapse include tamponade, pneumothorax, air way obstruction, hypoglycaemia, and hyponatraemia

## Challenges to diagnosis

- During pregnancy, early warning score (EWS) is not useful due to physiologic changes during pregnancy
- Modified Early Warning Scores (MEWS systems) are not highly effective. However, their use is recommended by NICE and MBRRACE-UK
- The National Early Warning Score 2 (NEWS2) is endorsed by National Health Service (NHS) England. However, it is recommendend for only women who are less than 20 weeks pregnant

## Challenging to resuscitation

Physiologic changes during pregnancy tend to make resuscitation more challenging, and to accelerate hypoxia, acidosis, and blood loss

### Physiologic changes during pregnancy

- Plasma volume: increases by 50% (oxygen carrying capacity decreases)
- Heart rate increases by 15-20 beats/min, and cardiac output increases by 40%
- Uterine blood flow is approximately 10% of cardiac output at term
- Blood pressure decreases by 10-15 mmHg with decrease in vascular resistance, and venous return
- O2 consumption increases by 20%, residual capacity decreases by 25%, respiratory rate increases, laryngeal oedema increases, and PaCO2 decreases
- Gastric motility decreases (which increases risk of aspiration), and oesophageal sphincter relaxes

- Aortocaval compression by the gravid uterus after 20 weeks decreases cardiac output by 30-40% and causes supine hypotension. Left lateral position should be adopted to eliminate this effect
- Chest compression achieves only 3% of cardiac output compared to 30% in non-pregnant women
- Hypoxia is more readily in pregnant women (higher oxygen consumption and respiratory rate, higher tidal volume and minute ventilation), and lower residual capacity)
- Difficult intubation due to laryngeal oedema and weight gain
- Aspiration risk is increased due to relaxation of oesophageal sphincter, delayed gastric emptying, and high intraabdominal pressure.
  Early intubation and prophylactic $H_2$ blockers are recommended
- Hyperdynamic circulation with rapid blood loss. Blood loss is less tolerated less due to pre-existing maternal anaemia

## Management

- **Initial management:**

| | |
|---|---|
| **Airway** | ▪ Airways should be secured with intubation as soon as possible<br>▪ A bag and mask ventilation should be conducted until intubation is available<br>▪ Supraglottic devices should be avoided (risk of aspiration)<br>▪ Waveform capnography is required to monitor tracheal tube placement<br>▪ Supplemental oxygen with a flow of 10–15 litre per minute is delivered |
| **Positioning** | ▪ Patients are positioned at a left lateral tilt (15-30°) on firm surface. Pillows are less effective<br>▪ The uterus may be displaced by kneeling or manual displacement to the left (up, off and over' method) if titling is not possible |
| **Chest compression** | ▪ Chest compression is applied immediately if breathing is absent and airways are clear<br>▪ The rate of chest compression is:<br>□ 30:2 ventilation<br>□ 100 compression/minutes and ventilation 10/minutes if intubated<br>▪ If cardiopulmonary resuscitation (CPR) is not effective within 4 minutes, delivery should be pursued |
| **Defibrillation** | ▪ If indicated, the same energy is utilized. Adhesive defibrillator pads are used with the left pad placed lateral to left breast.<br>▪ Uterine monitor transducers should be removed<br>▪ Defibrillation is safe to the baby<br>The same drugs and doses, used for CPR, are used in pregnant women |
| **Evaluation** | ▪ Bedside abdominal ultrasound should be performed if there is suspicion of intraabdominal or intrauterine haemorrhage |
| **IV access** | ▪ Two wide bore cannulas should be placed<br>▪ If peripheral venous access is not possible, central venous access, intraosseous access or venous cutdown should be considered |
| **Perimortem caesarean section** | ▪ It is indicated if there is no response to CPR within 4 mins of collapse or if CPR continues beyond 4 mins<br>▪ Delivery should be performed within 5 mins in the same site where resuscitation is done with the fastest approach |

- **Continued management:**

Patients are transferred to a high dependency unit under close supervision

| | |
|---|---|
| **Amniotic fluid embolism** | ▪ Inotropic medications (to prevent volume overload)<br>▪ Aggressive transfusion of fresh frozen plasma to prevent DIC. Recombinant factor VII should only be used if coagulopathy cannot be corrected<br>▪ Supportive management e.g. oxygen supplementation |
| **Cardiac disease** | ▪ Thrombolysis should be given to patients with coronary insufficiency (regardless of risk of placental bleeding)<br>▪ Percutaneous angioplasty is the best approach if readily available |
| **Sepsis** | ▪ Please refer to "Chapter 6: Bacterial sepsis in pregnancy" |
| **MgSO4 toxicity** | ▪ 10 ml of calcium gluconate (10%) given slowly intravenous |
| **Local anaesthetic toxicity** | ▪ Injection should be stopped immediately<br>▪ Intralipid 20% 1.5 ml/kg is given over 1 min followed by intralipid 20% 0.25ml/kg/min<br>▪ Arrythmias should be treated per protocol |
| **Anaphylaxis** | ▪ In addition to resuscitative measures, adrenaline 0.5 ml 1:1000 (intramuscular) or 0.5 ml 1:10.000 (intravenous)<br>▪ Chlorphenamine and steroids may be considered |

## Prognosis

Rate of survival is 65% if the cause of collapse is reversible

# Blodd Transfusion in Obstetrics

## Blood products

| Product | Indication and dosage | Target | Need for anti-D |
|---|---|---|---|
| **Packed red blood cells (RBCs)** | • The decision of transfusion and initial amount transfused is determined by clinical and haematological status of the patient<br>• Women with haemoglobin < 60 g/l should typically receive transfusion. Women with haemoglobin above > 100 g/l rarely requires transfusion<br>• In stable women with no active bleeding and with a haemoglobin less than 70 g/l, decision of transfusion should be made based on current symptoms and medical history<br>• During pregnancy, women should receive cytomegalovirus (CMV) seronegative blood. Any woman in her reproductive years should receive K antigen negative blood<br>• If blood type is unknown, O- Rh- blood should be given if there is emergency | Haemoglobin should at least rise above 7 g/l in a stable patient with no active bleeding | Rh negative women should receive Rh negative blood. Rh negative women who receive Rh positive blood for emergency situation should be managed by exchange transfusion |

| | | | |
|---|---|---|---|
| **Fresh frozen plasma (FFP)** | • It is given at a dose of 12-15 ml/kg every 6 units of transfused packed RBCs<br>• FFP of same blood group is recommended. However, if not available, any blood group can be used (if there is no high titre of anti-A or B)<br>• In most units, FFP is not virally inactivated (small risk of infection transmission) | Further transfusion of FFP is determined by blood results to achieve a target aPTT and PT < 1.5 of normal | No anti-D is required |
| **Cryo-precipitate** | Two 5-unit pools should be given early in major bleeding | Further dosage depends on fibrinogen level. Target fibrinogen is > 1.5 g/L. No anti-D needed | No anti-D is required |
| **Platelet concentrate** | • Platelet transfusion is indicated if platelet count is below 75.000/μL<br>• Transfused platelets should be group compatible include Rh status. ABO incompatibility may be acceptable if compatible group is not available (this is associated with less platelet increase; however, it should not be clinically significant)<br>• Do not give platelets through a set previously used for blood | Target Platelet count is above 50.000/μL. | If Rh-positive platelets were transfused, give anti-D antibodies at a dose of 250 iu (it should cover 5 units within 6 weeks) |

## Other treatment options

- **Factor VIIa:**
  It may be considered if available. Risk of thrombotic events with this treatment is 2.5%

- **Fibrinogen concentrate:**
  It is an experimental option and should not be used in clinical setting

- **Tranexamic acid (anti-fibrinolytic):**
  It is recommended in women with major bleeding

- **Cell salvage:**
  - It may be considered if anticipated blood loss is greater than 20% of total volume. A consent is necessary
  - After reinfusion, a dose of anti-D immunoglobulin (1500 iu) is indicated. Then, foeto-maternal haemorrhage is assessed 30-40 minutes after transfusion to determine further dosage
  - Predelivery autologous blood transfusion is not recommended

## Antenatal considerations

- **Patient consent:**
  - A Consent for transfusion of blood products should be obtained in high risk women. Refusal should be documented
  - If no consent was previously obtained and transfusion is indicated in emergency setting, information should be provided to the patient retrospectively

- **Antenatal labs:**
  - Group and screen is indicated at booking and at 28 weeks of pregnancy
  - In women at high risk of transfusion, group and screen should be repeated weekly. It should be valid for transfusion within 3 days

- In the presence of significant alloantibodies, group and screen should be performed every 3 days

## Intrapartum management

### Abstract

Management of labour presents the last stage and the most crucial part of antenatal care. Intrapartum management comprises conjugated care of 2 patients, with possible antenatal risk factors during pregnancy and potential risk factors that may rise during labour. Intrapartum factors participate the most to maternal and neonatal outcomes. In this chapter, we will discuss intrapartum care protocols and management of intrapartum and immediate postpartum events.

### Keywords

Intrapartum management, breech, perineal tear, postpartum haemorrhage

### Further readings

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# Thromboprophylaxis in Pregnancy and Puerperium

## Risk assessment

Risk factors for venous thromboembolism (VTE) in pregnancy and the puerperium are:

| | |
|---|---|
| **Pre-existing factors** | • Thrombophilia<br>• Medical comorbidities:<br>  ▪ Heart or lung disease<br>  ▪ Systemic lupus erythematous (SLE)<br>  ▪ Cancer<br>  ▪ Inflammatory conditions (inflammatory bowel disease or inflammatory poly arthropathy)<br>  ▪ Nephrotic syndrome (proteinuria > 3 g/day)<br>  ▪ Sickle cell disease<br>  ▪ Intravenous drug users<br>• Age > 35 years<br>• Body mass index [BMI] > 30 kg/m$^2$ as baseline or in early pregnancy<br>• Parity ≥ 3<br>• Smoking<br>• Gross varicose veins:<br>  ▪ Symptomatic<br>  ▪ Above the knee<br>  ▪ Associated phlebitis<br>  ▪ Oedema/skin changes<br>• Paraplegia |
| **Obstetric factors** | • Multiple pregnancy<br>• Assisted reproductive technology (ART)<br>• Pre-eclampsia<br>• Caesarean section |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_3

| | |
|---|---|
| | • Prolonged labour<br>• Mid-cavity rotational operative delivery<br>• Postpartum haemorrhage (> 1 litre) requiring transfusion |
| **New onset/transient factors** | • Surgical procedure in pregnancy or puerperium<br>• Hyperemesis and dehydration<br>• Ovarian hyperstimulation syndrome<br>• Admission or immobility<br>• Systemic infection (requiring antibiotics or hospital admission)<br>• Postpartum wound infection |

## Antepartum management

| Classification | Indications | Management |
|---|---|---|
| **High risk** | Previous VTE, not associated with major surgery | Antenatal low molecular weight heparin (LMWH) |
| **Intermediate risk** | • Previous VTE associated with surgery OR<br>• High risk thrombophilia OR<br>• Hospital admission OR<br>• Ovarian hyperstimulation syndrome OR Surgery (appendectomy) OR<br>• Medical co-morbidity (see before) | Antenatal low molecular weight heparin (LMWH)<br>If previous VTE is associated with major surgery with no additional risk, LMWH may start at 28 weeks |
| **Low risk** | • Age > 35 years<br>• Parity ≥ 3<br>• Smoker<br>• BMI > 30<br>• Pre-eclampsia<br>• Multiple pregnancy<br>• ART<br>• Low risk thrombophilia<br>• Asymptomatic antiphospholipid syndrome (APA) or persistent antibodies<br>• Gross varicose veins<br>• Family history of VTE in the first degree<br>• Immobility | • If there are 4 or more factors are present, antenatal LMWH is given + 6 weeks postpartum<br>• If 3 factors are present, prophylaxis starts from 28 weeks + 6 week postpartum<br>• If 2 factors are present, antenatal LMWH is not indicated and is given for 10 days postpartum |

## Previous VTE

- If VTE was not associated with major surgery, LMWH is given antenatally
- Antepartum LMWH should start once pregnancy test is positive. If on warfarin, women should shift to LMWH immediately (best if women shift within 2 weeks of missed period and before 6 weeks of pregnancy)
- If previous VTE is associated with anti-thrombin deficiency:
  - Antenatal LMWH (50%, 75% or full therapeutic dose) is given
  - Anti-Xa should be monitored (target is 0.5-1.0 at 4-hour peak)
  - Antithrombin replacement may be considered at onset of labour or before caesarean section
- If previous VTE is associated with lower risk hereditary thrombophilia, standard prophylaxis is used and continued postpartum for 6 weeks
- If previous VTE is associated with APA syndrome, antenatal and 6 weeks of postpartum thromboprophylaxis are indicated

If persistent antiphospholipid antibodies are present without previous VTE or other risk factors, close antenatal observation and LMWH for 7 days postpartum is enough

- If previous VTE is related to major surgery, LMWH may be considered starting at 28 weeks of gestation

## Screening for thrombophilia

- If there is family history of anti-thrombin deficiency or unknown thrombophilia, screen for Anti-thrombin deficiency
- If there is family history of a first degree relative with unprovoked or estrogen provoked VTE at a young age (< 50 years), screen for thrombophilias
- In women with prior unprovoked VTE, screen for APA

## Asymptomatic inherited thrombophilia

- Women with asymptomatic antithrombin, protein C or S deficiency or more than one defect should be offered antenatal LMWH and for 6 weeks postpartum.
- Other types are considered low risk thrombophilia and are managed accordingly

## Intrapartum management

- Patients should stop their injections once they start feeling contractions
- No regional anaesthesia should be used within 12 hours of a prophylactic dose or within 24 hours of a therapeutic dose
- Epidural catheter should not be removed within 12 hours of the last LMWH dose
- LMWH should not be given within 4 hours of spinal catheter removal
- If there is no risk of bleeding, start LMWH immediately after delivery. Otherwise, pneumatic compression devices, anti-embolism stocking should be considered. Unfractionated heparin (UFH) may be used if the risk of bleeding is high

## Postpartum management

| Risk factors | Duration of thromboprophylaxis |
|---|---|
| **2 or more minor risk factors *** | 10 days postpartum |
| **BMI greater than 40** | 10 days postpartum |
| **Previous VTE** | 6 weeks postpartum |
| **Asymptomatic thrombophilia with family history of VTE** | 6 weeks postpartum |
| **Caesarean section in labour** | 10 days postpartum |
| **Medical comorbidities** | 10 days postpartum |

* Minor risk factors include age > 35, BMI > 30, parity > 30, smoking, low risk thrombophilia, family history of VTE, gross varicose veins, pre-eclampsia, multiple pregnancy, immobility, current systemic infection, stillbirth, prolonged labor more 24 hours, elective caesarean delivery, operative delivery, Post-partum hemorrhage more than 1000 cc

## Medication profile

### Contraindication/cautions to heparin

- known bleeding disorders, active bleeding, high risk of major haemorrhage (e.g. placenta praevia), platelets count < 75,000/microlitre of blood
- Acute stroke in last 4 weeks,
- Severe liver disease
- Severe renal disease
- Uncontrolled Hypertension (> 200/120)

| Drug | Profile |
|---|---|
| **LMWH** | • Safe in pregnancy and breastfeeding<br>• Dose is based on booking appointment body weight<br>• Dose should be decreased if there is renal impairment<br>• Anti-Xa and platelet monitoring are not indicated |
| **UFH** | • It is used only if there is high risk of bleeding or if regional anaesthesia may be required<br>• Platelet count should be monitored every 2-3 days from day 4-14 or until heparin stops |
| **Fondaparinux (factor Xa inhibitor)** | • It may be used as a last option if heparin is not tolerated after consultation of a haematologist |
| **Warfarin** | • Not used in pregnancy. Few exceptions may be present including mechanical valves<br>• After delivery, warfarin may be resumed at day 5-7<br>• Safe with breastfeeding |
| **Dextran** | • It should be avoided in pregnancy and labour |
| **Aspirin** | • There is no role for aspirin in venous thromboprophylaxis |
| **Oral anticoagulants (non-vitamin K antagonist** | • They should be avoided in pregnancy and breast feeding |

# Postpartum Genital Hematomas

| | |
|---|---|
| **Background** | • 1 in 700 deliveries may have clinically significant hematomas<br>• Incidence of surgical intervention is 1 in 1000 deliveries |
| **Risk factors** | • Nulliparity<br>• Prolonged 2nd stage of labour<br>• Instrumental delivery<br>• Baby weight > 4 kg<br>• Genital tract varicosities<br>• Maternal age ≥ 30 |
| **Aetiology** | More than 80% are associated with repaired perineal tears or episiotomies |
| **Classifications** | • Classification according to relation to levator muscle:<br>▪ Supra-levator<br>▪ Infra-levator<br>• Classification according to position:<br>▪ Valval (infralevator)<br>▪ Vulvovaginal (infralevator)<br>▪ Paravaginal (infralevator)<br>▪ Sub peritoneal (supralevator) |
| **Management** | • Small hematomas < 5cm are typically treated conservatively<br>• Large hematomas require surgical evacuation<br>• Supralevator hematomas may require artery ligation or artery embolization (interventional radiology) to stop bleeding if surgical intervention is not sufficient |

| | Vulval and vulvovaginal Type | Paravaginal type | Supralevator/ Supravaginal or subperitoneal type |
|---|---|---|---|
| **Origin** | • It results from injury to branches of the pudendal artery<br>• Valval hematoma is limited by anterior urogenital diaphragm whereas vulvovaginal extends into paravaginal tissues | • It results from injury to the uterine artery<br>• It is bounded inferiorly by pelvic diaphragm and superiorly by the cardinal ligament | • It results from injury to the uterine artery in the broad ligament.<br>• Haematoma may dissect into the retroperitoneal space |
| **Clinical signs** | It is typically visible as vulval bulging | It is not obvious externally but evident on vaginal examination | It is not necessarily evident on examination and it may be seen bulging into upper vagina (some class those bulging into upper vagina as paravaginal) |

# Postpartum Psychosis

## Background

Postpartum psychosis is a severe psychiatric disorder that may develop shortly after birth, and manifests by mania, severe depression, hallucinations, delusions and confusion

## Incidence

- 1-2 per 1000 births
- Postpartum suicide is rare (1 in 100,000 pregnancies)

## Risk factors

50% of women who develop postpartum psychosis report no risk factors

- Women with bipolar disorder are at increased risk (25%)
- Women with bipolar disorder and personal or family history of postpartum psychosis (50%)
- Primiparity is another risk factor

## Preconception counselling

- Risk factors of postpartum psychosis should be identified and discussed prospectively
- Pre-conception counselling is best conducted by a perinatal psychiatrist

## Clinical presentation

- Baby blues are common (30-80% of births), and are characterised by transient emotional liability during the first postpartum week
- Psychotic symptoms differentiate postpartum psychosis from baby blues
- Symptoms of postpartum psychosis develop within 1-3 days postpartum in 50% of women. Most cases are diagnosed within 2 weeks of delivery
- High risk women should be followed-up for at least 3 months

## Management

- Patients should be admitted. A psychiatric team should be involved in treatment decision
- Safeguarding team may be involved to control the risk of child neglect or infanticide

# Postpartum care

## Abstract

Care after delivery is the least recognized part of obstetric care. This is unfortunate since pregnancy-related changes take 6-12 weeks to reverse, and during this period, such changes may increase the risk of some complications such as venous thromboembolism. Postpartum care may also include postoperative care if operative delivery was indicated, which brings other elements of care to traditional postpartum care. In this chapter, we will discuss common postpartum problems, their diagnosis, management, and prevention.

## Keywords

Haematoma, psychosis, thromboembolism

## Further readings

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# PART II

## Obstetrics: Complications of early pregnancy

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# Early Pregnancy Loss

## Background

- An early pregnancy assessment service (EPAS) should be available 7 days a week, and is responsible for diagnosing and caring for women with pain and/or bleeding in early pregnancy
- EPAS offer:
  - Early ultrasound
  - Assessment of hCG
  - Trained health professionals who can be involved sensitive discussions and delivering bad news
- EPAS accepts self-referrals of women with recurrent miscarriage or a previous ectopic or molar pregnancy

## Warning features

Warning symptoms and signs that may indicate ectopic pregnancy in early pregnancy include:

| | Symptoms | Signs |
|---|---|---|
| **Common** | Abdominal or pelvic pain, missed period, and vaginal bleeding | Pelvic tenderness, adnexal tenderness, and abdominal tenderness |
| **Others** | Breast tenderness, gastrointestinal symptoms, dizziness, fainting or syncope, shoulder tip pain, rectal pressure or pain on defecation | Cervical motion tenderness, rebound tenderness or peritoneal signs, pallor, abdominal distension, enlarged uterus, tachycardia or hypotension including orthostatic hypotension, and collapse |

One third of women with ectopic pregnancy has no known risk factors




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_4

## Referral to EPAS

| Immediate referral to EPAS | Routine referral to EPAS |
|---|---|
| Refer immediately to early pregnancy assessment service (or out-of-hours gynaecology service) if there is:<br>• Positive pregnancy test PLUS<br>• Pain and abdominal tenderness or pelvic tenderness or cervical motion tenderness | Refer to an early pregnancy assessment service (or out-of-hours gynaecology service) if:<br>• Women with bleeding and pain OR<br>• Pregnancy of 6 weeks' gestation or more OR<br>• Pregnancy of uncertain gestational age |

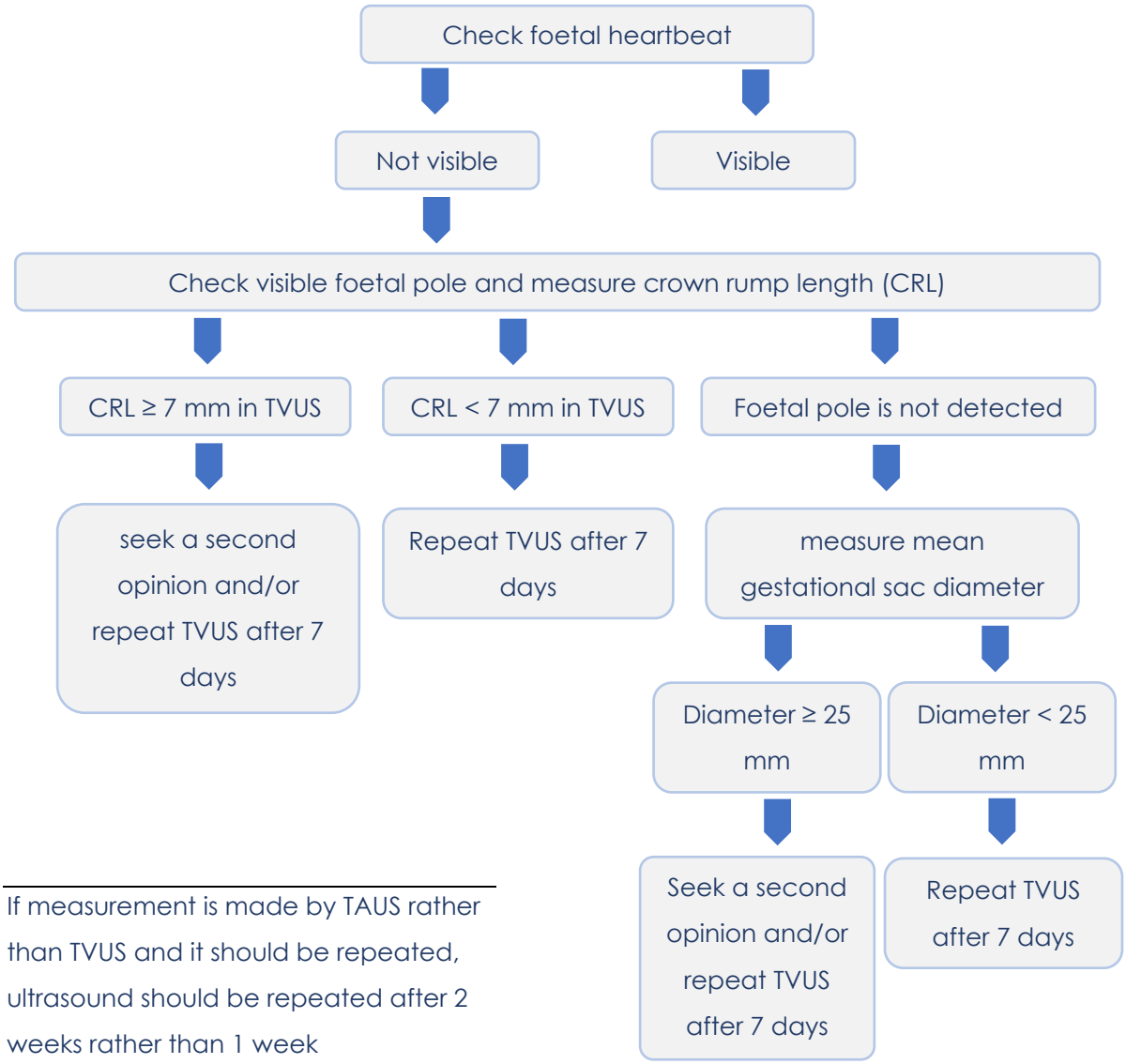
## Assessment of early symptoms

- **Observation:**

  Some symptomatic women may not need further assessment and can be expectantly managed

  - **Indications:**
    - If women present with bleeding AND
    - There is NO pain AND
    - They are less than < 6 weeks' pregnant AND
    - There are no risk factors (e.g. previous ectopic pregnancy)
  - **Outcomes:**
    - Women should return if bleeding continues or pain develops
    - Women should repeat a urine pregnancy test after 7–10 days. If positive, they should return for assessment
    - If symptoms and signs are getting worse, referral to EPAS immediately or within 24 hours

- **Ultrasound assessment:**
  - **Ultrasound method:**
    - Transvaginal ultrasound (TVUS) is the standard approach to determine pregnancy location, visualization of foetal pole and heartbeat
    - Transabdominal ultrasound (TAUS) is considered if:
      ① Uterus is enlarged, there are fibroids or ovarian cyst
      ② If TVUS is declines
  - **Ultrasound interpretation:**
    - A single ultrasound examination is not 100% accurate at very early gestational ages




If measurement is made by TAUS rather than TVUS and it should be repeated, ultrasound should be repeated after 2 weeks rather than 1 week

- Gestational age calculated from last menstrual period should not be used to determine foetal heart rate visibility
- When diagnosing complete miscarriage on TVUS while there was no previous scan that showed intrauterine pregnancy (IUP), possibility of a pregnancy of unknown location should be considered

| Sonographic findings related to ectopic pregnancy | |
|---|---|
| **Diagnostic signs in US** | Adnexal mass, moving separate to the ovary, comprising a gestational sac, containing a yolk sac or an adnexal mass, moving separately to the ovary, comprising a gestational sac and foetal pole |
| **Suggestive signs in US (high probability)** | • Adnexal mass, moving separately to the ovary, with empty gestational sac ('tubal ring' or 'bagel sign') or<br>• Complex, inhomogeneous adnexal mass, moving separate to the ovary |
| **Possible ectopic on US** | An empty uterus or pseudo-sac |

If suggestive or possible features are present, other intrauterine and adnexal features, clinical presentation and serum hCG levels should be assessed before making a diagnosis

- **Serum hCG:**
  - Serum hCG is used to determine subsequent management rather than to make a diagnosis
  - Serum hCG is checked 48 hours apart to determine management. Further checks should be decided by a senior healthcare professional:
    - If Serum hCG increases > 63% after 48 hours:
      - Pregnancy is likely IUP. Possibility of ectopic cannot be excluded
      - Offer TVUS 7-14 days later (or earlier if serum hCG ≥ 1500 IU/L). If viable IUP cannot be confirmed on a repeat US, refer for immediate clinical review by a senior gynaecologist
    - If serum hCG decreases by > 50% after 48 hours:
      - Pregnancy is unlikely to continue but that this conclusion is not confirmed

- Women should take a urine pregnancy test 14 days. If negative, no further action is required. If positive, return to the EPAS within 24 hours

□ If hCG levels decreases < 50%, or increase < 63%: refer for clinical review in the EPAS within 24 hours

## Management of miscarriage

- **Threatened miscarriage:**

Women with vaginal bleeding, IUP and visible foetal heartbeat should be observed:

- If bleeding gets worse, or persists for more than 14 days, reassessment is required
- If bleeding stops, start or continue antenatal care

- **Missed miscarriage:**
  - **Expectant management:**
    - □ Method:
      - Expectant management of miscarriage for 7 to 14 days can be the first line. In most women, no further treatment is required
      - If resolution of bleeding/pain occurs within 7 to 14 days, advise women to take urine pregnancy test after 3 weeks, and return for individualised care if positive
      - If bleeding/pain has not started or is persistent, offer a repeat TVUS scan
      - Women may choose to continue expectant management after 14 days after reviewing
    - □ Contraindications:

      ① High risk of haemorrhage (late first trimester, coagulopathies)

      ② Women who are unable to receive blood transfusion if needed

      ③ Previous adverse and/or traumatic experience

      ④ Evidence of infection

  - **Medical management:**
    - □ Indication: it should be offered if expectant management is declined
    - □ Method:
      - Offer vaginal misoprostol (oral route is also acceptable), using a single dose of 800 mcg (600-800 mcg if incomplete miscarriage), mifepristone should not be offered.

- If bleeding does not start within 24 hours, she should contact her healthcare professional to determine future management
- Side effects of treatment include pain, diarrhoea and vomiting. Offer women analgesics and anti-emetics during the period of treatment
- After medical management is complete, a urine pregnancy test is done after 3 weeks. If it is still positive, she should contact her health care professional
- Women should contact her provider if she experiences worsening symptoms

- **Surgical management:**

  Manual vacuum aspiration under local anaesthesia in an outpatient or clinic setting or Dilation and curettage in a theatre under general anaesthesia

## Management of ectopic pregnancy

- **Expectant management:**
  - **Candidates:**

| | |
|---|---|
| **Offer expectant management** | • Clinically stable and pain free women<br>• Ectopic sac < 35 mm with no heartbeat<br>• Serum hCG < 1,000 IU/L |
| **Consider expectant management** | • Clinically stable and pain free women<br>• Ectopic sac < 35 mm with no heartbeat<br>• Serum hCG between 1,000 and 1,500 IU/L |

  - **Method:**
    - hCG levels should be treated on days 2, 4 and 7 after the baseline test
    - If hCG drops ≥ 15% on days 2, 4, 7, repeat hCG weekly until it is negative (< 20 IU/L) or
    - If hCG level does not drop, senior advice is required
  - **Outcomes:**

    In properly selected patients, expectant management is comparable to medical treatment in success rate, risk of tubal rupture, time for ectopic pregnancy to resolve, and future fertility

- **Medical management:**
  - **Candidates:**

| | |
|---|---|
| **Offer systemic methotrexate** | • No significant pain<br>• Unruptured ectopic pregnancy<br>• Ectopic mass < 35 mm<br>• No heartbeat<br>• Serum hCG < 1,500 IU/L<br>• no intrauterine pregnancy<br>• Compliance |
| **Offer methotrexate or surgery** | • Serum hCG is 1,500-5000 IU/L<br>• Compliance<br>• No significant pain<br>• Unruptured ectopic pregnancy<br>• Adnexal mass < 35 mm<br>• No visible heartbeat<br>• No intrauterine pregnancy |

Methotrexate is not offered in the first visit unless ectopic pregnancy is definitely diagnosed and intrauterine pregnancy excluded

  - **Method:**
    - IM methotrexate, after assessment of baseline labs, is given
    - B-hCG is checked at day 1, days 4 and 7, then weekly until it is negative

- **Surgical management:**
  - **Candidates:**

① Patients cannot return for follow-up treatment
② Significant pain
③ Adnexal mass ≥ 35 mm
④ visible foetal heart rate
⑤ Serum hCG ≥ 5,000 IU/L

- **Method:**

  Laparoscopy is the standard approach

| | Indication | Follow-up |
|---|---|---|
| **Salpingectomy** | It is the standard management | Urine pregnancy test after 3 weeks |
| **Salpingotomy** | It is indicated if risk factors for infertility are present e.g. contralateral tube damage | Serum hCG after 7 days, then weekly until negative<br>up to 1 in 5 women (20%) may need further treatment (methotrexate and/or a salpingectomy) |

- **Anti-D immunoglobulins:**
  - Anti-D: 250 IU (50 micrograms) is given after surgical procedure for ectopic pregnancy or miscarriage
  - Do not offer anti-D rhesus prophylaxis to women who:
    - Received only medical management for ectopic pregnancy or miscarriage or
    - Have threatened miscarriage
    - Have spontaneous complete miscarriage
    - Have a pregnancy of unknown location
  - Do not use a Kleihauer test for quantifying foeto-maternal haemorrhage regardless of the indication

# Ectopic Pregnancy

## Incidence

- Overall incidence is 11:1000 (approximately 1%)
- Incidence of ectopic pregnancy in early pregnancy clinic is 2-3 %
- Incidence of caesarean scar pregnancy is 1:2000

## Risk factors

- IN-vitro fertilization (IVF)
- Previous pelvic surgery
- Previous pelvic infection
- Smoking

Majority of cases have no risk factors

## Diagnosis

**General**

| Ultrasound | Laboratory tests | |
|---|---|---|
| | Progesterone | HCG |
| Ectopic pregnancy appears as an adnexal mass that moves separate to the ovary. For tubal pregnancy, this mass can be:<br>• An adnexal gestational sac (foetal pole, yolk sac): a diagnostic sign<br>• Inhomogeneous mass or an empty sac: a suggestive sign<br>• If there is an empty uterus or a pseudosac: a possible sign | It has no role and should be used | • It should not be used in diagnosis<br>• It is used to determine future management<br>• A single value is prognostic of success of non-surgical treatment |

TVUS

Sensitivity: 88-99 %

Specificity: 94-100 %

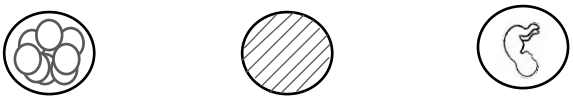
Findings

Ectopic (most commonly)

PUL (less commonly)

Adnexal mass

| Heterogenous mass | Empty sac | Gestational sac |
|---|---|---|
| (50-60 %) | (20-40 %) | (15-20 %) |



Empty uterus, no adnexal masses (too early / too small pregnancy)

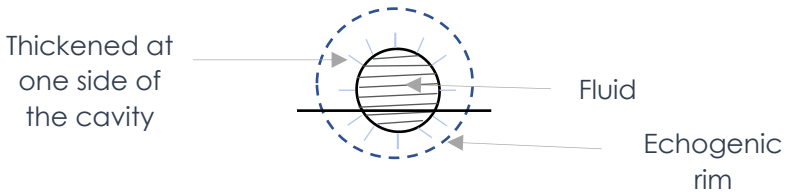
TVUS: Transvaginal ultrasound, PUL: Pregnancy of unknown location, DP: Douglas pouch

**Uterine findings in ectopic pregnancy**

20% of patients will have intrauterine fluid (pseudosac) which is a non-specific sign

**Uterine findings in intrauterine pregnancy**

Intra-decidual sign (double decidual sign), unlike the pseudocyst that is not diagnostic (early sac)




Positive pregnancy test + Intrauterine anechoic cystic structure + No adnexal mass

Probability of intrauterine pregnancy is 99.98 %

Fluid in DP (small amount)

Present in 28-56 % of cases of Ectopic pregnancy

May be present in Intrauterine pregnancy

Laparoscopy

Not a gold-standard in diagnosis of ectopic pregnancy

False negative rate with laparoscopy is 3 - 4.5 %

**Diagnosis of rare types of ectopic pregnancy**

| Type | Imaging features | Serum hCG |
|---|---|---|
| **Cervical ectopic (1% of all ectopics)** | • Ultrasound is diagnostic<br>• Ultrasound features are:<br>① Empty uterus<br>② Barrel-shaped cavity<br>③ Gestational sac below the level of the internal os<br>④ Blood flow around the sac<br>⑤ Sliding sign is negative<br>The last 2 signs differentiate it from incomplete abortion (with retained sac within the cervix) | Serum hCG is tested once at diagnosis (if HCG is above 10,000 iu/l, methotrexate treatment is likely to fail) |
| **Caesarean scar pregnancy (1:2000 pregnancies)** | • Caesarean scar pregnancy is misdiagnosed in 13% of cases<br>• Diagnosis is made by transvaginal ultrasound (TVUS) ± transabdominal ultrasound (TAUS)<br>• Ultrasound features include:<br>① Empty uterine cavity and cervical canal<br>② A sac/mass at the level of the internal os anteriorly (site of the scar)<br>③ Thin or no myometrium between the sac and the bladder<br>④ Prominent circulation on Doppler assessment<br>• If TVUS is equivocal, MRI may be considered | No role for hCG at the time of diagnosis. It may be useful for follow-up |
| **Interstitial ectopic (1-6% of ectopics)** | • Diagnosis is made by TVUS. It may be combined with 3D ultrasound or MRI to improve diagnostic accuracy<br>• Sonographic findings:<br>① Empty uterine cavity<br>② A sac is seen in the interstitial part of the tube, surrounded by < 5 mm of myometrium in all planes<br>③ Interstitial line sign: an echogenic line from the central uterine cavity to the periphery of the gestational sac (sensitivity is 80%, specificity is 98%)<br>• MRI findings: | A single HCG at the time of diagnosis (has no diagnostic role but may help in follow-up, may be repeated after 48 hours to decide the management) |

| | | |
|---|---|---|
| | ① Gestational sac surrounded by myometrium, lateral to the cornua<br>② Intact junctional zone between the uterine cavity and the sac | |
| **Cornual pregnancy (rarest type, 1:76000 pregnancies)** | • Sonographic features:<br>① The interstitial portion of the tube is seen in the uterine cavity<br>② The sac is mobile, surrounded by myometrium, and separate from the uterus<br>③ The sac is connected to a unicornuate uterus through a vascular pedicle | A single hCG is used to plan management along with clinical findings and sac size. It may be repeated, if necessary, for management planning |
| **Ovarian Pregnancy** | • Sonographic features (no specific criteria):<br>① Negative sliding organ sign<br>② Corpus luteum is seen separate from the sac<br>③ Foetal cardiac pulsations with colour Doppler within the ovary<br>• Final diagnosis is made by surgery and pathology | A single hCG is used to plan management. It may be repeated, if necessary |
| **Abdominal ectopic** | • Sonographic features: (diagnostic)<br>① Absence of intrauterine sac, adnexal mass or dilated tube<br>② Gestational sac surrounded by intestinal loops (separated by the peritoneum)<br>③ Wide mobility and fluctuation on pressure by the probe through the DP<br>• US and MRI show placental location and implantation to help planning surgical approach | Elevated hCG helps to confirm diagnosis |
| **Heterotopic pregnancy** | • Heterotopic pregnancy is suspected if there are:<br>▪ History of in-vitro fertilization<br>▪ Intrauterine pregnancy associated with ectopic symptoms<br>▪ Persistent increase in HCG after termination/miscarriage | HCG is of limited value. It is not necessarily higher than normal |

## Management

### General

#### ❶ Surgical management (Most common)

| ① | | ② |
|---|---|---|
| Laparoscopy | Vs. | Laparotomy |
| Generally preferable over laparotomy (e.g. less blood loss, less adhesions) | | No difference in subsequent successful pregnancy |
| Salpingectomy | Vs. | Salpingotomy |
| It is the standard surgery as long as the contralateral tube is healthy. In this group, subsequent pregnancy rate is 90% (comparable to salpingotomy). If fertility reducing factors are present, pregnancy rate is 40% (vs. 75% for salpingotomy) | | Selected if fertility reducing conditions are present such as:<br>① Contralateral tube is damaged<br>② History of PID (infection)<br>③ History of abdominal/pelvic surgery<br>④ History of ectopic pregnancy |
| | | • HCG should be followed up<br>• A second intervention may be needed in 20% of cases |

PID: Pelvic inflammatory disease

## ❷ Systemic methotrexate

### Candidates

- HCG < 1500 – 5000 iu/l
- Sac diameter < 3.5 cm
- Stable patients
- No cardiac pulsations
- No intrauterine pregnancy
- No sensitivity to treatment
- Compliant patient

⃠ Methotrexate should not be given in the 1st visit (intrauterine pregnancy should be excluded). A repeat hCG after 48 hours may be helpful

### Adverse effects

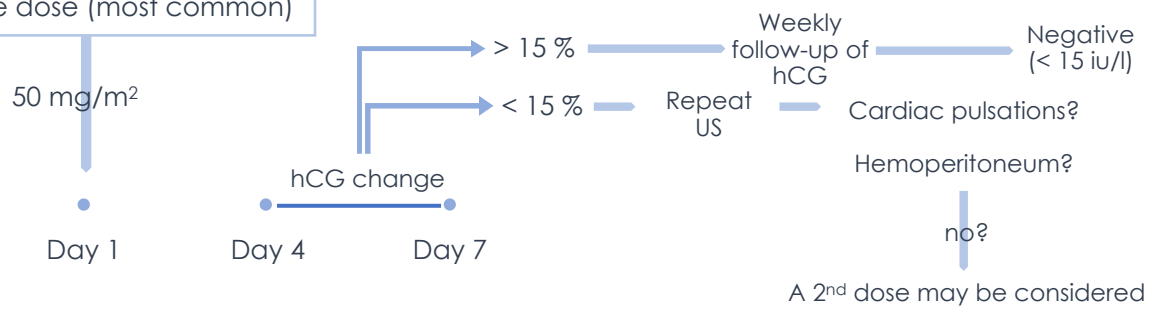
- Bone marrow suppression
- Pneumonitis
- Pulmonary fibrosis
- Gastric ulceration
- Liver cirrhosis
- Renal failure

### Contraindications

- Breastfeeding
- Alcoholism and liver disease
- Renal impairment
- blood dyscrasias
- Immunodeficiency
- Pregnancy

Methotrexate success comparable to surgery in properly selected cases

MTX single dose (most common)




| Success rate | | |
|---|---|---|
| | 65 - 95 % | 1st dose |
| | 3 - 27% | 2nd dose |

Pregnancy should be postponed to 3 months after completion of methotrexate therapy

| Predictors of success | |
|---|---|
| Initial HCG | • If < 1000 iu/l, success rate is 90%<br>• If > 5000 iu/l, success rate is 40% |
| US features | Positive predictors: No visible sac<br>Negative predictors: • Foetal pole • Cardiac activity • Yolk sac |
| Pretreatment change in hCG | The smaller the rise, the higher the rate of success (e.g. 11 - 20 % in 48 hours) |
| HCG change from day 1 - 4 | Decreased: 90 - 100 % success<br>Increased: 40 - 60 % success |

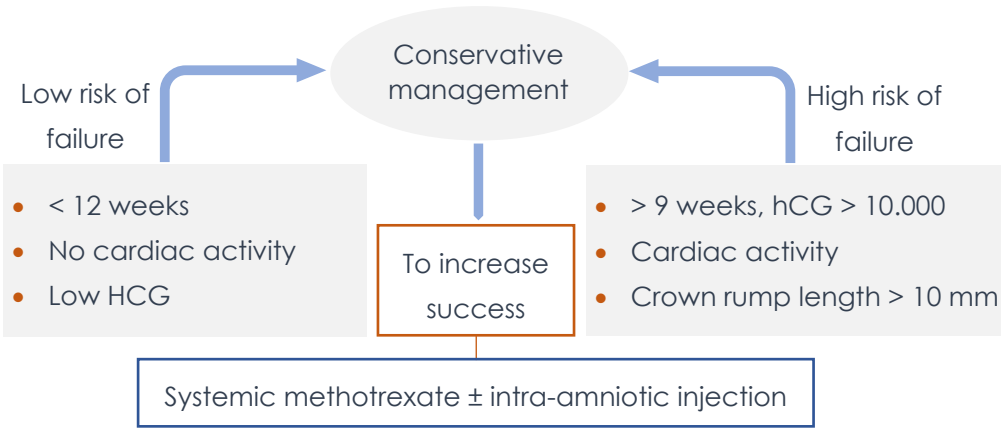
## ❸ Expectant management

| Candidates | Treatment success |
|---|---|
| • Stable patients<br>• Gestational sac diameter < 3.5 cm<br>• No cardiac activity<br>• HCG < 1500 iu/l and is trending down<br>• Compliant patient | • Comparable to methotrexate success if hCG is lower than 1500 iu/l<br>• Success rate is 60 - 100 % (96% if initial hCG is < 175, 66% if between 175-1500)<br>• Pretreatment hCG ratio over 48 hours. A ratio < 0.8 is indictive of success |

## Management of rare types of ectopic pregnancy

### Cervical pregnancy

① **First line is methotrexate (whenever possible):** Success rate is 91%

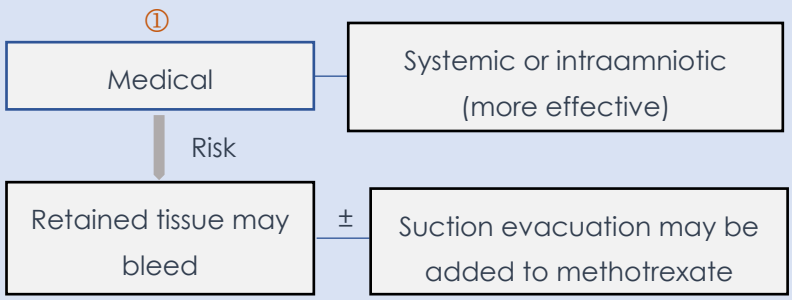


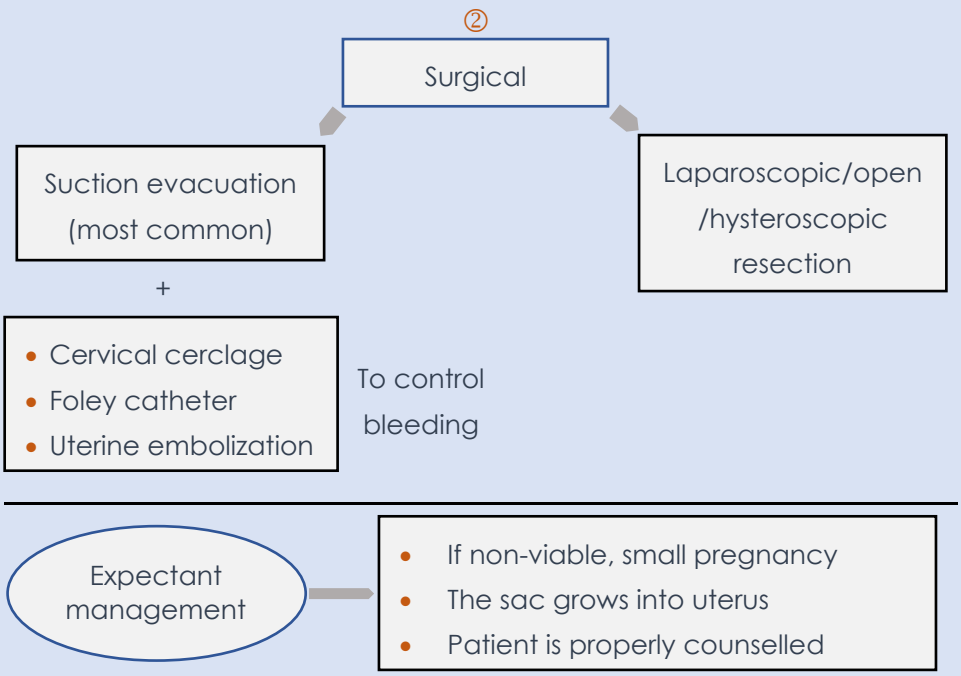

② **Surgery (dilation and curettage):** it has high failure rate and used only if there is life threatening bleeding

| | |
|---|---|
| Uterine artery embolization or ligation may decrease cervical bleeding | Hysteroscopic resection is another option |

### Caesarean scar pregnancy (a Life-threatening condition)

- **Surgical or medical (surgical management is more supported)**






2nd trimester viable pregnancy needs extensive counselling if a patient is interested in reaching viability (risk of bleeding, rupture and accreta)

**Interstitial pregnancy**

| Non-surgical | | Surgical |
|---|---|---|
| Medical | Expectant | • Cornual resection<br>• Salpingotomy<br>• Hysteroscopic resection under guidance |
| Methotrexate (systemic or Local) | If low or significantly falling HCG | |

**Cornual pregnancy**

Excision of the rudimentary horn

**Ovarian pregnancy**

| Surgery is the best option | Future fertility is good with surgery | Ovarian Laparoscpic excision is preferred |
|---|---|---|

| Surgical management | Medical management |
|---|---|
| • Enucleation<br>• Wedge resection<br>• Oophorectomy: only if there is<br>▪ Ovarian pathology or<br>▪ Significant bleeding | • Methotrexate (high failure rate; 40%). It is used if<br>▪ Surgery is risky<br>▪ There are persistent residual trophoblasts |

Bleeding control is achieved by electrocautery or sutures

**Abdominal pregnancy**

| Early | Late* |
|---|---|
| • Laparoscopic removal<br>• US guided feticide and systemic methotrexate | • Laparotomy:<br>▪ Localize placenta<br>▪ Place ureteric stents<br>▪ Bowel preparation<br>▪ Blood products<br>▪ preoperative angiographic embolization |

* Leaving placenta in situ is associated with less mortality but more morbidity (e.g. infection, ileus, fistula, bleeding, bowel obstruction). methotrexate and selective arterial embolization may be used

**Heterotopic pregnancy**

①

Medical (methotrexate) management

- If intrauterine pregnancy is not viable
- If intrauterine pregnancy is not desired

②

Surgical

- It is the first option if the patient is haemodynamically unstable
- If the patient is stable, it can still be considered

③

Local injection of potassium chloride or hyperosmolar glucose and aspirate (an option)

④

Expectant management

It may be considered in asymptomatic patients

Anti-D immunoglobulins

It is given to Rh-negative women with ectopic pregnancy if:

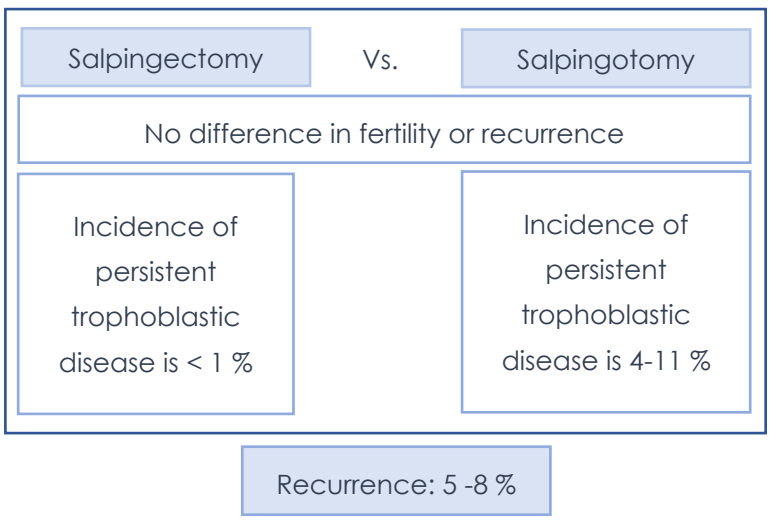
- Ectopic pregnancy was surgically managed
- There is heavy or repeated bleeding or abdominal pain (signs of disruption)

**Management of ectopic pregnancy and future fertility**

| In absence of tubal pathology or subfertility | In presence of subfertility history |
|---|---|
| No difference in rate of ectopic or pregnancy per management method | Expectant or medical management are superior to surgery |

Live births with subsequent pregnancies reported in women treated with uterine artery embolization and methotrexate

Patient support groups (ectopic pregnancy trust) should be offered to ectopic patients


Follow-up after salpingotomy

Check hCG 7 days postoperatively then weekly till it is negative

If it plateaus or increases, methotrexate is given. Methotrexate may be given prophylactically with salpingotomy

# Nausea and Vomiting with Pregnancy

## Background

- **Nausea and vomiting with pregnancy (NVP):**
  Nausea and vomiting in the first trimester after exclusion of other causes of nausea and vomiting
  Pregnancy-unique quantification of emesis (PUQE) score is used to classify severity of NVP

- **Hyperemesis gravidarum:**
  NVP with a triad of:
  - Weight loss >5%
  - Electrolyte imbalance
  - Dehydration

  After exclusion of other causes

## Epidemiology

- Incidence of NVP is 80%
- Incidence of hyperemesis gravidarum is 0.3 – 3.6%
- Average hospital stay associated with hyperemesis gravidarum is 3 – 4 days

## Clinical course

- NVP usually starts between 4 and 7 weeks and is most severe by the 9$^{th}$ week of gestation
- 90% of cases resolve by 20 weeks
- Symptoms starting beyond 10$^{+6}$ weeks are not typical and other causes should be excluded

## Clinical assessment

- **History:**
  - Ask about previous history of NVP or hyperemesis gravidarum
  - Ask about history and symptoms of other causes of nausea and vomiting
  - Ask about elements of PUQE score to determine severity:
    - Mild cases: score is 0-6
    - Moderate cases: score is 7-12
    - Severe cases: score is 13-15

- **Physical examination:**
  - Assessment of maternal weight and vital signs
  - Assessment of signs of dehydration and muscle wasting
  - Abdominal examination

- **Investigations:**

| | |
|---|---|
| **First line investigations** | • **Blood tests:**<br>▪ Full blood count<br>▪ Serum electrolytes and urea<br>▪ Glucose (if diabetic, to rule out diabetic ketoacidosis)<br>• **Urine tests:**<br>▪ Dipstick testing for ketonuria<br>▪ Midstream urinalysis for infection<br>• **Ultrasound:**<br>▪ Confirm foetal viability and gestational age<br>▪ Diagnosis of twins and molar pregnancy |
| **Second line investigations (in refractory cases)** | • Serum calcium and magnesium<br>• Thyroid function test<br>• Liver function test<br>• Serum amylase<br>• H. Pylori testing may be considered if indicated<br>• Upper endoscopy is safe in pregnancy and can be performed if indicated |

## Sequalae

- **Electrolyte effect:**
  - Hyponatremia, hypokalaemia, and hyperchloremia
  - Metabolic alkalosis (acidemia is present in severe cases)
  - Decrease in serum urea
  - Elevated hematocrit level
  - Ketonuria
- **Thyroid dysfunction:**
  - Hyperemesis gravidarum may be associated with biochemical thyrotoxicosis in 2/3 of cases (elevation of T4 with normal or decreased TSH)
  - The condition resolves spontaneously and does not need to be treated
- **Liver function:**
  - 40%, of women may have slightly elevated serum AST, ALT and bilirubin that resolves spontaneously
  - These findings are not associate with jaundice. Therefore, if jaundice is present, it should be investigated
- **Pancreatic function:**

  Amylase may be slightly elevated
- **Wernicke's encephalopathy:**
  - This disorder is caused by vitamin B1 (thiamine) deficiency
  - It is manifested by blurred vision, confusion, nystagmus, ophthalmoplegia, hyporeflexia, and ataxia
  - Complete remission occurs in only 30% of cases
  - Risk of intrauterine foetal death and termination of pregnancy is approximately 50%
- **Venous thromboembolism:**

  Risk of venous thromboembolism is these women is increased (2.5 – 4.5 times)
- **Low birth weight:**

  Women with severe hyperemesis gravidarum who have multiple admissions are at risk of small for gestational age (18%)

## Management setting

| Setting | Indication |
|---|---|
| **Community setting** | Mild NVP (PUQE score < 13) |
| **Ambulatory day care** | ① PUQE score < 13 (mild NVP)<br>② Failure of community management |
| **Inpatient management** | ① Continued NVP, cannot keep down oral antiemetics<br>② Continued NVP associated with ketonuria<br>③ Continued NVP associated with weight loss > 5%<br>④ Associated comorbidities e.g. urinary tract infection with no ability to tolerate antibiotics |

## Management

- **Medications:**
  - Phenothiazine (D2 antagonist): is safe in pregnancy
  - Diphenhydramine, doxylamine, cetirizine (H1 blockers): are safe in pregnancy
    - If one drug is not effective, treatment can be combined
    - If oral medications are not tolerated, IV or rectal route may be used
  - Metoclopramide (D2 and serotonin 5-$HT_3$ receptor blocker):
    - It is a second line treatment because of the risk of extrapyramidal manifestations, oculogyric crisis and tardive dyskinesia. It is important to rule out history of drug-induced extrapyramidal symptoms (phenothiazine and metoclopramide)
    - It is given as a slow infusion (over 3 minutes), 0.5 mg/kg/24 hours. Bolus injection should be avoided

Pyridoxine not recommended as a sole treatment. Diazepam is not recommended. Iron should be avoided in women with current or previous history of NVP

- Ondansetron:
  - It is used as a second line treatment because of the conflicting information on risks of cleft palate and cardiac abnormalities
  - It is more effective than first line medications and is comparable to metoclopramide with less side effects
- Steroids:
  - They are used if all other medical options failed
  - Treatment starts with hydrocortisone 100 mg twice daily till clinical improvement is achieved, and then prednisolone 40-50 mg once daily. The dose should be gradually tapered to the lowest possible dose that can control symptoms
- H2 blockers and proton pump inhibitors: if gastro-oesophageal reflux disease is present
- Thiamine: is indicated either orally or intravenously in women with prolonged vomiting
- Low molecular weight heparin is indicated during hospitalization

| | |
|---|---|
| **First line anti-emetics** | Cyclizine, chlorpromazine, prochlorperazine and promethazine |
| **Second line anti-emetics** | metoclopramide (used for no more than 5 days), domperidone, ondansetron |
| **Third line anti-emetics** | Steroids |

- **Intravenous hydration:**
  - Normal saline with potassium chloride is the best regimen
  - Fluid replacement is guided by daily electrolyte monitoring
  - Dextrose infusion should not be used except if:

    ① Serum sodium is normal

    ② Thiamine is administered (high dose of thiamine "100 mg" everyday IV dextrose is given)

- **Complementary therapy:**
  - Ginger:
    - It may be used in women with mild to moderate NVP who decline medical treatment
    - Ginger may cause stomach irritation, has anticoagulant effect and interacts with betablockers and benzodiazepines

Hypnosis is not recommended

- Acupuncture:
  It is safe to be used in pregnancy, and it may provide some benefit

A multidisciplinary team input is required in women with severe NVP and hyperemesis gravidarum (including a psychiatrist input)

- **Termination of pregnancy:**
  It may be offered if all other measures fail to control symptoms

- **Follow-up:**
  Women who have continued nausea and vomiting, which extend into the late second or third trimester, are at increased risk of foetal growth restriction and should be followed up with serial foetal growth scans

## Recurrence

- Risk of recurrence in subsequent pregnancies is 15%. The risk is 10% with the same parent and 16% with a different parent
- Risk may be reduced by early use of effective antiemetic, diet modification, and life-style modification before symptoms are aggravated

# Early pregnancy complications

## Abstract

First trimester pregnancy is a unique and crucial part of pregnancy. Early pregnancy is associated with risk of pregnancy loss, which conveys several causes, most of which are not preventable. The most catastrophic complication, specific to early pregnancy, is ectopic pregnancy, which may be associated with maternal morbidity and mortality. In this chapter, we will discuss complications of early pregnancy and evidence-based protocols for management of concerning symptoms.

## Keywords

Abortion, ectopic pregnancy, hyperemesis

## Further readings

1. Royal college of obstetricians and gynaecologists. Diagnosis and Management of Ectopic Pregnancy. Green-top Guideline No. 21: 2016.
2. National Institute for Health and Care Excellence. Ectopic pregnancy and miscarriage: diagnosis and initial management. NICE guideline NG126. Published date: 17 April 2019.
3. Royal college of obstetricians and gynaecologists. The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum. Green-top Guideline No. 69: 2016.

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# Antepartum Haemorrhage

## Definitions

- Antepartum haemorrhage (APH) refers to bleeding from or into the genital tract at or beyond 24 weeks of pregnancy and prior to birth

  - Spotting: minimal bleeding that is noted in the underwear or with wiping
  - Minor haemorrhage: bleeding less than 50 ml
  - Major haemorrhage: bleeding between 50 and1000 ml with no signs of clinical shock
  - Massive haemorrhage: bleeding that exceeds 1000 ml and/or bleeding associated with clinical signs of shock

## Causes

- Placenta Praevia
- Placental abruption
- Local pathology within the genital tract e.g. cervical polyps
- Unexplained antepartum hemorrhage




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_5

### Risk factors of placental abruption

- Most common risk factor is prior abruption:
  - Incidence is 1% in general population
  - Incidence is 4% after one occasion
  - Incidence is 20-25% after 2 occasions
- Pre-eclampsia
- Foetal growth restriction
- non-vertex presentation
- Polyhydramnios
- Advanced maternal age
- Multiparty
- low body mass index
- Assisted reproductive technology
- Premature rupture of membranes
- Trauma
- Smoking, cocaine or amphetamine

70% of cases occur without risk factors

### Risk factors of placenta praevia

- Previous praevia (risk increases by10 times)
- previous caesarean section:
  - 1 previous section: risk increases by 2 times
  - 2 previous sections: risk increases by 4 times
  - 3 previous sections: risk increases by 22 times
- Previous Termination of pregnancy
- Advanced maternal age (> 40 years)
- Multiparity
- multiple pregnancy
- Assisted reproductive technology
- Smoking
- Uterine scar, submucous fibroid, endometritis, prior dilation and curettage or manual placental removal (deficient endometrium)

- First trimester bleeding increases risk of APH from 1% to 1.4%
- First trimester hematoma is associated with relative risk of 5.6 for APH

## Complications of APH

| Maternal complications | Foetal complications |
|---|---|
| • Anemia<br>• Infection<br>• Maternal shock<br>• Renal tubular necrosis<br>• Disseminated intravascular coagulopathy (DIC)<br>• Post-partum haemorrhage<br>• Prolonged hospital stay<br>• Psychological complications<br>• Blood transfusion<br>• Maternal mortality | • Small for gestational age and foetal growth restriction<br>• Prematurity<br>• Intrauterine foetal death<br>• Perinatal morbidity and mortality |

| Complications associated with unexplained APH |
| --- |
| • Increased risk of fetal anomalies<br>• Oligohydramnios<br>• Premature rupture of membranes<br>• Preterm delivery<br>• Stillbirth<br>• Fetal growth restriction<br>• Induction of labour and caesarean section<br>• Neonatal intensive care unit admission<br>• hyperbilirubinemia |

## Management of APH

- **Prevention of APH:**
  - Elimination of modifiable factors (e.g. smoking, illicit drugs) may reduce risk of APH
  - Use of aspirin or heparin to treat thrombophilia is NOT supported
  - Women diagnosed with placenta praevia should not undergo pelvic examination, rectal examination, or have penetrative intercourse. There is no role for cerclage or prophylactic tocolysis in these patients

- **Management of active APH:**
  - First step is maternal stabilization, and transfer to a maternity unit with appropriate facilities. A patient who is not stable enough to provide good history should be immediately resuscitated prior to any fetal assessment
  - Second step is initial assessment, which includes history taking, maternal cardiovascular assessment, and evaluation of foetal status

## I. Initial assessment

| History | Examination | Maternal investigation | Foetal investigation |
|---|---|---|---|
| ▪ Pain and whether it is continuous or intermittent<br>▪ Foetal movements<br>▪ Association with premature rupture of membranes<br>▪ History of abnormal pap smear (incidence of cervical cancer with pregnancy is 7.5/100.000)<br>▪ Presence of risk factors (see before) | ▪ Assessment of general status and vital signs<br>▪ Abdominal assessment (soft non-tender uterus vs. tender woody uterus) including assessment of contractions<br>▪ Speculum examination: to assess cervical dilation and local genital causes of APH<br>▪ Pelvic examination may be performed once placenta praevia is ruled out by bedside ultrasound | ▪ Kleihauer test if maternal Rh is negative to adjust anti-D dose (but not for diagnosis of placental abruption)<br>▪ Ultrasound to rule out placenta previa (Sensitivity in diagnosing placental abruption is low; 24%)<br>▪ If bleeding is minimal, CBC, group and save are required. Coagulation screen is only required if platelet count is low<br>▪ If bleeding is major or massive: CBC, coagulation screen, electrolytes, Urea, Liver function tests are performed, and 4 units of blood are cross matched | ▪ Cardiotocography is done once the mother is stable or resuscitation commenced. It is likely abnormal in 70% of patients with abruption<br>▪ Cardiotocography may be performed immediately if vasa Praevia is suspected. Other tests for diagnosis of vasa praevia are complicated and inaccurate |

## II. Patient disposition

- **If bleeding is just spotting that resolved immediately:** if cardiotocography (CTG) is reassuring and no risk factors are present, dismiss home
- **If bleeding is more than spotting or bleeding is ongoing:** patient should be hospitalized at least till bleeding stops. She should be counselled by a paediatrician between 24-26 weeks of pregnancy

## III. Medications

- Single course of antenatal corticosteroids: this course should be given to pregnant women with APH if:
  ① Pregnant women are between 24+0 and 34+6 weeks
  ② Bleeding is greater than mild spotting

- Tocolysis is absolutely contraindicated in the presence of:
  ① Major haemorrhage
  ② Maternal instability
  ③ Foetal compromise
  ④ Placental abruption
  Otherwise, tocolysis is a relative contraindication in women with mild haemorrhage associated with placenta previa. Therefore, a senior obstetrician should take such a decision if tocolysis seems to be significantly beneficial.
  Nifedipine should be avoided due to its cardiovascular action

- Anti-D serum:
  - It should be given after an episode of APH regardless of routine doses (even if they were recently given).
  - If bleeding is continuous and pregnancy is beyond 20 weeks, give anti-D serum every 6 weeks
  - The dose of anti-D serum is 500 IU after 20 weeks of gestation, and feto-maternal haemorrhage should be tested after each bleeding episode

- Anticoagulation:
  - Women who are treated with anticoagulation for other indications should be hospitalized. In the presence of vaginal bleeding, anticoagulation should be stopped and a haematologist is consulted
  - If anticoagulation is inevitable and bleeding risk is high, the patient should be shifted to unfractionated heparin

## IV. Follow-up

- **Women with placental abruption or unexplained APH:**
  - Refer to high risk consultant for antenatal care during the rest of their pregnancy
  - Perform serial ultrasound to assess foetal growth

- **If bleeding is due to a local cause e.g. ectropion:**
  Antenatal care should continue with the same frequency and level of care

- **Intrapartum management and delivery:**

## Mode of delivery

- If there is maternal and/or foetal compromise, patient should be delivered immediately via caesarean section
- If foetal death is diagnosed, vaginal delivery is the standard route of delivery unless it is not possible e.g., transverse lie
- If APH is unexplained and both mother and fetus are stable, the decision of delivery mode and time is made by senior obstetrician

| Indications of continuous foetal monitoring | Indications of intermittent foetal auscultation |
|---|---|
| ▪ Active bleeding<br>▪ History of recurrent minor or major bleeding<br>▪ Suspected abruption<br>▪ Oligohydramnios<br>▪ Foetal growth restriction | One episode of minor bleeding that has resolved |

## management of delivery

### Caesarean section

- Regional anaesthesia is recommended in women who undergo caesarean section
- General anaesthesia is only recommended in the presence of maternal or foetal compromise. In these cases, general anaesthesia:
  ① Facilitates maternal resuscitation
  ② Facilitates quick delivery of the baby (timesaving)

### Vaginal delivery

Patient is at increased risk of postpartum haemorrhage. Therefore:

- Active management of 3rd stage of labour should be performed
- Syntometrine should be used if there is no hypertension. Its use is superior to syntocinon alone (20% greater reduction in postpartum haemorrhage)

### Neonatal team

Risk of neonatal anaemia and compromise

- Paediatric assistance should be present at delivery if there is continuous minor bleeding
- A paediatric consultant should attend if there is major bleeding or placenta previa anterior

### Management of postpartum haemorrhage

- In the presence of DIC:
  - Give 4 units of fresh frozen plasma and 10 units of cryoprecipitate while blood tests are pending
  - A haematologist should be involved
- Fresh frozen plasma to packed RBCs transfusion ratio is 1:1 – 1:1.4
- Transfusion of packed RBCs increases risk of acute tubular necrosis, while transfusion of whole blood increases risk of pulmonary oedema

- **Postpartum management:**
  - Thromboprophylaxis should be considered in patients who experienced major/massive bleeding.
  - Debriefing should be done, and clinical incident reporting is required

# Placenta Praevia

## Definitions

- **Placenta Praevia**: it refers to placenta covering the internal os after 16 weeks of gestation
- **Low lying placenta:** placental edge is present within 20 mm of the internal os after 16 weeks of gestation

## Epidemiology

Incidence of placenta Praevia is 1:200 (0.5%)

## Risk factors

- Previous caesarean sections (CS)
- Smoking
- Assisted reproductive technology
- Uterine pathology e.g. bicornuate uterus, uterine fibroids, adenomyosis, myotonic dystrophy
- Advanced maternal age: risk of placenta praevia increases by 1.3 times each year

## Clinical course

- If low lying placenta is diagnosed in the 2nd trimester, it will resolve in 90% of cases
- If low lying placenta is present at 32 weeks, it may resolve in 50% of cases
- If low lying placenta is present at 36 weeks, it will not resolve
- Risk of bleeding from placenta praevia significantly increases after 36 weeks:

| | |
|---|---|
| **35 weeks** | 5% |
| **36 weeks** | 15% |
| **37 weeks** | 30% |
| **38 weeks** | 60% |

- Risk of bleeding increases by 7 times if there is a short cervix
- Risk of massive bleeding and transfusion increases by 12 times during delivery compared to caesarean section performed for other indications
- Placenta praevia and anterior low-lying placenta have higher risk of bleeding

## Assessment

| Placental localization | Cervical length |
|---|---|
| • Placental site is screened in midtrimester routine Ultrasound scan:<br>  ▪ If placenta praevia or low lying placenta is detected: rescan at 32 weeks of gestation<br>  ▪ if it is persistent by 32 weeks, yet asymptomatic : rescan at 36 weeks of gestation<br>• Transvaginal utrasound is superior to abdominal ultrasound and should always be used to make the final diagnosis. It reclassifies 25-60% of diagnoses made by transabdominal ultrasound | Measurement of cervical length before 34 weeks predicts risks of preterm labour, emergent delivery and massive haemorrhage |

## Antepartum management

- **Hospitalisation:**
  - Patients who experience a bleeding episode are hospitalised till bleeding stops. Women who are dismissed home should have available assistance and should be living within 10-15 minutes from an equipped hospital and should present to hospital if they experience any bleeding or vague pain
  - In women with recurrent bleeding, decision of hospitalisation is individualized
  - Risk of preterm labour and haemorrhage should be considered in making the decision of hospitalisation
  - Venous thromboembolism prophylaxis should be weighed against risk of bleeding
- **Anaemia:** should be prevented/corrected during antenatal period
- **Corticosteroids**:
  - They should be given between 34 and 35+6 weeks.
  - Earlier administration is considered if there is increased risk of preterm labour
- **Tocolysis:**

  Tocolysis is may be considered if preterm labour is suspected and for 48 hours only to allow administration of antenatal steroids. However, if delivery is indicated for maternal or foetal indications, tocolytics should not be used. Cervical cerclage is NOT recommended

## Intrapartum management

**Time of delivery**

- Placenta praevia associated with history of vaginal bleeding OR risk factors of Preterm labour: planned delivery at 34-37 weeks
- Uncomplicated Placenta Previa: planned delivery 36-37 weeks

**Mode of delivery**

- Caesarean section is the standard mode. A senior consultant and senior anaesthetist should be present during planned delivery
- In women with asymptomatic low-lying placenta, decision of mode of delivery depends on distance of placental edge from the internal os, head position, and patient preference

**Interventions**

**Ultrasound**

Preoperative and intraoperative ultrasound scans are considered for placental localisation and determination of site of uterine incision

**Anaesthesia**

- Regional anaesthesia is preferred over general anaesthesia. It is associated with lower risk of bleeding
- Women should be consented for potential conversion to general anaesthesia in women with anterior placenta
- General anaesthesia is used in emergency situations

**Uterine incision**

- If foetal lie is transverse and pregnancy is less than 28 weeks: vertical skin and/or uterine incision is considered
- If the placenta is transected, the foetus should be delivered, and the cord is clamped immediately to avoid excessive foetal blood loss

**Fluid replacement**

- Rapid infusion and fluid warming devices should be available
- Cell salvage may be used in women with anticipated significant blood loss who declines transfusion. It is not associated with risk of amniotic fluid embolism

**Control of bleeding**

- Uterotonics
- If not effective, intrauterine tamponade and/or surgical haemostatic techniques should be used immediately
- Interventional radiology may be considered
- Hysterectomy if other measures fails

- **Success of balloon tamponade**:

  Balloon tamponade is successful in 75-85% of cases. Factors that are associated with tamponade failure are:

  ① prior caesarean section
  ② Anterior placenta
  ③ Thrombocytopenia
  ④ Coagulopathy
  ⑤ Post-partum haemorrhage > 500 ml within the first hour

# Placenta Accreta

## Epidemiology

- Incidence of placenta accreta is 2:10,000
- Risk of placenta accreta in the presence of placenta praevia increases by number of previous caesarean sections (CS):

| | |
|---|---|
| **Previous 1 CS** | 3% |
| **Previous 2 CS** | 11% |
| **Previous 3 CS** | 40% |
| **Previous 4 CS** | 61% |
| **Previous 4 CS** | 67% |

- The presence of history of uterine surgery, risk of placenta accreta increases by 3 times
- Maternal mortality associated with placenta accreta is 7%

## Risk factors

- Prior history of placenta accreta
- Prior CS or uterine surgeries (risk increase with number of surgeries)
- Placenta Praevia
- Maternal age
- Assisted reproductive technology

## Diagnosis

Placenta accreta is suspect if prior CS and anterior low-lying anterior are both present → Accreta is screened during second trimester scan (ultrasound is highly accurate)

MRI is comparable to ultrasound in most situations. MRI may be indicated to assess:

① Posterior placenta

② Parametrial invasion

Although IV gadolinium increases test sensitivity and specificity, information on long term safety on foetus is uncertain

## Intrapartum management

**Time of delivery**

If there are no risk factors for preterm labour: delivery is planned at 35-37 weeks of gestation

If there are risk factors for bleeding or preterm labour: delivery should be planned at 34-35 weeks of gestation

A plan for possible emergency delivery should be established with the patient. This includes the use of an institutional protocol and ongoing availability of matched blood products.

Median number of transfused units in women with placenta accreta is 5 units (2-8L loss).

**Patient consent**

- Discuss general risks of CS
- Discuss specific risks of placenta accreta e.g. massive haemorrhage, lower urinary tract injury (15% with conservative management vs. 60% with hysterectomy), risk of secondary hysterectomy after conservative management

## Approach

| | |
|---|---|
| **Anaesthesia** | Regional anaesthesia with possibility to convert to general anaesthesia |
| **Mode of delivery** | • Caesarean hysterectomy with placenta in situ<br>• If placental invasion is limited, uterus preserving procedures e.g. partial myometrial resection may be performed<br>• If hysterectomy denied, placenta in situ may be considered (without methotrexate). Strict follow-up is required because of risk of infection and secondary bleeding |
| **Ureteric stent** | Not required as a routine. However, it may be considered if bladder invasion is suspected |
| **Interventional radiology** | • It should be available specially in women declining transfusion<br>• Success rate is 90%<br>• Rate of secondary hysterectomy is 10%<br>• Use of prophylactic internal iliac balloon is controversial |

## Requirements of good care

- Supervising consultant obstetrician
- Anaesthesia consultant
- Available blood products
- Preoperative multidisciplinary plan
- Counselling and consenting
- Available level 2 critical care beds

# Vasa Praevia

## Definition

Vasa praevia is a term that describes the presence of umbilical vessels, unprotected by the umbilical cord, in the amniotic membranes within 2 cm of the cervix

## Incidence

- Incidence of vasa praevia is 1:3000 pregnancies
- Only 56% of these cases are diagnosed antenatally

## Risk factors

Most common risk factor is velamentous cord insertion
Other risk factors include:

- Low-lying placenta,
- Bilobed placenta
- Succenturiate placenta
- Assisted reproductive technology

## Diagnosis

### Antepartum diagnosis

- Routine scanning is not recommended. It may be considered only in high risk women (the presence of risk factors)
- Best diagnostic modality in pregnancy is combined transabdominal and transvaginal ultrasound with colour Doppler imaging (Sensitivity is 100%, specificity is 99%)
- If diagnosis is made in the second trimester, ultrasound should be repeated at 32 weeks (20% of cases may resolve by that time)

Antepartum diagnosis is associated with approximately 5% mortality

### Intrapartum diagnosis

- Pulsating foetal vessels deep to the internal os may be palpated during vaginal examination
- Rupture of membranes followed by Dark red vaginal bleeding and acute foetal compromise

Intrapartum diagnosis is associated with approximately 60% mortality

## Management

| | |
|---|---|
| **If the diagnosis is confirmed antenatally** | • If diagnosis is confirmed in the third trimester, elective caesarean section should be scheduled between 34 and 36 weeks of gestation<br>• Prophylactic hospitalization may be considered between 30 and 32 weeks of gestation, specially in the presence of other risk factors e.g. risk of preterm labour, multiple pregnancy<br>• Antenatal steroids are recommended at 32 weeks of gestation<br>• Emergency caesarean section should be performed in the presence of labour or premature rupture of membranes |
| **If diagnosis is made intrapartum** | • Immediate Caesarean section and neonatal resuscitation should be done<br>• Placental pathological examination to confirm diagnosis particularly if diagnosis is associated with stillbirth or acute foetal compromise and adverse neonatal outcomes |

# Antepartum haemorrhage

## Abstract

Antepartum haemorrhage is a broad term that conveys a spectrum of disorders hat cause bleeding from the genital tract during pregnancy. Such disorders may range from mild causes such as cervical ectopy or polyps, to more serious causes including placenta praevia and abruption. Unfortunately, many of these cases may remain unexplained and yet, they can be associated with complications. In this chapter, we will discuss causes of antepartum haemorrhage and management protocols in different clinical scenarios.

## Keywords

Placenta praevia, vasa praevia, placental abruption

## Further readings

1. Royal college of obstetricians and gynaecologists. Antepartum Haemorrhage. Green-top Guideline No. 63: 2011.
2. Royal college of obstetricians and gynaecologists. Placenta Praevia and Placenta Accreta: Diagnosis and Management. Green-top Guideline No. 27a: 2018.
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# PART III

## Obstetrics: Maternal and foetal medicine

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# Malaria with Pregnancy

## Epidemiology

- The most common type of malaria is falciparum (80%)
- Mortality rate with malaria:
  - Overall mortality is 0.5-1%.
  - Mortality with uncomplicated falciparum malaria is 0.1%
  - Mortality with severe malaria is 15-20% (up to 50% in pregnant women)
- Most common cause of mortality is misdiagnosis or delayed diagnosis

## Definitions

| | |
|---|---|
| **Uncomplicated malaria** | Malaria infection that is associated with < 2% parasitized red blood cells with no signs of severity or complications |
| **Severe and complicated malaria** | • Malaria infection that is associated with signs of severe infection after exclusion of other possible causes<br>• If 2% or more parasitized red blood cells are present, women are at high risk of developing severe malaria. Therefore, they are treated using severe malaria regimen |
| **Congenital malaria** | Foetal infection that results from vertical transmission of infected mothers |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_6

## Complications

- Premunition (prior exposure to anopheles bites) significantly impacts incidence and severity of symptoms and complications. UK residents are generally susceptible
- Complications in pregnancy include:
  - ① Maternal mortality
  - ② Miscarriage
  - ③ Stillbirth
  - ④ Preterm labour
  - ⑤ Low birth weight
  - ⑥Foetal growth restriction
  - ⑦ Foetal heart rate abnormalities

## Methods of malaria prevention

- Awareness of risks of malarial infection
- Bite prevention:

| | |
|---|---|
| **Skin repellents** | • 50% DEET (N, N-Diethyl-meta-toluamide) spray is safe in the first trimester<br>• It should be applied to exposed areas twice daily |
| **Knock-down mosquito sprays** | • Permethrin and pyrethroids can kill mosquitos |
| **Insecticide treated bed nets** | • Long lasting pyrethroid-impregnated bed nets are effectively protective |
| **Clothing** | • Clothing should cover as much of exposed areas through the whole day |
| **Room protection** | • Electrically heated mats can kill mosquitos |

- Chemoprophylaxis:
  - Pregnancy should be avoided during administration of chemoprophylaxis. However, it is not an indication of termination if pregnancy occurs
  - Medications used for chemoprophylaxis are:

| | Atovaquone-proguanil | Mefloquine |
|---|---|---|
| ***Type of chemoprophylaxis*** | Causal chemoprophylaxis (works against liver schizonts) | Suppressive chemoprophylaxis (works against RBC stage) |
| ***Duration of administration*** | They are taken for up to 7 days after leaving any endemic area | They are taken for 4 weeks after leaving any endemic area |
| ***Safety during pregnancy*** | Atovaquone-proguanil can be used during pregnancy. However, folic acid 5mg/day should be added prior to conception | Prophylactic dose (5mg/kg once a week) is safe in the second and third trimester. Use of Mefloquine in first trimester is reasonable if risk of falciparum infection is high |
| ***Excretion time*** | 3 months | 1 -2 weeks |
| ***Contraindications*** | Severe liver disease, pyruvate kinase and G6PD deficiency related anaemia | History of depression, psychiatric disorders or epilepsy |

Chloroquine and proguanil are not prescribed due to resistance. Primaquine is contraindicated as it causes RBCs hemolysis particularly in women with G6PD deficiency. Doxycycline is contraindicated in pregnancy

- Prompt diagnosis and treatment
- Avoidance of travelling to endemic area while pregnant:
  Risk of acquiring infection and mortality are doubled in pregnancy. However, if the trip cannot be postponed, women should:
  ① Seek guidance about prophylaxis from an experienced centre
  ② Consider malaria infection is they develop any flu-like illness during the trip and up to 1 year after returning home

## Diagnosis

### Clinical picture

| General clinical picture | Clinical picture of severe/complicated malaria |
|---|---|
| Diagnosis may be difficult because of clinical picture may be non-specific. However, history of travelling to an endemic area presents a clue to diagnosis<br>• Flu like symptoms<br>• Respiratory distress<br>• Fever<br>• Jaundice<br>• Pallor<br>• Sweating<br>• Splenomegaly | • Prostration<br>• Impaired consciousness<br>• Circulatory collapse and shock<br>• Abnormal bleeding (coagulopathy)<br>• Convulsions<br>• Respiratory distress<br>• Pulmonary oedema<br>• haemoglobinuria (in patients with G6PD deficiency)<br>• Algid malaria "gram negative septicaemia" |

## Investigations

Stepwise approach

### Rapid detection tests

Rapid detection tests are used for initial assessment. There are less sensitive than blood film, they may not detect low parasitaemia, which is common in pregnant women and has limited sensitivity to P. vivax

### Microscopic examination

Microscopic examination of thin and thick blood films is the gold standard and should be performed in all cases to determine degree of parasitaemia, species and stage of malaria

Stop malaria prophylaxis once admitted to hospital, so parasitemia is not suppressed and missed during assessment

Up to 3 films (12-24 hours apart) may be examined in febrile patients. All should be negative to rule out malaria

### Assessment of severity

Lab indicators of severity are:

- Severe anaemia (haemoglobin < 8 mg/dl)
- Thrombocytopenia
- Hypoglycaemia
- Acidosis
- Renal impairment
- Elevated lactate
- Hyperparasitaemia

Malaria should be reported to public health authorities and health protection agency

## Management

- **Emergency standby treatment:**
  - If malaria is suspected by the presence of flu-like illness and high temperature (38°c) in women traveling to endemic areas, a standby treatment should be started
  - Treatment consists of:

    ① Quinine 300mg 2 tablets 3 times/day for 5-7 days PLUS

    ② Clindamycin 150mg 3 tablets 3 times/day for 5-7 days FOLLOWED BY

    ③ Mefloquine for 1 week

    If vomiting occurs after treatment is given, it should be repeated:

    ① If vomited within 30 minutes, repeat the full dose

    ② If vomited within 30-60 minutes, give half the dose

- **Hospital admission:**
  - Pregnant women should be admitted to hospital
    - Uncomplicated malaria: admit to hospital
    - Complicated or severe malaria: admit to intensive care unit and follow up with blood film every 24 hours or more frequent if patient status is worsening
  - Monitoring:

| | |
|---|---|
| **Monitor blood glucose** | Hypoglycaemia can be profound and exacerbated by quinines |
| **Monitor central venous pressure (CVP)** | • CVP is monitored and right atrial pressure should be kept below 10 cm $H_2O$ to prevent pulmonary oedema<br>• Mortality rate of patients with severe malaria complicated by pulmonary oedema is approximately 50% |
| **Monitor blood pressure** | • Development of hypotension may indicate secondary bacterial infection, which should be treated with ceftriaxone |
| **Monitor haemoglobin** | • Severe anaemia should be treated with slow transfusion of packed RBCs plus furosemide to prevent pulmonary oedema. Exchange transfusion may be considered<br>• If anaemia is mild to moderate, iron and folic acid are given in the usual dose |

Thrombocytopenia resolves 7 days after treatment by 90% and by 100% after 14 days

- Treatment according to malaria species:

| | | |
|---|---|---|
| **P. falciparum** | ***Uncomplicated*** | Treatment with quinine plus clindamycin |
| | ***Severe*** | Treatment with IV artesunate (or quinine if artesunate is not available) * |
| **P vivax, ovale, malariae** | | Treatment with chloroquine |

* Quinine may cause cinchonism (blurring, tinnitus, headache, nausea, vomiting, diarrhoea, altered auditory acuity). Therefore, hospital treatment may improve compliance and decrease risk of self-discontinuation

- Symptomatic treatment:
  - Vomiting: it can be treated with metoclopramide. IV anti-malarial should be used instead of oral medications if vomiting is persistent. Infectious diseases specialist should be consulted
  - Fever: Treat with antipyretics (paracetamol). Fever should be efficiently controlled as it increases risk of preterm labor and fetal distress

- Venous thromboembolism prophylaxis:

  Risk should be calculated and weighed against the risk of haemorrhage specially in the presence of thrombocytopenia, and should stop if platelet count is below 100,000

- **Post-treatment follow-up:**
  - Antenatal care after recovery:
    - Regular assessment of hemoglobin, blood glucose and platelet count
    - Serial foetal growth scans
  - Preventing relapse during pregnancy (non-falciparum malaria):
    - Chloroquine 300 mg is given weekly (for P. vivax and ovale)
    - After delivery, relapse is prevented by administration of primaquine. It should start 3 months after delivery and after G6PD testing
  - Treatment of recurrence:

    Recurrence is treated by artemisinin for 7 days plus clindamycin

- **Peripartum management:**
  - Induction of labour is not indicated in women with uncomplicated malaria. Severe infection is not an indication for early caesarean delivery
  - Intrapartum fetal heart rate abnormalities may reflect maternal issues; fever and hypoglycemia should be ruled out
  - If malaria infection is peripartum, placental histology, placenta, cord, and baby blood films are indicated to rule out congenital malaria
  - Neonates should be screened by blood films after delivery and then weekly up to 28 days

# Bacterial Sepsis with Pregnancy

## Medical terms

- Sepsis = infection with systematic manifestations
- Severe sepsis = sepsis + organ dysfunction or hypoperfusion
- Septic shock = persistent hypoperfusion despite adequate fluid resuscitation

## Background

- Mortality rate: Severe sepsis with end organ damage is 20 to 40% and up to 60% if septic shock develops

## Risk factors of sepsis

- Obesity, impaired glucose tolerance/DM
- Impaired immunity, anaemia
- Vaginal discharge
- History of pelvic infection, History of GBS, amniocentesis
- Cervical cerclage, prolonged PROM
- GAS in close contacts, black group or minorities

## Clinical signs

- Fever, hypothermia
- Tachycardia, tachypnea
- Hypoxia, hypotension, oliguria
- Disturbed conscious level [use modified early obstetric warning score chart (needs annual training)]
- Diarrhea and vomiting (early toxic shock)
- Rash (generalized strept rash)
- Abdominal/pelvic pain & tenderness
- Offensive discharge
- Productive cough
- Urinary symptoms

## Toxic shock syndrome (TTS)

- Macular rash (most cases of staph. infection, 10% of strept. infection)
- Conjunctival suffusion is a classic sign

## Early presentation within 12 hours after birth

- Group A streptococci (GAS)
- Necrotizing fasciitis

**Warning signs & symptoms in puerperium**

- Fever > 38
- Tachycardia > 90
- RR > 20
- Abdominal or chest pain
- Vomiting/diarrhea
- Uterine/renal tenderness
- Generally unwell

**Non-genital tract causes of sepsis**

| | |
|---|---|
| **Mastitis** | • Can cause abscess, TSS, necrotizing fasciitis<br>• Refer to hospital if recurrent, persistent despite 48 hr antibiotics, patient is unwell or severe or unusual symptoms |
| **UTI (gm-ve)** | • Diagnosis with symptoms, blood/protein/leukocytes in mid-stream sample (send for culture)<br>• May be resistant to usual antibiotics (use carbapenem) |
| **Pneumonia** | • Treat with B-lactam + macrolides (send sputum sample)<br>• Hemoptysis = pneumococcal pneumonia<br>• Severe hemoptysis + low WBC count = PVL-associated staph necrotizing pneumonia (70% mortality) |
| **Skin/soft tissue infection (particularly associated with TSS)** | • Caesarean section (CS) site, episiotomy site, IV sites<br>• Recurrent abscess including labial = PVL-producing staph<br>• Remove any indwelling device, record and inspect IV site twice daily<br>• Necrotizing fasciitis is deep and later appears on the skin (suspect by agonizing pain out of proportion to signs requiring more pain management) |
| **Gastroenteritis** | • Rare<br>• Nausea and vomiting can be related to TSS or profound sepsis |
| **Pharyngitis** | • Typically viral, 10% with group A streptococci (GAS)<br>• Diagnose with 3/4 Centor criteria (fever, tonsillar exudate, cervical LNs, no cough) |
| **Spinal abscess** | • Staph, strept, gm -ve, sterile (15% each) |

## Pathogens

### Most common lethal bacteria

- GAS
- E. coli
- Coliform infection is seen with UTI, PROM and cerclage

### Major pathogens of sepsis

- GAS, E. coli
- Staph, Pneumococci
- MRSA (2% of mothers in puerperium)

### Unpasteurized milk

- Salmonella
- Listeria
- Campylobacter

- Chlamydophila: contact with infected cheap abortus or birds
- Coxiella: Q fever due to inhalation from birthing animals

- High risk of staph and strept:
  - IV drug users
  - Chronic illness
  - Endocarditis
  - Blood-borne virus

---

### Investigations

- Blood culture prior to Abs (screen for MRSA)
- Lactate within 6 hours (> 4 = hypoperfusion)
- Relevant imaging (find source)
- ABG for hypoxia
- Routine blood tests (CBC, CRP, urea, electrolytes)

- Consider throat swab if suspected
- If MRSA unknown (nose swab for screening)

- IV drug users (risk of abscess spread and infective endocarditis), MRSA swab of injection site, use central venous catheter or peripherally inserted central catheter (difficult IV access)

## Management

*Suspected sepsis should be referred to secondary care*

**Indications of ICU transfer (cardiac output monitor, respiratory support)**

- Hypotension or persistent lactate > 4 despite resuscitation (needs inotropes)
- Pulmonary edema, airway protection and mechanical ventilation
- Renal dialysis
- Disturbed conscious level
- Hypothermia
- Uncorrected acidosis
- Multiorgan failure

**If severe sepsis is suspected**

↓

**IV broad spectrum antibiotics within 1 hour**

- Co-amoxiclav: not covering MRSA or pseudo + necrotizing enterocolitis
- Clindamycin: covers most staph and strept including many MRSA, decrease exotoxin production, decrease mortality
- Piper-tazobactam: cover all except MRSA
- Gentamicin: needs level monitoring if given regularly, only for normal renal

**Treatment of infections**

- Mastitis: flucloxacillin + clindamycin [vancomycin + clindamycin (vancomycin trough level 5-20)]
- CS wound infection or IV site: flucloxacillin + clindamycin (Or vanc + clinda: MRSA)
- Endometritis: once gentamicin + cefotaxime + metronidazole
- Pyelonephritis: cefotaxime + once genta
- TTS: flucloxacillin (or vancomycin) + clindamycin + gentamicin

**IVIG**

- For severe invasive staph and strept not responding to treatment (but not gram negative bacteria)

---

- Early presentation within 12 hours after birth (GAS, necrotizing fasciitis), start immediate high dose IV antibiotics

- Fever + tachycardia > 90 + abdominal pain, antibiotics and senior review

- Suspicion of necrotizing fasciitis indicates involvement of ICU team and plastic/reconstructive surgeries
- Invasive GAS is notifiable, alert infection control team and isolate patient in a single room

### Sepsis during puerperium

- Umbilical area should be examined
- Either the mother or baby infected with GAS, both should be treated

### Management during puerperium

- Treat the cause + broad spectrum antibiotics:
  - Piperacillin/tazobactam OR
  - Carbapenem/clindamycin may be used

### If diarrhea develops after antibiotics or if offensive

- Send for C. Difficile and treat empirically with oral vanc or oral metro (30% mortality if not treated)

### Treatment of hypotension/oliguria

- Aggressive IV, which increases risk of pulmonary edema postpartum and needs ICU (may require vasopressors)

- No epidural or spinal with sepsis but do general only
- NSAIDs avoided in sepsis as they decrease capacity of polymorphs to fight GAS
- Cefuroxime is not used (associated with C. Difficile)

### Antibiotic prophylaxis

1. To newborn of women with group A strept
2. To healthcare team
3. To close contacts (seek medical if symptoms) or prophylaxis

- Close contacts with recent GAS should be noted

### Cardiotocograph (CTG) during labour

- Continuous CTG during labor in sepsis
- Continuous CTG is indicated also if pyrexia > 38 or 37.5 twice
- CTG changes: consider maternal acidemia, hypoxia or low mean BP

- CTG is not sensitive predictor of early neonatal sepsis

# Genital Herpes in Pregnancy

## Incidence

- Incidence of neonatal herpes in the UK is 1.7:100.000
- About 2% of women may acquire primary genital herpes simplex virus (HSV) infection in pregnancy

## Classification

| Type | Percentage | Morbidity and mortality |
|---|---|---|
| **Localized disease to skin, eye, mouth** | 30% of neonatal herpes | Morbidity rate < 2% (best prognosis) |
| **Local central nervous system (CNS) disease** | 70% of disseminated infection and/or local CNS infection (60% of them do not show localized disease features) | Morbidity rate is 70%, mortality rate is 6% (presentation is late, between 10 days and 4 weeks) |
| **Disseminated infection with multiple organ involvement** | | Morbidity rate is 17%, mortality rate is 30% (worst prognosis, more common in preterm babies) |

## Aetiology

- **Causative organism:**
  - Neonatal herpes may be caused by herpes simplex virus type 1 (HSV-1) or herpes simplex virus type 2 (HSV-2) (50 % each)
  - Congenital herpes may occur as a result of transplacental transmission, and is extremely rare

- **Route of infection:**
  - Infection is commonly acquired through birth canal during vaginal delivery
  - 25% of cases are acquired postnatally from contact persons (oro-labial herpes)

- **Risk of transmission:**
  - The risk is high with primary genital herpes if acquired in the third trimester, particularly within 6 weeks of vaginal delivery (risk is 40%)
  - Trans-placental maternal antibodies cannot prevent viral spread to neonatal brain
  - Risk of transmission in recurrent genital herpes is low (0-3%). It is likely to cause local CNS disease or skin, eye, mouth disease

## Clinical picture

- Maternal infection presents as multiple painful shallow erythematous ulcers in the affected area
- Disseminated infection in adults is rare (e.g. encephalitis, hepatitis, or skin lesion). However, the risk may increase in pregnancy particularly immunocompromised women (high mortality rate)

## Antepartum management

<table>
<tr><th colspan="2">Primary infection (first episode)</th></tr>
<tr><th>First or second trimester</th><th>Third trimester</th></tr>
<tr><td>
<ul>
<li>There is no risk of spontaneous abortion or anomalies</li>
<li>Once genital herpes is suspected, patients should be referred to genitourinary unit to confirm diagnosis using PCR and plan for immediate management</li>
<li>Treatment options include:
<ul>
<li>Oral acyclovir 400 mg 3 times per day for 5 days (IV for disseminated infection)
<ul>
<li>Acyclovir is safe during pregnancy</li>
<li>It may cause transient neonatal neutropenia but no significant maternal or neonatal complications</li>
<li>Valaciclovir or famciclovir are not recommended as a first line (less available data)</li>
</ul></li>
<li>Paracetamol and lidocaine 2% gel may be used for symptomatic management</li>
<li>Suppression treatment will be given at 36 weeks of gestation to decrease viral infection, incidence of CS, and asymptomatic viral shedding</li>
</ul></li>
</ul>
</td><td>
<ul>
<li>There is risk of perinatal morbidity (preterm labor and low birth weight)</li>
<li>Infection is treated with oral (or IV for disseminated infection) acyclovir 400 mg 3 times per day for 5 days, with the continuation of suppression therapy till the time of delivery</li>
<li>Because 15% of cases of late pregnancy infection are recurrent, antibody testing is indicated (IgG and IgM) to determine type of infection:
<ul>
<li>Primary infection within 6 weeks of delivery: Caesarean section (CS) is indicated</li>
<li>Recurrent infection: CS is not indicated</li>
</ul></li>
<li>Within 6 weeks, if delivery did not occur, expectant management with anticipated vaginal delivery are allowed</li>
</ul>
</td></tr>
<tr><th colspan="2">Recurrent episode</th></tr>
<tr><td colspan="2">
<ul>
<li>There is no increased risk of preterm labour, feotal growth restriction or foetal anomalies.</li>
<li>The Risk of neonatal herpes is low, despite the presence of lesions at birth by 0-3%.</li>
<li>Many episodes resolve within 7-10 days without treatment. Symptomatic treatment may be used</li>
<li>Suppression therapy using acyclovir 400 mg 3 times per day at 36 weeks of gestation and till delivery is recommended to reduce risk of recurrence at time of delivery</li>
</ul>
</td></tr>
</table>

Sequential PCR culture to predict viral shedding at birth is not recommended

## Intrapartum management

Management of primary or recurrent lesions at labour include:

**primary lesions**

- CS is indicated for all women if infection is diagnosed in labour or within 6 weeks of labour
- Benefit of CS decreases if rupture of membranes occurs for more than 4 hours. However, CS should still be performed

**If a patient refuses CS**

- Intrapartum IV acyclovir is given to the mother (5mg/kg every 8 hrs) and to the baby (20mg/kg every 8 hours). It is not clear whether intrapartum treatment reduces neonatal herpes
- Foetal scalp electrode, foetal blood sampling, amniotomy and/or instrumental delivery should be avoided during labor

**Recurrent lesions**

- CS should not be offered as a routine. Mothers should be counselled and allowed to make a decision
- risk of neonatal herpes with vaginal delivery is 0-3%. The risk increases with foetal scalp electrode, foetal blood sampling, amniotomy and/or instrumental delivery.

## Certain circumstances

### Genital herpes and preterm prelabour rupture of membranes (PPROM)

| Lesion | Management |
|---|---|
| **Primary lesion** | • Decision is guided by a multidisciplinary team discussion involving the obstetricians, neonatologists, and genitourinary medicine physicians.<br>• CS will be indicated if the decision is immediate delivery or delivery within 6 weeks of diagnosis of infection<br>• Otherwise, IV acyclovir 5mg/kg every 8 hours and prophylactic corticosteroids should be given. |
| **Recurrent lesion** | If PPROM occurs before 34 weeks, expectant management, including oral acyclovir 400 mg 3 times daily for the mother, is recommended |

### Genital herpes in HIV-positive women

| | Primary HSV infection | Recurrent HSV infection | |
|---|---|---|---|
| | | Women with HIV positive antibodies and history of genital herpes | Seropositive women for HSV-1 or 2 without history of genital herpes |
| **Suppression treatment** | Management of third trimester primary infection follows general guidelines of management of HSV in pregnancy (see before) | Indicated at 32 weeks to decrease risk of transmission of HIV specially if vaginal delivery is anticipated | Not indicated |
| **Mode of delivery** | | Mode of delivery is decided according to HIV in pregnancy guidelines | |

## Neonatal management

**Neonates of mothers with primary HSV infection in the third trimester delivered by CS**

- Risk of transmission is very low
- swabs or active treatment is not indicated
- The baby can be discharged after 24 hours if the baby is well
- Parents should be informed about prevention of postnatal infection including good hand hygiene.
- Parents should seek medical advice if they notice any neonatal concerns e.g. skin, eye, mucus membrane lesions, lethargy, irritability, or poor feeding

**Neonates of mothers with primary HSV infection in the third trimester delivered by vaginal delivery**

**If the baby is well**

- Swab for PCR is taken from:
  - Conjunctiva
  - Skin
  - Oropharynx
  - Rectum
- Empirical treatment with 20 mg/kg/8 hours

**If the baby is sick**

- Swabs are taken for PCR
- Lumbar puncture is done to rule out CNS infection even in absence of CNS features
- Empirical treatment with 20 mg/kg/8 hours

**Neonates of mothers with recurrent HSV infection with or without lesions at delivery**

- Risk of transmission is very low
- Swabs or active treatment is not indicated
- The baby can be discharged after 24 hours if the baby is well
- Parents should be informed about prevention of postnatal infection and should seek medical advice if any neonatal concerns are noted

**Neonatal concern**

**(Clinical evidence of sepsis or poor feeding)**

- Swabs and blood are taken for culture and PCR
- Empirical treatment is given
- Further management is guided by neonatology team

# Group B Streptococci in Pregnancy

**Incidence**

- Prevalence of group B streptococci (GBS) colonization is 20-40% (not affected by pregnancy)
- Incidence of neonatal early onset group B streptococcal disease (EOGBS) is:
  - 0.6:1000 births as a baseline
  - 5:1000 in the presence of intrapartum pyrexia
  - 1:400 if maternal GBS status is positive
  - 1:700 in women with positive GBS in a previous pregnancy (2-2.5 times higher than baseline)
  - 1:50000 if maternal GBS status is negative
  - 2:1000 in preterm babies (22% of all EOGBS cases)
- History of recurrence of GBS positive status is 50%
- Mortality rate with EOGBS is 2-3% in term babies, 20-30% in preterm babies

**Risk factors (present in 35% of cases)**

① Previous baby with GBS disease

② GBS bacteriuria

③ Positive GBS rectovaginal swab

④ Pyrexia > $38^0$ during labour

*90% of cases of EOGBS demonstrate clinical signs within 12 hours of*

| Clinical situation | Management |
|---|---|
| *GBS was present in previous pregnancy* | Offer intrapartum prophylaxis versus bacteriological screening in late pregnancy |
| *Previous history of early or late onset GBS disease* | Offer intrapartum prophylaxis |
| *GBS bacteriuria in current pregnancy* | Offer intrapartum prophylaxis |
| *GBS urinary tract infection in current pregnancy (> 105 cfu/ml)* | Immediate treatment at time of diagnosis and intrapartum prophylaxis |
| *Positive GBS in current pregnancy and planned caesarean section (CS), she had prelabour rupture of membranes (PROM)* | Offer intrapartum prophylaxis and perform category 2 or 3 CS |
| *Positive GBS status, planning for vaginal delivery, she had term PROM* | Immediate intrapartum prophylaxis and induction of labour (IOL) as soon as possible |
| *GBS status is negative or unknown, she had term PROM* | Offer immediate IOL versus expectant management for 24 hours |
| *Intrapartum pyrexia (38°c or more)* | Broad spectrum antibiotics covering GBS |
| *Women in preterm labour who will deliver vaginally with unknown GBS status* | Offer intrapartum prophylaxis |
| *Preterm labour, planned CS with intact membranes* | Prophylaxis is not indicated |

Ideal time for GBS testing is 35-37 weeks or 3-5 weeks prior to anticipated delivery (32-34 in twins)

Bacteriological testing is not offered on maternal request

Universal testing is not recommended as 20% with positive swabs will be negative at delivery, 6% of negative swabs will be positive at delivery

PCR is not currently recommended for testing

GBS carrier status does not alter induction of labor method and is not a contraindication to membrane sweeping or water birth

Treatment is not indicated if CS is planned with absence of labour and intact membranes

Preterm prelabour rupture of membranes (PPROM)

Bacteriological testing is not recommended

Give intrapartum prophylaxis regardless once labor is confirmed or induced

If GBS status is positive or current pregnancy

Expedite delivery if gestational age is > 34 weeks (but not if < 34 weeks)

Antibiotics for expectantly managed PPROM

Oral erythromycin 250 mg 4 times a day for 10 days (oral penicillin is the second line)

Screening for GBS status in pregnancy (rectovaginal swab)

Taken from lower vagina and anorectum (2 swabs or 1 swab are fine)

Keep in non-nutrient transport medium (Amies, Stuart)

Transport and proceed as soon as possible (or refrigerate). Recovery of isolates decreasing over 1-4 days. Enriched medium is used for culture

Positive rectovaginal GBS swab is not treated routinely. But patients are offered intrapartum

*Intrapartum prophylaxis*

It should be given regularly till delivery

Benzylpenicillin (Penicillin G) starts by loading dose 3 g then 1.5 g every 4 hours

If non-severe allergy to Penicillin

Cephalosporins (cefuroxime)

1.5g loading dose then 0.75g every 8hrs

If severe allergy to Penicillin

Vancomycin

1g/12hr

| Maternal risks of intrapartum prophylaxis | Neonatal risks of intrapartum prophylaxis |
|---|---|
| • Anaphylaxis<br>• Increase medications in labor<br>• Development of antibiotic resistant infection specially with broad spectrum antibiotics | • Altered neonatal bowel flora (inconsistent findings)<br>• Abnormal child development e.g. diabetes, obesity, allergy (theoretical) |

Intrapartum prophylaxis decreases risk of EOGBS (< 7 days of age, RR 0.14) but not late onset neonatal group B streptococcal disease (LOGBS) (7 days or more)

If declined

- Advise close monitoring of the newborn for 12 hours after birth
- Discourage neonatal very early discharge

*Intrapartum vaginal cleansing does not increase risk of neonatal GBS disease*

Intrapartum pyrexia should be treated with amoxicillin 2 g/6 hours or cefuroxime 1.5g/6 hours

Warning signs of the neonate to seek medical advice

- Abnormal behavior (inconsolable crying or listlessness)
- Floppy, difficulty with feeding
- Temperature < 36 or > 38 °C
- Rapid breathing
- Change in skin color

If the mother received adequate intrapartum prophylaxis (for more than 4 hours before delivery) and the baby appears well

No special observation of the baby is needed after birth

Inadequate intrapartum prophylaxis or history of previous baby with GBS disease

Well babies are evaluated at birth and their vital signs are checked at 0, 1, 2 hours and then 2-hourly for 12 hours

Asymptomatic term babies without risk factors

Postnatal antibiotic prophylaxis is not indicated

If clinical signs of EOGBS are present

Treat baby with penicillin and gentamicin within 1 hour of the decision to treat

Beast-feeding is encouraged regardless of GBS status

EOGBS outcomes in not treated: 7% disability rate, 5% case fatality rate

# Human Immunodeficiency Virus (HIV) in Pregnancy

## Antenatal care

- **Medical management:**

  Antenatal management of women with HIV should be guided by a multidisciplinary team

### I. Assessment

- **Screening for depression:**

  Women with HIV are screened for depression at booking, 4-6 weeks postpartum, and 3-4 months postpartum

- **Sexual health screening:**
  - In women with newly diagnosed HIV, sexual health screening is recommended
  - In women with known HIV, sexual health screening is suggested

- **HIV resistance testing:**
  - HIV resistance testing should be completed, and results should be made available prior to initiation of treatment except if the patient presents late beyond 28 weeks of gestation.
  - Postpartum, combination antiretroviral therapy (cART) is recommended, women who opt for stopping cART should undergo further resistance test to assess review changes after the off-treatment interval

- **Assessment of CD4:**
  - If the patient is on cART: check CD4 at baseline and at delivery

- If patient commences cART in pregnancy: check CD4 at initiation of treatment and at delivery

- **Assessment of viral load:**

  Viral load is checked:

  - 2-4 weeks after starting treatment
  - At each trimester
  - At 36 weeks
  - At delivery

If viral load is suppressed by cART, review adherence to treatment, perform resistance test, consider therapeutic drug monitoring (TDM), optimize and intensify treatment regimen

- **Liver function test (LFT):**

  LFT is checked:

  - At initiation of cART
  - With each blood work

## II. Medical treatment

- **Choice of medications:**
  - If a woman is on cART regimen prior to pregnancy, she should continue the same treatment

*Indications of changing regimen:*

① Non-standard regimen e.g. protease inhibitor monotherapy

② Medications with decreased pharmacokinetics in pregnancy e.g. darunavir/cobicistat, elvitegravir/cobicistat

③ Absence of pharmacokinetic information during pregnancy e.g. raltegrarvir

④ Dolutegravir (risk of neural tube defect)

- Women who are not on treatment should be managed as follows:
  - Standard regimen is:

    Tenofovir OR abacavir

    **PLUS**

    Emtricitabine OR lamivudine

    **PLUS**

    Efavirenz OR atazanavir
  - Darunavir: it may be used in a high dose if there is known resistance
  - Dolutegravir: it may be considered after 6 weeks of gestation
  - Integrase inhibitor regimen: it is the third line if viral load is still above 100.000 despite cART treatment
  - Zidovudine monotherapy: it is not recommended except if:

    ① Women declining cART AND

    ② Viral load is < 10000 AND

    ③ Planning for caesarean section

> Do not use protease inhibitor monotherapy, darunavir/cobicistat, elvitegravir/cobicistat

- Women who are not on treatment who present after 28 weeks of gestation:
  - Start cART immediately
  - If viral load is unknown or above 100.000, treatment should consist of 3-4 medications containing raltegravir 400 mg twice daily OR dolutegravir 50 mg once daily
- Women who are not on treatment who present at labour:
  - Treatment should include the following:

    Nevirapine 200mg PLUS

    Oral zidovudine 300 mg PLUS

    Lamivudine 150mg BD PLUS

    Raltegravir 400 BD PLUS

    IV zidovudine during the duration of labour
  - A double dose of tenofovir should be considered in preterm labour

If women present with rupture of membranes or in labour and HIV status is unknown, urgent HIV testing should be done and management should be started immediately if tests are positive

- Women with HIV-2:
  - Management should involve an expert in HIV-2 treatment
  - A boosted protease inhibitor-based regimen (darunavir) is recommended

- **Time of treatment initiation:**

  Women who are not on cART during pregnancy should start treatment:
  - If viral load is ≤ 30.000, she should start treatment as early as possible in the second trimester
  - If viral load is 30.000-100.000, treatment should start at the onset of second trimester
  - IF viral load > 100.000 and/or CD4 < 200, treatment should start in the first trimester

  Thereby, all women should start by week 24 of gestation

- **Dosing:**
  - Doses are similar to those used in non-pregnant women except raltegravir (should be given 400mg BID)
  - Therapeutic drug monitoring should be considered if tenofovir and atazanavir are combined

- **Obstetric management:**
  - Combined screening for aneuploidy and non-invasive prenatal testing is recommended for high risk women to preclude the need for invasive testing
  - If invasive testing cannot be avoided, the following considerations should be taken:
    - Viral load should be less than 50
    - Women who are not on treatment should be treated immediately
    - cART should contain raltegravir
    - A single dose of nevirapine 2-4 hours prior to procedure
  - External cephalic version should not be performed unless viral load is below 50

## Intrapartum management

- **Mode of delivery:**
  - Mode of delivery is determined by viral load at 36 weeks:
    - If viral load is below 50, planned vaginal delivery is recommended. Vaginal birth after caesarean can be tried
    - If viral load is 50-399, consider prelabour caesarean section (CS) after reviewing viral load, duration of treatment, and obstetric circumstances
    - If viral load > 400, prelabour CS is recommended
  - Candidates for vaginal delivery are managed per routine protocol. However, duration of rupture of membranes should be minimized
  - Women with rupture of membranes:
    - All women with prelabor rupture of membranes (PROM) should deliver within 24 hours:
      - If viral load is less than 50, immediate induction or augmentation of labour is recommended
      - Women with viral load 50-399, recommend CS after reviewing other factors
      - Viral load ≥ 400, recommend immediate CS
    - Preterm prelabour rupture of membranes > 34 weeks, management is similar to women with PROM. Group B streptococcal test and prophylaxis are required
    - Preterm prelabour rupture of membranes < 34 weeks is managed by antenatal steroids, viral load should be optimized, and decision of time and mode of delivery are made by a multidisciplinary team

- **Timing of delivery:**

  If caesarean section is decided, it should be performed:
  - Between 38-39 weeks of gestation if indicated for a high viral load
  - After 39 weeks of gestation if planned for obstetric indications

- **Delivery setting (place):**
  - Delivery should be planned where immediate access to paediatric care is available
  - Water birth is supported if viral load is lower than 50

- **Intrapartum treatment:**

  Intrapartum IV zidovudine is indicated if:

  ① Viral load is above 1000 in women who present for labour, PROM or planned CS

  ② Untreated woman with unknown viral load admitted in labour or with PROM

  ③ It may be considered if patients are on cART and viral load is between 50 and 1000

## Neonatal management

| | Definition | Treatment |
|---|---|---|
| **Very low risk** | • cART was given to the mother for more than 10 weeks AND<br>• 2 viral load tests were less than 50 at least 4 weeks apart AND<br>• Maternal HIV was less than 50 at or after 36 weeks | 2 weeks of zidovudine |
| **Low risk** | The above criteria are not met BUT<br>• Viral load less than 50 at or after 36 weeks OR<br>• Infant born before 34 weeks with the most recent viral load less than 50 | 4 weeks of zidovudine |
| **High risk** | • Viral load > 50 OR<br>• Unknown viral load (but likely > 50) | Combination postexposure prophylaxis (PEP) immediately after birth (within 4 hours): zidovudine, lamivudine, nevirapine<br>PEP should be limited to 4 weeks even with breast feeding unless there is significant ongoing exposure<br>Consider raltegravir instead of nevirapine in women with HIV-2 |

- **Antibiotic prophylaxis:**

  If the baby has positive HIV PCR or is diagnosed HIV, co-trimoxazole should be given from 1 month of age (prophylaxis against pneumocystis pneumonia)

- **Vaccinations:**
  - Rotavirus vaccine is not contraindicated unless baby has HIV and is severely immuno-compromised
  - BCG vaccine should not be delayed if the baby is at low or very low risk of transmission

- **Assessment of viral load:**

| Non breast-fed babies | Breast fed babies |
|---|---|
| Assessment should be performed:<br>• Within the first 48 hours<br>• Prior to discharge<br>• At 2 weeks (if at high risk)<br>• At 6 weeks (2 weeks after stopping treatment)<br>• At 12 weeks (8 weeks after stopping treatment)<br>HIV antibody testing is performed at 18-24 months of age to ensure seroconversion | Assessment should be performed:<br>• Within the first 48 hours<br>• Prior to discharge<br>• At 2 weeks<br>• Monthly during breast feeding and for 2 months after cessation<br>HIV antibody testing is performed at 18-24 months of age to ensure seroconversion |

## Postpartum management

- **Medical treatment:**

  cART should be continued postpartum. It may be modified to adjust to contraceptive choice

- **Surveillance:**
  - Women should be followed up by a multidisciplinary team at 4-6 weeks postpartum
  - Assess mental health. Discuss contraception
  - Cervical cytology should be performed 3 months after delivery
  - If HIV diagnosis is new, the partner and other children should be evaluated

- **Breast feeding:**
  - Safest approach to breast feeding is formula milk. Cabergoline should be given to suppress milk production

- Women who are interested in breast feeding should be adherent to cART:
  - Decision should be supported after counselling on the low risk of transmission
  - Monthly follow-up of foetal viral load is required and for 2 months after cessation
  - Maternal cART is recommended to minimize risk of transmission during breast feeding

## Hepatitis and HIV

| Hepatitis B and HIV | Hepatitis C and HIV |
|---|---|
| • If hepatitis B is newly diagnosed:<br>▪ Test hepatitis B virus (HBV) DNA<br>▪ Test antigen status<br>▪ Screen for hepatitis A, C, and D<br>▪ Screen liver function<br>• After starting cART, LFT should be repeated at 2-4 weeks and then regularly thereafter to detect hepatotoxicity and immune reconstitution inflammatory syndrome (IRIS)<br>• Regimen should include Tenofovir AND emtricitabine OR lamivudine in women with wild type HIV/HBV:<br>▪ Emtricitabine is superior to lamivudine in this regimen (more effective)<br>▪ Emtricitabine or lamivudine should not be used alone to treat HBV (concerns on resistance)<br>• Women should receive hepatitis A vaccine if not immune:<br>▪ After first trimester (0 and 6 months)<br>▪ A 3rd dose is given if CD4 is < 300<br>• Treatment should continue postpartum<br>• Decision of vaginal delivery is made by HIV viral load regardless of HBV viral load<br>• Newborn should receive immunization with or without HBV immunoglobulins | • If hepatitis C is newly diagnosed:<br>▪ Access quantitative RNA<br>▪ Screen liver function<br>• After starting cART, LFT should be checked after 2-4 weeks and regularly thereafter<br>• Discontinue/do not use Ribavirin-based directly acting anti-viral therapies immediately. If the patient is not currently pregnant and is planning to become pregnant, expedite treatment with Ribavirin-based directly acting anti-viral therapies prior to conception<br>• HBV vaccine should be given to non-immune women after the first trimester<br>• Women should receive hepatitis A vaccine if not immune:<br>▪ After first trimester (0 and 6 months)<br>▪ A 3rd dose is given if CD4 is < 300 (0, 1, 6 months)<br>• Decision of vaginal delivery is made by HIV viral load regardless of HBV viral load<br>• cART should be continued postpartum in all women with both HCV/HIV |

# Maternal infection with pregnancy

## Abstract

Pregnancy presents a physiologic cause of immunodeficiency, which brings women to high risk of complications when exposed to infection. In fact, maternal infection may have foetal and neonatal sequalae as well either through maternal morbidity or through congenital and vertical transmission. In this chapter, we will discuss some important maternal infections, their complications, and their diagnosis and management strategies.

## Keywords

Malaria, sepsis, herpes, GBS, HIV

## Further readings

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# Epilepsy and Pregnancy

## Epidemiology

- Incidence of epilepsy in pregnancy is 0.5-1%
- Diagnosis of epilepsy is not necessarily permanent. Patients are considered no longer having epilepsy if:
  ① 10-years seizure-free (with the last 5 years off the anti-epileptic drugs "AEDs") OR
  ② Childhood epilepsy syndrome with no further seizures during adulthood

## Course of epilepsy in pregnancy

- Among women with epilepsy:
  - 67% of women do not experience seizures in pregnancy on average
  - 60% of women with focal epilepsy do not experience seizures in pregnancy
  - 74% of women with generalized epilepsy do not experience seizures in pregnancy
  - 75-90% of women do not experience seizures in pregnancy if they were seizure-free for 9-12 months prior to conception

  The most predictive factor of remission is seizure-free interval prior to conception
- 15% of women self-discontinue their medications in pregnancy for fear of foetal risk




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_7

## Risks of epilepsy on pregnancy

**Obstetric complications**

Spontaneous miscarriage, antepartum haemorrhage, hypertensive disorders, preterm labour, induction of labour, caesarean section, postpartum haemorrhage

**Foetal risks**

- Risk of congenital anomalies is low if the patient is not on AEDs and is comparable to baseline (2.8%).
- Risk of recurrence of major malformations if there is a previous history of foetal anomalies is 17% regardless of seizures type
- Most common congenital anomalies with AEDs are neural tube defects, congenital heart disorders, urinary, skeletal anomalies and cleft palate
- Risk of congenital abnormalities depends on drug type, number and dose

| | |
|---|---|
| **Lamotrigine and carbamazepine monotherapy** | If used in the lowest possible dose, they carry the lowest risk of congenital anomalies |
| **Valproate** | Associated with neural tube defects, facial defect, and hypospadias<br>Risk of anomalies is relatively high compared to other AEDs |
| **Phenobarbital** | Associated with cardiac anomalies |
| **Phenytoin** | Associated with cardiac anomalies and cleft palate |
| **Carbamazepine** | Associated with cleft palate |

Valproate and AED polytherapy should be avoided unless it is not safe to change treatment

**Other AEDs risks**

- Foetal growth restriction (risk of Small for gestational age is 3.5 times higher)
- Neonatal intensive care unit admission

## Diagnosis of epilepsy

- If diagnosis of epilepsy was not made prior to conception, it should only be made by a medical expert (a neurologist)
- If seizures occur in the second half of pregnancy, patients should be managed as eclampsia and magnesium sulphate. Final diagnosis should be made based on previous history of seizures/epilepsy and risk factors of preeclampsia and full neurological assessment.
- CT and MRI are safe in pregnancy to assess women with seizures

**Other causes of seizures**

- Cerebral venous sinus thrombosis
- Posterior reversible leukoencephalopathy syndrome
- Space occupying lesions
- Reversible cerebral vasoconstriction syndrome
- Syncope
- Hypoglycaemia
- Hyponatremia and Addisonian crisis
- Psychogenic seizures

## Antepartum management

**Maternal care**

- All patients should receive 5 mg/day of folic acid starting 3 months prior to conception and till the end of the first trimester
- Antenatal care should involve designated epilepsy care team
- Women who unintentionally get pregnant while on AEDs:
  ① Should not stop AEDs
  ② Should be offered an urgent epilepsy consultation
- Discuss safe environment, continuous observation and assistance with the patient and her family. **Close monitoring of epilepsy is recommended in patients who experienced seizures within 1 year prior to conception**
- Women with history of epilepsy who are not at high risk of seizures can be managed as "low risk"
- Perinatal mental health team should assess any mood or cognitive concerns

Women with non-epileptic attack disorder should not be treated with AEDs

**Foetal care**

- Detailed anatomy US scan at 18-20+6 weeks
- Serial growth scans for women exposed to AEDs to diagnose small for gestational age

Serum AED level monitoring, antepartum foetal surveillance with cardiotocography, and increasing the dose of antenatal steroids (if indicated) are **NOT** recommended

## Intrapartum management

- **General principles:**
  - Epilepsy is not an indication for planned caesarean delivery or induction of labour. Induction medications are NOT contraindicated in patients with epilepsy. However, elective caesarean section may be indicated in women with recurrent and prolonged seizures during pregnancy who are at high risk of status epilepticus
  - One-to-one midwife care is recommended
  - Continuous foetal monitoring is indicated in women:
    ① At high risk of intrapartum seizures or
    ② After occurrence of intrapartum seizures
  - Water birth should only be offered after a discussion with an epilepsy specialist in women who are not on AEDs and, have no history of seizures for a long time

- **Intrapartum medications:**

| | |
|---|---|
| **Pethidine (for analgesia)** | It should be avoided (lower seizures threshold). Diamorphine may be used instead |
| **Ketamine (for anaesthesia)** | It should be avoided (lower seizures threshold) |
| **Sevoflurane (for anaesthesia)** | It should be avoided (epileptogenic) |
| **Clobazam (long acting benzodiazepines)** | The medication may be considered in women at significant risk of peripartum seizures |

- **Prevention of seizures:**

Although risk of peripartum seizures is low, it is relatively high compared to antepartum period.

- Adequate analgesia during labour
- AED should continue during labour

- **Management of seizures:**

Intrapartum seizures can cause foetal hypoxia with subsequent bradycardia and reduced variability. Uncontrolled tonic clonic seizures are the most significant factor of sudden unexpected death in epilepsy (SUDEP). As a role, any seizures longer than 5 minutes are not anticipated, and they present a risk factor for status epilepticus

**Intrapartum seizures**

- Incidence of seizures in labour is 3.5%
- Risk of tonic-clonic seizures is 1-2% in labour and 1-2% within 24 hours postpartum
- Risk of status epilepticus is 1%

| | |
|---|---|
| **Positioning** | Patient should be positioned in a left lateral tilt. Airway and oxygenation should be maintained |
| **Control of seizures** | • Lorazepam IV (0.1 mg/kg, usually 4 mg bolus followed by 2nd dose after 10-20 minutes) is the standard treatment<br>▪ Diazepam 5-10 mg slow IV may be used as an alternative<br>▪ Rectal diazepam 10-20 mg (can be repeated once after 15 minutes) may be used if there is no IV access<br>▪ If no response, consider phenytoin (or fosphenytoin). Loading dose is 10-15 mg/kg by IV infusion |
| **Tocolytics** | • Tocolytics are indicated if there is persistent uterine hyper tonus<br>• Continuous foetal monitoring should be performed during and after seizures |
| **Delivery** | Immediate delivery is indicated If:<br>① Foetal heart rate does not recover within 5 minutes or<br>② Seizures are recurrent, expedite delivery |

Peripartum use of benzodiazepine and AEDs should be reported to paediatric team to consider risk of neonatal withdrawal syndrome

## Postpartum management

- **Maternal care:**
  - Prevention of risk factors of seizures e.g. sleep deprivation, stress, poor pain control. Risk of seizures is high in the first 3 postpartum days specially in women who had recent seizures (within a month before pregnancy)
  - Women should be advised to continue their AEDs postpartum.
  - The dose should be reviewed within 10 days postpartum to avoid toxicity if the dose was changed during pregnancy. Providers should be aware of signs of AED toxicity e.g. drowsiness, diplopia, or unsteadiness. Urgent neurological review is indicated if toxicity is suspected
  - Dose of AEDs should be tapered to pre-pregnancy baseline
  - Breast feeding should be encouraged
  - Postpartum screening for depression is recommended

- **Neonatal care:**
  - Neonates should be closely monitored for signs of adverse effects of AED in-utero exposure or withdrawal
  - All babies born to women on enzyme-inducing AEDs should be offered 1 mg IM vitamin K to prevent haemorrhagic disease of the newborn

## Contraception

| | Drugs | Suitable contraceptives | Notes |
|---|---|---|---|
| **Enzyme-inducing AEDs** | ▪ Carbamazepine<br>▪ Phenytoin<br>▪ Phenobarbital<br>▪ Primidone<br>▪ Oxacarbazine<br>▪ Topiramate<br>▪ Eslicarbazapine | ▪ Copper intrauterine devices (IUD), levonorgestrel-releasing intrauterine system and medroxyprogesterone acetate injections<br>▪ Copper IUD is preferred for<br>▪ emergency contraception | ▪ Risk of failure of oral contraceptives is 3 times higher (3.1%)<br>▪ Topiramate at doses less than 200mg/day does not cause drug interactions |
| **Non enzyme-inducing AEDs** | ▪ Valproate<br>▪ Lamotrigine<br>▪ Levetiracetam<br>▪ Gabapentin<br>▪ Pregabalin<br>▪ Tiagabine<br>▪ Vigabatrin | All methods of contraception | Oestrogen-containing contraception decreases serum level of lamotrigine by 20% in the first 3 days and 25-70% in general. Therefore, it increases risk of seizures |

# Headache and Pregnancy

## Classification

| | |
|---|---|
| **Primary headache (90% of causes)** | • Migraine<br>• Tension headache |
| **Secondary headache** | Examples include:<br>• Hypertension<br>• Subarachnoid haemorrhage<br>• Drug-related e.g. nifedipine<br>• Post-dural puncture<br>• Meningitis<br>• cerebral venous thrombosis<br>• Anaemia<br>• Caffeine withdrawal<br>• Arteriovenous malformation |

## Assessment

- **History:**

  History should cover the following points:

  - Characters of headache e.g. site, severity, type of pain, exacerbating and alleviating factors, relation to time during the day
  - Associated symptoms e.g. auras, change in vision, nausea and vomiting
  - Medical history and current medications
  - Prior investigations and treatment

- **Physical examination:**
  - **Neurological examination:**
    - Fundoscopy for assessment of papilledema
    - Pupillary reaction
    - Visual field assessment
    - Cranial nerve assessment e.g. eye movement, speech and swallowing
    - Muscle tone and coordination
    - planter response for upper motor neuron lesion
    - Assessment of gait
  - **Cardiovascular assessment:**
    - Assessment of preeclampsia after 20 weeks of gestation (blood pressure, proteinuria, clonus)

- **Investigations:**
  - **Magnetic resonance imaging (MRI):**
    - It should be avoided in first trimester because of the risks associated with hyperthermia and acoustic noise. However, it is generally superior to ionising radiation
    - T2-weighted MRI and magnetic resonance venography (MRV) is the best modality to diagnose central venous thrombosis.

Gadolinium-based contrast is safe in pregnancy and breast feeding

  - **Computerized tomography (CT):**
    - It is the standard modality in women with headache or focal neurological signs
    - Head CT is associated with low foetal exposure (<0.005 mGY)

Iodine-based contrast media should be avoided in pregnancy. If its use was inevitable, thyroid function of the neonate should be checked

| Epidemiology | |
|---|---|
| Most cases occur in childbearing periods. Frequency and severity without aura decrease in pregnancy. There is 17-fold risk in risk of stroke, 4-fold risk of acute myocardial infarction and 2-fold increase in risk of preeclampsia | **Migraine** |
| Incidence is 0.5-2.5% after epidural anaesthesia. Incidence of headache after dural puncture is 70-80% | **Postural puncture headache** |
| It is more prevalent in obese women | **Idiopathic intracranial hypertension** |
| Headache associated with preeclampsia is limited to women who are pregnant or in the puerperium,<br>and occurs after pre-eclampsia or eclampsia is diagnosed | **preeclampsia** |
| The condition is associated with preeclampsia | **Posterior reversable encephalopathy syndrome** |
| The condition occurs in postpartum period and is associated with arterial constriction and dilation | **Reversible cerebral vasoconstriction syndrome** |
| The highest risk occurs in the third trimester and for 4 weeks postpartum.<br>Incidence during pregnancy and puerperium is 1:2500 to 1:10000. The most common site is sagittal sinus or one of the cortical veins | **Cerebral venous thrombosis** |

| Clinical features |
| --- |
| Unilateral pulsating moderate to severe headache, that builds up over minutes to hours. It is aggravated by routine physical activity and is associated with nausea ± vomiting ± sensitivity to light/sound. Aura may present, which evolve over > 5 minutes and resolves within 60 minutes |
| It develops 24-48 hours post-puncture. It is a fronto-occipital headache that radiates to the neck, it is aggravated by standing. It typically lasts for 7-10 days but may last up to 6 weeks if untreated |
| Generalized, non- throbbing headache, associated with diplopia (38%), visual loss with papilledema (31%). Diagnosis is based by exclusion. Elevated cerebrospinal fluid pressure on lumbar puncture (above 20cm$H_2O$) |
| Diagnosis is made by at least 2 of the following features: (1) Temporal headache. (2) Either/or both: **A.** worsened in parallel with worsening of pre-eclampsia or eclampsia. **B.** improved in response to improvement of pre-eclampsia.<br>(3) at least two of them (bilateral location, pulsating quality, aggravated by physical activity) |
| Headache, vomiting, visual disturbance, seizure, and alerted mental status. MRI shows oedema in the posterior circulation of brain |
| Recurrent severe headache of sudden onset that develops over 1-3 weeks, commonly associated with nausea, vomiting, photophobia, confusion and blurred vision. Definitive diagnosis is by diffuse arterial beading on cerebral angiography, Resolution may occur in 1-3 months |
| Headache is the most common symptom (80-90%). It is acute or subacute, localized, continuous, moderate to severe headache that develops over hours or weeks, associated with papilledema, focal deficits, alerted consciousness, seizures, diplopia ($6^{th}$ nerve palsy, psychosis, and focal neurological signs. CT is insensitive (30%), T2-weighted MRI or MRV are the best modalities |

| Management |
| --- |
| ❶ Avoid precipitating factors, recommend rest, hydration, regular meals, and relaxation. ❷ Paracetamol and antiemetics, If inadequate, sumatriptan (safe) and NSAIDs (in first and second trimester only). ❸ Consider prophylactic treatment with propranolol or amitriptyline 25-50 mg at night if there is recurrent headache (3-4 times per month) |
| ❶ Hydration and simple analgesics ❷ Epidural blood patch (60-90% cure rate) |
| Visual fields and acuity should be monitored. Advise on controlling weight gain. Therapeutic lumbar puncture or acetazolamide 500mg twice daily may be used to improve headache and visual loss |
| Presence of preeclampsia related headache is a feature of severe preeclampsia. Patients should be admitted, and magnesium sulphate should be started. Decision of delivery is made based on gestational age, maternal and foetal status, and laboratory findings |
| Recognition and management are required to avoid irreversible sequalae. Management of preeclampsia, control of blood pressure, prevention and treatment of seizures and prompt delivery |
| Treatment with Calcium channel blockers, high dose corticosteroid, and magnesium sulphate |
| Refer to a neurologist, low molecular weight heparin is used for 6 months, if deterioration occurs, endovascular therapy should be performed. Follow-up with MRV after 3-6 months.<br>It is not a contraindication to future pregnancy, but heparin prophylaxis will be indicated |

# Stroke and pregnancy

## Epidemiology

- Stroke is a neurological deficit caused by acute focal injury of the central nervous system that is attributed to a vascular cause (cerebral infarction, cerebral vein thrombosis (CVT), intracranial haemorrhage (ICH) and subarachnoid haemorrhage)
- Risk of strokes is 3 times higher among pregnant women vs. nonpregnant population of the same age

**Obstetric risk factors**

- Maternal age >35 years
- Migraine
- Gestational diabetes
- Preexisting hypertension
- Pre-eclampsia or eclampsia.

## Clinical presentation

| Symptoms and signs of stroke relate to the affected area of the brain | | | | | |
|---|---|---|---|---|---|
| **Frontal lobe** | **Parietal lobe** | **Temporal lobe** | **Occipital lobe** | **Cerebellum** | **Brainstem** |
| • Higher cognitive functions<br>• Motor control<br>• Emotional expression | • Processing sensory input<br>• Sensory discrimination<br>• Body orientation<br>• Primary and secondary somatic areas | • Auditory reception<br>• Expressed behaviour<br>• Receptive speech<br>• Visual memory<br>• language comprehension | • Visual reception<br>• Visual interpretation | • Coordination<br>• Control of voluntary<br>• movements | • Alertness<br>• Breathing<br>• Digestion<br>• Heart control<br>• Blood vessel control |

Clinical assessment includes a brief history of onset, symptoms, medical history, and contraindications to thrombolysis. Scores on the National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) are doucmented

| Modified Rankin Scale (mRS) | |
|---|---|
| **Score** | **Description** |
| **0** | No symptoms at all |
| **1** | No significant disability: able to carry out all usual duties and activities |
| **2** | Slight disability: able to look after own affairs without assistance |
| **3** | Moderate disability: requiring assistance, but able to walk without assistance |
| **4** | Moderately severe disability: unable to walk or attend to own bodily needs without assistance |
| **5** | Severe disability; bedridden and incontinent (requiring constant nursing care) |
| **6** | Dead |

## Investigations

- **Diagnostic investigations:**
  - **CT scan:**

| | |
|---|---|
| **Non contrast CT scan** | All patients with suspected stroke should have non-contrast computed tomography (CT) with lead shielding on arrival to hospital |
| **CT angiogram** | For candidates for mechanical thrombectomy to evaluate for large vessel occlusion. Less radiation exposure than CT perfusion |
| **CT perfusion** | Theoretical risk of fetal thyroid suppression. Therefore, neonatal thyroid function should be monitored in the initial 2 weeks of life |

In eclampsia, posterior reversible encephalopathy syndrome (PRES) can be suggested on CT scan (e.g., ill-defined subtle white matter hypodensities in frontal, parietal and occipital regions)

Most accurate assessment is done by a combination of CT perfusion and CT angiogram

- **MRI:**
  - MRI is the preferred first-line imaging modality in pregnancy (no radiation)
  - Gadolinium can be used to enhance MRI. However, it passes the placenta and may accumulate in the amniotic fluid. It should be used with caution and informed consent should be obtained

In eclampsia, posterior reversible encephalopathy syndrome (PRES) is visible as white matter lesions that are hyperintense on T2 and hypointense on T1

- **Investigations for underlying cause:**

| Investigation | Value |
|---|---|
| **12-lead ECG** | • Possible underlying arrhythmia, such as atrial fibrillation or cardiac ischaemia. |
| **Early 24-hour cardiac/Holter monitoring** | • For all patients with ischaemic stroke. |
| **Prolonged cardiac monitor or implantable loop recorder** | • Should be considered for cryptogenic strokes potentially caused by paroxysmal atrial fibrillation |
| **Transthoracic echo** | • The preferred first-line investigation |
| **A 'bubble test' or contrast echocardiogram** | • Can demonstrate an intra-atrial shunt. |
| **Transoesophageal echocardiogram (TOE)** | • Rule out aortic arch atheroma, left atrial appendage thrombus, and patent foramen ovale |
| **Doppler imaging of the extracranial carotid and vertebral arteries** | • Rule out the presence of dissections, stenosis and occlusions |
| **Full blood count, liver function tests, urea, electrolytes and uric acid** | • If pre-eclampsia is suspected, checked to rule out HELLP syndrome or thrombocytopenia. |
| **Thrombophilia Screening** | • Persistent lupus anticoagulant was more associated with ischaemic stroke<br>• Testing for inherited thrombophilia is of limited benefit in pregnancy. However, testing for inherited gene mutations and acquired thrombophilias can guide treatment |

## Management

- **Management of stroke:**
  - **Management of ischemic stroke:**

**Intravenous thrombolysis:**

- Pregnancy is a relative contraindication for the use of thrombolytics, however, recombinant tissue plasminogen activator (rt-PA) may be considered when the benefits outweigh the increased risks of uterine bleeding (e.g., moderate or severe stroke)
- Major surgery as CS or difficult vaginal delivery within 2 weeks is a relative contraindication for thrombolytic therapy.
- Its safety during breastfeeding is unknown

**Obstetric complications of thrombolytic treatment**

- maternal deaths
- Bleeding episodes
- Foetal deaths
- Neonatal death
- Miscarriages
- Preterm delivery

**Mechanical thrombectomy:**

- Mechanical thrombectomy with stent retriever devices is superior to intravenous rt-PA alone in acute anterior circulation ischaemic stroke (10% only)
- Eligible patients with a large vessel occlusion on CT angiogram should be urgently referred to a neuro-interventional centre
- Fetal radiation exposure can be minimised by using low-doses, pulsed fluoroscopy and radiation shields.
- Care includes ICU setting until stable, with foetal wellbeing assessment

  - **Management of haemorrhagic stroke:**

Immediate treatment is directed towards haemostasis, correction of coagulopathy and hyper/hypoglycaemia, blood pressure control and venous thromboembolism prophylaxis

- **Correction of coagulopathy and thrombocytopenia:** e.g., patients on warfarin with a prolonged INR should receive IV vitamin K and prothombin complex.
- **Aggressive blood pressure control:** target blood pressure is 140 mmHg
- **Thromboprophylaxis:** using intermittent pneumatic compression is indicated in all patients with ICH

- **Antiepileptic medications:** for patients with clinical seizures or EEG changes.
- **Surgical decompression:** for patients with cerebellar haemorrhage with deteriorating neurological function, or with brainstem compression and/or hydrocephalus

- **Management of Cerebral Venous Thrombosis (CVT):**
  - **Anticoagulation:** with either LMWH or unfractionated heparin.
    If anticoagulation is contraindicated, or if the patient does not respond to anticoagulation, thrombolysis or thrombectomy can be considered
  - **Intravenous mannitol:** is given if there are signs of increased intracranial pressure
  - **Decompressive craniectomy:** is considered in cases of impending herniation.

- **Management of pre-eclampsia/eclampsia and posterior reversible encephalopathy syndrome (PRES):**
  - Magnesium sulphate is an essential treatment
  - Blood pressure optimization
  - Delivery of the foetus

  In most cases, PRES resolves spontaneously, with recovery within days to weeks.

## Secondary prevention strategies

- Recurrent strokes account for 25–30% of all strokes
- Aggressive blood pressure management should be considered
- Administration of aspirin is recommended with ischaemic stroke within 24–48 hours of onset
- Dual antiplatelet therapy (aspirin and clopidogrel) is indicated in women with transient ischaemic stroke and mild stroke within 24 hours and for 21 days
- Clopidogrel should be stopped 7–10 days before delivery
- Women on clopidogrel who has spontaneous labour should not undergo neuroaxial anaesthesia
- If there is ischaemic stroke and atrial fibrillation, anticoagulation should start within 4–14 days of the onset of symptoms.
- Statin therapy should be stopped pre-conceptually and throughout pregnancy

- **Obstetric management:**

A multidisciplinary team should be involved in the care of a pregnant woman with stroke, including obstetrics, neurology, radiology, neurosurgery, cardiology, naesthesiology and haematology

- **Pre-conceptual care**
  - No consensus on the best protocol for secondary prevention of stroke in pregnancy.
  - Statins, clopidogrel and vitamin K antagonists are usually discontinued
  - BP control is optimised using pregnancy-safe medications pre-conceptually.
  - Aspirin is safe
  - In women with a high thrombotic risk, LMWH is also commenced.
  - Future pregnancies should be closely monitored:
    - Stroke recurrence is 0–1.8% in pregnancy
    - Stroke recurrence is 0.5% outside of pregnancy
    - If concurrent thrombophilia is present, the risk is up to 20%

- **Mode of delivery**
  - Mode of delivery requires multidisciplinary input and should be individualized
  - If vaginal delivery is considered:
    - Consider early epidural reduces fluctuation in BP
    - Consider operative vaginal delivery to shorten the second stage. Thereby, prevent prolonged Valsalva and increased intracranial pressure

- **Postpartum management:**
  - The postpartum period is the highest risk period for venous thromboembolism and stroke.
  - Anticoagulation should be continued for at least 6 weeks postpartum.
  - Multidisciplinary approach to postnatal care is important.
  - A complete thrombophilia screen should be arranged 6 weeks postnatally.
  - Warfarin, low molecular weight heparin (LMWH), clopidogrel and aspirin are safe to take while breastfeeding.
  - Combined hormonal contraception is contraindicated.
  - No increased risk in stroke in women taking progesterone-only contraception.

# Multiple Sclerosis with Pregnancy

## Definition

Multiple sclerosis (MS) is a chronic demyelinating neurologic disorder that results in progressive neurological dysfunction and disability

## Epidemiology

- MS is 2-3 times more common in women than in men
- Mean age of onset is 30 years
- Incidence of MS in the general population is 1 in 330
- Recurrence risk with one affected child is 2.7% (genetic predisposition)

## Classification

- Depending on relapse and progression of the disease, it is classified to:
  ① Relapsing remitting MS (RRMS) (85%)
  ② Secondary progressive MS (SPMS)
  ③ Primary progressive MS (PPMS) (10-15%)
- Disease progression is monitored using the expanded disability status scale (EDSS). This is a 20-point step scale with 0.5 increments. It ranges from 0 = 'normal' to 10 = 'death caused by MS'

## Clinical presentation

| Primary symptoms (a direct result of demyelination) | | Secondary symptoms (complications of primary symptoms) |
|---|---|---|
| **Most common** | **Least common** | |
| • Visual symptoms: optic neuritis (often the first symptoms in 20–30%), diplopia, blurring of vision, poor colour vision<br>• Fatigue<br>• Spasticity<br>• Cognitive symptoms<br>• Mood changes<br>• Numbness, tingling/prickling<br>• Loss of balance and dizziness<br>• Acute and chronic pain<br>• Urinary incontinence or retention<br>• Constipation or anal incontinence | • Dysarthria<br>• Dysphonia<br>• Dysphagia<br>• Seizures<br>• Tremors<br>• Breathing problems<br>• Headache<br>• Hearing loss | • Recurrent urinary tract infections<br>• Poor postural alignment<br>• Decreased bone density<br>• shallow, inefficient breathing<br>• Sexual dysfunction (30–70% in MS patients) |

## MS and assisted reproduction

- The rate of relapse is higher following assisted reproductive techniques (ART). Relapse commonly occurs 3 months after ART
- The rate of relapse is significantly higher after unsuccessful attempts and following GnRH agonist protocols

**ART-related factors that cause relapse**

- Discontinuation of medications prior to initiation of ART
- Immunological changes during ART e.g., pro-inflammatory cytokines
- Stress associated with infertility treatment

## MS and pregnancy

| Effect of pregnancy and breastfeeding on MS | Effects of MS on pregnancy |
|---|---|
| • Fewer relapses occur during pregnancy<br>• Most new relapses involve different symptoms that have not presented before (vs. 'pseudo relapses' present as a flare-up of all symptoms)<br>• Pregnancy does not affect the risk of MS or long-term progression<br>• Pregnancy worsens some symptoms e.g., fatigue, back pain, bladder/bowel problems, urinary tract infection (UTI)<br>• 20-30% relapse rate during the first 3–4 months postpartum (pre-pregnancy relapse rate is the most predictive factor of postpartum relapse)<br>• Exclusive breastfeeding for at least the first 2 months postpartum reduces relapse in the immediate postnatal period | **Maternal effects:**<br>• Many women will choose to terminate their pregnancy (fear of disability, inheritance of the disease, or discontinuing medications)<br>• Higher rate of antenatal hospitalisation<br>• Higher rate of caesarean delivery<br>• Slightly higher incidence of operative vaginal deliveries (in women with greater disability)<br>**Fetal effects**<br>• No major increase in adverse outcomes in infants<br>• No increase in the rate of miscarriage, congenital abnormality, still births and perinatal mortality<br>• Small risk of preterm delivery<br>• Higher risk of foetal growth restriction (increases by 1.7 times) |

## Obstetric management

- **Pre-pregnancy counselling:**
  - Pre-pregnancy counselling should be done with the MS clinical team.
  - The discussion should include importance of conceiving during remission and of good disease control during pregnancy.
  - There is no evidence that pregnancy with MS is harmful.
  - The safety of medications used during pregnancy and breastfeeding should also be discussed including risk of some medications on the foetus and the risk of stopping DMTs during pre-conception counselling
  - MS is not a hereditary disease, the risk of having children developing the disease is very small.

- Women should be encouraged and supported to stop smoking because it increases the risk of disease progression.

**MS medications' safety in pregnancy**

- Glatiramer acetate and interferons, are relatively safe to use during early pregnancy.
- Some patients with highly active disease on DMTs are at risk of significant rebound of disease activity (within 3 months) and these women may stay on their DMT, e.g., natalizumab, or restart them early in the postpartum period to reduce the risk of relapse
- Other immunosuppressants and DMTs are contraindicated during pregnancy and breastfeeding

- **Antenatal management:**

Multidisciplinary setting involving a neurologist with an interest in MS and pregnancy, an MS specialist nurse, an obstetrician with expertise in MS, a general practitioner (GP) and a community midwife should manage the patient:

- Frequent rest and avoiding stress may be helpful for fatigue
- Monthly midstream urine sampling is indicated in women with bladder symptoms and neurogenic bladder
- Adequate hydration, high-fibre diet and occasional laxatives in women experiencing constipation
- Consider thromboprophylaxis with compression stockings and LMWH in women with reduced mobility or wheelchair-bound and have additional risk factors
- Amitriptyline may help with neurogenic pain
- Diazepam can improve spasticity
- Anaesthetist review: It is safe to use pethidine, nitrous oxide, a transcutaneous electrical nerve stimulation machine and regional anaesthesia during labour

**Management of relapse**

- Relapse during pregnancy is more probable during the first and second trimesters
- MRI can confirm a relapse (but MRI with gadolinium contrast should be avoided in pregnancy)
- Management involves oral or IV corticosteroids
- Women with MS relapse receive steroids for less than 4 weeks before birth. Additional oral doses or parenteral hydrocortisone are indicated during delivery and in the immediate postpartum period to lower the risk of acute adrenal crisis (stress dose)

- Fetal scan surveillance in the third trimester should be considered because of the risk of small-for gestational-age infants.

- **Intrapartum management:**
  - MS does not affect timing and mode of delivery and they should be determined by obstetric indications. However:
    - Planned caesarean section may be considered in women with severe neurological problems.
    - Women with higher EDSS scores might require induction of labour
  - The bladder should be emptied periodically during labour, and it is advisable to use an indwelling urinary catheter with epidural anaesthesia
  - Increased fatigue and maternal exhaustion may increase incidence of assisted delivery

- **Postpartum management:**
  - The MS team should formulate a postnatal plan in the late third trimester.
  - Women should be encouraged to breastfeed. Breastfeeding is contraindicated when they restart on a DMT in the immediate postpartum period
  - Breastfeeding is safe during steroid therapy but advised to be 4 hours post-administration to minimise infant exposure.
  - Patients with very active disease prior to pregnancy usually restart their MS treatment immediately after delivery and choose not to breastfeed.
  - Effective contraception is necessary to prevent unintended pregnancies in women with MS. Most contraceptive methods are safe to be taken.

# Spinal Cord Injury and Pregnancy

## Background

- Spinal cord injury (SCI) results in temporary or permanent alternation in motor, sensory or autonomic function of nervous system
- Pregnancy exacerbates most complications of spinal cord injury. Women with lesions above the level of T6 of the spinal cord are susceptible to autonomic dysreflexia (AD), spasms, breathing difficulties, bradycardia and hypotension.
- Other complications of SCI include pressure ulcers, anaemia and urinary tract infections
- Spinal cord injury during pregnancy is a less common scenario that is associated with greater risks to both the mother (risk of venous thromboembolism in the first 3 months) and foetus (risk of miscarriage and foetal anomalies)

## Preconception counselling

| Issue | Points to discuss |
|---|---|
| **Spinal cord injury and disability** | • Woman's understanding of her condition<br>• Extent of spinal and injury<br>• Impact on pregnancy and delivery; pelvic contractures<br>• Review medication for potential teratogenicity |
| **The effect of pregnancy** | • Worsening mobility with advancing pregnancy<br>• Worsening breathing with advancing pregnancy<br>• Possible change in bladder care and need for an indwelling catheter by the end of pregnancy<br>• Complications of spinal injury that may be aggravated by pregnancy: autonomic dysreflexia, spasms |
| **Care in pregnancy** | • GP, community midwife, local obstetric unit, obstetric unit at place of delivery if different, occupational therapy<br>• Anaesthetic review early in pregnancy<br>• Social services |
| **Delivery** | • Vaginal delivery is the best route of delivery<br>• Admission to delivery suite should be considered early in labour |
| **Postnatal issues** | • Resources for neonatal care should be available<br>• Adaptive equipment e.g. low baby-changing tables |

## Antenatal care

- Multidisciplinary team should manage antenatal care according to active health issues. Care may be provided in collaboration with a local obstetrician and community midwife for patients who live far from a specialist care
- Women should be admitted late in the third trimester (to avoid unattended birth)

**Multidisciplinary team**

- Obstetrician
- Obstetric anaesthetist
- Spinal nurse
- Specialist midwife and nurse
- Physiotherapist
- Occupational therapist

## Obstetric complications

- Lesions above T10 are associated with altered perception of foetal movement and of contractions (preterm labour may be unnoticed)
- Patients are taught to palpate foetal movement and contractions.
- There is increased incidence of malpresentation, and external cephalic version may be offered

## Bladder

- Women who use intermittent catheterization for bladder emptying may switch to indwelling catheterization later in pregnancy (due to incontinence and limited mobility)
- If a woman has suprapubic catheter (SPC) in place, it should be changed within 24 hours of surgery to decrease surgical infection
- Urinary retention should be avoided as it may precipitate AD episodes

## Renal

Pregnancy increase urinary incontinence and Urinary tract infection

## Thromboprophylaxis

Venous thrombo-embolism risk increases up to 6 months after SCI then returns to baseline. In assessing antenatal risk, Otherwise, SCI may increase risk of thrombo-embolism due to immobility

## Cardiac

- Blood pressure and pulse should be recorded at booking to determine baseline and then at each antenatal
- Increase In systolic blood pressure by 20-40 mmHg above baseline is a sign of AD.

## Skin

- Risk of decubitus ulcers is increased
- In these cases, patients should be admitted for skin care, use of pressure relieving mattresses, and position change every 2 hours
- Postpartum pressure mapping is recommended before discharge

## Bowel

Pregnancy increases constipation which may precipitate AD, bowel care includes oral fibres, scheduled bowel movements, laxatives or digital evacuation

## Respiratory system

- **Lesion above T4:**
  It is associated with paralysis of ventilation muscles, with subsequent breathing difficulties
- **Lesion above T6:**
  This s an indication for:
  - Antenatal respiratory Function assessment: Vital capacity < 12-15 ml/kg is an indication for mechanical ventilation)
  - If respiratory function is impaired, chest physiotherapy, CPAP or mechanical ventilation are indicated

## Spasms

- Only 16% of patient report worsening of spasms in pregnancy
- Spasms are treated with baclofen
- Baclofen is better delivered by intrathecal pump. Oral baclofen may cause neonatal withdrawal symptoms
- Bladder spasms are treated with oxybutynin

## Autonomic dysreflexia

### Symptoms

- Nausea
- Anxiety
- Malaise
- Prickling sensation in skull
- Ringing in the head
- Throbbing headache
- Sweating, blushing, tremor, nasal congestion, spasms and twitching

### Triggers

- Vascular: Deep vein thrombosis, pulmonary embolism
- Urinary triggers: Bladder distension, calculi, catheter blockade, catheterization, infection
- Gastrointestinal tract: Active haemorrhoids, constipation, gallstones, gastric ulcers
- Skin: Constrictive clothing, blisters, burns, pressure ulcers
- Reproductive system: Intercourse, labour, and delivery
- Habits: excessive alcohol or caffeine intake, substance abuse

| General signs | Cardiac signs | Foetal signs |
|---|---|---|
| • Increased blood pressure > 20 mmHg, papillary dilatation<br>• transient loss of consciousness<br>• retinal bleed,<br>• subarachnoid haemorrhage, cerebrovascular accident, stroke | • Reactive sinus bradycardia<br>• Prolonged PR interval<br>• Atrioventricular blocks (Most common is second degree)<br>• Ventricular ectopic beats | Foetal bradycardia |

### Treatment

- Eliminate the triggering factor
- Use nifedipine (bite and swallow, 10 mg every 15 min) to manage blood pressure. IV labetalol or hydralazine may be used
- GTN (glyceryl trinitrate) patch or spray nitroglycerin 2% ointment is applied to skin above lesion level

## Labour and delivery

- **Symptoms and diagnosis of labour:**
  - Women with a lesion below T10 can perceive painful contractions (signals from uterine contractions enter the spinal cord at T10 and from cervical dilation at T11-12)
  - In women with lesions above T10, labor may start and progress unnoticed. Therefore:
    ① Daily cardiotocography starting at 36+6 weeks of gestation (4 hourly monitoring of contractions)
    ② Home labor monitors may be used.

- **Anaesthesia:**

| Lesions above T6 | Lesion below T6 |
|---|---|
| • Regional analgesia should be initiated early in labour (once labour is diagnosed) to control AD<br>• Absence of AD indicates effective epidural | • Anaesthesia is determined by patient preference<br>• Lesion above T10 may not require analgesia |

- **Vaginal delivery:**

| | |
|---|---|
| **First stage** | • Early epidural (specially in women with higher SCI<br>• Insertion of indwelling catheter to prevent distended bladder<br>• Vaginal examination should be gently performed. A local anaesthetic may be used. Otherwise, it may precipitate AD or spasms |
| **Second stage** | • Optimal positioning (depending on woman's disability and preference)<br>• Instrumental delivery may be indicated to shorten second stage if AD is uncontrollable despite standard analgesia<br>• Rapid spinal anaesthesia may be performed for prompt control of severe AD |
| **Third stage** | • Both physiologic and active management are reasonable<br>• Ergometrine should be avoided in women at risk of AD. Otherwise, it can be used as indicated |
| **Episiotomy** | • Use standard analgesia regardless of patient's perception of pain to reduce risk of triggering spasms and AD.<br>• Repair and postpartum pain care should be similar to general population |

- **Caesarean section:**

  Caesarean section is not a routine and should be performed as obstetrically indicated. However, incidence of caesarean delivery is high in women with SCI (47% if the lesion is at T5 or above, 26% if the lesion is below T5).

| | |
|---|---|
| **Preoperative** | • Suprapubic catheter should be changed 24 hours before surgery<br>• If general anesthesia is considered, rocuronium should be used instead of suxamethonium if SCI is recent (between 3 days to 9 months post-injury) to avoid risk of hyperkalemia and cardiac arrest) |
| **Operative** | • Skin incision is made 2 cm above SPC insertion, if present<br>• Non-absorbable sutures are used for rectus and skin closure (to decrease risk of wound dehiscence) |
| **Postoperative** | • Gentle early physiotherapy (to decrease risk of thrombosis). Patients should be turned every 2 hours to decrease risk of decubitus ulcers<br>• Regular physiotherapy is recommended on 5$^{th}$ day<br>• Sutures are removed on 10$^{th}$ day |

## Postpartum care

- **Breastfeeding:**
  - Breastfeeding should be normal. AD is rare with breast feeding
  - Breastfeeding difficulties may be present if SCI is above T4. Visual stimulation or oxytocin nasal spray may be helpful
  - Baclofen is safe with breastfeeding

- **Contraception (fertility is not impaired)**
  - Progesterone only pills, injections, implants, sterilization are the most favourable options
  - Combined oral contraceptives should be performed (risk of thrombosis)
  - Intrauterine device may not be suitable because insertion may trigger AD and strings' check may be challenging

## Neurologic disorders with pregnancy


### Abstract

Although neurologic disorders do not common coincide with young reproductive ages, the risk is still present. Such disorders may be hard to diagnosis and are absolutely challenging to manage. In its most prevalent form, headache is a common symptom in pregnancy, and it may convey an uneventful condition. However, it may be a symptom of a more serious underlying disorder. Pregnancy may increase the risk of certain neurological disorders such as sinus venous thrombosis and may alter the course of an existing disorder. In this chapter, we will discuss some neurological disorders that may be encountered in pregnancy, their obstetric and medical impact, and the best approach to manage them.



### Keywords

Headache, stroke, multiple sclerosis, spinal cord injury


### Further readings


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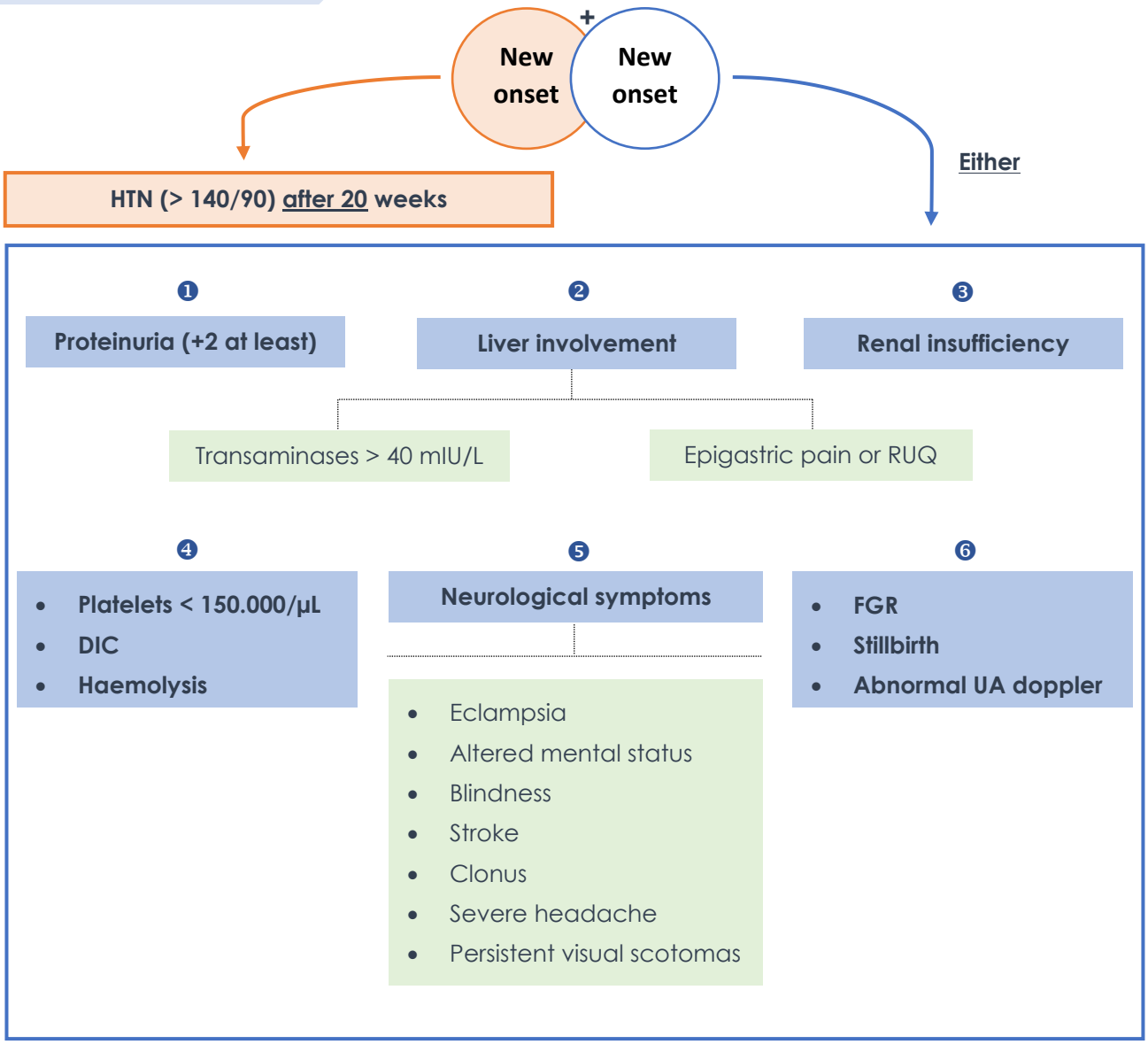
# Hypertension in Pregnancy

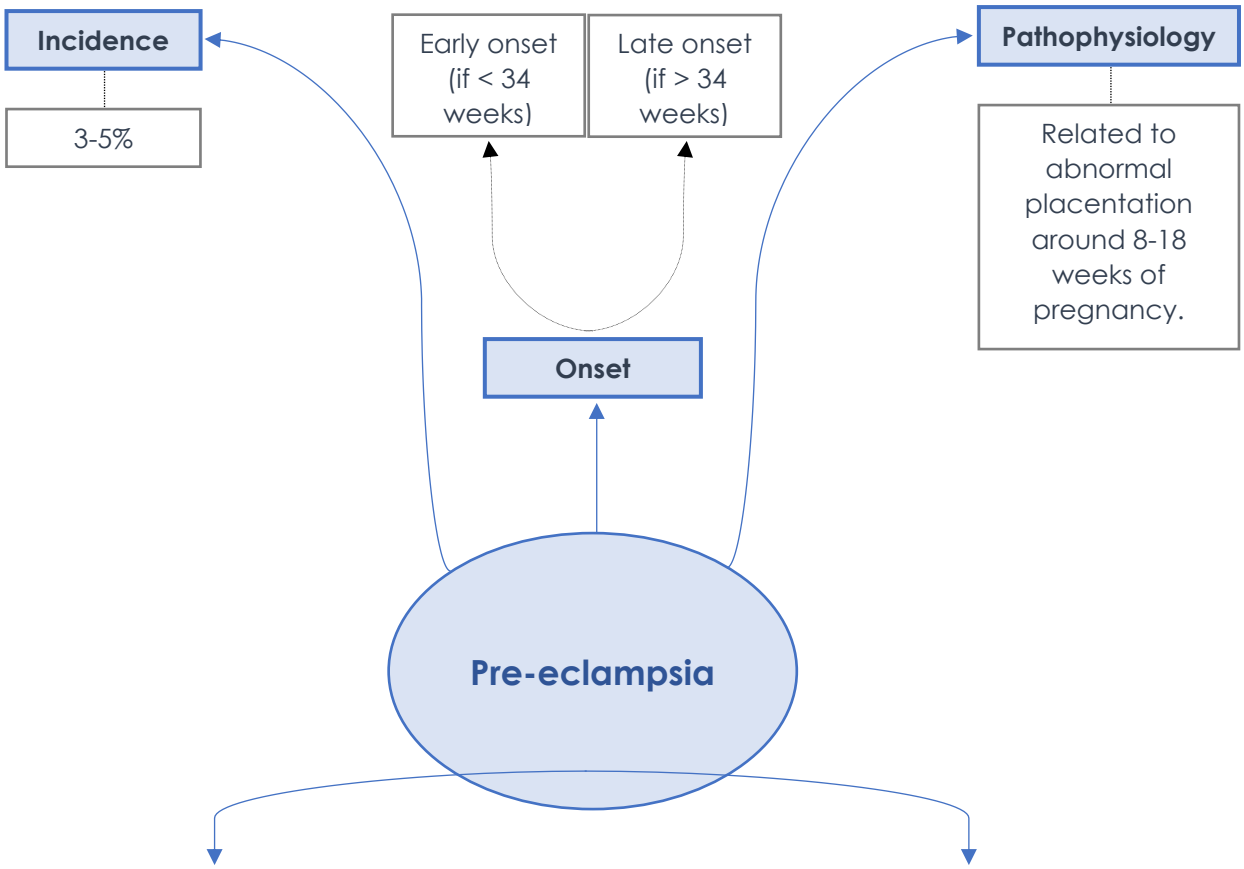
## Definition of pre-eclampsia







S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_8




| Symptoms | Complications |
|---|---|
| Severe headache | Stroke |
| Severe pain below the ribs | Eclampsia |
| Vomiting | Multiorgan failure |
| Visual symptoms (blurring or flashing) | Fetal growth retardation (FGR) |
| Sudden swelling of the face, hands and feet | Preterm labor (PTL) |
| | Intrauterine fetal death (IUFD) |

## Screening for preeclampsia

***Risk determination at booking visit (1st trimester risk assessment)***

### Model 1

**Maternal history** to define risk factors such as:

- Nulliparity
- High BMI
- Afro-Carribean race
- Ovulation induction
- Personal or family history of preE (specially if onset or delivery was early)

- Predicts 47% of preE (early and late onset)
- Predicts 35% of GHTN
- FP rate is 10%
- For early onset disease, most significant factor is AMA followed by high BMI.

### Model 2

**Model 1 + 1st trimester MAP**

- Predicts 60% of preE,
- Predicts 40% of GHTN
- FP rate is 10%

### Model 3

**Model 1 + placental biomarkers** such as:

- Placental-like growth factor ↓
- PAPP-A ↓
- FMS-like tyrosine kinase 1 ↑

- Predicts 80% of early onset preE
- Predicts 65% of late onset
- Predicts 40% of GHTN
- FP rate is 10%

### Model 4

**Model 1 + UA doppler**

- 80% detection of early onset preE
- predicts 45% for late onset

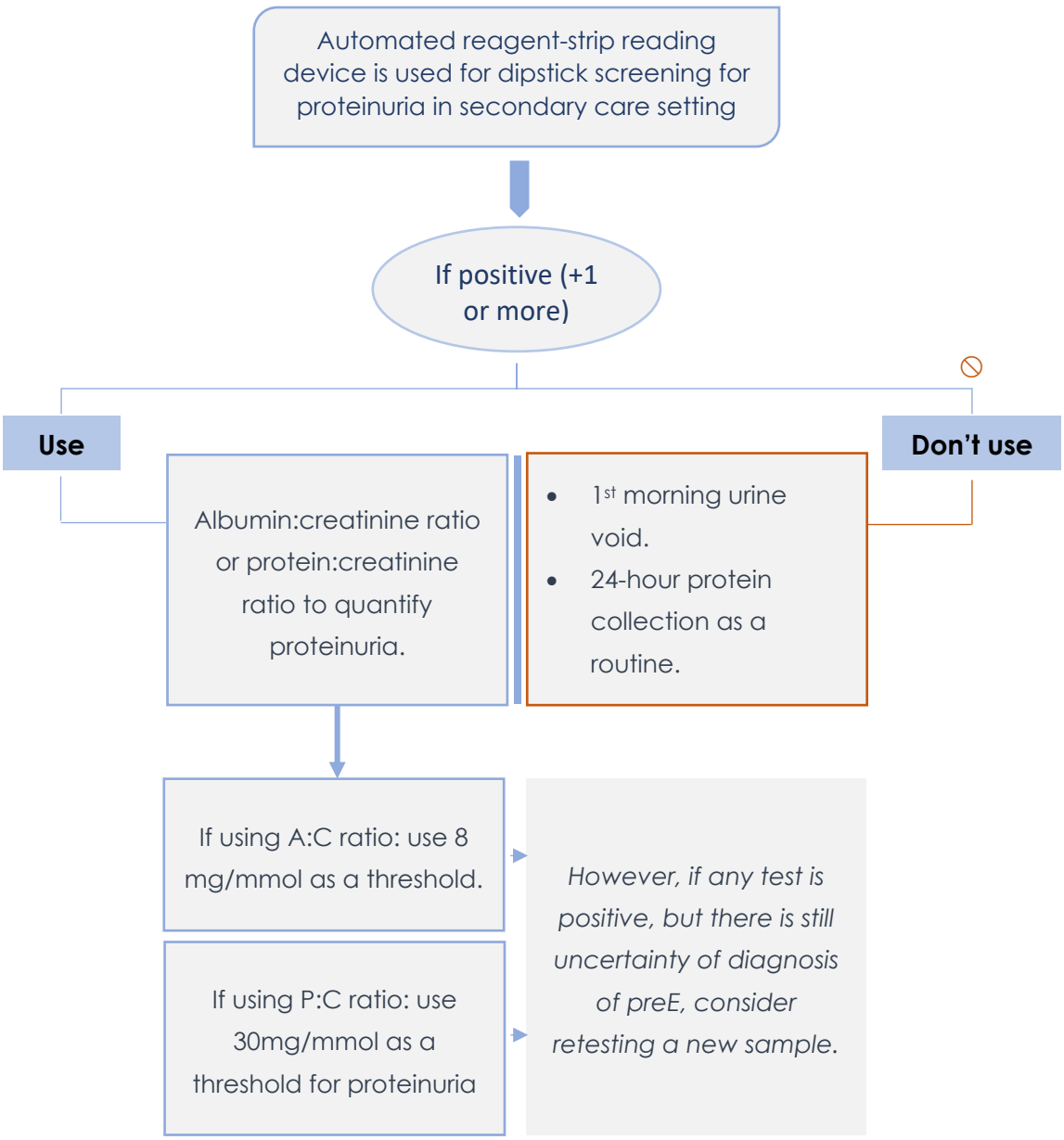
### Model 5

**Model 1 + 2 + 3 + UA doppler between 11-14 weeks**

- Predicts 89% of early onset
- Predicts 47% of late onset
- Predicts 35% of GHTN
- FP rate is 5%
- Consider cost effectiveness

## Assessment of proteinuria

Proteinuria interpretation should be in the context of symptoms, signs and other investigation



## Management of chronic hypertension in pregnancy

### ① Prepregnancy

- Refer to a specialist in hypertensive disorders of pregnancy
- Advise stopping ACEIs or ARBs before conception, alternatives should be discussed with the treating physician
- If she becomes pregnant, consider stopping these medications and start an alternative within 2 days of pregnancy notification
- Women on thiazides or thiazide-like diuretics should also stop them before conception (risk of congenital abnormalities and neonatal complications)
- *Other medications:* limited evidence, but no known increase risk of congenital anomalies

### ② Treatment of chronic hypertension

- Offer advice on weight management, exercise, healthy eating, and salt reduction in diet
- Continue existing medications if safe in pregnancy (or their alternatives) unless sustained systolic < 110, sustained diastolic < 70 or symptomatic hypotension
- If patients are not on treatment, offer treatment if sBP ≥ 140 or diastolic ≥ 90 (Target pressure is 135/85)
- Treatment options:
  - ① Labetalol
  - ② Nifedipine "2nd option"
  - ③ Methyldopa "3rd option"
- Give aspirin 75-150 mg
- Placental growth factor-based testing may help to rule out preE between 20-35 weeks if chronic HTN is suspected to develop preeclampsia

| ③ Antenatal visits | ④ Delivery time | ⑤ Postnatal investigations |
|---|---|---|
| A visit is scheduled every week if BP is poorly controlled, every 2-4 weeks if well controlled | • Delivery before 37 weeks is not indicated if a woman has blood pressure < 160/110 with or without medications.<br>• After 37 weeks, time should be determined after a discussion between the patient and senior obstetrician | • BP should be measured daily in the first 2 days, once between 3-5 days postpartum, then as clinically indicated if BP medication was changed after birth<br>• Target pressure is < 140/90. Continue treatment during postpartum period if necessary.<br>• Offer a review of antihypertensive treatment after 2 weeks with her GP or a specialist<br>• If methyl-dopa is used, it should be stopped within 24 hours postpartum.<br>• Patients with chronic HTN should be offered medical review after 6-8 weeks |

## Management of gestational hypertension

| | Hypertension 140/90 to 159/109 | Severe hypertension |
|---|---|---|
| **Admission** | Not routine | Admit, but if BP < 160/110 mmHg, manage as hypertension |
| **Medications** | Offer treatment of BP > 140/90 | Offer to all women |
| **Target BP** | 135/85 or less | |
| **BP follow-up** | Once or twice weekly till < 135/85 | Every 15-30 min till BP < 160/110 |
| **Dip stick proteinuria** | Once or twice weekly with BP | Daily while hospitalized |
| **Blood test** | Complete blood count (CBC), liver function test (LFT), renal function test (RFT) at baseline then weekly | |
| **Placental growth factor -based testing** | Carry out in 1 occasion if there is suspicion of preeclampsia | |
| **Fetal assessment** | ▪ Fetal heart rate (FHR) auscultation at each visit<br>▪ Fetal growth scans at diagnosis and every 2-4 weeks if normal<br>▪ CTG when clinically indicated | ▪ FHR auscultation at each visit<br>▪ Fetal growth scans at diagnosis and every 2 weeks if severe HTN persists<br>▪ CTG at baseline and when clinically indicated |

**Risk factors that require additional assessment and follow-up**

- Nulliparity
- Age 40 or more
- Pregnancy interval > 10 years
- FH of preeclampsia
- Multifetal pregnancy
- BMI of 35 or more
- Gestational age at presentation
- Previous history of preE or GHTN
- preexisting vascular disease, preexisting kidney disease

**Treatment options**

- Labetalol
- Nifedipine "2nd option"
- Methyldopa "3rd option"

**Timing of birth**

- Delivery < 37 weeks is not indicated if a woman has blood pressure < 160/110 with or without medications.
- After 37 weeks, delivery time should be decided by the patient and a senior obstetrician

**Postnatal**

- BP is measured daily in the first 2 days, once between 3-5 days postpartum, then as clinically indicated if BP medication was changed after birth
- Counsel patients that duration of postnatal treatment will be similar or may be longer than antenatal period
- Decrease the dose if BP is < 130/80 mmHg.

  If on methyl-dopa in pregnancy, stop it within 24 hours postpartum
- If she is not on any treatment during pregnancy, BP is treated only if > 150/100 postpartum
- *A written care plan should be provided when transferring the patient to the community care including:*
  - ① Who will provide f/u care and medical review
  - ② Frequency of BP monitoring
  - ③ Threshold for reducing or stopping the medications
  - ④ Indication for referral to primary care for BP review
- Patients should be offered medical review after 6-8 weeks
- *Do not offer bed rest in hospital.*

## Management of preeclampsia

① **Assessment**

② **Treatment**

③ **Timing of birth**

④ **Postnatal care**

❶

### Assessment

Full clinical assessment at each antenatal visit

| Indications of admission to hospital | Risk prediction models |
|---|---|
| ① Sustained systolic BP > 160<br>② New or persistent:<br>• Rise in creatinine (> 1 mg/dl)<br>• ALT > 70 mIU/ml<br>• Plt < 150.000/µL<br>③ Signs of:<br>• Severe preeclampsia<br>• Impending eclampsia<br>• Pulmonary edema<br>• Fetal compromise | Use these models to determine place of care<br>FullPIERS: Used any time in pregnancy<br>PREP-S: Only up to 34 weeks<br>★ These models do not predict risk on babies |

2

## Treatment of preeclampsia

| | Hypertension 140/90 to 159/109 | Severe hypertension |
|---|---|---|
| **Admission** | If any of the above indications is present OR if fullPIERS or PREP-S indicates high risk of adverse outcomes | Admit, but if BP < 160/110 mmHg, manage as hypertension |
| **Medications** | Offer treatment of BP > 140/90 | Offer to all women |
| **Target BP** | 135/85 or less | |
| **BP follow-up** | At least every 48 hours | Every 15-30 min till < 160/110 then at least 4 times/day while admitted as inpatient |
| **Dip stick proteinuria** | Only if clinically indicated e.g. diagnosis is uncertain | |
| **Blood test** | CBC, LFT, RFT twice a week | CBC, LFT, RFT 3 times a week |
| **Fetal assessment** | • FHR auscultation at each visit<br>• Fetal growth scans at diagnosis and every 2 weeks if severe HTN persists<br>• CTG at baseline and when clinically indicated | |

## ❸ Timing of birth

**Indications of early delivery (< 37 weeks)**

- Inability to control BP despite ≥ 3 classes of medications at appropriate dose
- Progressive deterioration of LFT, RFT, hemolysis or platelets
- Severe intractable headache, repeated scotomas, eclampsia
- Reversed end-diastolic flow in umbilical artery Doppler
- Pulse oximetry < 90%
- Placental abruption
- NRFHT

| Week | Timing of birth |
|---|---|
| < 34 weeks | Continue surveillance unless of any indication of delivery occurs |
| From 34 to $36^{+6}$ | Continue surveillance unless one of the above indications arises |
| ≥ 37 weeks | Initiate birth within 24-48 hours |

## 4 Postnatal care

### Blood pressure monitoring

| Patients are not on any anti-hypertensive | Patients on antihypertensive treatment |
|---|---|
| Measure BP at least 4 times a day while inpatient | Measure BP at least 4 times a day while inpatient |
| Measure BP once between 3-5 days | Then every 1-2 days for up to 2 weeks till BP is normal without medications |
| If high | Continue antenatal medications |
| Measure BP on alternate days till BP is normal | Consider reducing dose if BP is < 140/90 |
| Start treatment if BP is >150/100 | Reduce the dose if < 130/80 |

★ Review headache and epigastric pain every time BP is checked

**Patient can be transferred to community care if**

① No symptoms of preeclampsia
② BP < 150/100 with or without treatment
③ Blood tests are stable or improving

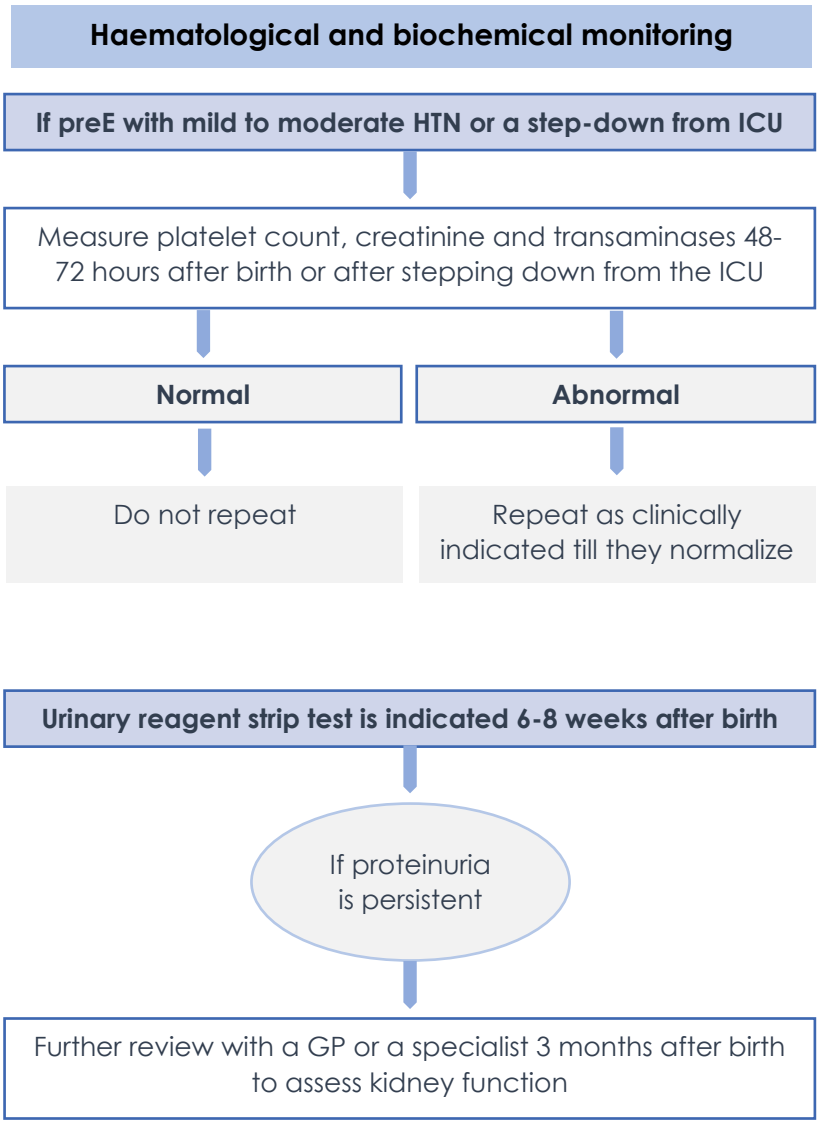
When transferring to community care, provide a written care plan

**Offer women with preE and on treatment**

Medical review with GP or specialist 2 weeks after transfer to community care

**Offer all women with preE**

Medical review at 6-8 weeks


Haematological and biochemical monitoring
If preE with mild to moderate HTN or a step-down from ICU
Measure platelet count, creatinine and transaminases 48-72 hours after birth or after stepping down from the ICU
Normal
Abnormal
Do not repeat
Repeat as clinically indicated till they normalize
Urinary reagent strip test is indicated 6-8 weeks after birth
If proteinuria is persistent
Further review with a GP or a specialist 3 months after birth to assess kidney function

## Fetal monitoring

**Chronic hypertension**

- Serial US for foetal growth
- AF assessment
- Umbilical artery Doppler velocimetry at 28, 32, 36 weeks

CTG is done only when clinically indicated

**Gestational HTN**

- Serial US for foetal growth
- AF assessment
- Umbilical artery Doppler velocimetry at baseline

**If normal**

Repeat every 2-4 weeks if clinically indicated

CTG is done only when clinically indicated

**Preeclampsia or severe GHTN**

- CTG at diagnosis
- Serial US for fetal growth
- AF assessment
- umbilical artery Doppler velocimetry at diagnosis

US is repeated every 2 weeks

CTG is not repeated if normal

CTG is repeated if

- Maternal condition deteriorates
- Vaginal bleeding
- Abdominal pain
- Reduced foetal movement

**Additional fetal monitoring**

- If there is history of severe preE
- If there is history of preE resulting in labor before 34 weeks
- If there is history of Pre-E associated with birth weight < 10$^{th}$ percentile, abruption, or IUFD

## Intrapartum care

**Blood pressure**

- Measure BP hourly
- Measure BP every 15-30 min if severe HTN
- Continue treatment during labor

**Blood tests**

- Determine need for labs using the same antenatal criteria even if regional anesthesia is considered

**Epidural analgesia**

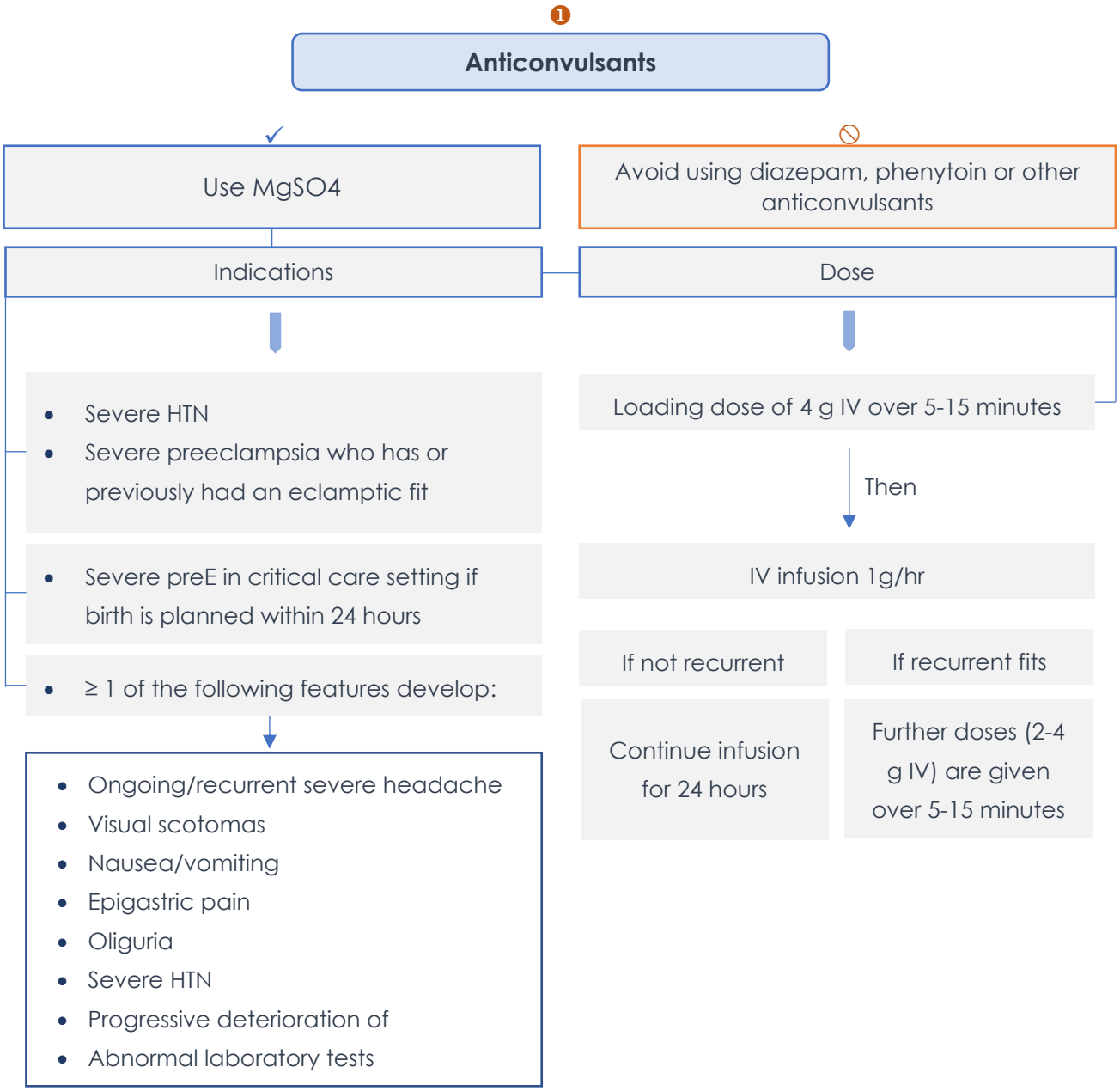
- Before using regional analgesia, do not preload patients with severe PreE with IV fluids

**2nd stage of labour**

- Do not routinely cut short second stage of labor
- Assisted or operative delivery may be indicated if there is severe HTN not responding to initial treatment

## Critical care

Medical management of severe hypertension, severe pre-eclampsia or eclampsia in a critical care setting:



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## Antihypertensives

| Labetalol | Nifedipine | Hydralazine |
|---|---|---|
| Oral, IV | Oral | IV |

**Indications**

Management of severe HTN in critical care during pregnancy or after birth

- Monitor BP to ensure response
- Modify treatment as indicated
- Identify adverse maternal or foetal effects
- Consider up to 500 ml of crystalloid fluid before or with the 1st dose of hydralazine

❸

## Corticosteroids

✓ Give antenatal steroids if preterm labour is anticipated within 7 days

⃠ Do not give steroids for HELLP syndrome

❹

## Fluid balance:

- Do not use volume expansion unless hydralazine is used as antihypertensive
- Limit IV fluid to 80 ml/hour unless there is ongoing fluid loss e.g. bleeding

## Referral to critical care

3 Levels

| | |
|---|---|
| **Level 3 care** | • Severe preE needing ventilation |
| **Level 2 care** | • Step-down from level 3 or If there is:<br>▪ Eclampsia<br>▪ HELLP<br>▪ Hemorrhage<br>▪ Hyperkalemia<br>▪ Severe oliguria<br>▪ Coagulation support<br>▪ IV antihypertensives<br>▪ Initial stabilization of BP<br>▪ Evidence of cardiac failure<br>▪ Abnormal neurology |
| **Level 1 care** | • Step down from level 2 after delivery<br>• Preeclampsia with HTN<br>• Ongoing conservative management of preterm with severe HTN |

## Postnatal treatment

Use meds that are used once daily whenever possible

1. **Enalapril** — Monitor maternal potassium and renal function

2. **Nifedipine** Or **Amlodipine** — Preferred for black Africans or Caribbean family origin with hypertension during postnatal period
   - If previously effective

3. **Enalapril + Nifedipine** — If one of the above medication is not effective

If not effective or not tolerated

4. **Atenolol** Or **Labetalol** — Add them to the combination treatment OR Substitute for one of the above medications

---

**Diuretics**
**ARBs**

⊘ Avoid whenever possible during postnatal period if a woman is breast-feeding or expressing milk

- Patients on antihypertensives can breastfeed
- Medications pass in breast milk in a very little amount that is unlikely significant
- Reassure women that any nanufacturer information/warning is related to lack of testing rather than established safety concerns

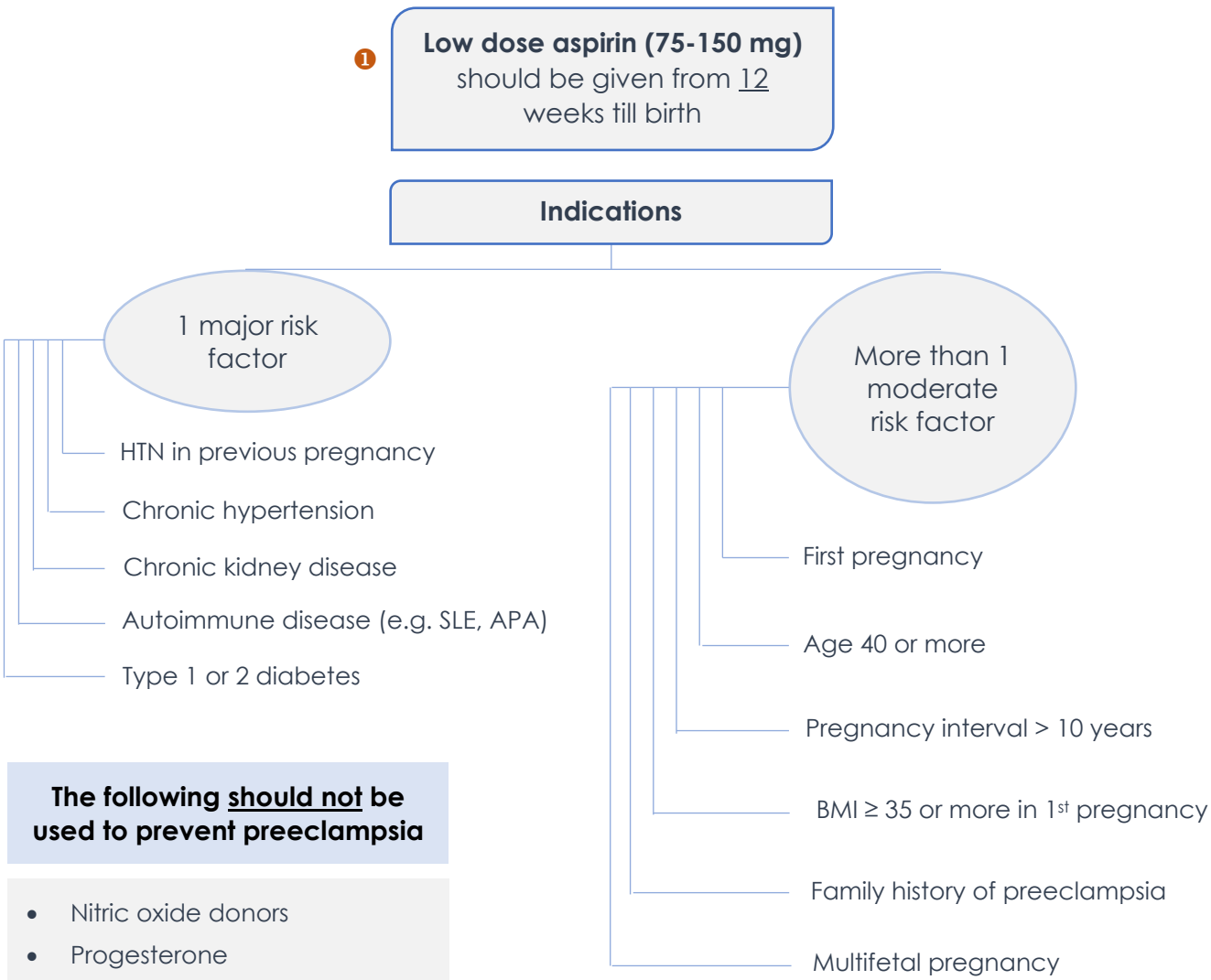
- While breast feeding and using medications, monitoring BP of babies is advised especially preterm babies who have symptoms of low BP in the first few weeks.
- When discharged home, advise women to monitor neonatal drowsiness, lethargy, pallor, cold peripheries or poor feeding

## Follow-up

- **Risk of recurrence:** 1:5 (20%)
- **Pre-pregnancy counseling:** it is recommended in future pregnancies specially in women with;
  - Previous preE
  - Hypertension with early labor < 34 weeks
- **Patients that are at increasing risk of long-term complications:**
  - HTN: 2-4 times
  - Stroke: 1.5 times
  - Major CVD: 2 times
  - CV mortality: 2 times

  Women with history of preE but no HTN or proteinuria at 6-8 weeks after birth are at relative risk of end stage renal disease. However, the overall risk is low, and no follow-up is indicated
- **Counselling:**
  - Maintaining healthy weight and lifestyle is essential
  - Risk of recurrence increases if interpregnancy interval is > 10 years
- **Do not offer:**
  - Screening for thrombophilia in patients with preE

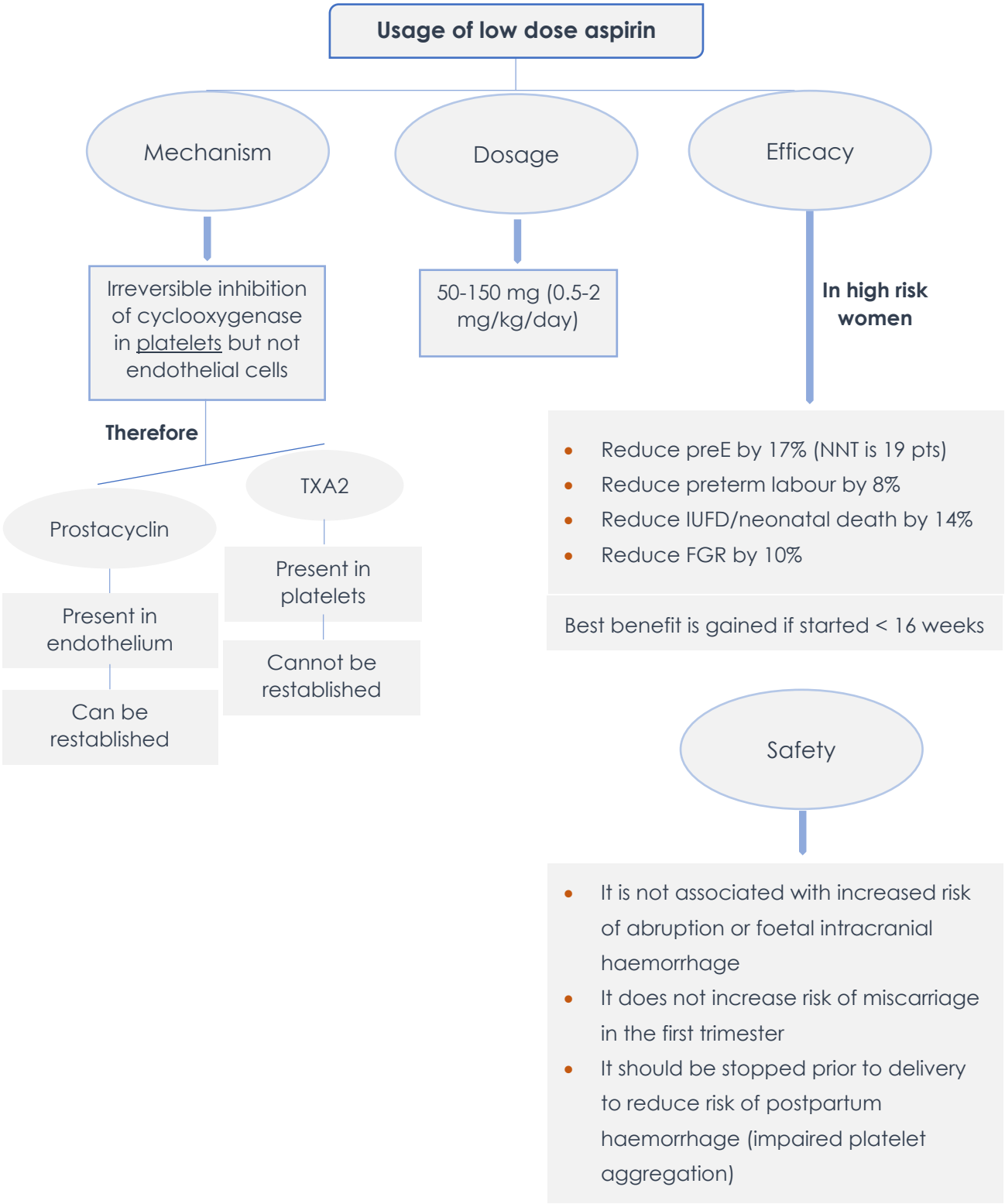
## Low-dose aspirin and calcium in prevention of preeclampsia




**The following should not be used to prevent preeclampsia**

- Nitric oxide donors
- Progesterone
- Diuretics
- Heparin
- Magnesium
- Folic acid
- Antioxidants (vit C and E)
- Garlic
- Fish oil or algal oils
- Salt restriction

*Advise women that exercise, rest and work in women with hypertension is similar to healthy pregnant women*


Usage of low dose aspirin
Mechanism
Dosage
Efficacy
Irreversible inhibition of cyclooxygenase in platelets but not endothelial cells
50-150 mg (0.5-2 mg/kg/day)
In high risk women
Therefore
TXA2
Prostacyclin
Present in platelets
Present in endothelium
Cannot be restablished
Can be restablished
Reduce preE by 17% (NNT is 19 pts)
Reduce preterm labour by 8%
Reduce IUFD/neonatal death by 14%
Reduce FGR by 10%
Best benefit is gained if started < 16 weeks
Safety
It is not associated with increased risk of abruption or foetal intracranial haemorrhage
It does not increase risk of miscarriage in the first trimester
It should be stopped prior to delivery to reduce risk of postpartum haemorrhage (impaired platelet aggregation)

## ❷ Calcium supplementation

### Introduction

- Maternal serum level is decreased specially in the third trimester due to active transport to the fetus (accumulates 25-30 g during pregnancy)
- Absorption of calcium is increased (due to increasing in 1,25 vitamin D)
- Parathormone and calcitonin are increased in pregnancy

Calcium level is lower in patients with preE

- Required intake is 1000mg/day (only 6% reach this level)

### Maternal risks

- Osteopenia &Osteoporosis
- Tremors
- Paresthesia
- Muscle cramps and Tetany

| | |
|---|---|
| **Indication** | Prevention of preE |
| **Duration** | From 20 weeks of gestation until the end of pregnancy |
| **Target group** | • All pregnant women, particularly those at higher risk of preE<br>• population where calcium intake is low (< 600 mg) |
| **Dosage** | 1.5-2 g elemental calcium |
| **Frequency** | Daily, divided on 3 doses preferably taken at mealtime (do not exceed the upper limit 3000mg) |
| **Side effects** | • Difficulty in swallowing<br>• Urinary tract stones<br>• Infection<br>• Malabsorption of other minerals (should not be given with iron if both given) |

### Effect of calcium supplementation

- Reduces risk of preE by 55%
- Reduces risk of preterm labour by 24%
- Reduces risk of maternal morbidity and mortality by 20%
- Risk of HELLP syndrome may increase 2.7 times

## Abbreviations

**Pre-E:** Pre-eclampsia

**RUQ:** Right upper quadrant

**Plt:** Platelets

**DIC:** Disseminated intravascular coagulopathy

**FGR:** Foetal growth retardation

**UA:** Uterine artery

**PTL:** Preterm labour

**IUFD:** Intrauterine foetal death

**AMA:** advanced maternal age

**BMI:** Body mass index

**FP:** False positive

**MAP:** Mean arterial pressure

**CTG:** Cardiotocography

**NRFHT:** Non-reassuring foetal heart tracing

**US:** Ultrasound

**AF:** Amniotic fluid

**MgSO4:** Magnesium sulfate

**SLE:** Systemic lupus erythematosus

**APA:** Anti-phospholipid antibody syndrome

**BMI:** Body mass index

# Myocardial Infarction and Pregnancy

## Incidence

Cardiovascular disease (CVD) complicates 0.2-4% of all pregnancies

CVD is the leading cause of overall maternal deaths (20%) Most common cause is acquired heart disease

Acute myocardial infarction in pregnancy is rare (0.7:100.000). Risk is is 3-4 times higher than non-pregnant

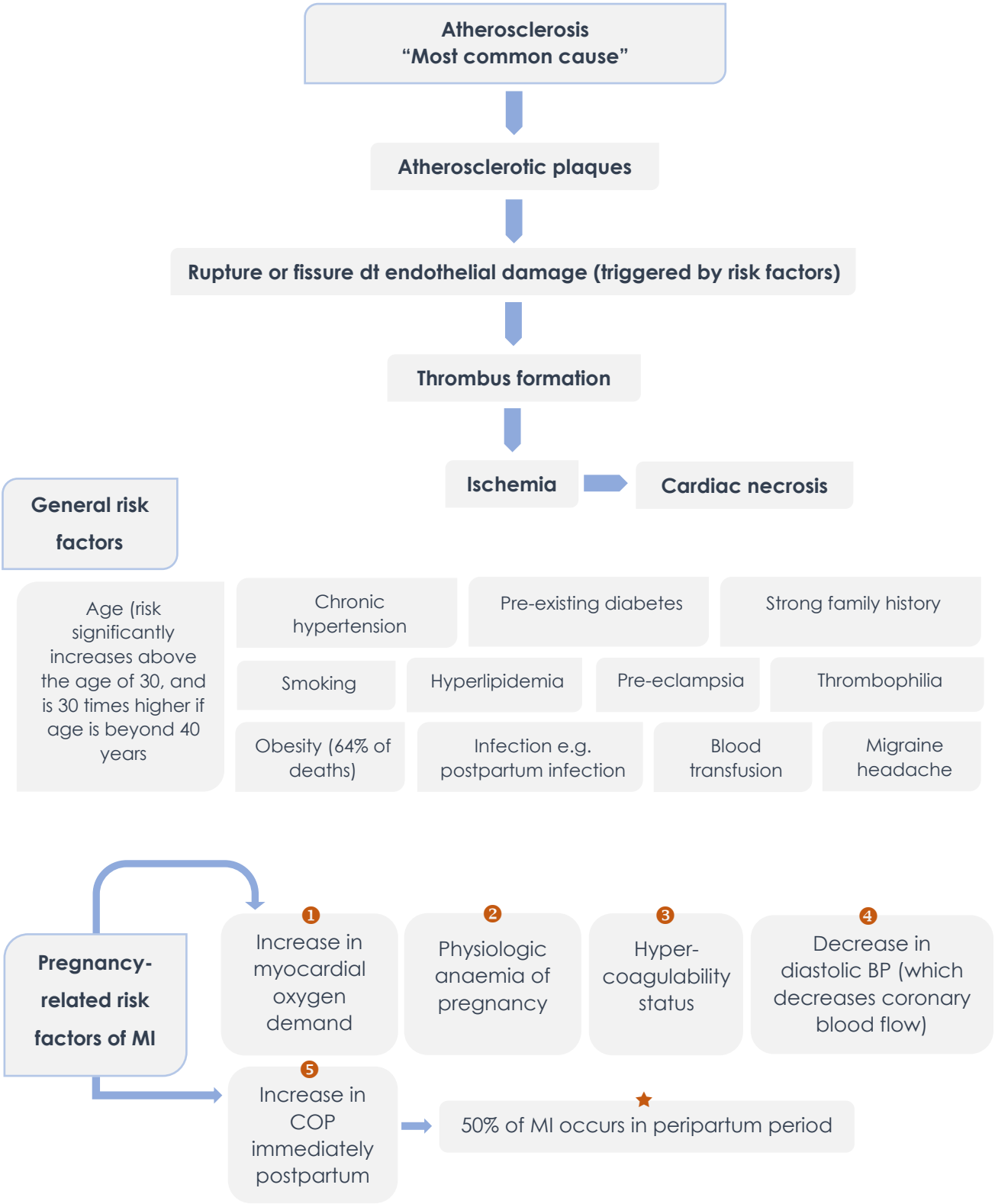
## Physiological changes in pregnancy

| | |
|---|---|
| **Plasma volume** | Plasma volume increases by 50% during pregnancy<br>This starts as early as 6 weeks and plateaus at 32 weeks |
| **COP** | • COP increases by 40% in pregnancy<br>• It Increases steadily till 25 weeks of gestation<br>• 300-400 ml of blood is pushed from the placenta to the circulation with each labour contraction. COP increases by 50% during contractions |
| **BP** | Vascular resistance and BP decrease by 10-15 mmHg during pregnancy |
| **Hematologic changes** | • Factor 7, 8, 10, fibrinogen and VWF increase, protein S decreases, C4b and plasminogen activator inhibitor type 1 increase resulting in a hypercoagulable state<br>• Reversal of haematologic changes occurs within 8 weeks after delivery |
| **HDL** | It increases in pregnancy |

**ANP** = **A**trial **N**atriuretic **P**eptide / **COP** = **C**ardiac **O**ut**p**ut / **BP** = **B**lood **P**ressure
**CVP** = **C**entral **V**enous **P**ressure / **AMI** = **A**cute **M**yocardial **I**nfarction

Cardiovascular changes are reversed between 4 and 12 weeks postpartum

## Pathophysiology of acute myocardial infarction (MI)



**Pathological causes of MI**

- **Atherosclerotic**
  - Associated with risk factors
    - Atheroma 50%
- **Non-atherosclerotic**
  - Coronary dissection (22%)
  - Thrombosis (14%)
  - Spasm

**Coronary artery dissection in pregnancy**

- It occurs without risk factors
- It may be caused by progesterone action on vessel wall, lytic action of proteases from eosinophils and lack of prostacyclin
- Highest risk is between third trimester and up to 3 months
- Left anterior descending branch is involved in 80% of cases (30-40% mortality)

**Coronary artery thrombosis**

Obstetric risk factors

- Thrombophilic state of pregnancy
- Hereditary thrombophilia
- Smoking in pregnancy

**Classification (same aetiology)**

- **STEMI (ST segment elevation MI)**
  - Partial coronary occlusion
- **NSTEMI (non-ST segment elevation MI)**
  - Complete coronary occlusion

## Diagnosis

Low index of suspicion should be considered for, particularly in the presence of risk factors, if these symptoms develop:

- Chest pain
- Nausea & vomiting
- Epigastric pain or
- Dizziness

## Investigations

### ① ECG

- First line. Sensitivity is 50% and therefore, other markers should be used in combination with ECG
- Most sensitive and specific sign is ST elevation (it appears within a few minutes)
- Other findings include ST depression, symmetrical T wave inversion, newly developed Q waves

Normal ECG changes in pregnancy are:

- 15-20° left axis deviation
- ST segment depression
- T wave inversion in inferior & lateral leads
- Inverted T in V1, V2 and occasionally V3
- Small Q wave and inverted T in lead III
- Q wave in lead AVF

### ② Cardiac markers

- Cardiac-specific Troponin I and T are the markers of choice
- Unlike other markers, they are not affected by anaesthesia, labour or caesarean section
- Although Troponin may increase with preE, PE, and GHTN, the rise is small and is still within standard range
- Initial negative results should not be used to exclude MI as it may take 12 hours for them to peak

### ③ Echocardiogram

- It is used primarily to rule out other causes of chest pain (e.g. aortic dissection)
- Its role in diagnosing MI is limited. It may reveal left ventricular dysfunction and wall motion abnormalities

### ④ Coronary angiography

- It is best done through radial access, with abdomen shielded and fluoroscopic time minimized
- Maternal exposure is 7 mGy, and fetal exposure is 1.5 mGy
- Doses < 50 mGy do not cause foetal loss, congenital malformation, intellectual disability, or foetal growth restriction*

**PreE** = **P**re-eclampsia / **PE** = **P**ulmonary **E**mbolism / **GHTN** = **G**estational **H**ypertension / **MI** = **M**yocardial **I**nfarction

* Foetal exposure to 1 mGy is associated with very low risk of childhood cancer

## Treatment

**ICU admission with continuous foetal monitoring**

### Reperfusion therapy

① **For STEMI**

- Treatment of choice is coronary angiography and primary percutaneous coronary intervention (PPCI)
- Bare metal stents are preferred to drug-eluting stents because they lack safety data
- If significant delay is anticipated, thrombolysis with tissue plasminogen activator (tPA) is an alternative. It does not cross the placenta and is not teratogenic. Risk of maternal hemorrhage is 8%

② **For NSTEMI**

- Antiplatelet drugs are the first line
- If ischaemia continues or if haemodynamically unstable, stenting for revascularization can be performed
- Angiography may still be used after ischaemia resolves if patient is at high risk (multidisciplinary decision)

### Medications

① **Aspirin**

- Safe dose is 60-150 in pregnancy (no adverse maternal or foetal side effects apart from slight increase in need for postdelivery transfusion)

② **Low molecular weight heparin and UFH**

- Safe in pregnancy
- Should stop 24 hours prior to labour

③ **Nitrates and labetalol**

- Safe in pregnancy
- IV nitroglycerin may be associated with bradycardia and loss of beat-to-beat variability
- Nifedipine should be avoided in acute coronary events as it may increase mortality. Otherwise, it is safe in pregnancy.

④ **Antiplatelet drugs**

- It is indicated after stenting
- 75 mg clopidogrel can be used in pregnancy. However, it should be given for the shortest duration possible

---

- ACEIs and ARBs are <u>contraindicated</u> in pregnancy (1st trimester: cardiac and CNS anomalies, 2nd trimester: renal dysgenesis, oligohydramnios, pulmonary hypoplasia, foetal growth restriction, fetal demise)
- Statins: <u>not recommended</u> in pregnancy; safety information is limited

ACEIs: Angiotensin-Converting Enzyme Inhibitors (ACEIs), ARBs: Angiotensin II Receptor Antagonists

## Timing and mode of delivery

- Timing and mode of delivery are a multidisciplinary team decision (including a cardiologist, obstetrician, obstetric anaesthetist, neonatologist)
- If possible, delivery should be delayed to 2-3 weeks after acute MI (to reduce risk of maternal mortality during this time)
- VD and CS are comparable in terms of maternal mortality

| Vaginal delivery | Elective caesarean section |
|---|---|
| • Less bleeding<br>• Less infection<br>• Lower risk of venous thromboembolism | • Less hemodynamic fluctuations<br>• Planned circumstances with availability of Multidisciplinary team (MDT) |

- Timing of vaginal delivery may depend on foetal status and cervix favourability (long labour increases preload from uterine contractions and increases cardiac workload)

### Management during vaginal delivery

| | |
|---|---|
| **Analgesia** | • Epidural analgesia to decrease pain and urge to push |
| **Position** | • Left lateral position, supplementary oxygen |
| **Monitoring** | • Continuous cardiovascular monitoring: with pulse oximetry and ECG<br>• If left ventricular function is significantly impaired or there was a recent cardiac event, invasive monitoring with an arterial catheter is recommended<br>• Continuous foetal monitoring |
| **Treatment of ischemia during labour** | • IV nitroglycerin<br>• Labetalol<br>• Calcium antagonists can be used<br>Nitroglycerin and calcium antagonists are tocolytics and may prolong labour |
| **After delivery** | • Slow IV oxytocin infusion < 2 U/min to decrease postpartum bleeding<br>• Ergometrine is <u>contraindicated</u><br>• Monitoring in high dependency unit or ICU for at least 24-48 hours |

# Cardiac Disease with Pregnancy

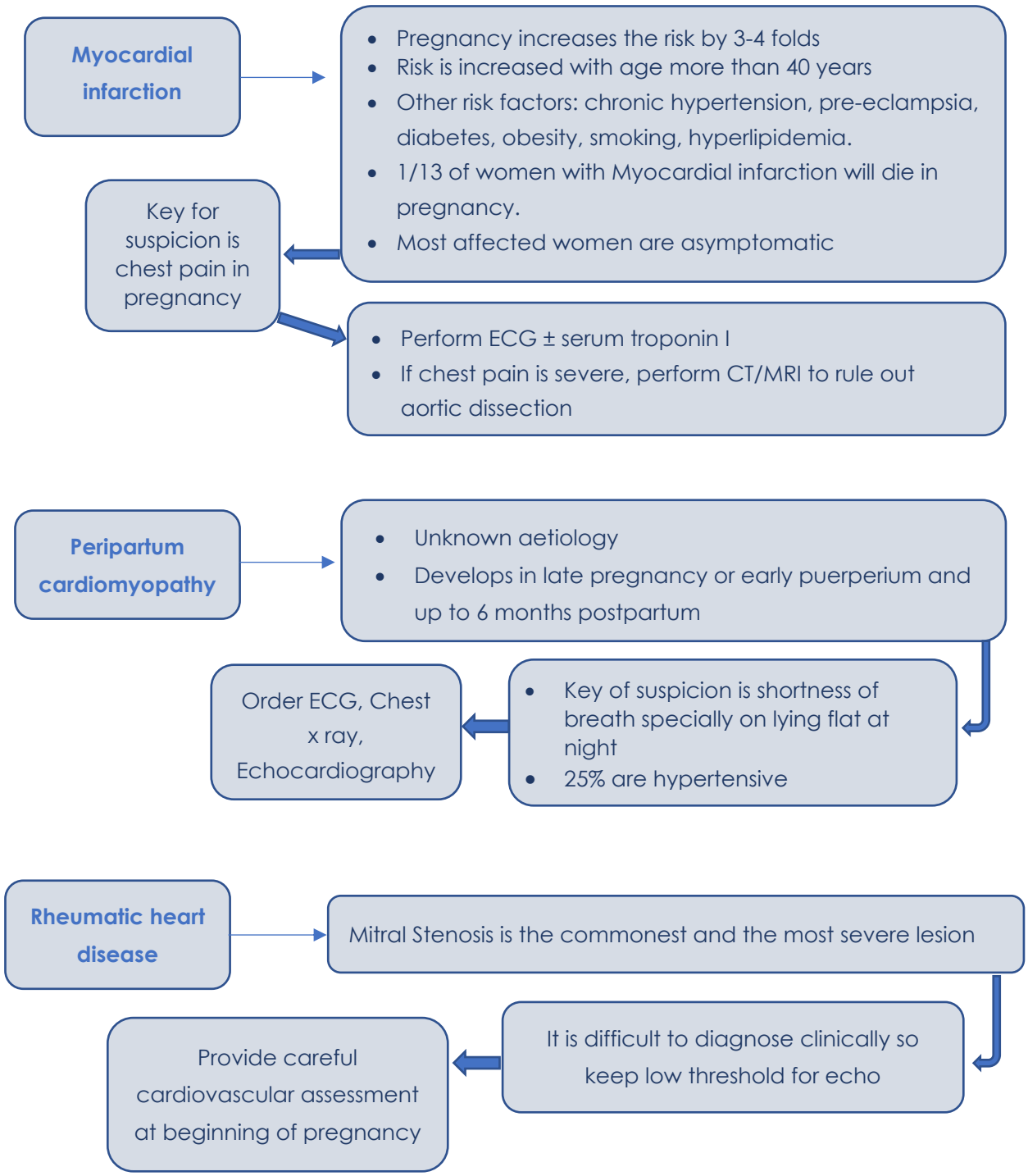
## Epidemiology

- Deaths related to cardiac diseases with pregnancy:

| Cause | % of total deaths |
|---|---|
| *ischemic heart disease/myocardial infarction* | 33% |
| *peripartum cardiomyopathy* | 33% |
| *Rheumatic heart disease* | 5-10% |
| *congenital heart disease* | 5-10% |
| *pulmonary hypertension* | 5-10% |

- Aortic dissection:
  - Systolic hypertension is a major contributor to death from aortic dissection
  - It can occur as a complication of Marfan syndrome
- Congenital heart disease complicates 0.8% of all pregnancies

## Diagnosis of heart diseases with pregnancy



## Management of cardiac diseases with pregnancy

| stage | Management |
|---|---|
| ***Preconception*** | • At the age of puberty, girls with congenital heart disease should be referred to cardiac/Obstetric gynecological clinic to discuss contraception and preconception counselling<br>• Issues associated with pregnancy and congenital heart disease should be generally discussed in the first visit to the joint clinic<br>• In preconception visit, details on the following topics should be discussed:<br>① Risk of mortality<br>② Risk of congenital heart disease in offspring<br>③ Antenatal care in pregnancy and frequency of medical surveillance |
| **Antepartum** | • Early in pregnancy, women with history of cardiac defect or with murmurs during physical examination should be assessed by a joint clinic (cardiology/obstetrics/anesthesia) for risk assessment<br>▪ If low risk: women can be returned to routine obstetric care<br>▪ If high risk: women should be followed-up regularly in antenatal care clinic, better by the same obstetric consultant<br>• At each subsequent visit: Cardiovascular assessment should be performed:<br>▪ Blood pressure assessment manually<br>▪ Assessment of pulse and rhythm (1st sign of volume overload)<br>▪ Auscultation for change in murmurs<br>▪ Assessment of signs of pulmonary oedema<br>• Each trimester: oxygen saturation should be checked in women with cyanotic heart disease. More frequent checks may be indicated<br>• In the second trimester: women with congenital heart disease should be offered fetal echocardiography by an accredited paediatric/fetal cardiologist<br>• At 32-34 weeks of gestation: a multidisciplinary meeting should be held to discuss delivery plan including:<br>▪ Delivery attending team<br>▪ Safety and appropriateness of caesarean section<br>▪ Safety of bearing down in second stage of labour<br>▪ Prophylaxis against Postpartum haemorrhage<br>▪ Need for venous thromboprophylaxis<br>▪ Length of hospital stay<br>▪ Timing of obstetric/cardiac review |

| | |
|---|---|
| **Intrapartum** | • General principle to minimize cardiovascular stress include:<br>▪ Early slow incremental epidural<br>▪ Cutting short the second stage of labour e.g. assisted vaginal delivery<br>• Use of oxytocin may result in cardiovascular adverse effects e.g. hypotension. Therefore:<br>▪ Low dose oxytocin in recommended with vaginal delivery<br>▪ Uterine compression sutures may be used as an alternative to oxytocin in caesarean section |

# Postural Tachycardia Syndrome and Pregnancy

## Introduction

Postural tachycardia syndrome (POTS) is an autonomic dysfunction that commonly affects women in childbearing years that primarily affects women between the ages of 15 and 50 years

## Diagnosis

- **Trigger:** Classic presentation is usually evoked within 10 minutes by moving to an upright posture
- **Response:** persistent heart rate of >30 beats/minute (standing heart rate of >120 beats/minute in severe cases) in absence of orthostatic hypotension. Symptoms may be severe enough to interfere with life activities
- **Relief:** Majority of symptoms are relieved by lying down

| Symptoms* | Signs |
|---|---|
| • Light headedness/syncope<br>• Headache/migraine<br>• Nausea<br>• Exercise intolerance<br>• Sweating<br>• Shortness of breath<br>• Tremor<br>• Blurred vision<br>• Palpitations and chest pain<br>• Fatigue<br>• Gastrointestinal upset<br>• Anxiety | • Pallor<br>• Sweating<br>• Tachycardia<br>• Acrocyanosis<br>• Tilt table test is contraindicated in pregnancy. Stand test may be used instead |

* Diagnosis is made by presence of criteria of POTS for at least 6 months

## Effect of pregnancy on POTS

60% reports symptom improvement (particularly if medicated)

20-30% report worsening of symptoms (most common: migraine, presyncopal and syncopal episodes)

12-15% report stable symptoms

### Predictors

- Patients with severe POTS are at greater risk of decompensation during pregnancy
- Patient not on medications before pregnancy are at low risk of exacerbation during pregnancy

Symptoms may be severe enough to warrant admission and IV fluids

**When?**

1/3 of women at first trimester

1/3 of women at 24 weeks onward

1/3 throughout pregnancy

Women who experience symptoms in the first half typically experience improvement in the second half (fluid retention may improve symptoms)

## Effect of pregnancy on POTS

- POTS is a benign condition in pregnancy and is not associated with adverse effects
- However, women with POTS may be at higher risk of severe vomiting and hyperemesis gravidarum in 1st trimester (50-60%)

## Management in pregnancy

<table>
<tr><td>Pre-pregnancy counselling</td><td colspan="2">• Review orthostatic blood pressure and pulse changes outside pregnancy<br>• Review and discuss POTS status (current symptoms and medications)<br>• Stop unsafe medications prior to conception<br>• Discuss impact of pregnancy on POTS, and POTS on pregnancy</td></tr>
<tr><td>Antenatal care (consultant led)</td><td colspan="2">• Individualized multidisciplinary care (an obstetrician and a physician with experience in POTS)<br>• Support prompt recognition of symptoms. Syncope may result in maternal and foetal injury<br>• Consider medications if symptoms exacerbated or debilitating (see next)</td></tr>
<tr><td>Intrapartum care</td><td>Vaginal delivery<br>• Vaginal delivery is the standard route. Success rate is high (80-85%)<br>• Continuous foetal monitoring is indicated<br>• Avoid prolonged dehydration, upright/standing postures *. Warm baths and warm environment may exacerbate symptoms<br>• Regional anaesthesia is acceptable if required. If there is severe tachycardiac response, consider early analgesia and anaesthesia.<br>• Intrapartum medications that produce vasodilation should be used cautiously. They may worsen tachycardia (Prostaglandins, magnesium, oxytocin, glyceryl trinitrate)<br>• Keep anaesthesia and paediatrics team aware of POTS</td><td>Caesarean section<br>• Early elective caesarean section may be indicated in women with severe decompensation<br>• Regional analgesia is appropriate.</td></tr>
<tr><td>Postnatal care</td><td colspan="2">Symptoms improve in the majority within 6-12 months (due to physical reconditioning). No particular management is required</td></tr>
</table>

* Squatting may relieve syncopal symptoms.

## Treatment of POTS in pregnancy

- Treat underlying reversible causes
- Blood volume expansion
- Physical manoeuvres
- Medications
- Cognitive behavioural therapy

**The mainstay of conservative treatment for POTS**

- Fluid intake should increase up to 2-3 L/day
- Salt intake is increased up to 10-12 g/day
- Physical manoeuvres when the patient is symptomatic (making a fist, bending forward, placing a foot on a chair, pumping calves before standing)
- Exercise (aerobic and resistance training) may benefit (but if new exercise regimen, start slowly and gradually)
- Compression stockings
- Caffeine intake should be limited

| *medications* | Safety in pregnancy | Indication |
|---|---|---|
| *Beta blockers* | • Labetalol and propranolol are safe (category C)<br>• Maternal and foetal side effects are not anticipated with standard doses of propranolol used for POTS | Hyperadrenergic state |
| *Fludrocortisone* | • current date supports safety in all trimesters | Non-specific |
| *Midodrine (a1 receptor agonist)* | • It should be used with caution as data on safety are limited<br>• Although there is no evidence of associated anomalies, vasoconstrictive effect may result in foetal vascular insult | Neuropathic POTS (rapid action) |
| *Ivabradine (sinus node blocker)* | • contraindicated in pregnancy and breast feeding | - |
| *Octreotide* | • limited data but appears safe | Refractory cases |
| *Pyridostigmine* | • Safe in pregnancy and breast feeding (Category C) | Non-specific |
| *Clonidine* | • Safe (category C), given every 8 hours in pregnancy | Non-specific |

# Cardiovascular disorders with pregnancy


## Abstract

Cardiovascular disorders are increasingly encountered in pregnancy. In part, because care of congenital heart disease has significantly improved that more girls survive their childhood and get into their reproductive years. In addition, rheumatic heart disease is common among some immigrant groups and they may be first diagnosed in pregnancy. In this chapter, we will discuss common cardiovascular diseases in pregnancy and how diagnosis should alter antenatal, intrapartum, and postpartum care. We will also cover hypertension disorders of pregnancy in this chapter.



## Keywords

Hypertension, myocardial infarction, postural tachycardia, rheumatic heart, congenital heart disease


## Further readings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# Diabetes Mellitus in Pregnancy

## Preconception management

- **Glycaemic control:**

| Parameter | Target | Value |
|---|---|---|
| **Plasma glucose** | • Target fasting capillary plasma glucose is 5-7 mmol/L<br>• Premeal plasma glucose level is 4-7 mmol/L before meals | Preconception glycaemic control decreases (but does not preclude) risks of miscarriage, congenital anomalies, stillbirth and neonatal death |
| **HgbA1C** | Target HgbA1C is 6.5% (48 mmol/mol) | • Optimizing HbA1C level decreases risk of congenital anomalies<br>• If HbA1C is above 10% (86 mmol/mol), pregnancy should be avoided |

- **Pregnancy counselling:**
  - Discuss with the patient the effect of diabetes on pregnancy and pregnancy on diabetes including:
    - Diet, weight gain, and exercise in pregnancy
    - Risk of hypoglycaemia in the presence of nausea and vomiting specially in the first trimester
    - Impaired awareness of hypoglycaemia during pregnancy
    - Risk of large for gestational age baby and its complications
  - You should discuss risks of diabetes and/or obesity to the baby in later life.




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_9

- **Contraception:**
  - Contraception should be encouraged to avoid unplanned pregnancy. It should be continued till glycaemic control is achieved
  - Oral contraception can be used unless otherwise contraindicated

- **Weight loss:**

  If body mass index is greater than 27 prior to pregnancy, advise women on weight loss and offer individualized dietary recommendations

- **Diabetic monitoring:**
  - Patients are offered a glucometer for self-monitoring. HbA1C is checked monthly prior to conception
  - If medication regimen is changed to provide strict control, frequency of monitoring should increase and include fasting and mixture of premeal and after meal measures
  - Patients should be provided ketone testing strips. They can be used if they develop significant hyperglycaemia or feels unwell

- **Drug therapy:**
  - **Oral hypoglycaemics:**
    - Before conception, metformin may be used as an alternative or adjuvant to insulin. This can continue during pregnancy
    - Other oral hypoglycaemics should be stopped
  - **Insulin:**
    - NPH is the first choice in pregnancy. However, if long-acting insulins (e.g. glargine and detemir) achieve good glycaemic control before pregnancy, they can continue in pregnancy
    - Rapid acting insulins (e.g. aspart and lispro) do not adversely affect pregnancy
  - **Other medications:**
    - Statins, angiotensin-converting enzyme (ACE) inhibitors and an angiotensin receptor blockers (ARB) should stop before conception
    - Folic acid should start before conception and continues till 12 weeks of pregnancy (5mg/day)

- **Retinal assessment:**
  - Retinal assessment is indicated if annual assessment was not done in the last 6 months.
  - If test is normal, it should be pursued by annual screening

Avoid rapid optimization of blood glucose till retinal assessment is done

- **Renal assessment:**
  - Check serum creatinine prior to conception
  - Refer to a nephrologist before contraception if:
    ① Serum creatinine is 120 micromol/litre or more
    ② eGFR less than 45 mL/min
    ③ Albumin:creatinine (A:C) ratio more than 30

## Gestational diabetes (GDM)

- **Screening and diagnosis:**
  - **Indications of screening:**

    At booking appointment, GDM testing is offered if any of these risk factors present:

    ① Body mass index > 30
    ② Previous macrocosmic baby 4.5 kg or more.
    ③ Previous GDM
    ④ Family history of diabetes (1st degree relative with diabetes),
    ⑤ Ethnic origin with high prevalence of diabetes

In addition, presence of glycosuria +2 or more at 1 occasion or +1 at 2 or more occasions by reagent strip testing during routine antenatal care may indicate undiagnosed GDM. This requires further tests to rule out GDM

  - **Methods of screening:**
    - If 1 or more risk factors are present, 75g 2-hour oral glucose tolerance test (GTT) should be done between 24-28 weeks
    - In women with prior GDM, offer early diagnosis by:
      ① Self-monitoring of blood glucose OR

② 75g 2-hour oral GTT as early as possible

If normal, repeat 75g 2hr oral GTT between 24-28 weeks

- **Diagnostic criteria:**

  Diagnosis of gestational diabetes is made if fasting glucose is 5.6 mmol/L or above OR 2-hour plasma glucose is 7.8 or above.

- **Management:**
  - **Patient counselling:**

    Counsel the patient that:

    - Failure to diagnose or manage GDM is associated with small increase in risk of labour complications including shoulder dystocia
    - Diagnosis of GDM leads to frequent monitoring and increased intervention rate in pregnancy and labour
    - In some women, GDM is controlled by exercise and diet. The majority will be managed by medications or insulin
    - Good glycaemic control is associated with decreased risk of:

      ① Foetal macrosomia

      ② Trauma during birth

      ③ Induction of labour

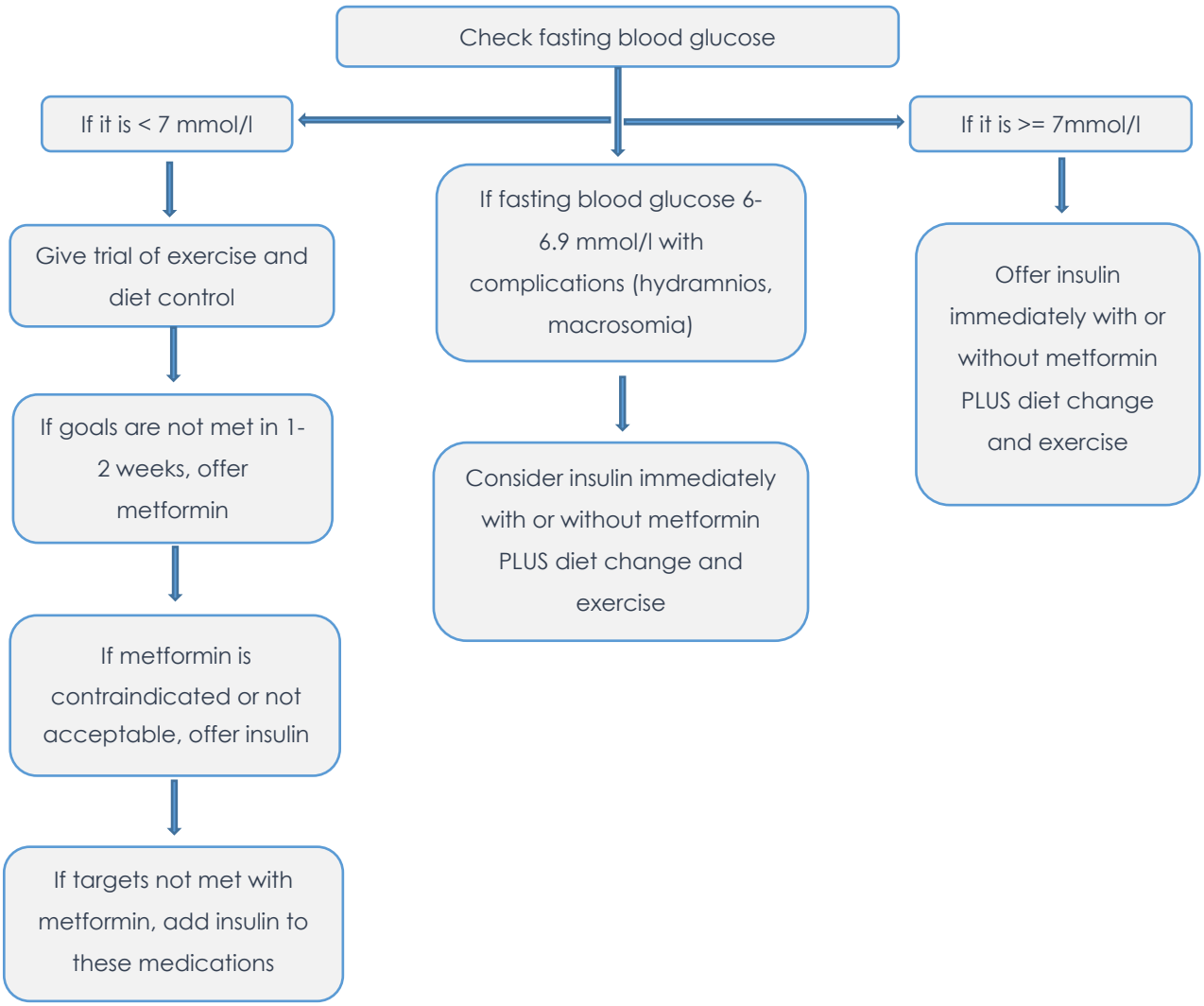
      ④ Caesarean section

      ⑤ Neonatal hypoglycaemia

      ⑥ Perinatal death
    - Diet should be healthy with low glycaemic index. All patients should be referred to a dietitian
    - Exercise is recommended. Approximately 30 minutes of walking after a meal are beneficial

    Women should be educated to self-monitor and to follow the same target glucose level of non-pregnant women

- **Drug therapy:**




If insulin is declined and metformin cannot be tolerated or if it fails to achieve glycaemic goals, Glibenclamide may be considered

## Antenatal care

| ① Antenatal scheduling | |
|---|---|
| **Book appointment - 10 weeks (joint diabetes-antenatal care appointment)** | • Provide information on diabetes and pregnancy<br>• Review medical history and medications<br>• If not done preconception, take clinical history to determine extent of complications, review medications and their complications<br>• Offer retinal assessment (if not done in the last 3 months)<br>• Offer renal assessment (if not done in the last 3 months)<br>• Measure HbA1C to determine the level of risk<br>• Offer self-monitoring vs. immediate 75g 2-hour GTT to women with previous GDM<br>• Confirm viability at 7-9 weeks of pregnancy<br>• Discuss diet, exercise and target blood glucose<br>• Contact with joint diabetes/obstetric team should be scheduled every 1-2 weeks |
| **16 weeks** | • Offer retinal assessment at 16-20 weeks to women with pre-existing diabetes if retinopathy is present at booking appointment |
| **20 weeks** | • Routine anatomy scan should include foetal heart assessment (the 4 - chamber view, outflow tract and the 3-vessel view) |
| **25 weeks** | • Offer nulliparous women all routine investigations offered normally at 31 weeks. |
| **28 weeks** | • Offer ultrasound (US) for foetal growth and amniotic fluid volume assessment<br>• Offer retinal assessment to all women with pregestational diabetes<br>• If GDM is diagnosed between 24-28 weeks, patients should enter this care pathway |
| **32 weeks** | • Offer US for foetal growth and amniotic fluid volume assessment<br>• Offer nulliparous all routine investigations offered normally at 31 weeks |
| **34 weeks** | • Routine antenatal care visit |
| **36 weeks** | • Offer US for foetal growth and amniotic fluid volume assessment |

| | |
|---|---|
| | • Provide information and discuss plan of birth and postnatal care, change in medications, contraception and follow-up |
| **37-39 weeks** | • Offer induction of labour of caesarean section as indicated in type 1 and 2 diabetes<br>• In women with GDM, anticipate spontaneous labour |
| **38 weeks** | • Offer testing for foetal well being |
| **39 weeks** | • Offer testing for foetal wellbeing.<br>• Advise GDM to deliver by 40+6 weeks |

### ② Glycaemic management

- **Frequency of monitoring:**
  - Women on multiple daily insulin injections: check fasting, premeal, 1-hour post-meal and bedtime blood glucose level daily during pregnancy
  - Women on diet, exercise, oral hypoglycaemics or one daily dose of intermediate acting or long-acting insulin: check fasting and 1-hour post-prandial glucose daily

- **Target glucose level:**
  - Fasting capillary glucose: 5.3 mmol/l AND
  - 1-hour postprandial glucose: 7.8 mmol/l OR
  - 2-hours postprandial glucose: 6.4mmol/l

- **Precautions:**
  - Patients with type 1 diabetes should be provided with ketone blood testing strips. If the patient develops hyperglycaemia or appears unwell, she should rule out diabetic ketoacidosis (DKA) using these strips (type 1 diabetes).
  - Women with type 2 or GDM should seek urgent advice if these develop these manifestations
  - Patients with If DKA should be admitted to level 2 critical care for medical and obstetric care

- **HbA1c follow-up:**
  - HbA1C should be measured in all women with pregestational diabetes at booking to

determine risks in early pregnancy. HbA1C measurement may be considered in the 2nd and 3rd trimester to determine the level of peripartum risk rather than to assess glycaemic control

- Risk increases if HbA1C is higher than 6.5% (48 mmol/mol).
- HbA1c should be checked in all women at time of diagnosis of GDM to rule out pre-existing diabetes

**③ Insulin treatment**

**insulin**

- Rapid-acting insulin analogues have an advantage over soluble human insulin during pregnancy and their use is recommended
- Insulin pump is offered if adequate control cannot be achieved with multiple injections without developing hypoglycaemia

**Caution**

- Patients should be aware of risk of hypoglycaemia and impaired awareness of hypoglycaemia in first trimester
- Fast acting glucose must be always available with patients (e.g. dextrose tablets or drinks)
- Provide glucagon to type 1 if needed and instruct her and her family in its use. It is particularly indicated in women with hypoglycaemia and distributed consciousness

**Continuous glucose monitoring**

Do not offer routinely. Indications are limited to:

- Problematic severe hypoglycemia with or without awareness
- Unstable blood glucose.
- Collecting information on fluctuating blood glucose levels

## ④ Organ assessment

- **Retinal assessment during pregnancy:**

Assess the retina in women with pregestational diabetes using mydriasis and digital imaging at booking appointment and 28 weeks

If diabetic retinopathy is present

Re-assess at 16-20 weeks

Retinopathy is not a contraindication to rapid optimization of glucose if high HbA1C in early pregnancy is found and is not a contraindication to vaginal delivery

If pre-proliferative retinopathy or any referable retinopathy is present

Ophthalmological follow-up for at least 6 months after birth

- **Renal assessment during pregnancy:**

Offer it to women with pregestational diabetes at booking visit if it was not done in the last 3 months

If creatinine >= 120, albumin: creatinine ratio > 30 or total protein excretion > 0.5 g/day*

Refer to a nephrologist

* eGFR is not used in pregnancy.
Consider thromboprophylaxis in women with nephrotic range proteinuria > 5 g/day or albumin: creatinine ratio > 220mg/mmol

### ⑤ Foetal assessment

- Foetal anatomy scan, which includes cardiac assessment
- Foetal growth and amniotic fluid assessment every 4 weeks from 28 to 36 weeks.
- Routine foetal well-being assessment (e.g. ultrasound, Doppler, non-stress test or biophysical profile BPP) is not recommended before 38 weeks unless there is risk of foetal growth restriction (e.g. macrovascular disease, nephropathy)

## Intrapartum care

Birth plan should be discussed in the third trimester. Woman are advised to give birth where advanced neonatal resuscitation is available for 24 hours

| | |
|---|---|
| **Time of delivery** | • Type 1 or 2 diabetes without complications: 37 - 38+6 weeks.<br>• Type 1 or 2 with metabolic, maternal or foetal complications: delivery may be indicated before 37 weeks<br>• GDM without complications: expectant management may continue till 40+6 weeks |
| **Mode of delivery** | • If there is suspected foetal macrosomia, discuss risks and benefits of vaginal delivery versus caesarean section with the patient<br>• Diabetes is not a contraindication to vaginal birth after caesarean |
| **Anaesthesia** | • Anaesthetic assessment in the 3rd trimester should be offered to women with diabetes and associated comorbidity (e.g. obesity or autonomic neuropathy)<br>• If general anaesthesia is indicated during labour, blood glucose should be measured every 30 minutes till the woman becomes fully conscious |
| **Blood glucose control** | • Blood glucose is checked every hour intrapartum. Goal is 4-7 mmol/l<br>• Women with type 1 diabetes are treated with IV dextrose and insulin infusion from the onset of established labour. The same treatment is offered to any diabetic woman if glucose cannot be maintained within target range |

## Neonatal care

Glycaemic control during labour and early neonatal feeding decrease risk of neonatal hypoglycaemia

- Women should feed their babies within 30 minutes of birth and then every 2-3 hours
- Check baby's glucose at 2-4 hours after birth.
- If babies develop abnormal signs, rule out polycythaemia, hyperbilirubinemia, hypocalcaemia or hypomagnesemia.
- If babies have signs of congenital heart disease or cardiomyopathy (e.g. heart murmur), echocardiography should be performed
- Babies should not be transferred to community care before 24 hours postnatal. They should be able to maintain normal glucose levels and feed well by then.

**Indications of admission to neonatal intensive care unit**

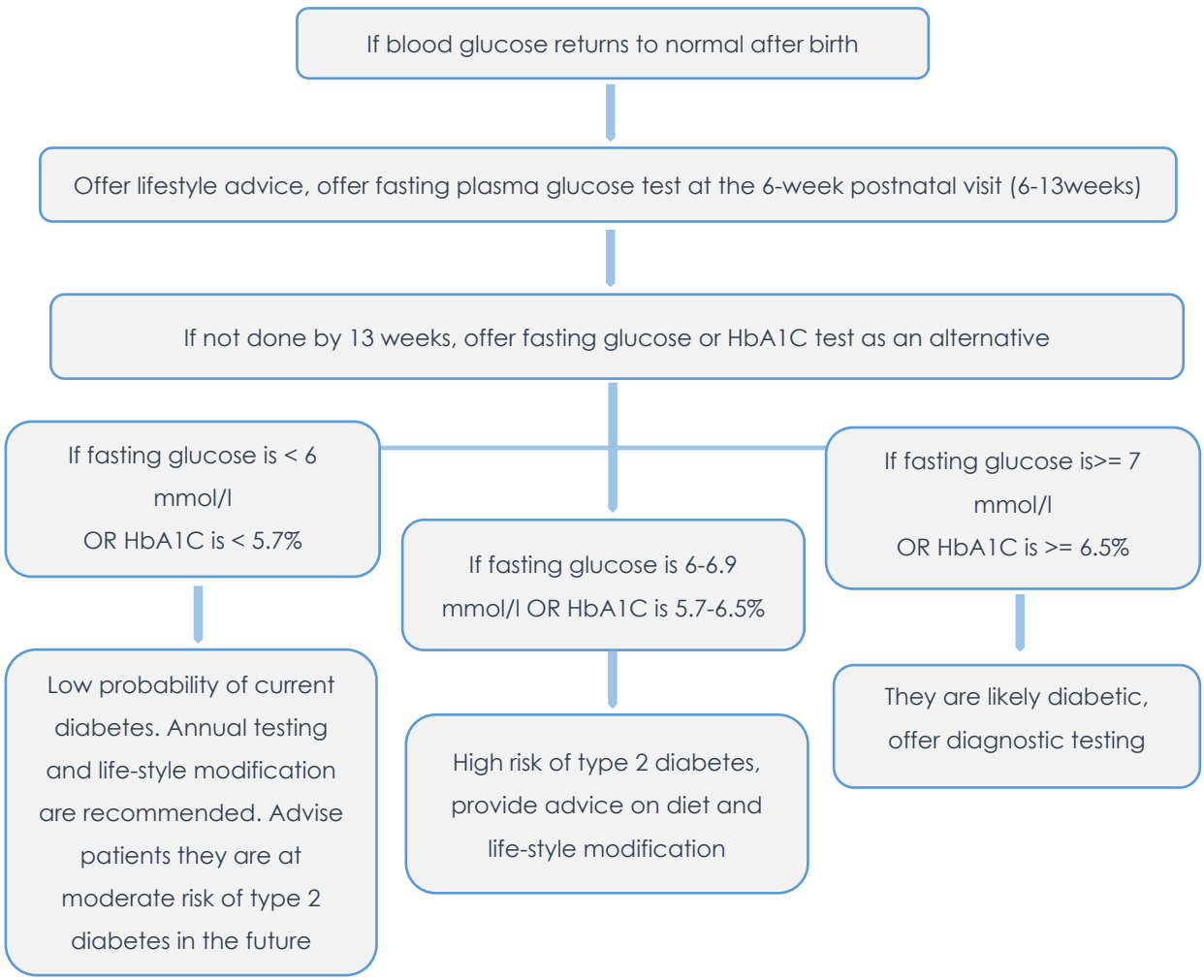
Hypoglycaemia associated with abnormal clinical signs e.g.

- Signs for cardiac decompensation
- signs of encephalopathy
- Signs of polycythaemia that may warrant partial exchange transfusion.
- Need for IV fluids or tubal feeding due to:
  Poor oral feeding
  Failure to maintain pre-feeding glucose above 2 mmol/l in 2 consecutive occasions despite maximum feeding support
- Jaundice requiring frequent monitoring or intense phototherapy

## Postnatal care

| | |
|---|---|
| **Women with insulin-treated pregestational diabetes** | • Insulin dose should be lowered, and blood glucose should be monitored to determine appropriate dose<br>• Patients are more liable to hypoglycaemia postnatally specially with breastfeeding. They should be advised to have a meal or snack before or during feeding<br>• Discuss future pregnancy and contraceptive options<br>• They should be referred to their routine diabetes care |
| **Women on oral hypoglycaemics (type 2 diabetes)** | • Metformin or glibenclamide can be used immediately after birth and during breastfeeding<br>• Other medications are avoided |
| **Women with GDM** | • Women with GDM should stop treatment immediately after birth<br>• They can be referred to community care once persistent postnatal hyperglycaemia is ruled out |

## Follow-up of GDM after birth



# Thyroid Dysfunction with Pregnancy

## Hyperthyroidism with pregnancy

### Incidence

Incidence of hyperthyroidism in pregnancy is 2 in 1,000 pregnancies in the UK

### Treatment options

| | |
|---|---|
| **Antithyroid Drugs** | ▪ Propylthiouracil is the first choice in pregnancy. It crosses the placenta less readily than carbimazole. Therefore, it is safe in early pregnancy<br>▪ Shifting to carbimazole may be considered after the first trimester due to risk of hepatotoxicity with Propylthiouracil |
| **Radioiodine** | It is contra-indicated in pregnancy |
| **Beta-Blockers** | It may be used. However, treatment course should not prolonged |
| **Surgery** | ▪ Surgery may be the treatment of choice if she plans to get pregnant<br>▪ Surgery may be considered during pregnancy if absolutely indicated |

### Follow-up

**During pregnancy**

- Thyroid hormones should be kept in the upper third of the reference range
- TSH receptor antibody (TRAb) is checked at 24-28 weeks to determine risk of fetal and/or neonatal hyperthyroidism. If it remains high, thyroid function test should be checked in neonates

**After delivery**

- In the mother: check thyroid function test at 6 weeks and 3 postpartum
- In the neonate: 6 hours and a few days later

## Complications

Poorly controlled hyperthyroidism during pregnancy may cause the following complications:

**Maternal complications**

- Pregnancy-induced hypertension
- Pre-eclampsia
- Heart failure
- Premature labour
- Thyroid storm

**Fetal/neonatal complications**

- Miscarriage
- Intrauterine growth restriction
- Low birthweight
- Stillbirth
- Thyroid dysfunction

# Hypothyroidism with pregnancy

## Incidence

- Incidence of hypothyroidism is 1:1000
- The most common cause is Hashimoto disease

## Diagnosis

- **Indications of testing:**

  Indications of testing of thyroid function are:

  ① Personal history of thyroid disease

  ② Symptoms of the disease

  ③ Significant goiter (not within the 30% expected)

  ④ Distinct nodules

- **Results:**

  Serum TSH is measured first. Free T4 is indicated if serum TSH is abnormal

| Serum TSH | Normal range |
|---|---|
| **First trimester** | 0.1- 2.5 mIU/L |
| **Second trimester** | 0.2 - 3.0 mIU/L |
| **Third trimester** | 0.3 - 3.0 mIU/L |

## Complications

### Maternal complications

- Spontaneous abortion
- Placental abruption
- Preeclampsia
- Preterm labour
- Fetal death

### Fetal/neonatal complications

- Low birth weight
- Impaired neuropsychiatric development
- Antibodies rarely crosse to the foetus

## Management

- Hypothyroidism is treated with levothyroxine at 1-2 mcg/kg or 100 mcg/day
- If women are on levothyroxine before pregnancy, pre-pregnancy dose should increase by 25%
- Dose is adjusted by TSH level. TSH should be checked every 4-6 weeks and dose adjusted by 25-50 mcg each time till TSH is normalized

# Postpartum thyroiditis

## Definition

Thyroid dysfunction within 12 months postpartum. This includes hypo-, hyperthyroidism, or both

## Incidence

- 5-10% of all pregnancies
- The underlying mechanism is autoimmune

## Management

- First phase: manifested by thyrotoxicosis (due to release of thyroid hormones secondary to thyroid destruction by autoantibodies)
  Treat with thioamides is ineffective. Beta-blockers are used to control symptoms if severe
- Second phase: manifested by hypothyroidism, usually between 4-8 months postpartum
  Treatment is with levothyroxine 25-75 mcg/day for 6-12 months.

## Prognosis

Most cases resolve. However, one third of patients may develop permanent hypothyroidism

# Diabetes Insipidus with Pregnancy

## Incidence

- It affects 2 to 4 per 100,000 pregnant women
- It usually occurs in the third trimester and resolves spontaneously 4-6 weeks postpartum

## Risk factors

- Diabetes insipidus may be associated with conditions complicated by hepatic dysfunction e.g., HELLP syndrome

## Classification

| Classification | Explanation |
|---|---|
| **Neurogenic** | • Anti-diuretic hormone (ADH) deficiency due to diminished production of ADH from the hypothalamus/posterior pituitary axis<br>• It is caused by central nervous system pathology |
| **Nephrogenic** | • It is due to reduced sensitivity of the kidneys to ADH |
| **Gestational** | • It is a transient deficiency of ADH |
| **Psychogenic** | • It is caused by excessive water consumption |

## Diagnosis

- Classic symptoms are polydipsia (drinking > 3 litres/day) and diluted polyuria (> 3 litres urine/day)
- There are no physical signs
- Laboratory diagnosis is made by assessment of blood osmolality (> 285 mOsmol/kg) and urinary osmolality (<300 mOsmol/kg). There is associated hypernatremia

## Endocrine disorders with pregnancy

## Abstract

On the top of the list of endocrine disorders comes diabetes mellitus, which yields several maternal, foetal, and neonatal outcomes. Type 1 diabetes, which is associated with higher risk of acute complications, more challenging management, coincides with reproductive age. Pregnancy is associated with significant immunologic and metabolic changes that may render diabetes harder to control and more liable to cause complications. On the other side, uncontrolled diabetes increases risk of pregnancy loss, congenital anomalies, macrosomia, polyhydramnios, and other obstetric complications. In this chapter, we will discuss management of endocrine disorders in pregnancy including medical and obstetric care of these patients.

## Keywords

Diabetes, thyroid disorder, diabetes insipidus

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# Liver Masses and Pregnancy

| Incidence | Risk factors |
|---|---|
| 20% of general population have a benign liver lesion, predominantly liver cysts | • Alcoholism<br>• Viral hepatitis<br>• Metabolic conditions<br>• Use of oral contraceptive pills (OCPs)<br>• Examination for stigma of liver disease and palpable liver abnormalities |

**Investigations**

❶ Imaging strategies

| Non-contrast Ultrasound (US) | Contrast-enhanced US | CT liver protocol | Contrast-enhanced liver MRI |
|---|---|---|---|
| Sensitivity of US in diagnosis of liver tumors > 90%, differentiate solid from cystic mass. Usually, further imaging modalities may be required | It involves injection of microbubbles to improve visualization. No adverse clinical effects in pregnancy | Foetal exposure is 1-10 mGy (1:10,000-1:100,000 risk of childhood cancer). Therefore, it is performed only if medically justified | MRI with use of gadolinium is considered safe in pregnancy |

| ❷ Laboratory tests | ❸ Liver biopsy |
|---|---|
| • Standard liver function tests<br>• Tumor markers in pregnancy are unreliable | Not usually necessary (MRI with contrast is usually diagnostic, biopsy is associated with risk of bleeding and cancer spread) |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_10

## Specific masses

### ❶ Hepatic hemangiomas

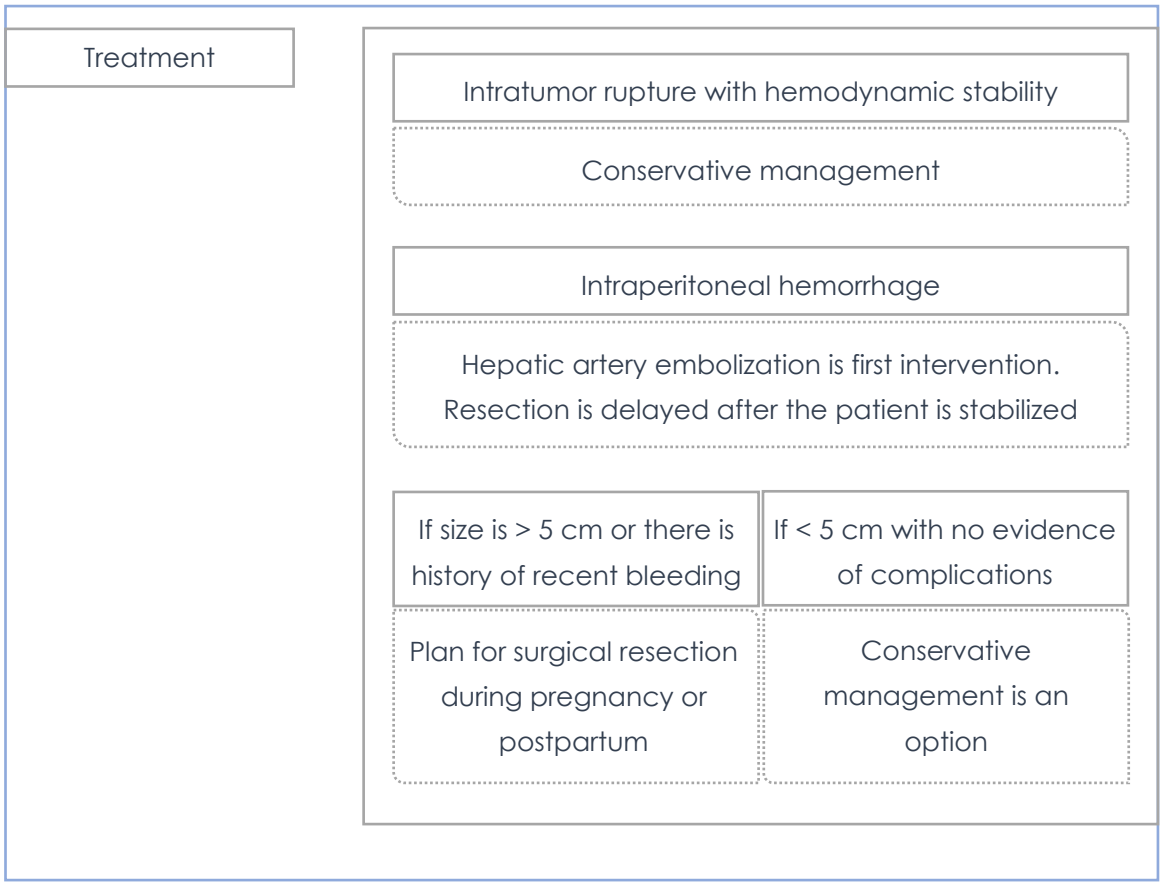
| | |
|---|---|
| Incidence | The commonest benign tumor (2-20% of healthy population) |
| Pathology | • It is a slowly growing tumor. It may have estrogen receptors and growth may be accelerated during pregnancy and with OCPs<br>• They may reach large sizes (up to 20 cm)<br>• They are supplied by hepatic artery |
| Symptoms | • It is rarely symptomatic. It may be complicated by necrosis, infarction or thrombosis. It rarely ruptures<br>• Risk factors for bleeding:<br>▪ 10 cm lesion<br>▪ Rapidly expanding lesion |

There is no evidence that OCPs or pregnancy affect hemangioma size or increase risk of complications

| | |
|---|---|
| Investigations | Ultrasound:<br>• The mass appears well circumscribed and hyperechogenic |
| | Contrast enhanced CT:<br>• The mass is characterized by progressive centripetal fill and retains contrast in delayed phase |
| Kassabach-Merritt syndrome | Triad of:<br>• Expanding hemangioma<br>• Thrombocytopenia<br>• hypofibrinoginemia |
| Treatment | • Conservative<br>• If > 5 cm, it needs to be monitored closely |

| ❷ Focal nodular hyperplasia | |
|---|---|
| Incidence | • The second most common benign lesion (3% of adult)<br>• 80-90% occur in females in reproductive years |
| Pathology | • 78% are solitary<br>• 84% are sized < 5 cm, but it may reach up to 15 cm<br>• The lesion is district, isolated, surrounded by pseudo-capsule |
| Symptoms | • Asymptomatic<br>• Risk of rupture is extremely rare<br>• No risk of malignant transformation |
| Effect of pregnancy and OCPs is not clear. OCPs does not cause the lesion to develop but may accelerate growth | |
| Investigations | US:<br>• Hypoechoic or isoechoic mass with occasional visualization of a central scar (thin hyperechoic zone) |
| | CT and MRI:<br>• Hepatic mass associated with homogenous pseudocapsule and central scar |

| ❸ Hepatic adenoma | |
|---|---|
| Incidence | Rare, it occurs in young women on OCPs |
| Pathology | • 32% are solitary, 45% are multiple, 23% are liver adenomatosis (10 or more lesions)<br>• Average size is 8 cm (but may reach up to 30 cm)<br>• 75% are present in the right lobe of the liver<br>• May be pedunculated |
| Symptoms | • Most patients are asymptomatic<br>• Lifetime risk of haemorrhage is 27%, rupture rate is 16% |
| Risk factors | • Young women with OCPs (30-40 per million vs 1.3 per million if not using OCPs)<br>• Non-contraceptive oestrogen, androgenic steroids<br>• Diabetes<br>• Glycogen storage disease, galactosemia and iron overload |
| Investigations | US:<br>• Non-specific hepatic mass |
| | CT and MRI:<br>• Hypervascular lesion with large peripheral vessels |
| Complications | • Bleeding<br>▪ 60% of Patients with epigastric pain and tenderness have signs of bleeding<br>▪ Bleeding can occur with any size, but the risk is high if the mass is > 10 cm and in the 3rd trimester<br>▪ Risk of bleeding is not related to number<br>▪ Risk of intraperitoneal hemorrhage is higher with lesions close to the capsule (maternal mortality is 44%, foetal mortality is 38%)<br>• Risk of malignant transformation: 4-10% (4% if < 5 cm) |




### ❹ Hepatocellular carcinoma

- Highest rate is noted in early onset cirrhosis in Asian countries with high prevalence of Hepatitis B and C
- It may rupture in pregnancy

### General clinical presentation

- Asymptomatic
- Compressive symptoms
- Pain due to capsular stretching (by mass growth or development of hematoma)
- Hepatic bleeding (present with severe epigastric pain radiating to back with signs of hypovolemic shock)
- Intraperitoneal bleeding, foetal hypoxia and maternal, foetal mortality (very rare)

## Interventions

- Once a liver mass is detected, a multidisciplinary team care should be offered

| | | |
|---|---|---|
| Elective surgery: in non-pregnant, incidence of mortality is 1%, risk of significant morbidity is 16% (data with pregnancy is limited) | Trans-arterial embolization is the best approach in emergency setting | Radiofrequency ablation is safe in pregnancy for lesions < 5 cm that are accessible (which have the lowest initial bleeding risk) |

## Pregnancy specific issues

| Pregnancy risk | Perinatal risk | Postpartum risk |
|---|---|---|
| If acute haemorrhage occurs in pregnancy:<br>• Resuscitation and arterial embolization.<br>• Emergency operative strategies include:<br>▪ Liver packing<br>▪ Primary resection<br>▪ Orthotopic liver transplantation (rare)<br>• After management of acute bleeding episode, further imaging will be unreliable due to present hematoma | • Unplanned early delivery is unlikely (except in emergency situations e.g. rupture)<br>• Women with hepatic adenoma are safe to deliver vaginally | • With postpartum drop in maternal hormones, risks of degeneration and bleeding increase<br>• Imaging is needed after delivery<br>• Counsel patients with hepatic adenoma that OCPs and anabolic steroids should be avoided and keep strict follow-up because risk of enlargement is present even if these medications are avoided |

# Constipation in Pregnancy

## Epidemiology

Constipation is a common complaint in pregnancy:

- 35% of pregnant women in the first and second trimester
- 21% in the third trimester
- 17% in the puerperium

## Clinical picture

- Women complain of infrequent emptying, dry hard stool, pain and straining with bowel movements
- Straining may cause pudendal nerve damage which can cause pelvic floor weakness and/or incomplete emptying

## Treatment

- **Dietary modifications:**

  Dietary fibres, fluid intake, bran or wheat fibres, Linseed (short term treatment, safety is unknown) safety) and /or probiotics

- **Laxatives:**
  - **Bulk forming laxatives:**
    - ***Characteristics:*** They are the **safest** and **best** choice in pregnancy. They are not absorbed from the gastrointestinal tract e.g. wheat bran, methylcellulose
    - ***Mechanism of action:*** They bulk faecal material and stimulate peristalsis

- ***Contraindications:***
  - faecal impaction
  - It is not suitable for acute cases, since it takes few days to work

- **Osmotic laxatives:**
  - ***Characteristics:***
    - Polyethylene glycol (PEG) and lactulose are poorly absorbed. Therefore, PEG is the treatment of choice of chronic constipation in pregnancy.
    - Lactulose should be avoided in diabetic women and patients who require low galactose diet (Galactosemia)
  - ***Mechanism of action:***

    They act by Increasing osmolar tension, which increases water content in the colon, thus, stimulating peristalsis
  - ***Side effects:***
    - Flatulence and abdominal bloating
    - Theoretical risk of electrolyte imbalance with chronic use

- **Stimulant laxatives:**
  - ***Characteristics:*** e.g. Senna, bisacodyl

    They are more effective than bulk forming

    Bisacodyl is minimally absorbed (5%) and is a safe and good choice in pregnancy
  - ***Mechanism of action:***

    They reduce water absorption and stimulate colonic peristalsis
  - ***Side effects:***
    - They should be used with caution in the third trimester (risk of uterine contractions)
    - Docusate should be used with caution, only in low doses if other measures fail because of risk of neonatal hypomagnesemia with maternal overuse
    - Senna and Docusate should be used with caution during breastfeeding (partially absorbed and excreted in breast milk)

- Laxatives should be withdrawn gradually
- If multiple medications are administered, stop one medication at a time, starting with **stimulant laxatives**
- Withdrawal of laxatives may take several months

- **Suppositories and enemas:**
  - Glycerine suppositories can be used in pregnancy. They should be discontinued once bowel movements are restored without difficulty
  - Data on safety of enemas in pregnancy is limited

**Avoid in pregnancy**

- Anticholinergics and antispasmodics are contraindicated in pregnancy
- Lubiprostone (chloride channel activator) is contraindicated in pregnancy
- Prucalopride (5-HT4 receptor stimulant) is contraindicated in pregnancy and its use non-pregnant women should be combined with contraception use

## Gastrointestinal disorders with pregnancy

### Abstract

Gastrointestinal symptoms are common in pregnancy and their severity varies and fluctuates throughout pregnancy. In this chapter, we will discuss constipation, as a common symptom specially in late pregnancy, and we will also cover liver mases with pregnancy, and the effect of pregnancy on these masses.

### Keywords

Haemangioma, liver masses, constipation

## Further readings

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# Asthma in Pregnancy

## Definition

It is a chronic inflammatory disorder of respiratory airways which results in intermittent episodes of wheezing, breathlessness and cough, which are observed more at night and on exposure to triggers

## Epidemiology

- Prevalence of asthma in pregnancy is 4-12%
- It is the most common chronic disorder in pregnancy

## Differential diagnosis

- Normal respiratory rate is 12-20/minutes at rest. Persistent respiratory rate > 24 is abnormal
- Breathlessness is common in pregnancy and is **not necessarily** due to asthma
- Causes of breathlessness in pregnancy include:

| | | |
|---|---|---|
| **Respiratory** | • Asthma<br>• Amniotic fluid embolism<br>• Pneumothorax<br>• Pneumonia (chest infections) | • Interstitial lung disease<br>• Thromboembolism<br>• Dysfunctional breathing |
| **Cardiovascular** | • Ischemic heart disease<br>• Arrythmias<br>• Acute haemorrhage | • Cardiomyopathy<br>• Chronic anaemia |
| **Endocrine** | • Acute renal failure with acute ketoacidosis<br>• Thyrotoxicosis<br>• Diabetes with acute ketoacidosis | |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_11

## Asthma and pregnancy

| Effect of pregnancy on asthma | Effect of asthma on pregnancy |
|---|---|
| • The course of asthma in pregnancy is variable; 1/3 improve, 1/3 deteriorate, 1/3 remains stable<br>• Asthma control deteriorates more commonly with severe (60%) than mild asthma (10%)<br>• Deterioration of asthma most commonly occurs between 24-36 weeks<br>• Most common trigger factors of asthma exacerbation are:<br>▪ Viral infection (34%)<br>▪ Poor adherence to corticosteroids (29%) | • Airway hyper-responsiveness may predict pre-eclampsia in pregnancy<br>• Asthma is associated with increased probability of caesarean section<br>• Poorly controlled severe asthma increases the risk of low birth weight infants.<br><br>Women with well controlled asthma have no/ minimal additional obstetric risk |

## Management

Women with moderate to severe asthma (step 3 and up) need to be managed by conjoint obstetrician and respiratory physician care

| | |
|---|---|
| **Mild intermittent asthma** | • Inhaled short acting B2 agonist as needed |
| **Regular preventive therapy** | • Add inhaled steroids 200-800 mcg/day |
| **Initial add-on therapy** | Add inhaled long acting B2 agonist<br>• If adequate response is achieved, continue treatment<br>• If there is inadequate response, increase inhaled steroids dose<br>• If no response is achieved, stop this treatment and increase the dose of inhaled steroids<br>• If no response is achieved, consider leukotriene receptor antagonist or sustained release theophylline |
| **Persistent poor control** | • Increase inhaled steroids to 2000 and add a 4$^{th}$ drug (leukotriene receptor antagonist, sustained release theophylline, B2 agonist tablet) |
| **Continuous or frequent use of steroids** | • Add oral steroids |

## Management during pregnancy

- **Non-pharmacological management:**
  - Treatment includes avoiding asthma triggers and patient education
  - Patients should be counselling that poor asthma control carries higher risk than asthma medications on the foetus and that they are overall safe to use in pregnancy

- **Pharmacological management:**

  Asthma medications can continue in pregnancy. The dose usually does not need to be changed:

| | |
|---|---|
| **Inhaled steroids** | They are the best choice in pregnancy (they decrease incidence of exacerbation in pregnancy) |
| **Salmeterol** | Salmeterol is safe but is not used alone in pregnancy |
| **Theophylline** | Theophylline level needs to be monitored safe in pregnancy |
| **Leukotriene blockers** | Leukotriene blockers have limited evidence of efficacy. Therefore, shifting to inhaled steroids ± long acting B2 agonists before pregnancy is recommended |
| **Oral steroids** | Oral steroids may be associated with small increase in the risk of cleft lip/palate in the first trimester (< 0.3%). Therefore, it can still be used in pregnancy |
| **Anti-IgE** | Anti-IgE medications are not recommended in pregnancy |

- **Management of asthma exacerbation in pregnancy:**

  Treatment should include oral steroids, nebulized B2 agonist, oxygen, and other additional supportive care measures

## Management during labour and delivery

- Asthma does not affect labour and delivery. Only 1/5 of patients may experience exacerbation, which is rarely severe
- The following precautions should be taken in labour:
  ① Avoid PGF2 alpha (associated with bronchospasm). PGE2 is safe
  ② Ergometrine and syntometrine may cause bronchospasm and should be used with caution
  ③ If patient is on oral steroids, she may need IV hydrocortisone during labour (stress dose protocol)

## Postpartum management

- There is no increased risk of exacerbation. Severity of asthma returns to pre-pregnancy level within few months
- Medications that are safe in pregnancy can continue. Non-steroidal anti-inflammatory drugs (NSAIDs) should be used with caution as they may cause bronchospasm (unless there is known tolerance to NSAIDs)

# Cystic Fibrosis in Pregnancy

## Epidemiology

- Prevalence of carrier state of cystic fibrosis (CF) is 1:25
- CF is associated with shorter life expectancy. With modern management strategies, median survival is 31 years, and life expectancy is above 50 years
- Most common cause of death is respiratory failure due to progressive bronchiectasis, persistent lung infection with virulent organism e.g. pseudomonas, staph aureus

Other complications include pancreatic insufficiency, diabetes, osteoporosis, liver disease, and gall stones

## Aetiology

- CF is an autosomal fibrosis disease
- The disease is caused by mutations in CFTR (cystic fibrosis transmembrane conductance regulator) gene, which is located on the long arm of chromosome 7. The gene encodes chloride channels in epithelial cell membrane

## CF and fertility

- **Effect of CF on fertility:**
  - Menarche is slightly delayed (the most significant determinant is body mass index)
  - Menstrual cycles are typically regular. Amenorrhoea is seen in women with poor lung function
  - Almost all men with CF are infertile
  - Women have almost normal fertility. However, cervical mucus is thick throughout the cycle

- **CF and Contraception:**
  - Combined oral contraceptives (COCs) are commonly used:
    - Theoretically, they may be less effective in women with CF due to frequent use of antibiotics. However, this has not been proven to increase failure rate
    - Condoms may be used in addition to COCs when on antibiotics
  - Long acting methods (injectables, implants, Mirena) are effective options
  - Both medical and surgical methods can be used as usual if termination of pregnancy is indicated

## CF and pregnancy

| Effect of CF on pregnancy | Effect of pregnancy on CF |
|---|---|
| • No increase in the risk of miscarriage<br>• No increase in the risk of congenital anomalies<br>• Risk of prematurity is 25% (the risk is related to poor lung function)<br>• Less maternal weight gain in pregnancy (5-10 kg vs. 10-12 kg) with no associated impairment of foetal growth<br>• Higher risk of pregestational and gestational diabetes (14-20%) and associated complications<br>• Spontaneous live birth is 70-90% | • Pregnancy does not affect life expectancy even among women with poor lung function<br>• In some patients, deterioration of general status may occur during pregnancy<br>• Mortality rate is 20% within 10 years of delivery, and 40% in women with poor lung function. This is likely not related to the effect of pregnancy and represents the nature course of the disease |

## Management

- **Preconception management:**
  - **Assessment:**

    Prior to conception, clinical assessment should include:
    - Assessment of disease severity and rate of progression is indicated

- Partner testing to assess risk of inheritance. Inheritance risk is less than 1:250 if the partner has no known mutation, and is 1:2 (50%) if the partner is a carrier
- Testing of glycaemic status (risk of pregestational diabetes)

Folic acid should be administered prior to conception

- **Pregnancy decision:**

| Pregnancy candidates | Contraindications to pregnancy |
|---|---|
| • Women are anticipated to have good obstetric outcomes and low mortality if pre-pregnancy good lung function (FEV1 > 70% of expected)<br>• Stability of lung function may be more important than the absolute value | • *Absolute contraindication:* Pulmonary hypertension and cor pulmonale<br>• *Relative contraindications:* Infection with Burkholderia capacia (associated with poor pregnancy outcome and high mortality) |

Women who underwent lung or heart-lung transplant should postpone pregnancy for 2-3 years to ensure graft stability and decrease risk of rejection and prematurity

- **Antenatal management:**

A multidisciplinary team composed of a physician, physiotherapist, dietitian, obstetrician, midwife, and obstetric anaesthetist should be involved

- **Sonographic assessment:**
  - First trimester ultrasound is used for dating
  - Second trimester ultrasound is done for anomaly scan. If the patient is diabetic, foetal echocardiogram should be offered
  - Third trimester ultrasound is performed serially to assess foetal growth and wellbeing

- **Medical assessment:**
  - Observation of nutritional status and weight gain. If weight gain is poor, nutritional supplementation through the enteral route may be considered
  - Pulmonary function should be monitored throughout pregnancy

- Oral glucose tolerance test should be performed in the first trimester. If the test is normal, it should be repeated between 28 and 32 weeks of pregnancy

- **Medical treatment of CF:**
  - General treatment of CF consists of chest physiotherapy, pancreatic enzymes, nutritional supplements, pancreatic enzymes, mucolytics, long term nebulized antibiotics, frequent courses of IV antibiotics. Most medications are safe during pregnancy
  - Exacerbations of infection should be treated aggressively with hospital admission, physiotherapy and IV antibiotics
  - Women may need to be admitted in the third trimester for optimization of lung function prior to delivery through physical therapy and antibiotics

- **Intrapartum management:**
  - **Mode of delivery:**
    - Mode of delivery is not influenced by CF and is guided only by obstetric indications
    - Women who deliver vaginally are at higher risk of instrumental delivery (40%). This may be because patients get tired more quick than normal specially in the presence of diminished lung function
  - **Timing of delivery:**

    Elective preterm delivery may be indicated if
    - Lung function is declining or
    - In the presence of foetal growth restriction

- **Postpartum management:**

  Because breast feeding is exhausting and consumes calories from the mother, women who have difficulties maintaining their weight may be advised to consider other options

## Respiratory disorders with pregnancy


### Abstract

Respiratory disorders are not uncommon during pregnancy. Bronchial asthma is a prevalent disease in pregnancy and the interaction between pregnancy and asthma is inconsistent. Women should be counselled that asthma should be controlled in pregnancy and that medications should not be stopped for fear of teratogenicity. In this chapter, we will discuss respiratory disorders, particularly asthma and cystic fibrosis, in pregnancy, their complications, and management protocols.



### Keywords

Cystic fibrosis, asthma, inhaled steroids


### Further readings


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# Systemic Lupus Erythematosus and Pregnancy

## Prevalence

- Systemic Lupus Erythematosus (SLE) affects women more than men (10:1)
- Prevalence of SLE among women in the child-bearing period is 1:500

## Clinical features

| | | | |
|---|---|---|---|
| **Dermatologic** | • Malar rash (flat or raised)<br>• Discoid rash (raised, with adherent scaling)<br>• Photosensitivity<br>• Painless oral ulcers | **Hematologic** | • Haemolytic anaemia<br>• Reticulocytosis<br>• Leukopenia<br>• Lymphopenia<br>• Thrombocytopenia |
| **Immunologic** | Anti-DNA or anti-Smith antibodies | **Renal** | • Persistent proteinuria<br>• Cellular casts |
| **Neurologic** | Seizures and psychosis | **Metabolic** | • Uraemia<br>• Ketoacidosis<br>• Electrolyte imbalance |
| **Inflammatory** | Pleuritis and pericarditis | **Skeletal** | Non erosive arthritis |

## SLE and fertility

SLE itself does not affect fertility. However, secondary causes that impact fertility include:

- Ovarian insufficiency caused by medications e.g. cyclophosphamide
- Lupus nephritis with end stage renal disease
- Inhibition of cyclooxygenase and ovulation by non-steroidal anti-inflammatory drugs (luteinized unruptured follicle syndrome)




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_12

## Preconception management

- **Initial assessment:**
  - Assessment of disease activity:
    - Anti-dsDNA antibodies
    - Complement C3/C4 levels
  - Assessment of organ involvement:

| System | Risks | Assessment |
|---|---|---|
| **Cardiac** | Pulmonary hypertension, valvular heart disease, cardiomyopathy | Echocardiography |
| **Respiratory** | Pulmonary fibrosis | chest X-ray and CT scan<br>Lung function tests if there is underlying restrictive respiratory involvement |
| **Renal** | Lupus nephritis | Urine dipstick and protein: creatinine ratio to screen and quantify Proteinuria and Haematuria<br>Renal function tests to assess pre-existing renal dysfunction |
| **Haematologic** | Anaemia, leukopenia, thrombocytopenia | Complete blood count |

  - Assessment of antiphospholipid antibodies (risk of thrombosis, recurrent miscarriage, foetal growth restriction, foetal loss, preterm delivery)
  - Assessment of the presence of anti-Ro/La antibodies (risk of congenital heart block and neonatal cutaneous lupus syndrome)
  - Review of medications

- **Preconception counselling:**

- Women are counselled on obstetric risks associated with SLE:
  - Risk of miscarriage is 6-35%
  - Risk of stillbirth is 0-22%
  - Risk of preeclampsia, preterm delivery, and foetal growth restriction (FGR) is 2-4 folds higher than baseline
  - Prelabour rupture of membranes (PROM) occurs in 20% of SLE patients. Steroid treatment may increase the risk
  - Risk of FGR is 25-35% in women with SLE (35% with lupus nephritis)
  - Risk of congenital heart block is 2-3% in women with anti-Ro and Anti-La antibodies. Recurrence is 16% in subsequent pregnancy
- If the disease is quiescent (with negative antiphospholipid antibodies, no hypertension, or renal involvement), risks of miscarriage, still birth, and FGR do not significantly increase compared to baseline

**Contraindications to pregnancy**

- **Pulmonary hypertension:**
  - It is present in 4% of women with SLE
  - Mortality rate is 33%
- **Active disease particularly active lupus nephritis**

**Congenital heart block**

- Anti-Ro and Anti-La antibodies destroy the foetal cardiac conductive system
- It develops mostly between 18-28 weeks
- It presents with fixed bradycardia at 60-80 beats/minute
- 50% require pacing in the 1st year of life
- Hydrops may occur

**neonatal cutaneous lupus**

- It appears within 2 weeks of delivery and may persist for up to 6 months
- Neonatal lupus and congenital heart block rarely coexist in the same neonate

**Indications of termination of pregnancy**

- Uncontrolled hypertension
- Worsening renal function despite treatment (this may be due to early onset preeclampsia or lupus nephritis flare)
  Women with active lupus nephritis with worsening renal function is managed by cyclophosphamide and mycophenolate. These medications are teratogenic in the first trimester

## Antepartum management

- **Antenatal surveillance:**

| | |
|---|---|
| Low risk group (women with stable disease) | Regular assessment of foetal growth, blood pressure and proteinuria every 4 weeks |
| Women at higher risk of FGR and/or preeclampsia (presence of active disease or prior history of FGR or preeclampsia) | More frequent assessment is required |
| Higher risk group (active SLE, active nephritis, anti-Ro & anti-La, APA (active disease) | Hospital admission is commonly indicated |
| Women with anti-Ro/La antibodies | • Foetal heart rate should be assessed at each visit<br>• Echocardiography is indicated at 18-20 weeks and at 28 weeks of gestation |

- **Management of thromboembolism:**
  - Risk of thromboembolism should be assessed as early as possible prior to conception and at each hospital admission
  - If there is previous history of venous thromboembolism, low molecular weight heparin (LMWH) is given throughout pregnancy and for 6 weeks postpartum

- **Management of SLE flares:**
  - Most flares can be managed expectantly
  - Nephritis flare should be differentiated from preeclampsia. Therefore, blood pressure and proteinuria should be monitored closely and compared to baseline. New-onset lupus nephritis is unusual and therefore, development of high blood pressure and proteinuria for the first time in the second trimester is consistent with preeclampsia

  - If the disease was active within 3-6 months prior to conception, patients are at high risk of SLE flare during pregnancy
  - Most flares occur in the second trimester

  - Presence of haematuria or red cell casts, increased dsDNA titre or decreased complement level, lupus activity in other organs is consistent with lupus flare
  - The only definitive test is renal biopsy. It is not performed in pregnancy unless indicated for decision-making particularly in early pregnancy (first and second trimester). Women with lupus nephritis may be conservatively manged with prolongation of pregnancy compared to early onset preeclampsia
  - Treatment of lupus nephritis includes:
    - Steroids and azathioprine (safe in pregnancy)
    - If treatment is inadequate, mycophenolate or tacrolimus may be considered after discussing treatment plan with a nephrologist and rheumatologist
    - Blood pressure should be kept under 140/90

- **Foetal management:**

  There is an increased risk of miscarriage (even in absence of antiphospholipid antibodies)
  - Scanning with Doppler ultrasound:
    - Foetal growth scan is performed every 4 weeks
    - Uterine artery doppler is performed at 20 weeks and is repeated after 4 weeks if there are any abnormalities (to assess risk of preeclampsia)

- **Postpartum care:**
  - Risk assessment of venous thromboprophylaxis
  - Oestrogen-containing contraceptives should be avoided
  - Close monitoring is indicated because of the increased risk of lupus flare in the postpartum period

## Drug therapy of SLE

| Drugs | Recommendations |
|---|---|
| **Corticosteroids** | Continue during pregnancy |
| **Non -steroidal anti inflammatory** | Discontinue prior to conception |
| **Azathioprine** | Safe to continue in pregnancy (should not be discontinued without Don't stop without guidance from a rheumatologist) |
| **Methotrexate** | Stop prior to conception (contraindicated in pregnancy) |
| **Mycophenolate Mofetil** | It is contraindicated in pregnancy and breastfeeding. Patients should switch to azathioprine prior to conception |
| **Cyclophosphamide** | • It should not be used in pregnancy. However, a rheumatology consult is indicated in women with flare<br>• It should be avoided with breastfeeding |
| **Ciclosporine** | • Decision should be made by following rheumatology and nephrology consult<br>• Breastfeeding is likely safe |
| **Hydroxychloroquine** | Continue throughout pregnancy and breastfeeding. Cessation may precipitate a flare |

Metabolic disorders

# Phenylketonuria in Pregnancy

## Definition

Phenylketonuria (PKU) is an autosomal recessive disease, caused by phenylalanine hydroxylase deficiency. The disease is managed by phenylalanine restricted diet

## Epidemiology

- Incidence of PKU is 1:10.000
- Incidence is more common among Turkish and Irish population

## Classification

| | |
|---|---|
| **Classic PKU** | • Complete absence of phenylalanine hydroxylase<br>• Serum Phenylalanine > 1200 mmol/l (normal level is < 120 mmol/l) |
| **Non-classic PKU** | • Complete absence of phenylalanine hydroxylase<br>• Serum phenylalanine is either:<br>▪ Serum Phenylalanine is 900-1200 mmol/l (moderate PKU)<br>▪ Serum Phenylalanine is 600-900 mmol/l (mild PKU) |

Hyperphenylalaninemia refers to serum phenylalanine that is higher than normal, yet less than 600 mmol/l

## Maternal PKU syndrome

- Maternal PKU syndrome in the neonate is caused by untreated maternal PKU or hyperphenylalaninemia and exposure of the foetus to high concentration of phenylalanine
- Clinical features are similar to foetal alcohol syndrome and include:
  - Microcephaly
  - Congenital heart disease
  - Facial dysmorphism
  - Eczematous rash
  - Intellectual and developmental delay
  - Foetal growth restriction and low birth weight
- Babies of women with maternal PKU may inherit the disease. Disease features in untreated children include:
  - Microcephaly
  - Intellectual and behavioural impairment
  - Epilepsy
  - Musty odour
  - Hair/skin pigmentation
  - Eczema

Phenylalanine is actively transported through the placenta (foetal concentration is 1.25 -2.5 times higher than maternal concentration)

## Management

- **Preconception management:**
  - Reliable contraception is required, preferably by combined oral contraceptives (COCs)
  - If pregnancy is planned, phenylalanine level should be optimized during pregnancy or less optimally before 10 weeks (120-300 mmol/l)
  - COCs are stopped 3-6 months prior to planned conception and women are transitioned to barrier methods

- Maternal PKU programme is followed with diet restriction and phenylalanine is checked by twice weekly blood spot
- Once the level is < 350 in 3-4 blood spots, allow unprotected intercourse
- Folic acid is given prior to conception

- **Antenatal management:**
  - A multidisciplinary team is involved (obstetrician, midwife, dietitian, metabolic consultant)
  - Blood spot testing is performed 3 times/week and diet is adjusted accordingly. Diet adjustment may require admission in women with nausea and vomiting
  - Nutritional status should be assessed before dating ultrasound and at 20 weeks including aminoacid profile, vitamins, minerals, trace elements, and complete blood count
  - Tyrosine should be supplied starting at 16 weeks of gestation
  - Weight gain should be monitored (60% of cases of microcephaly occur when weight gain is less than 70% of optimal)
  - ultrasound surveillance:
    - First trimester ultrasound: to check viability
    - Second ultrasound scan of congenital anomalies, including Foetal echocardiography between 20 and 22 weeks
    - Serial ultrasound scans for assessment of foetal growth

Microcephaly is suspected if head circumference is < 2 standard deviations below mean, and is diagnosed if < 5 standard deviation below mean

- **Intrapartum management:**

  Mode of delivery is determined by obstetric indications. No precautions are required

- **Postpartum management:**
  - Neonatal PKU screen is conducted on day 5
  - The mother should be followed up with a metabolic consultant after 3 months postpartum
  - Breastfeeding is safe

## Immunologic and metabolic disorders with pregnancy


### Abstract

In this chapter, we will discuss systemic lupus erythematosus, an immunologic disorder, with pregnancy. The disease is more common in women and commonly starts at the age of 20-40, making its chance to coincide with pregnancy considerably high. Disease severity may be altered by pregnancy and the disease itself can cause adverse obstetric outcomes. We will also discuss phenylketonuria, an example of an inherited metabolic disorder. Such disorders have become increasingly important in obstetrics since care development of these disorders has improved survival and has brought more children to reach their reproductive years.



### Keywords

SLE, phenylketonuria, inherited metabolic disorders


### Further readings


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# Acute Kidney Injury in Pregnancy

## Definition

- In pregnancy, the threshold for diagnosis of acute kidney injury (AKI) is lower than non-pregnant women and creatinine > 90 micromol/l in pregnancy is considered diagnostic
- In patients with chronic kidney disease (CKD), superimposed AKI may be considered if serum creatinine rises above pre-pregnancy levels
- Normally, serum creatinine decreases by 35 micromol/l in pregnancy

## Incidence

- Most common cause in pregnancy is preeclampsia
- It accounts for 1.4% of obstetric admissions
- 40% of AKI may pass unrecognized




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_13

## Causes

| Gestation | Diagnosis | Clinical features |
|---|---|---|
| *Early* | Hyperemesis | Severe nausea and vomiting |
| | Septic abortion | Abdominal pain, vaginal bleeding, fever, vaginal discharge |
| | Acute retention | Retroflexed uterus |
| *Mid-late* | Pre-eclampsia | New onset hypertension and proteinuria after 20 weeks |
| | Ureteral obstruction | A possible complication of multiple pregnancy, polyhydramnios, a single functioning kidney, autonomic neuropathy (MS or type 1 diabetes), and obstructed labour |
| | Abruption | Abdominal pain, uterine tenderness, vaginal bleeding |
| | Acute fatty liver | Anorexia, vomiting, jaundice, hypoglycaemia, elevated liver enzymes, lactic acidosis |
| | Micorangiopathic haemolytic anaemia (TTP, HUS) | Haemolysis, end organ damage (renal injury with HUS, neurological symptoms with TTP) in the 2nd or 3rd trimester or postpartum |
| *Peripartum* | Chorioamnionitis | Fever, uterine tenderness, abnormal lochia and risk factors |
| | Postpartum haemorrhage | Bleeding, hemodynamic instability |
| | Ureteric injury | Operative delivery, fever, leucocytosis, pain, persistent ileus |
| | NSAIDs | Hyperkalaemia, fluid retention, worsening of hypertension |
| *Any trimester* | Urosepsis | Dysuria, flank pain, renal angle tenderness, fever |
| | Lupus nephritis | Proteinuria +/- haematuria, systemic symptoms of lupus |
| | Glomerulonephritis | Persistent proteinuria before 20 weeks; P:C ratio > 30 mg/mmol |
| | Interstitial nephritis | New drug exposure e.g. NSAIDs, PPIs, antibiotics (penicillin, cephalosporins), $H_2$ antagonists WITH OR WITHOUT systemic symptoms (fever, rash) |
| | Renal stones | Renal colic, specially in the presence of a single kidney |
| | Intravascular volume depletion | A possible complication of sepsis, hyperemesis, or diabetic ketoacidosis |

MS: Multiple sclerosis, TTP: Thrombotic thrombocytopenic purpura, HUS: Haemolytic uremic syndrome

## Non-steroidal anti-inflammatory drugs (NSAIDs)

Most common cause of acute interstitial nephritis, and kidney injury

Regardless of selectivity of COX inhibition, risk is similar

All NSAIDs have dose-dependent adverse effects on kidney

Within the first month of exposure, risk of acute renal failure is doubled

Impaired renal function increases risk of toxicity of NSAIDs

- Significant effect → 1-5%
- Renal failure → 0.5-1%
- Complications → 20%

If preexisting risk factors of AKI

- Volume depletion
- Pre-eclampsia
- Antenatal or peripartum AKI
- Preexisting chronic kidney disease

→ NSAIDs are contraindicated

The risk of AKI should also be considered if combined nephrotoxic medications are used (NSAIDs and gentamicin)

| | |
|---|---|
| **Naproxen** | Highest risk of acute renal failure |
| **Indomethacin** | More nephrotoxicity (higher risk of nephritis and hyperkalaemia) |
| **Fenoprofen** | Highest risk of nephrosis |
| **Meloxicam** | Least effect on kidney but no data safety with breast feeding |
| **Ibuprofen** | At dose < 1200 mg/day, it does not increase risk of heart failure or myocardial infarction. Risk may not increase if used for a short duration (< 6 months) |

**Bleeding risk of NSAIDs**

| **Aspirin** | **Analgesic-NSAIDs (e.g. ibuprofen, diclofenac)** |
|---|---|
| Effect on inhibiting platelet aggregation is irreversible for the lifetime of these platelets | Effect is reversible and dose dependent, no increase in postoperative bleeding |

**Postpartum use of NSAIDs**

Low risk if used by a healthy woman with dose 400mg 3 times/day (1200 mg)

Parenteral med of choice is fentanyl (metabolized by liver)

Contraindications

① Preeclampsia
② Prior AKI (unless completely resolved, with no ongoing risk)
③ Impaired cardiac function
④ High risk of vascular events

Transmission through breast milk is minimal

Alternatives to NSAIDs

- Paracetamol is an alternative for mild pain
- If not sufficient, codeine may be considered. Conversion to morphine is CYP2D6-dependent (variable) and therefore, there is theoretical risk on the baby. However, there is no clinical data that supports any increasing risk

## Management

Supportive treatment to maintain kidney perfusion

Clinical assessment is challenging in pregnancy as pregnant women compensate for hypovolemia and hypotension

Tachycardia is the critical sign

Keys to management

Fluid status assessment

Medication review

Fluid replacement

Appropriate diagnostic workup

Early involvement of a nephrologist

Indications of renal replacement

Metabolic acidosis

Hyperkalemia

Fluid overload refractory to medical treatment

Urea > 17 mmol/l despite medical treatment

*Values are pregnancy-specific because urea is teratogenic*

If there is hyperkalemia

- Calcium salts can be given for cardiac stabilization
- Insulin administration with glucose may be used temporarily to manage hyperkalemia

Specific conditions and their managements

## ❶ Pre-eclampsia

### Incidence

- It is complicated by AKI in 2% of cases
- The commonest glomerular disease in the world
- Pathology consists of glomerular endotheliosis correlated to severity with decrease in glomerular filtration rate

### Outcome

- AKI in preeclampsia affects maternal but not neonatal outcome

### Management

- If urine output is < 20/hour or creatinine > 90 micromol/l, magnesium sulphate should be reduced by 50% (1 g/hr to 0.5 g/hr). loading dose should be the same (4 grams)
- Check serum magnesium every 4-6 hrs in the presence of AKI (2-3.5 mmol/l is advised)
- Fluid management:
  - Aggressive fluid management should be avoided even in presence of oliguria
  - Fluid restricted to 80/hour to decrease risk of pulmonary oedema
  - In immediate postpartum period, oliguria should not be aggressively treated (urine output > 40 ml in 4 hours is acceptable)

## ❷ HELLP syndrome

### Incidence

- Risk of AKI is 3-15%
- Risk is higher with placental abruption, disseminated intravascular coagulopathy, sepsis, haemorrhage, and intrauterine foetal death

### Prognosis

- Presence of AKI with HELLP syndrome worsens prognosis and renal replacement may be temporarily required
- AKI is mostly reversible

### Management

- Supportive management. Steroids should not be used
- HELLP parameters may deteriorate in the first 48 hours postpartum. However, if renal function and platelet count do not resolve thereafter, HUS & TTP should be ruled out

## ❸ Thrombotic microangiopathy (TTP, HUS)

### Incidence

- It is rare (1:25.000)
- Prenatal mortality is high (30-80%)

### Types

| TTP | HUS |
|---|---|
| ▪ Primarily present with neurologic symptoms | ▪ Predominantly associated with renal dysfunction |
| ▪ It is caused by abnormalities in ADAMTS13*, which breaks down Von Willebrand factor | ▪ It is caused by complement pathway dysfunction |
| ▪ It presents in the 2nd, 3rd trimester and postpartum | ▪ It usually presents after delivery |

* ADAMTS13 physiologically decreases in the 2nd, 3rd trimester

### Differential diagnosis

This disease consists of microthrombi formation with subsequent consumptive thrombocytopenia, hemolysis, and end-organ damage. Therefore, it is difficult to distinguish from HELLP syndrome. 20% of TTP patients has co-existing HELLP syndrome

Keys to differential diagnosis are:

- Complement dysfunction is seen in HELLP syndrome and HUS
- Clotting abnormalities are only seen in 20% of HELLP syndrome
- Elevated antithrombin and fibrinogen suggest diagnosis of TTP

### Management

- Fresh frozen plasma infusion and/or plasma exchange (it decreases maternal mortality of TTP from >50% to <10%).
- Early treatment with eculizumab (anti-C5 blocking antibody) decreases morbidity if given to atypical HUS with ADAMTS13 activity is > 10%

## ❹ Acute fatty liver

### Incidence

- It is a rare but a serious disease (5:100.000)
- 14% of patients develop renal impairment
- 3.5% of patients eventually require renal replacement therapy

### Aetiology

- The disease may be caused by foetal homozygosity to beta-fatty acid oxidation, which results in excessive fatty acid load on the heterozygote mother
- Kidney pathology shows tubular free fatty acid deposition

### Differential diagnosis

Features that distinguish it from HELLP syndrome are hypoglycemia, hyperammonemia and prodromal vomiting

### Management

- Supportive management, and immediate delivery
- Most cases recover their hepatic and renal function

## ❺ Systemic lupus erythematosus (SLE)

### Incidence

- Renal involvement is present in 20-50%.
- Renal disease (lupus nephritis) activation occurs in 16% of cases in pregnancy. Risk of flare extends to the postpartum period
- Acute renal failure develops in 10% of women with lupus nephritis in pregnancy

### Management

- Prednisolone, hydroxychloroquine and tacrolimus.
- Mycophenolate is teratogenic and should be replaced by azathioprine prior to conception

### ❻ Obstructive nephropathy

#### Incidence

- It is rare
- It is more likely to develop if there is a single functioning kidney or with renal transplant

#### Causes

- Autonomic neuropathy: which results in urine retention e.g. complicated diabetes, multiple sclerosis
- Obstruction: renal infection (e.g. renal abscess or pyonephrosis), retroflexed uterus in the 1st trimester, postpartum urinary retention (15% of patients), renal stones

#### Diagnosis

- Diagnosis of obstructive nephropathy is challenging in pregnancy because of the physiologic dilation in the upper urinary tract starting at 6-10 weeks of gestation
- Suggestive signs of diagnosis:
  - ① Dilated ureter distal to pelvic brim
  - ② Obstruction does not decompress by placing woman in all-fours position
  - ③ Absent ureteric jets (even in contralateral position)

#### Management

- Management is guided by the cause e.g. stones are treated with analgesia and hydration. Uteroscopic stone removal is the first option if intervention is needed.
- If AKI and infection develop, they should be managed by percutaneous nephrostomy or delivery if gestational age is appropriate

## Renal disorders with pregnancy

### Abstract

Acute kidney injury is a serious complication that may be encountered in pregnancy. In addition to other causes of acute kidney injury in the general population, pregnancy may bring some additional causes specific to pregnancy, namely preeclampsia and acute fatty liver of pregnancy.

In addition, obstetric complications may indirectly cause acute kidney injury, as a result of hypoperfusion such as postpartum haemorrhage. In this chapter, we will cover these causes in more details as well as their diagnosis and management.

## Keywords

Preeclampsia, HELLP, acute fatty liver of pregnancy, renal failure, AKI

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# Dermatoses of Pregnancy

| | Intrahepatic cholestasis of pregnancy | Atopic eruption of pregnancy (prurigo gestationis) | Polymorphic eruption of pregnancy | Pemphigoid gestationis |
|---|---|---|---|---|
| **Incidences** | Overall incidence is 0.7%. Incidence is 1.2–1.5% among Indian–Asian or Pakistani–Asian women | Incidence is 1:300 pregnancies (most common dermatosis of pregnancy)<br>It is more common in women with family history of atopy<br>It presents in the second and third trimesters | Incidence is 1:160 to 1:300<br>It usually presents in the third trimester or in the postpartum period<br>**Risk factors:**<br>① Nulliparity<br>② Multiple pregnancy<br>③ Over distention of abdomen | Incidence is 1:700-1:150.000<br>It usually presents in the second trimester, or rarely postpartum |
| **Symptoms and signs** | • Itching, more at night<br>• It affects hands, feet and pressure sites<br>• Hyperpigmentation secondary to scratching may be present | • Erythematous papules or nodules affecting the face, neck, chest, trunk and extensor surfaces<br>• 80% are primary, 20% are exacerbations<br>• It Improves after delivery with no postpartum exacerbation | • Symptoms start with pruritis<br>• Erythematous papules within abdominal stria, they progress to the trunk and limbs<br>• Lesions merge to form plaques or wheals<br>• There is periumbilical | • Papules and plaques around umbilicus, they extend to the trunk, extremities, palms and soles<br>• They coalesce and form bullae<br>• There is mucosal sparing<br>• Large tense blisters may be present |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_14

| | | | | |
|---|---|---|---|---|
| | | | sparing, sparing of palms, soles and face<br>• Lesions resolve within 4-6 weeks | • Symptoms may improve towards delivery. It commonly flares up at delivery (75%)<br>• Postnatal flaring may occur for 2-6 weeks |
| **Complications** | **Obstetric risks:**<br>• Risk of stillbirth<br>• Preterm labour<br>• Meconium passage<br>• Caesarean section delivery<br>• Postpartum haemorrhage<br>• Risk of recurrence is 45%-90%<br>**Neonatal risks:**<br>Small theoretic risks of:<br>• Neonatal haemolytic anaemia<br>• Hyperbilirubinemia<br>• Kernicterus | No maternal or foetal adverse complications | • No maternal or foetal complications<br>• Recurrence is rare | **Maternal risks:**<br>• Association with other autoimmune diseases (graves)<br>• Recurrence is possible (more with earlier onset and more severe symptoms). It may recur with oral contraception or menstruation<br>**Foetal/neonatal risks:**<br>• Foetal growth restriction<br>• Preterm labour<br>• Self-limited skin disease of the newborn |
| **Investigations** | • Monitoring of liver function and bile acids for diagnosis of intrahepatic cholestasis and | • Histopathological assessment is non-specific | • Diagnosis is clinical<br>• Histopathology is performed only if the diagnosis is not clear or lesions are | • Biopsies are taken from perilesional skin<br>• Histopathology shows |

| | | | | |
|---|---|---|---|---|
| | ruling out other causes<br>• Viral screen, liver ultrasound, and assessment of pre-eclampsia may be indicated if other causes are suspected | • Immuno-fluorescence is negative | not responsive to treatment<br>• Early findings include lymphocytic vasculitis and eosinophilia<br>• Late findings include spongiosis and hyper or parakeratosis<br>• fluorescence is negative | degenerative changes of basal cells and blister formation<br>• Immuno-fluorescence is positive (C3 deposition along basement membrane, 50% of cases are associated with IgG complement fixing)<br>• Indirect immuno-fluorescence from blood or blister fluid may be performed |
| **Treatment** | • Ursodeoxycholic acid is the standard treatment (improves pruritis, liver function tests and may improve foetal outcomes)<br>• Dose 15 mg/kg one dose or 2 divided doses<br>• Topical emollient and anti-histaminics for symptomatic treatment | Symptomatic treatment e.g. oatmeal baths, emollients, topical antipruritic preparations e.g. topical steroids, topical benzoyl peroxide, erythromycin and zinc acetate lotion | • Topical steroids are the first line treatment<br>• Anti-histaminic treatment<br>• Emollients | • Topical or oral steroids<br>• Antihistaminic treatment<br>• Cyclosporin (not with breastfeeding)<br>• Immunophoresis may be used in women cases refractory to systemic steroids (up to 7.5 mg of prednisolone). Blood pressure |

| | | | | |
|---|---|---|---|---|
| | • Water soluble vitamin K may be offered | | | and renal function should be monitored<br>• Because of the risk of flare around delivery time, treatment may start or increase if blisters increase by that time |
| **Referrals** | Referral to an obstetric consultant is indicated because of obstetric risks | Referral to a dermatologist | Referral to a dermatologist | Referral to an obstetric consultant and dermatologist |

## Dermatologic disorders with pregnancy

### Abstract

Skin conditions in pregnancy are not uncommon and they may result in significant discomfort. However, skin conditions may indicate an underlying process that may be threatening to the foetus. In this chapter, we will discuss common dermatologic conditions of pregnancy, and how to differentiate and manage them.

### Keywords

Skin eruption, atopic eruption of pregnancy, intrahepatic cholestasis, pemphigoid gestastionis, polymorphic eruption of pregnancy

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# Thalassemia in Pregnancy

## Background

- Beta-thalassemia is an autosomal recessive disease
- Beta-thalassemia is classified into 3 types:
  - Thalassemia major (2 defective β globin genes)
  - Thalassemia minor (trait)
  - Thalassemia intermedia

## Obstetric risks

| Maternal risks |
| --- |
| • Cardiomyopathy (due to iron overload). Approximately 50% of mortality cases are cardiac in origin<br>• Pregestational and gestational diabetes, hypothyroid, and hypoparathyroid disorders (particularly if no chelation is done for 9 months) |
| **Foetal risks** |
| • Foetal growth restriction<br>• Risk of operative delivery due to foetal hypoxia |

## Preconception care

- **Infertility:**
  - Women with beta-thalassemia may suffer from delayed puberty and infertility due to pituitary affection of iron overload
  - In these patients, ovulation induction with gonadotrophins may be indicated




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_15

- **Contraception:**
  - Women should be counselled on risk associated with pregnancy. Women who desire to conceive may still use contraception till her clinical status is optimized
  - Hormonal contraception is NOT contraindicated in these patients

- **Chelation:**
  - Aggressive chelation is required prior to conception to reduce risk of end organ failure and cardiomyopathy
  - Chelating agents:

| | |
|---|---|
| Deferasirox and deferiprone | • They are potentially teratogenic<br>• They should be discontinued 3 months before conception and women may be shifted to deferoxamine |
| Deferoxamine | • It is safe to be used after 20 weeks of gestation<br>• Low doses are recommended in pregnancy |

- **Genetic counselling:**

  Options of genetic testing should be discussed with women:

  - The partner may be tested. If the partner is not a carrier, the baby will not be at risk of thalassemia major
  - If the partner is positive for thalassemia genes (high risk couples), pre-implantation genetic diagnosis or sperm/egg donation may be offered
  - if partner testing is not available, prenatal genetic testing and possible termination of pregnancy is offered

- **Antibody screening:**
  - ABO and full blood group genotype should be assessed
  - Antibody titers should be measured
  - Risk of alloimmunization is 16%

- **Organ assessment:**

### Pancreas

- Good glycemic control should be achieved prior to pregnancy
- To assess glycemic control, fructosamine is superior to HgBA1c.
- Fructosamine target is < 300 for at least 3 months prior to conception

### Bone

- Women should be screened for preexisting osteoporosis and vitamin-D deficiency
- Bisphosphonates are contraindicated in pregnancy. It should be stopped 3 months prior to conception

### Heart

Cardiac assessment is indicated using:

- ECG
- Echocardiography: diminished ejection fraction is a relative contraindication to pregnancy
- T2 cardiac MRI (Cardiac T2):
  - T2 Cardiac MRI > 20 ms prior to conception is optimal
  - T2 cardiac MRI < 10 ms is associated with high risk of heart failure

### Liver

Liver assessment is indicated using:

- FerriScan or Liver T2:
  - Liver iron load < 7 mg/g dw: is recommended prior to conception
  - If iron load > 15 mg/g dw, risk of myocardial loading is high. Therefore, low dose deferoxamine between **20-28 weeks** is recommended.
- Ultrasound: for assessment of gall bladder stones and liver cirrhosis

### Thyroid

Thyroid function should be screened prior to conception

- **Preconception medications and vaccines:**

| | |
|---|---|
| Pneumococci vaccine | • In women who underwent splenectomy, pneumococci vaccine should be taken every 5 years |
| Hemophilus B/ meningococcal C vaccines | • In women who underwent splenectomy, pneumococci vaccine should be taken once |
| Hepatitis B vaccine | • It should be given to all women who test negative for HBsAg<br>• In these women, hepatitis C status should be assessed. If positive, a hepatologist should be involved |
| Penicillin | • It should be given to high risk splenectomised women for prophylaxis |
| Erythromycin | • It should be given to high risk splenectomised women for prophylaxis in women allergic to pencillin |
| Folic acid | • It should be given in high dose (5mg) 3 months prior to conception |

## Antenatal care

- **Antenatal care visits:**

  Antenatal care visits are scheduled every 4 weeks till 28 weeks then every two weeks

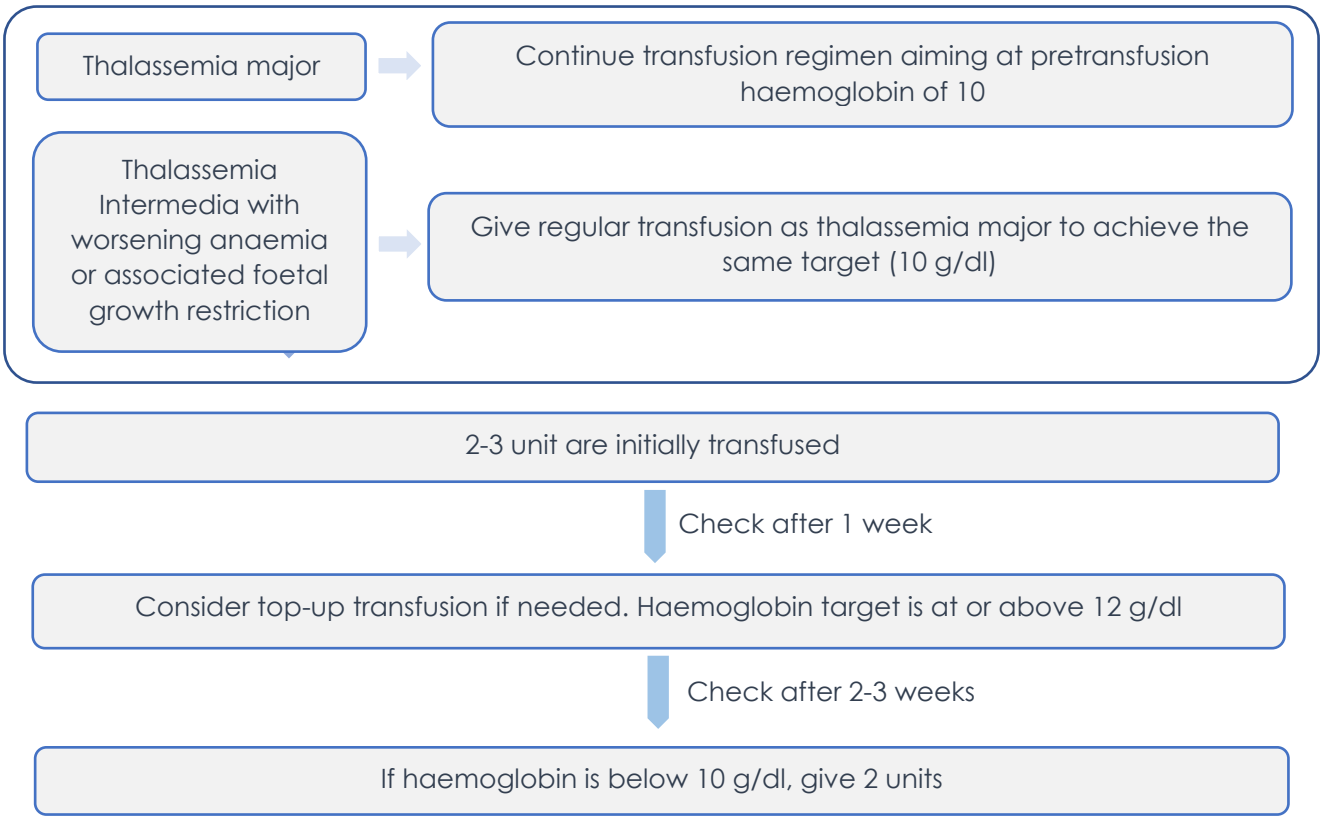
- **Ultrasound assessment and follow-up:**
  - Early ultrasonography scan (7–9 weeks) is offered to diabetic women (risk of early pregnancy loss) and women undergoing ovulation induction
  - First trimester routine scan at 11-14 weeks
  - Second trimester routine scan at 18-21 weeks
  - Foetal growth assessment every 4 weeks starting at 24 weeks

- **System-specific assessment:**
  - Endocrine assessment:
    - Fructosamine should be monitored monthly in patients with diabetes
    - Thyroid function should be monitored in patients with hypothyroidism

- Cardiac assessment:
  - Routine assessment is done at 28 weeks and as indicated
  - Women with palpitations should be assessed by ECG Holter monitoring. Chelation therapy may be indicated in these patients

- **Management of thalassemia:**

### ❶ Transfusion therapy




### ❷ Chelation therapy

- Iron chelation is managed by an experienced haematologist.

| | |
|---|---|
| **Indications** | ▪ If T2 Cardiac MRI < 10 ms during pregnancy (cardiac MRI is not done prior to conception, it is done during pregnancy)<br>▪ If liver iron is > 15 mg/g dw |
| **Dose** | Deferoxamine (20 mg/kg/d) SC 4-5 days/week from 20-24 weeks |

- **Thromboprophylaxis:**
  - Low dose aspirin: for women who had splenectomy OR has platelet count > 600 x $10^9$/l
  - Low dose aspirin PLUS low molecular weight heparin (LMWH): for women who had splenectomy AND has platelet count > 600 x $10^9$/l

## Intrapartum care

- For women who have red cell antibodies, cross matched blood should be available. Otherwise, a group and save is enough. Two units should be cross-matched if haemoglobin is < 10
- Intrapartum IV deferoxamine 2g/24 hours is given to reduce risk of free radical damage and arrhythmia from labor stress and high toxic non transferrin bound iron
- Continuous electronic foetal monitoring is recommended
- Active management of third stage of labour is recommended

## Postnatal care

- LMWH is given during hospitalization plus:
  - 7 days after vaginal delivery
  - 6 weeks after caesarean section
- Breast feeding should be encouraged

# Sickle Cell Anaemia with Pregnancy

## Background

### Definitions

Sickle cell disease (SCD) is an inherited autosomal recessive disorder caused by single gene mutation involving haemoglobin structure

This mutation causes formation of abnormal haemoglobin making red blood cells become liable to haemolytic anaemia, and vaso-occlusion in the small blood vessels

### Types

| | | |
|---|---|---|
| **Homozygous** | This is called sickle cell anaemia (HbSS). This gives the typical picture of the disease | |
| **Heterozygous** | Combination with normal haemoglobin (A), This is called sickle trait (HbAS) | Asymptomatic except for increased risk of UT infections and microscopic haematuria |
| | Combination with haemoglobin C (HbSC)<br>Combination with beta thalassaemia (HbSB)<br>Combination with haemoglobin D, E or O-Arab | Symptomatic with varying severity |

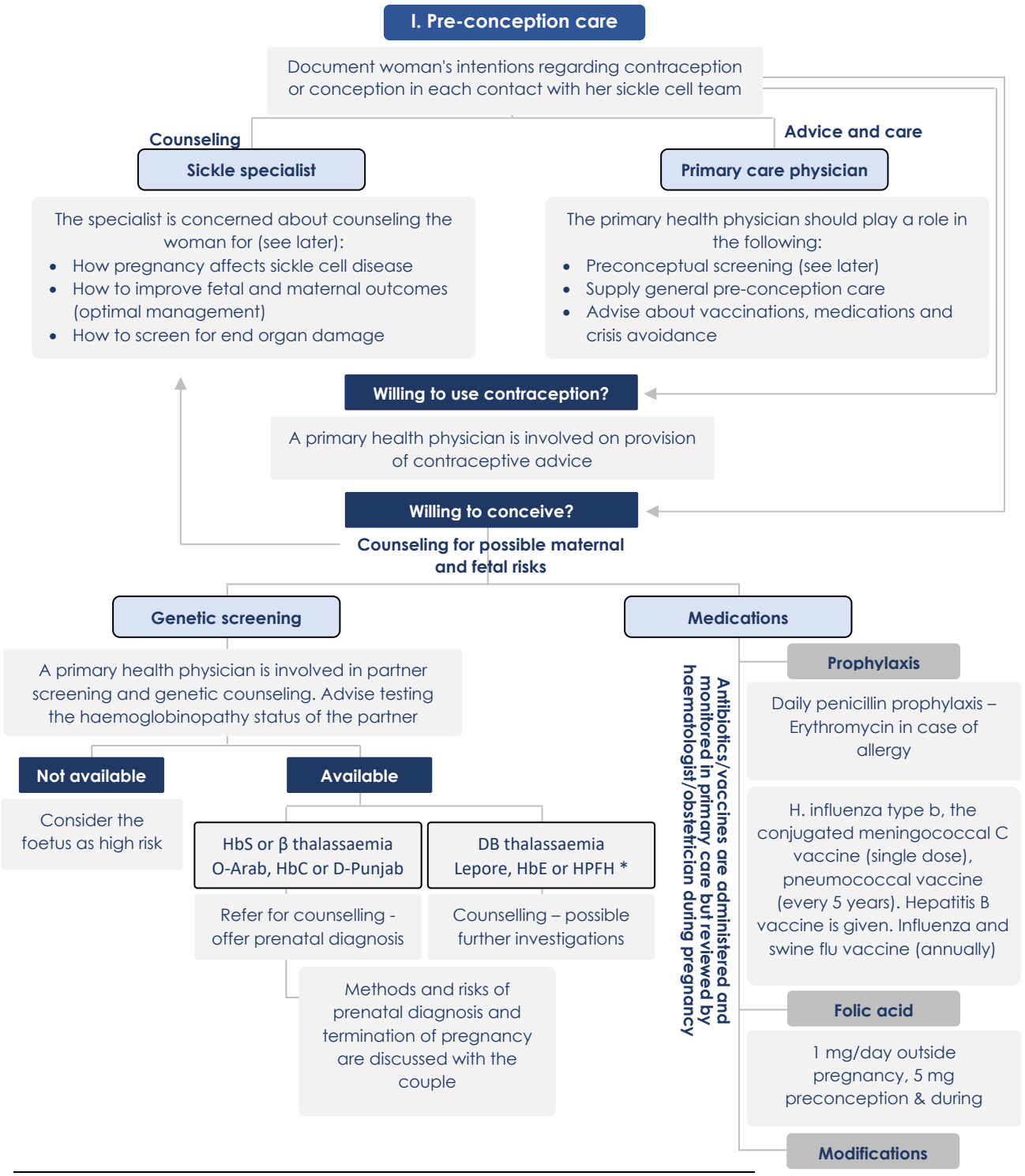
### Incidence

- It is the most common inherited condition worldwide (300,000 children per year)
- The disease is most common in African descent, in the Caribbean, Middle East, India and the Mediterranean, and South and Central America
- In the UK, 100–200 women with SCD get pregnant per year in the UK

### Complications

- Haemolytic anaemia.
- Vaso-occlusion in the small blood vessels and acute painful crises.
- Stroke, pulmonary hypertension, renal dysfunction, retinal disease and leg ulcers.
- Cholelithiasis.
- Avascular necrosis (the femoral head is commonly affected)

## Preconception management




* Hereditary persistence of fetal hemoglobin (HPFH)

** If pregnancy occurs while on treatment, do not terminate but offer level 3 ultrasound for fetal anomalies

## Counseling women with SCD who plan to conceive (RCOG recommendation)

- Inform women about factors that participate sickle cell crises e.g. dehydration, cold, hypoxia, overexertion and stress. This includes nausea and vomiting in pregnancy due to dehydration.
- Inform about the risk of worsening anaemia, the increased risk of crises and acute chest syndrome (ACS) and the risk of increased infection (urinary tract infection) during pregnancy.
- Inform about the increased risk of fetal growth restriction, fetal distress, induction of labour and caesarean section. Risk of SCD in the offspring should be discussed.

## Screening women with SCD for disease complications

| | |
|---|---|
| **Screening for pulmonary hypertension** | • Screening is carried out with echocardiography.<br>• The risk is higher with SCD. Screening is performed if no screening has been done in the last year.<br>• Tricuspid regurgitant jet velocity > 2.5 m/second is associated with a high risk of pulmonary hypertension. |
| **Screening for hypertension, renal and hepatic complications** | • Blood pressure and urinalysis is performed to screen for hypertension and/or proteinuria.<br>• Renal and liver function tests are performed annually for sickle nephropathy and/or hepatic complications. |
| **Retinal screening** | Preconception retinal screening is recommended because proliferative retinopathy is common in patients with SCD, especially patients with HbSC. |
| **Screening for iron loading (women with repeated transfusions)** | • High ferritin level and T2 cardiac magnetic resonance imaging helps to assess iron loading.<br>• If a woman is heavily loaded with iron, aggressive iron chelation before conception is recommended. |
| **Screening for red cell antibodies** | Red cell antibodies are screened because they are associated with an increased risk of haemolytic disease of the newborn. |

## Antenatal care

**II. Antenatal care**

**Consider multidisciplinary team including high-risk pregnancy experienced obstetrician, midwife, and a haematologist**

**First appointment**

**Primary care or hospital appointment**

**Counseling and providing information**

- Counsel the couple and offer partner testing if this has not been achieved preconceptual.

**Evaluating current clinical status**

- Take a clinical history to assess the complications of SCD.
- Document baseline oxygen saturations and blood pressure.
- Offer retinal, renal and cardiac assessments (if not performed in the last year).
- Send midstream urine for culture.

**Reviewing current treatment**

- Stop taking hydroxycarbamide, ACE inhibitors or ARBs.
- Advise taking 5 mg folic acid.
- Advise taking antibiotic prophylaxis.
- Discuss vaccinations.

**7-9 weeks**

Perform an ultrasound to confirm viability and assess gestational age

**10 weeks (Booking appointment)**

**High-risk pregnancy experienced mid-wife**

**Counseling and providing information**

- Counsel the woman about the effect of pregnancy on SCD and the potential maternal and fetal risks.
- Give clear information and advice including the crisis participating e.g. extreme temperatures, dehydration and overexertion and the risk of persistent vomiting.

**Evaluating current clinical status**

- Assess renal function test, urine protein/creatinine ratio, liver function test and ferritin.
- Assess extended red cell phenotype.

**Reviewing test results & treatment**

- Review partner genetic results. Discuss further steps according to the results including the risks and benefits of prenatal diagnosis if indicated.
- Consider low dose aspirin from the 12th week of gestation. Iron is given only if indicated (iron deficiency).

**16 weeks**

**Mid-wife and multidisciplinary team**

Routine antenatal care - Repeat midstream urine culture - Multidisciplinary check (consultant obstetrician and haematologist)

**20 weeks**

**Mid-wife and multidisciplinary team**

Detailed fetal ultrasound scanning - Repeat midstream urine culture – repeat fetal blood count

**24 weeks**

**Multidisciplinary team**

Ultrasound monitoring and follow up of fetal growth and amniotic fluid - Repeat midstream urine culture

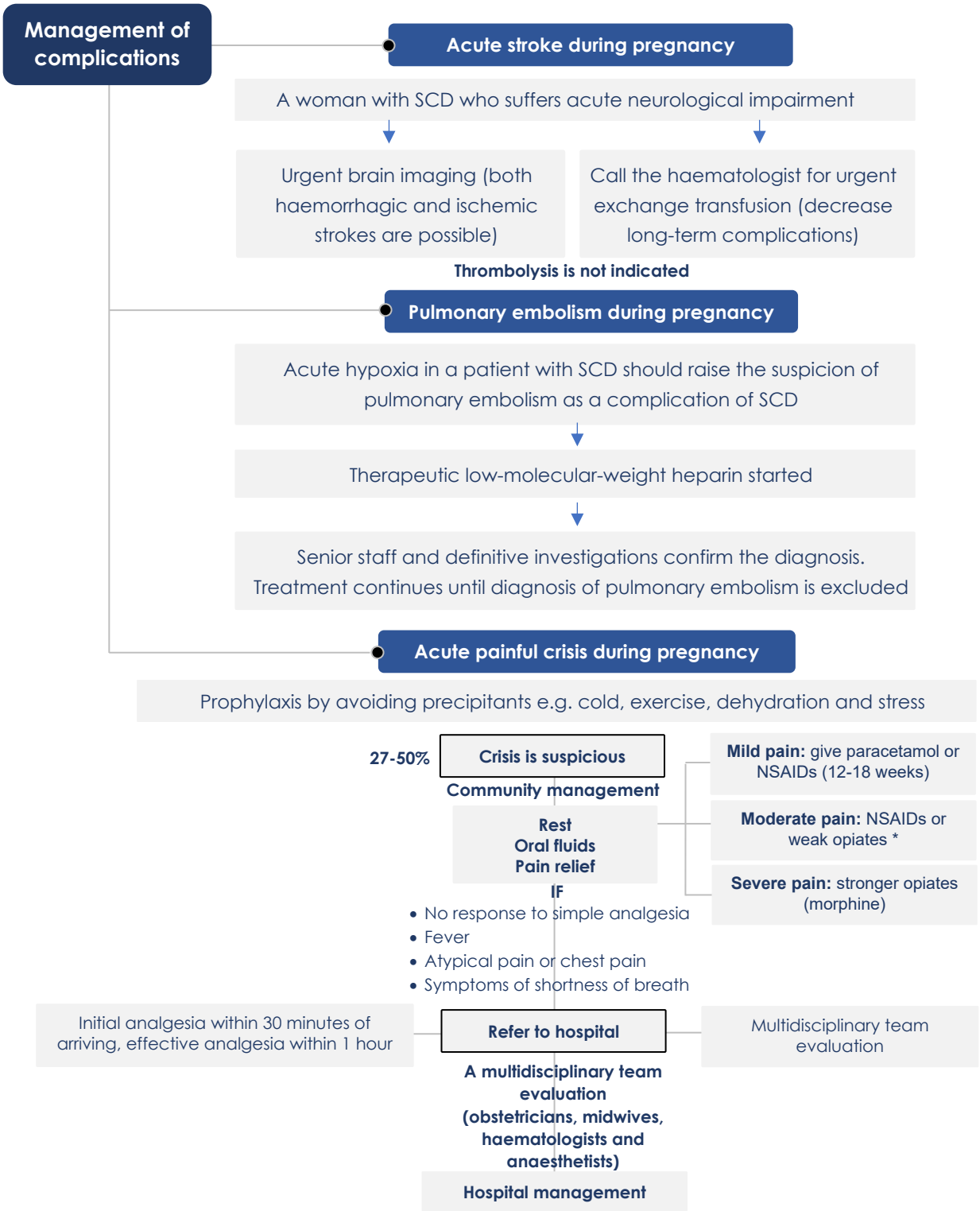
**26 weeks**

**Mid-wife**

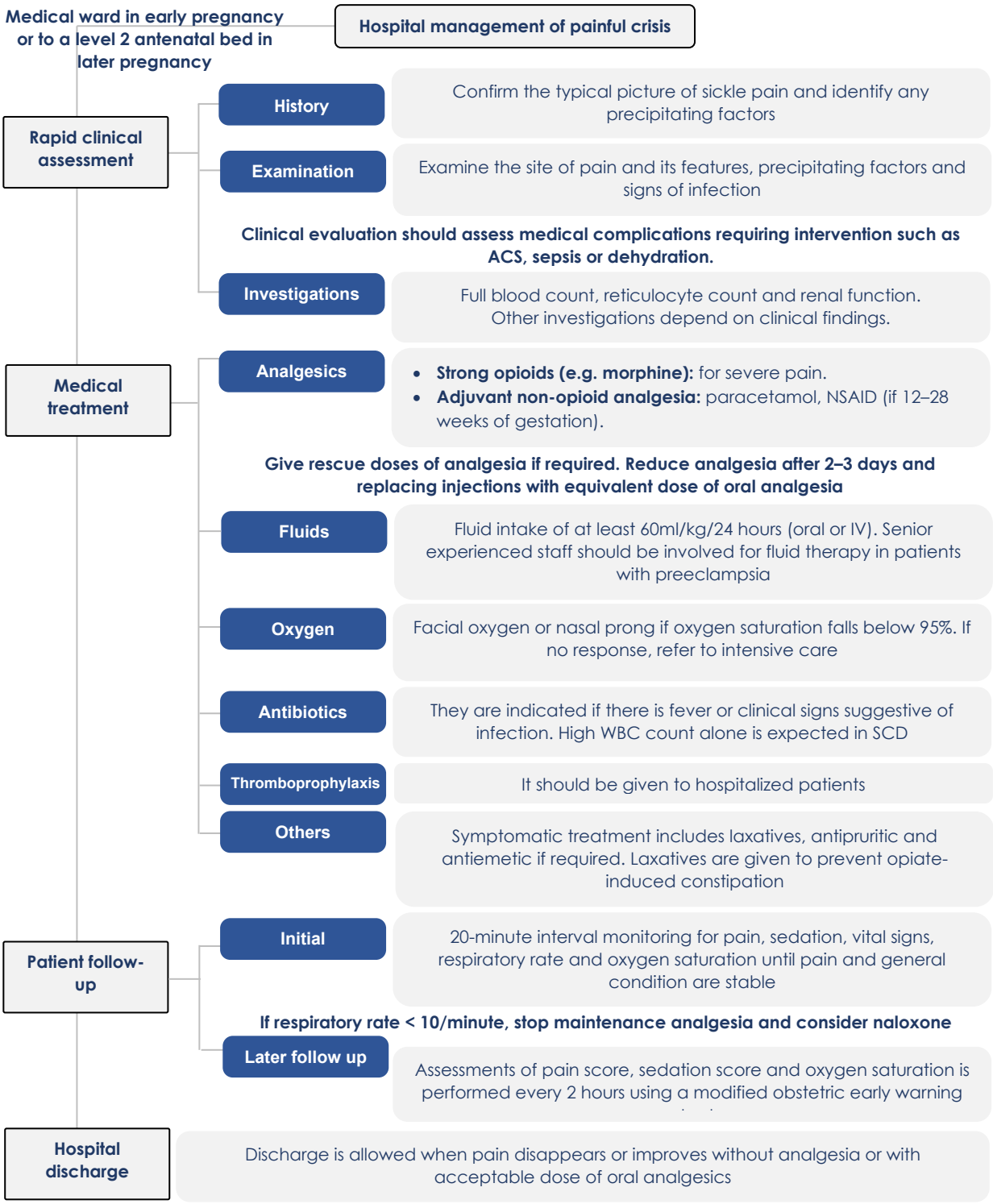
Routine antenatal care visit with routine check including measurement of blood pressure and assessment of proteinuria

| | | |
|---|---|---|
| **28 weeks**<br>**Multidisciplinary team** | | Ultrasound monitoring and follow up of fetal growth and amniotic fluid - Repeat midstream urine culture – Repeat fetal blood count, group and antibody screen |
| **30 weeks**<br>**Mid-wife – ANC classes** | | Routine antenatal care visit with routine check including measurement of blood pressure and assessment of proteinuria |
| **32 weeks**<br>**Multidisciplinary team** | | Routine antenatal check visit - Ultrasound monitoring and follow up of fetal growth and amniotic fluid - Repeat midstream urine culture – Repeat fetal blood |
| **34 weeks**<br>**Mid-wife** | | Routine antenatal care visit with routine check including measurement of blood pressure and assessment of proteinuria |
| **36 weeks**<br>**Multidisciplinary team** | **Evaluating current clinical status** | • Routine antenatal check visit<br>• Ultrasound monitoring and follow up of fetal growth and amniotic fluid |
| | **Counseling and providing information** | • Discuss timing, mode and management of the birth<br>• Discuss analgesia and anaesthesia; arrange anaesthetic assessment<br>• Offer information about baby care after birth |
| **38 weeks**<br>**Mid-wife - obstetrician** | | Routine ANC check - Discuss induction of labour or caesarean section between 38 and 40 weeks of gestation |
| **39 weeks**<br>**Mid-wife** | | Offer routine ANC check – Advise the woman and arrange to deliver by 40 weeks of gestation |
| **40 weeks**<br>**Obstetrician** | | Offer routine ANC check – Offer fetal monitoring if the woman declines delivery by 40 weeks of gestation |

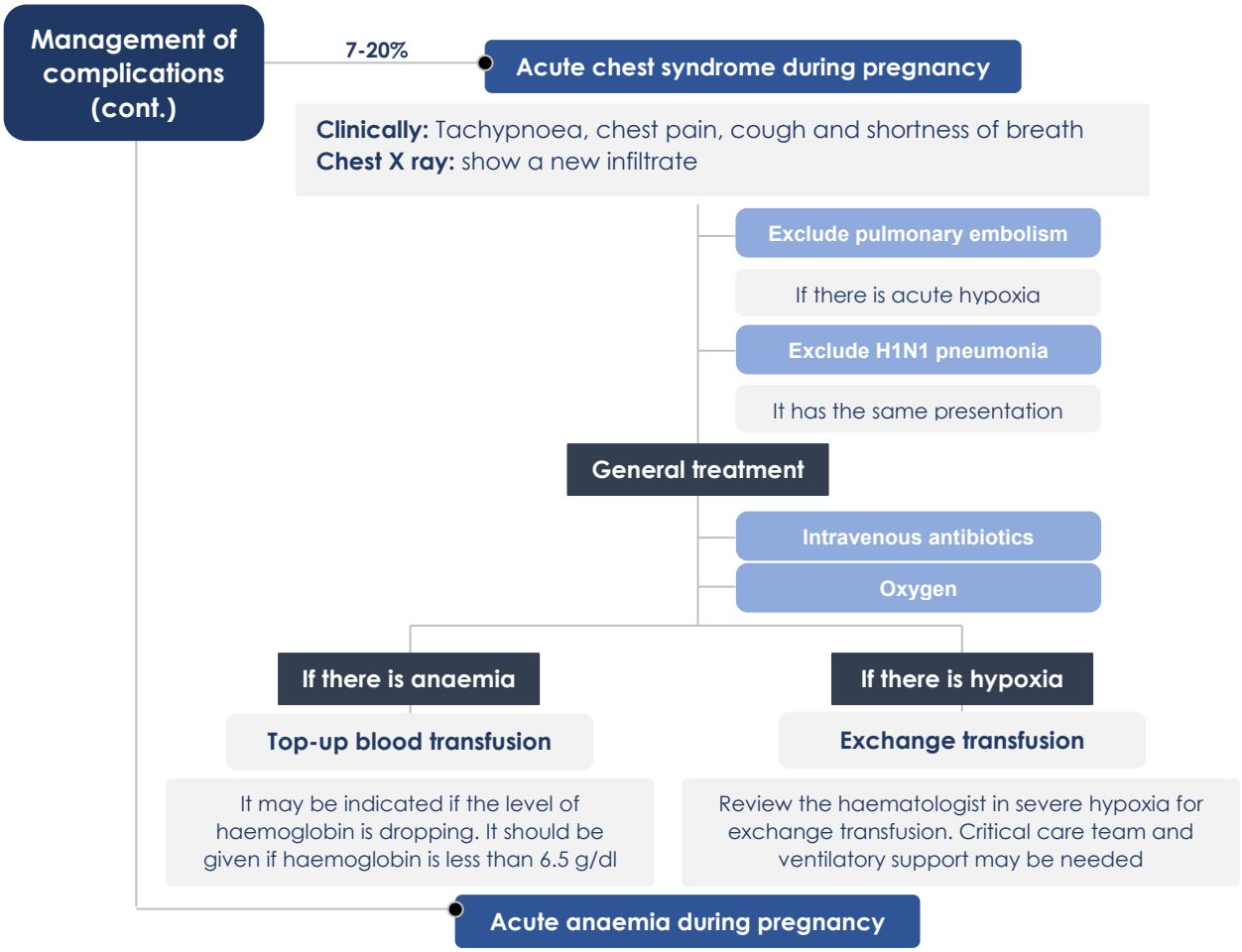
## Management of complications




* Weak opioids include co-dydramol, co-codamol or dihydrocodeine. Pethidine should be avoided because of the risk of toxicity and seizures in SCD




* Morphine or diamorphine can be given by the oral, subcutaneous, intramuscular or intravenous route. Parenteral opiates can be given by intermittent bolus or patient-controlled systems. This depends on woman's preference. Opiates are not associated with teratogenicity or congenital malformation. They may cause transient suppression of fetal movement and a reduced baseline fetal heart variability. Observe the neonate for signs of opiate withdrawal if the mother receives prolonged course of opiates in late pregnancy.


Management of complications (cont.)
7-20%
Acute chest syndrome during pregnancy
Clinically: Tachypnoea, chest pain, cough and shortness of breath
Chest X ray: show a new infiltrate
Exclude pulmonary embolism
If there is acute hypoxia
Exclude H1N1 pneumonia
It has the same presentation
General treatment
Intravenous antibiotics
Oxygen
If there is anaemia
If there is hypoxia
Top-up blood transfusion
Exchange transfusion
It may be indicated if the level of haemoglobin is dropping. It should be given if haemoglobin is less than 6.5 g/dl
Review the haematologist in severe hypoxia for exchange transfusion. Critical care team and ventilatory support may be needed
Acute anaemia during pregnancy
Blood transfusion
Woman isolation
Consider reticulocyte count:
Low count: this may indicate aplastic crisis caused by erythrovirus (a cause of hydrops fetalis) - Refer to a fetal medicine specialist.
High count: indicates hemolytic crisis.

## Intrapartum management

**Pre-labour assessment and considerations**

**III. Intrapartum care**

- Advise and arrange for the place of birth. Hospitals that can manage high-risk pregnancies and complications of SCD (e.g. abruption, pre-eclampsia, peripartum cardiomyopathy and acute sickle cell crisis) are recommended.
- Discuss suitable positioning during fetal delivery in women who had hip replacements due to avascular necrosis
- Anaesthetic assessment is performed in the third trimester

**Smooth maternal course and normal fetal growth?**

**Pregnancy is 38+0 weeks or more**

**Elective birth**

- ***Blood preparation:***
  - Cross-matched blood if atypical antibodies are present (saves time).
  - A 'group and save' if there are no atypical antibodies.
- ***Multidisciplinary team:***
  A senior midwife, senior obstetrician, anaesthetist and haematologist are notified once labour is confirmed.

**No obstetric contraindication to vaginal birth**

**Vaginal birth (preferred)**

**Avoid protracted labour**
**Labour > 12 hours increases painful crisis risk**

**If there is any obstetric indication**

**Cesarean section**

Regional analgesia is recommended

**Continuous intrapartum electronic fetal heart rate monitoring is indicated.**

| | |
|---|---|
| **Venous access** | Achieve early and consider anaesthetic review for possible difficulties. Such women may have repeated admissions and venous access may be difficult. |
| **Hydration** | Adequate hydration is given orally or by intravenously (if oral fluids are intolerable) using a fluid balance chart. |
| **Warmth** | Keep the patient warm during labour |
| **Oxygen** | Follow up hypoxia using pulse oximetry and arterial blood gas analysis. Give Oxygen therapy if oxygen saturation ≤ 94 |
| **Analgesia** | Avoid pethidine (risk of seizures). Consider epidural analgesia as usual |
| **Antibiotics** | Not used as a routine for prophylaxis. However, temperature is observed hourly. If it is > 37.5, investigate the cause. Be more worried than usual for infection. |

## Postpartum management

### IV. Postpartum care

**The probability of complications of SCD including acute crisis continues during puerperium. The risk of sickle cell crisis is 25% and is more after general anaesthesia. Accordingly, the same level of care and caution that is considered during pregnancy should continue during puerperium**

#### Maternal care

**Oxygen/hydration**

Give adequate hydration and oxygen (if oxygen saturation < 94%) until discharge

**Mobilization**

Encourage early mobilization of the patient

**Breast-feeding**

Allow and encourage breast-feeding

**Thromboprophylaxis**

Low-molecular-weight heparin is given during hospitalization and 7 days post-discharge (after vaginal delivery) or 6 weeks (after caesarean section). Antithrombotic stockings are recommended

**NSAIDS**

They are given routinely postpartum (not contraindicated with breastfeeding)

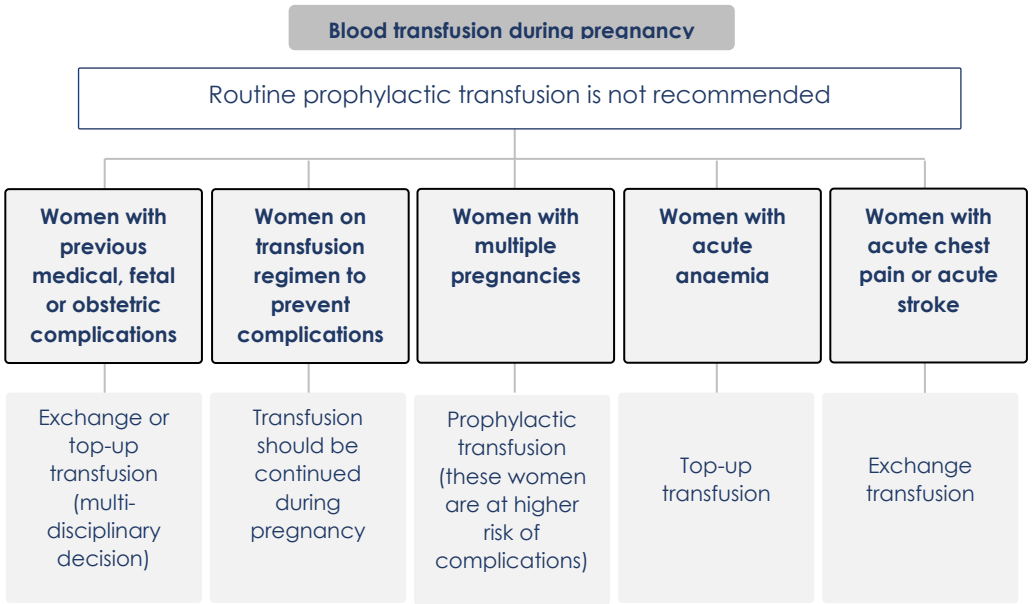
**Contraception**

- Progestogen-containing contraceptives (bills, injectables and intrauterine system) are the first line.
- Estrogen-containing contraceptives are second-line agents (theoretical risk of venous thromboembolism in these women).
- Copper IUD devices are also second line agents

#### Newborn care

Consider early newborn testing using capillary sample if the father is a carrier or a patient

**Appendix** **Indications of transfusion during pregnancy**




- Blood used for transfusion should be cytomegalovirus negative.
- Blood should be matched for full rhesus typing (C, D and E) and Kell typing (an extended phenotype). Alloimmunisation is common in SCD.

# Iron Deficiency Anaemia in Pregnancy

## Definition

Because of dilutional effect of increased plasma volume in pregnancy, definition of anaemia in pregnancy is different from non-pregnant status. Anaemia is defined as a haemoglobin level below 110 g/l (11 g/dl) in first trimester, 105 g/l (10.5 g/dl) in second trimester, and < 100 g/l (10 g/dl) postpartum

## Epidemiology

- 30% of women with heavy menstruating blood have anaemia; 60% of these cases are severe
- 40% of pregnant women have anaemia
- 50% of cases of anaemia in pregnancy are caused by iron deficiency

## Body iron

- Iron input comes from daily iron absorption (1 – 2 mg/Day) and haem recycling inside the body (40 – 60 mg/Day)
- Hepcidin regulates iron absorption and is deficient in cases of iron deficiency
- Daily requirements of haem iron in women is 18 mg/day. Dietary sources include e.g. meat, poultry and fish
- Total pregnancy requirements are 1200 mg

### Blood loss

Every 1 ml of blood loss is associated with loss of 0.5 mg of iron

if iron loss exceeds 5 mg/day, it cannot be physiologically compensated, and iron supplements will be required

## Risk factors

- Previous anaemia
- Multiparity
- Recent history of bleeding
- Two successive deliveries less than one year apart

## Diagnosis

- **Clinical picture:**

| | General features | Features associated with severity |
|---|---|---|
| **Symptoms** | ▪ Fatigue, poor concentration, irritability, and weakness<br>▪ Tinnitus<br>▪ Headache<br>▪ Pruritis and hair loss<br>▪ Taste disturbance and pica<br>▪ Shortness of Breath | ▪ Shortness of Breath at rest<br>▪ Anginal pain<br>▪ Ankle swelling<br>These symptoms may indicate a haemoglobin below 70 g/l |
| **Signs** | ▪ Pallor<br>▪ Angular cheilitis<br>▪ Atrophic glossitis<br>▪ Koilonychia (spoon-shaped with striae) | ▪ Murmurs<br>▪ Cardiac enlargement<br>▪ Heart failure<br>▪ Ankle oedema |

Women with chronic blood adapts to many of these symptoms and usually present with poor concentration and fatigue only

- **investigations:**

  - **Serum haemoglobin:**

    During pregnancy, screening for anaemia is done at booking visit and 28 weeks' gestation. Postpartum haemoglobin testing is indicated if:

    ① Antepartum anaemia was present and was not corrected

    ② Peripartum blood loss is greater than 500 ml

    In these cases, complete blood count is repeated within 48 hours and if anaemia is diagnosed (haemoglobin < 100 g/l), 40-80 mg of oral iron is given for 3 months

  - **Serum ferritin:**

    - Serum ferritin is used to diagnose iron deficiency. if ferritin level is below 30ng /ml, diagnosis of iron deficiency is made by greater than 90% sensitivity and specificity
    - Even in the presence of haemoglobinopathies, serum ferritin may be measured to rule out concomitant iron deficiency

    **Ferritin in pregnancy**

    Ferritin first increases in pregnancy and then decreases gradually till 32 weeks when it reaches 50% of pre-pregnancy level

  - **Serum transferrin saturation:**

    - It may be considered as an alternative to ferritin when other causes of elevated ferritin are present:
      ① Acute and chronic inflammation
      ② Hepatocellular damage
      ③ Malignancies
    - A level below 12% is considered abnormal

## Obstetric complications

### Antepartum complications

- Prematurity
- Low body weight
- Peripartum blood loss
- Maternal infection
- Isolated iron deficiency alone may affect maternal cognition, capacity to work and cause maternal depression and affect foetal brain maturation

### Postpartum complications

- Postpartum depression
- Postpartum haemorrhage (secondary to uterine atony)
- Puerperal sepsis
- Perinatal morbidity and mortality
- Affected neurodevelopment of the infant

## Treatment

- **Oral iron:**
  - **Regimen:**
    - It is the 1st line of treatment. Ferrous containing preparations are preferred
    - In women with iron deficiency, 100 mg of elemental iron should be given daily
    - In women with iron deficiency anaemia, 100-200 mg of elemental iron (2-3 divided doses) should be given
    - information on routine use of oral iron in all pregnant women is limited
    - Oral iron should be given:
      ① At night or more than 1 hour before the next meal
      ② Better with vitamin C (e.g. orange juice)
      ③ Not with milk or tannins (e.g. tea)

- **Side effects:**
  - GI upset
  - Nausea and vomiting.
  - Constipation
  - Dark stool

  Women with nausea and epigastric discomfort may try alternate day dosing or lower iron dose. Iron polymaltose (ferric iron and maltose) is associated with less GI discomfort and better absorption with food.

- **Follow-up:**
  - Check haemoglobin level 2 weeks after initiation of treatment. Expected rise should be 1.2 g/l/day (20 g/l every 3-4 weeks)
  - In no response is found, the following causes should be ruled out:
    ① Poor compliance
    ② Poor absorption (e.g. celiac disease, atrophic gastritis, inflammatory bowel disease, gastric bypass, H pylori infection)
    ③ Concomitant medications e.g. proton pump inhibitors
  - Treatment should continue for 3 months and for 6 weeks after restoring normal iron levels

- **Parenteral iron:**
  - **Indications:**
    ① Lack of response to oral iron after 2-3 weeks
    ② Late gestation (> 34 weeks) with haemoglobin level below 100 g/l
    ③ Severe anaemia (< 70 g/l)
    Parenteral iron should be avoided in the first trimester

  - **Response:**
    - Parenteral iron may elevate haemoglobin by 20 g/l in 7 days (it increases production of erythrocytes by 6 times vs. 3 times with oral iron)
    - Carboxymaltose preparation achieves target haemoglobin with fewer injections and less infusion time compared to other preparations

- **Adverse effects:**
  - Anaphylaxis (within 30 minutes of starting infusion)
  - Hypotension and malaise
  - Nausea and vomiting
  - Arthralgia
  - Abdominal pain

  Side effects of parenteral iron are generally less than oral iron. Side effects are more with dextran preparations and less with sucrose and carboxymaltose

- **Blood transfusion:**

  Blood transfusion is the last resort when other options fail to increase haemoglobin level. Each blood unit increases haemoglobin by 10 g/l

If a woman reaches time of delivery with haemoglobin level below 100 g/l, she should be managed in an obstetric-led unit

# Thromboembolic Disease in Pregnancy

## Background

- Risk of Antenatal venous thromboembolism (VTE) is 4-5 folds higher compared to non-pregnant women. Highest risk is present during puerperium (increases by 20 folds)
- Untreated deep venous thrombosis (DVT) may be complicated with pulmonary embolism (PE) in up to 20%; case fatality rate is up to 15%. Fatality occurs within 30 minutes of development of embolism in 66% of cases
- Greatest risk of recurrence is within 2 weeks of initial VTE. Risk of recurrent PE and fatality may be reduced from 20% to 10% with the use of unfractionated heparin (UFH)
- Diagnosis of PE is confirmed in only 2-6% of women with suspected PE

## Investigations

**Electro-cardiogram (ECG)**

- It is an essential investigation in all women with clinical suspicion of PE e.g. chest pain
- Significance of ECG:
  ① Ruling out Ischemic heart diseases
  ② Diagnosis of PE: ECG abnormalities are present in 40% of cases:
  - T-wave inversion; most common (20%)
  - SQT patterns (15%)
  - Right bundle branch block (18%, 4% in puerperium)

**Arterial Blood Gases (ABG)**

It has a limited diagnostic value; only 10% of patients has $PO_2$ less than 60

**Chest X ray (CXR)**

- Significance of CXR:
  ① Ruling out other pulmonary cause that may explain symptoms
  ② Diagnosis of PE (limited role): Positive findings include atelectasis, effusion, pulmonary edema, regional oligemia, and focal opacities. CXR is negative in 50% of cases.
- Radiation hazards are limited in pregnancy (CXR dose is 0.01 mSV, which is negligible)

**Compression duplex ultrasound**

- It is the standard diagnostic test for DVT. It is used in women with symptoms of DVT or PE
- If the test is positive for DVT: it is diagnostic for VTE and it indicates initiation of therapeutic anticoagulation (which covers both DVT and PE)
- If negative: PE cannot be excluded

**Ventilation/ perfusion (V/Q) scan**

- V/Q scan is considered the standard diagnostic test for acute PE by many physicians in comparison to CT pulmonary angiogram (CTPA)
- Advantages:
  ① High negative predictive value (99%-100%)
  ② Less radiation dose to maternal breasts (lower risk of breast cancer) compared to CTPA
- Indications over CTPA:
  ① Prior exposure to CT chest
  ② Family history of breast cancer
- Disadvantages:
  Although maternal exposure is lower compared to CTPA, foetal exposure is higher (Fetal Exposure is 0.5 mGy). Therefore, there is small risk of childhood cancer. An informed consent should be obtained after discussing these risks
- Precautions:
  To minimize radiation, ventilation component may be omitted, and low dose perfusion is used

**CTPA scan**

- Its use is comparable to V/Q scan. In addition, CTPA can diagnose other pulmonary conditions that may be associated with symptoms
- Hazards:
  - Higher exposure of maternal breasts to radiation (high risk of breast cancer). Lifetime risk of breast cancer in young women increases from 0.1% to 13% when exposed to 10 mGy of radiation
  - Although fetal exposure is less (0.1 mGy), risk of childhood cancers is present
- Precautions:
  Bismuth shields decrease radiation dose by approximately 20-40%.

There is no role for D-dimer and 2 level wells score in diagnosing VTE during pregnancy

## Management

### I. Management strategy

**Venous thrombo-embolism (VTE)**

Treatment with low molecular weight heparin (LMWH) is recommended if the diagnosis is clinically suspected (unless It is contraindicated)

**Compression Duplex US is performed**

**Positive**

Complete treatment regimen

**US venography**
It is considered if Iliac vein thrombosis is suspected (buttock and back pain, swelling of entire limb)

**Negative**

**Clinical suspicion**

**Low**

Stop LMWH. No further action is required

**High**

stop LMWH and repeat US on day 3 and day 7

**Acute pulmonary embolism (acute PE)**

**Perform CXR, ECG and ABG**

**No clinical evidence of DVT**

**Abnormal CXR**

CTPA is superior to V/Q scan

**Normal CXR**

V/Q scan versus CTPA scan

**If CTPA or V/Q scan is negative**

**Low clinical suspicion**

No further action required

**High clinical suspicion**

① Imaging test may be repeated, or the other test may be performed
② Continue treatment till PE is ruled out

**Clinical evidence of DVT**

Diagnosis using Compression Duplex US

**Positive**

Treatment of VTE. No further investigations

**Negative**

VTE is excluded

**Massive PE with maternal collapse**

This is a critical case that should be managed through a multidisciplinary team. Management may be either:

- Medical therapy (UFH, thrombolytic therapy)
- Surgical intervention (thoracotomy, embolectomy)

**Massive PE with cardiovascular compromise**

- First line assessment is **CTPA and echocardiography** which should be performed within 1 hour of onset
- If diagnosis is confirmed, thrombolytic therapy should be immediately initiated followed by UFH infusion without loading dose

## II. Management options

### ① Anti-coagulants

| | LMWH | UFH |
|---|---|---|
| ***Indication*** | • It is the standard anticoagulant unless contraindicated<br>• It is superior to UFH because:<br>① it is not associated with high risk of osteoporosis<br>② It is associated with lower risk of heparin induced thrombocytopenia (HIT)<br>③ Incidence of complications is generally lower (0.04% vs 2% with UFH) | • Because of its short half-life, It is indicated if the patient is at high risk of active bleeding<br>• Examples if UFH indications include:<br>① VTE at term<br>② Massive PE |
| ***Dosing*** | • **Therapeutic dose *:**<br>Dose is determined by pre-pregnancy or early pregnancy weight e.g.<br>▪ ***Enoxaparin:***<br>– If weight is less than 50kg: 40mg twice daily or 60mg once daily<br>– If weight is 50-69kg: 60 mg twice or 90mg once daily<br>– If weight is 70-89kg: 80mg twice or 120mg once daily<br>▪ ***Dalteparin:***<br>– < 50kg: dose is 5000 IU twice or 10000 IU once daily<br>– 50-69kg: 6000 IU twice or 12000 IU once daily<br>– 70-89kg: 8000 IU twice or 16000 IU once daily | • **Therapeutic dose:**<br>80 Unit/kg (loading dose) followed infusion of 18 Unit/kg/hour (maintenance dose). Loading dose is not indicated if the patient is on treatment<br>• **Dose adjustment:**<br>▪ If aPTT level is less than 1.2: increase the dose by 4/kh/hr andrebolus with 80 units/kg<br>▪ If aPTT is 1.2-1.5, increase the dose by 2 U/kg/hr and rebolus with with 40 U/kg.<br>▪ If aPTT is 2.5-3: decrease the dose by 2U/kh/hr<br>▪ If aPTT > 3, decrease the dose by 3U/kg/hr and stop infusion for 1 hour |

| | | |
|---|---|---|
| | • **Maintenance:** The therapeutic dose should continue for at least 3 months (and 6 weeks postpartum) | |
| ***Monitoring*** | • Routine monitoring with anti-Xa activity is NOT routinely indicated in women treated for VTE<br>• Peak anti-Xa monitoring is may be indicated if:<br>① Maternal weight < 50 or < 90 kg<br>② Renal impairment<br>③ Recurrent VTE<br>Anti-Xa target level is 0.5-1.2 for LMWH (0.35-0.7 for UFH) | • aPTT is used to monitor UFH treatment. It should be measured 4-6 hours after initiation of treatment or dose change. Target aPTT is 1.5-2.5<br>• Once target aPTT level is reached, aPTT should be measured daily<br>• In postoperative patients, platelet count should be monitored every 2-3 days from day 4-14 or till UFH stops |
| ***Session of treatment*** | • 24 hours before planned delivery (elective caesarean section or induction of labour)<br>• 24 hours before regional anaesthesia<br>• LMWH should be stopped for 4 hours after spinal anaesthesia or after removal of epidural catheter** | • Subcutaneous UFH should stop 12 hours before induction of labour or regional anaesthesia<br>• Intravenous UFH should stop 6 hours before induction of labour or regional anaesthesia |

* There is no evidence of superiority of using LMWH once or twice daily

** Epidural catheter should not be removed within 12 hours of the last dose of LMWH

Fondaparinux, argatroban, r-hirudin, danaparoid are alternatives to heparin if there is heparin allergy or intolerance

### ② Thrombolytics

- Streptokinase, urokinase, rtPA "alteplase" may be indicated in patients with massive PE
- Treatment is associated with risk of maternal and foetal bleeding (3%, 2%, respectively)

③ **IVC filter**

- **Indications:**
  - ① Iliac vein VTE
  - ② Proven DVT with recurrent PE despite treatment
- **Risks:**
  - ① Migration
  - ② It increases risk of DVT, caval thrombosis and risk of infection (rare)

## Postpartum management

- Start with prophylactic dose of LMWH 4 hours after delivery
- Switch to the therapeutic dose of LMWH 8-12 hours later

| Warfarin | LMWH |
|---|---|
| • Safe in Breast feeding.<br>• It requires monitoring particularly in the first 10 days.<br>• Warfarin initiation may be delayed for at least 5 days (or more with high bleeding risk) | • Safe in Breast feeding.<br>• It does not need monitoring.<br>• Used for 12 weeks postpartum to decrease risk of post-thrombotic syndrome. |

- Patients on therapeutic dose LMWH are advised to have 2 drains placed during caesarean section (abdominal, rectus sheath). Skin incision is closed with interrupted sutures

# Inherited Bleeding Disorders in Pregnancy

## Hemophilia

### Definition

It is an X-linked disorder that causes reduction or absence of factor VIII (hemophilia A) or factor IX (hemophilia B) with subsequent bleeding symptoms

### Obstetric risks

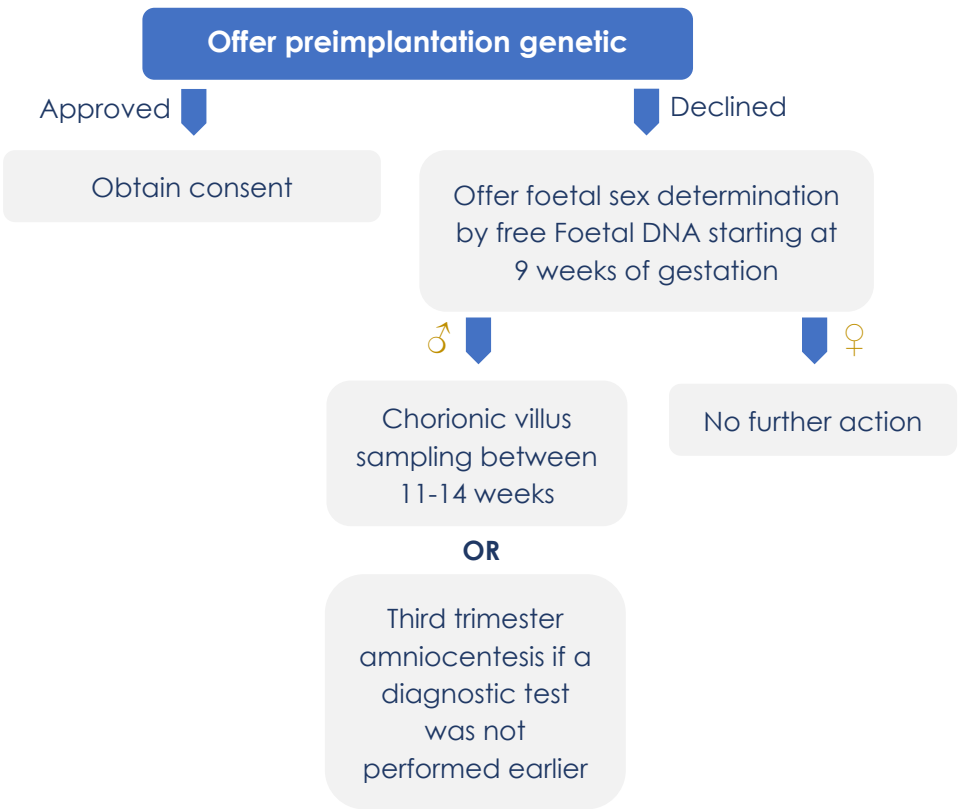
- **Risks to mother and baby:**

| Mother | Baby |
|---|---|
| • Carriers may have low factor VIII/IX levels and thus, increased risk of bleeding with invasive procedures, termination, and spontaneous miscarriage and at the time of delivery<br>• Therefore, carriers should be tested for factor VIII/IX level before invasive Procedures or with bleeding symptoms | • Male neonates with hemophilia are at increased risk of bleeding, including intracranial hemorrhage (ICH) and extracranial hemorrhage (ECH)<br>• Male neonates with hemophilia are at risk of iatrogenic bleeding at delivery |

- **Risk of inheritance:**
  - A female carrier has a chance of having 50% affected males and 50% female carriers
  - 50% of male babies with severe haemophilia have no previous family history. The chance that the mother is a carrier is 90%

## Preconception care

- Baseline factor level should be assessed prior to pregnancy
- Iron deficiency should be assessed and corrected
- Genetic counselling and prenatal diagnosis should be offered and discussed, and relevant consents should be obtained:



## Antenatal care

Antenatal care should be delivered by multidisciplinary team including a haematologist and an obstetrician with expertise in these disorders

| | Follow-up | Treatment |
|---|---|---|
| **During pregnancy** | • Factor VIII/IX should be checked at booking and in the third trimester<br>• Factor VIII levels rise in pregnancy, factor IX level does not change | • Tranexamic acid is given:<br>▪ As a single treatment in women with levels above 0.5 iu/ml if clinically indicated<br>▪ In combination with other treatments if levels are below 0.5 iu/ml<br>• Desmopressin (DDAVP) may be used to raise factor VIII levels. During treatment, fluid should be restricted to 1 liter/day<br>• If DDAVP is not sufficient or ineffective, recombinant factor VIII should be used<br>• Recombinant factor XI should be used if levels are below 0.5 iu/ml<br>• Following miscarriage, treatment should be continued until bleeding stops |
| **Pre-procedure** | • Factor VIII/IX levels must be at least 0.5 iu/ml to cover any procedure or spontaneous miscarriage<br>• If treatment is indicated, it should aim for levels of 1.0 iu/ml | |
| **After treatment** | Response to treatment is monitored by measuring plasma clotting factor concentration before and after infusion, and 4-6 hours after treatment to adjust dosing | |

- **External cephalic version:** It should be avoided in a male foetus or a female foetus who could be a carrier of severe haemophilia
- **Delivery plan:** A clear plan for the intrapartum care should be established in advance of 37 weeks of gestation. This should include a visit to the anaesthetic clinic

## Intrapartum management

### Obstetric care

- **Mode of delivery:**
  - Option of **planned lower segment caesarean section:** to deliver affected male babies should be discussed during pregnancy and pros and cons of this route should be explored with the patient
  - If **vaginal delivery** is planned:
    - Spontaneous labour is preferred
    - Ventouse and midcavity forceps should be avoided in delivering male babies
- **Intrapartum foetal assessment:**
  - Foetal blood sampling (FBS) and foetal scalp electrode (FSE) contraindicated in foetuses with potential moderate/severe haemophilia.
  - FBS and FSE may be considered in foetuses with known mild haemophilia if the benefit (e.g. avoiding caesarean section) overweighs the risk. The decision is made by a senior obstetrician. Pressure under direct vision may be beneficial after FBS

No particular plan/percussions are indicated in **female foetuses**. Nevertheless, female foetuses that are carriers of severe haemophilia B are at theoretical risk of Intracerebral haemorrhage

### Analgesia and anaesthesia

- Insertion or removal of epidural/spinal anaesthesia or intramuscular injections should be avoided if factor VIII or IX levels are less than 0.5 iu/ml
- To maintain factor VIII/IX in the normal range, corresponding factor replacement or DDAVP may be used in conjugation with tranexamic acid

**Haemostatic management**

- Active management of third stage of labour is recommended to reduce risk of bleeding
- Factors VIII/IX should be kept above 0.5 iu/ml for:
  - At least 3 days following vaginal delivery or
  - At least 5 days following instrumental delivery or caesarean section
- Tranexamic acid should be continued after delivery and until lochia is minimal
- Thromboprophylaxis is contraindicated if factor level is at or below 0.6 iu/ml unless patients are at high risk of thrombosis after weighing benefits and risks of anticoagulation

## Neonatal management

- **Neonatal assessment:**
  - All male babies to haemophilia carrier mothers should have their cord blood tested. Testing is not recommended in female babies
  - In the presence of manifestations of ICH, cranial magnetic resonance imaging should be considered
  - Cranial ultrasound is considered in the presence of moderate/severe haemophilia prior to discharge

- **Medications:**
  - Oral vitamin K should be given to neonate with low factor levels per neonate bloodspot screening
  - Short-term primary prophylaxis is indicated in the presence of:
    ① Moderate or severe haemophilia AND
    ② High risk of bleeding e.g. prematurity, birth trauma

## Von Willebrand disease (VWD)

**Classification**

- Type 1: partial quantitative deficiency of Von-Willebrand factor (WVF)
- Type 2: qualitative deficiency of WVF
- Type 3: severe quantitative deficiency of WVF

**Obstetric risks**

Maternal risk of antepartum, primary and secondary postpartum haemorrhage

**Antenatal assessment**

- Factor VIII levels and VWF antigen level should be checked at booking, third trimester and before any invasive procedures
- Bleeding phenotype should be assessed:
  - Type 1 VWD: it can be managed in a standard obstetric unit. Referral is not indicated
  - Type 2, type 3, or severe type 1 VWD: she should be referred to high risk obstetric service with a haemophilia centre

**Disease management**

- Target level of factor VIII and VWF ristocetin cofactor (VWF:RCo) activity before procedures is 0.5 iu/ml or above
- If these levels are below 0.5, they should be treated with:
  - DDAVP (blood-derived factor concentrates)
  - VWF-containing concentrates
  - Tranexamic acid may be added
- Target peak VWF activity levels are above 1.0 iu/ml and levels. It should be kept above 0.5 iu/ml until haemostasis is achieved

**DDAVP**

- DDAVP treatment requires fluid restriction to avoid hyponatremia).
- It may be associated with thrombocytopenia in patients with type 2B VWD
- It is contraindicated in pre-eclampsia

## Intrapartum management

- Normal vaginal delivery is allowed unless obstetrically contraindicated
- Foetuses with type 2 or 3 VWD should not undergo:
  ① FBS
  ② External cephalic version
  ③ FSE placement
  ④ Ventouse delivery and midcavity forceps
- If VWF activity is below 0.5 iu/ml, tranexamic acid should be considered in conjugation with treatment. If it is above 0.5 iu/ml, tranexamic acid may be considered alone if clinically indicated (oral or IV) starting prior to delivery
- Platelet transfusions and VWF factor replacement may be indicated in women with type 2B VWD
- Use of non-steroidal anti-inflammatory drugs and intramuscular injections should be avoided unless factor VIII and WVF activity are greater than 0.5 iu/ml

| Central neuraxial anaesthesia | |
|---|---|
| **Type 1 VWD** | Safe if VWF activity is normal |
| **Type 2 VWD** | Should be avoided if VWF activity < 0.5 iu/ml |
| **Type 2N VWD** | Should be avoided if factor VIII level < 0.5 iu/ml |
| **Type 3 VWD** | Not safe |

## Postpartum management

- VWF activity and factor VIII levels should be kept > 0.5 iu/ml for:
  - At least 3 days after uncomplicated vaginal delivery
  - At least 5 days following instrumental delivery or after caesarean section.
- Tranexamic acid (1g 3-4 per day) is given for 1-2 weeks (2–3 weeks or more if indicated)
- Low-molecular-weight heparin (LMWH) may be given if venous thromboprophylaxis is indicated if VWF:RCo and factor VIII levels are normal/corrected
- Patients with type 3 may need to be treated with VWF concentrate for 2-3 weeks postpartum

**Neonatal management**

- Babies at risk of type 2 or 3 VWD should have their cord blood tested for VWF activity
- Oral vitamin K should be given unless VWF activity tests normal
- Short-term prophylaxis with factor concentrate is indicated in babies with type 3 VWD who were exposed to significant birth trauma
- Babies with type 3 VWD should undergo routine cranial imaging prior to discharge

## Factor XI deficiency

**Inheritance**

- Autosomal disorder, recessive and dominant
- Incidence in the non-Jewish population is 1/1 000 000
- Incidence of heterozygosity among Ashkenazi Jews in 8% and incidence of homozygosity is 0.2–0.5%

**Phenotypes**

- **Homozygosity:** Spontaneous bleeding is rare. These patients are at risk of bleeding with surgery or trauma
- **Heterozygosity:** It is associated with mild or moderate reduction in factor XI levels

**Risks**

- Highest risk with bleeding genotype, group O blood type
- Check platelets and VWFs to rule out other issues
- Factor XI does not usually increase during pregnancy, Check at booking, 28 weeks and before procedure

**Treatment options**

- Factor XI or tranexamic acid is not usually indicated antenatally
- Prophylactic factor XI replacement is indicated in women with homozygous/compound heterozygous, if there is history of bleeding

**Anaesthesia**

- Avoid central neuraxial in patients with bleeding phenotype and low factor level
- In women with non-bleeding phenotype, counselling is indicated

## Platelet dysfunction

| | Bernard Soulier syndrome | Glanzmann thrombasthenia |
|---|---|---|
| **Aetiology** | An inherited disorder of platelet function that is caused by deficiency of glycoprotein (GP) Ib-IX-V receptor and is associated with severe bleeding tendency | An inherited disorder of platelet function that is caused by abnormality of glycoprotein IIb/IIIa (GpIIb/IIIa), which is the receptor of fibrinogen |
| **Inheritance** | Autosomal recessive inheritance* | Autosomal recessive disorder |
| **Risks** | High risk of primary and secondary postpartum hemorrhage, and wound hematoma | • High risk of intrapartum and postpartum hemorrhage<br>• Foetal thrombocytopenia and bleeding may develop if maternal alloimmunization develops to paternal-derived foetal platelet Antigens (GP IIb/IIIa) |
| **Management** | • Prophylactic HLA-matched platelet transfusion is indicated if there is bleeding History<br>• Tranexamic acid should be given before caesarean section or from the onset of labour and till lochia is minimal<br>• Neuraxial anaesthesia should be avoided.<br>• DDAVP has no role as a single treatment | • Prophylactic HLA matched platelet transfusion or recombinant factor VIIa at delivery if history of bleeding<br>• DDAVP has no role<br>• Give Tranexamic acid at delivery and till lochia is minimal<br>• Maternal alloimmunization to paternal derived fetal platelet Antigens (GP IIb/IIIa) may cause fetal thrombocytopenia and bleeding.<br>• Screen for platelet-specific alloantibodies at booking, 28 weeks, 34 weeks:<br>▪ If positive: referral to foetal Medicine unit is indicated, consider Intravenous Immunoglobulins and steroids. |

| | | |
|---|---|---|
| | | Caesarean section may be considered according to risk. Otherwise, cautions should be made during vaginal delivery<br>▪ If there is paternal heterozygosity, consider amniocentesis and platelet typing<br>▪ If negative for alloimmunization: no further action is required in this regard |

* Test the father for GP Ib surface density in areas with high consanguinity

## Haematologic disorders with pregnancy

### Abstract

Anaemia, is the most common medical disorder, in pregnancy. This is because of the high prevalence of iron deficiency among women in their reproductive years. However, there are other causes of anaemia that are more challenging to manage. In this chapter, we will discuss common causes of anaemia and their manage during pregnancy. We will also cover bleeding disorders and their impact on obstetric care.

### Keywords

Anaemia, thalassemia, sickle cell, iron deficiency, bleeding tendency

### Further readings

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# Appendicitis in Pregnancy

## Incidence

- Incidence is 1:800 to 1:1500 in pregnancy. Incidence is higher in non-pregnant women
- It most commonly occurs in the 2nd trimester

## Presentation

| Classic presentation | Atypical presentation |
|---|---|
| • Right iliac fossa pain, at McBurney's point 6 cm from anterior superior iliac spine towards the umbilicus<br>• Anorexia, nausea<br>• Fever up to 39.3$^0$ C<br>• Slight increase in white blood cell (WBC) count<br>• Rebound and guarding (surgical abdomen)<br>• Rovsing's sign | • Gastrointestinal symptoms e.g. heart burn, constipation, diarrhea<br>• Urinary symptoms<br>• General malaise<br>• Pain at any point on the right side of the abdomen (rather than McBurney's point)<br>• Rebound and guarding may not be present |

## Investigations

**❶ Imaging**
- Ultrasound: it shows dilated tubular structure in right iliac fossa > 6 mm
  *Sensitivity 67-100%, specificity 90% depending on gestational age, body mass index and the sonographer*
- Magnetic resonance imaging: If ultrasound is not conclusive (sensitivity 91%, specificity 98%)

**❷ Elevated CPR** — It is indicative of inflammation but is non-specific

**❸ WBC** — It may be misleading because a count as high as 29 x10$^9$/L may be normal in pregnancy




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_16

## Differential diagnosis

- Ectopic pregnancy
- Threatened miscarriage
- Gastroenteritis:
  - Diarrhoea or vomiting
  - Recent travel
  - Sick contacts
  - Fast food
- Musculoskeletal pain:
  - Gradual onset, exacerbated by movement, localized tenderness
  - No systemic signs
- Oral iron supplements:
  - Mild gastrointestinal upset
  - Dark stool
- Pyelonephritis:
  - Flank pain, renal angle tenderness and pyuria
  - Symptoms of dysuria or urinary frequency
- Preeclampsia or HELLP syndrome:
  - Abdominal pain
  - Hypertension
  - Proteinuria
  - Abnormal labs
- Placental abruption:
  - Acute abdominal pain
  - Foetal distress
  - Uterine tenderness
  - Vaginal bleeding, collapse
  - Most commonly in the 3rd trimester
- Chorioamnionitis:
  - Prolonged rupture of membranes
  - Fever, offensive vaginal discharge, foetal tachycardia
  - Occult chorioamnionitis with intact membranes occurs with listeriosis
- Ovarian vein thrombophlebitis (Postpartum):
  - Fever
  - Abdominal pain & tenderness in lower abdomen, patient unwell
  - Gastrointestinal symptoms are unusual

## Maternal and foetal morbidity

It Increases significantly in relation to severity

### Risk of foetal loss

- 1.5% with simple appendicitis
- 6% with generalized peritonitis
- 36% with perforated appendix

### Perforated appendix

- Risk of foetal loss
- Risk of Preterm labor
- Risk of Severe sepsis
- Risk of subsequent pelvic adhesions and subfertility

### Prevention

- Keep a low threshold of suspicion. A negative laparotomy rate (up to 35%) is acceptable
- Even if the appendix looks grossly normal, it should be removed

### Management

- Immediate laparotomy and extensive irrigation
- If the patient is critically ill, the foetus should be delivered to permit maternal resuscitation

## Management

| Appendectomy | | |
|---|---|---|
| Performed through vertical incision at the point of maximum tenderness | If diagnosis is uncertain, low midline vertical incision may be used to allow exposure | If CS is indicated, surgery can be performed through the same incision but will be extended |
| Laparoscopic appendectomy is becoming more popular. However, there is increase in the risk of foetal loss (relative risk = 1.9) compared to open surgery | | |

CS = Caesarean section

| ⃠ **Antibiotic management <u>alone</u> should not be used** |
|---|
| Perioperative antibiotics should cover gram negative, gram positive, and anaerobic bacteria (cephalosporins + metronidazole) |
| ✓ Clindamycin, erythromycin and azithromycin are safe |

**Management of chronic appendicitis**
(a ruptured appendix that has walled itself off)

| In non-pregnant | In pregnant women |
|---|---|
| Conservative management with fluids, IV antibiotics and observation (recovery is quicker than surgery) | If women are generally well, definitive treatment may be delayed until after delivery |

| Management of appendicitis for pregnant women in labour |
|---|
| Appendicitis diagnosis is not possible in labour. It should be postponed till after delivery |

| Anesthetic management | |
|---|---|
| **General anaesthesia** | **Regional anaesthesia** |
| • 17-fold higher in complications compared to regional in pregnant women because of:<br>▪ Failed intubation (3.3%)<br>▪ Aspiration of gastric contents<br>▪ Higher liability to develop hypoxia<br>Pregnant women tend to desaturate quicker (3 minutes vs. 9 minutes in non-pregnant women). The risk increases with increased body mass index<br>• Although all induction and maintenance medications cross placenta, their effect is transient. Ventilatory support may be needed for these babies till drug effect is worn off | • It is preferred whenever possible<br>• The main risk with regional anaesthesia is hypotension |

Tocolytics are not indicated (general anaesthesia has a tocolytic effect)

A left lateral tilt is considered during surgery to avoid the need for uterine or cervical manipulations

During laparoscopic surgery, intra-abdominal pressure should not exceed 12 mmHg

- Preoperative and postoperative foetal monitoring is required
- Intraoperative monitoring is only indicated if intervention is planned in case of non-reassuring foetal heart tracing. Otherwise, it should not be done routinely
- Foetal status is usually stable if uterine perfusion and maternal oxygenation is maintained intraoperatively.
- Anaesthetics may decrease variability and baseline heart rate
- Foetal heart rate changes are usually corrected by maternal oxygenation and correction of hypovolemia.

Opiates are safe around surgery

**Effect of surgery**

No increased risk of miscarriage (10%, similar to baseline)

- Best time for semi-urgent surgery is early 2nd trimester to:
  - Avoid period of organogenesis (4-10 weeks)
  - Lower risk of preterm labor compared to 3rd trimester surgery (1% vs. 9%)
- Long term neonatal outcomes after appendectomy are favorable.

- If there is high risk of preterm labour, consider antenatal steroids (betamethasone IM 12mg 24 hours apart), unless there is maternal sepsis
- Maximum benefit of steroids is between 48 hours and 1 weeks after the second dose, surgery should be planned during this interval if possible

- Preterm labor > 34 weeks can be allowed to proceed
- Presence of recent abdominal incision is not a contraindication to pushing in the 2nd stage of labour

- CS (unless indicated for resuscitation) should be avoided at the time of appendectomy to avoid intrauterine infection, subsequent adhesions and fertility issues

In septic patients

- Foetal heart rate changes (tachycardia, decrease variability) are anticipated
- Preoperative antibiotics, hydration and pain relief usually restore normal feotal heart rate
- If these abnormalities persist, arrange CS at time of appendectomy

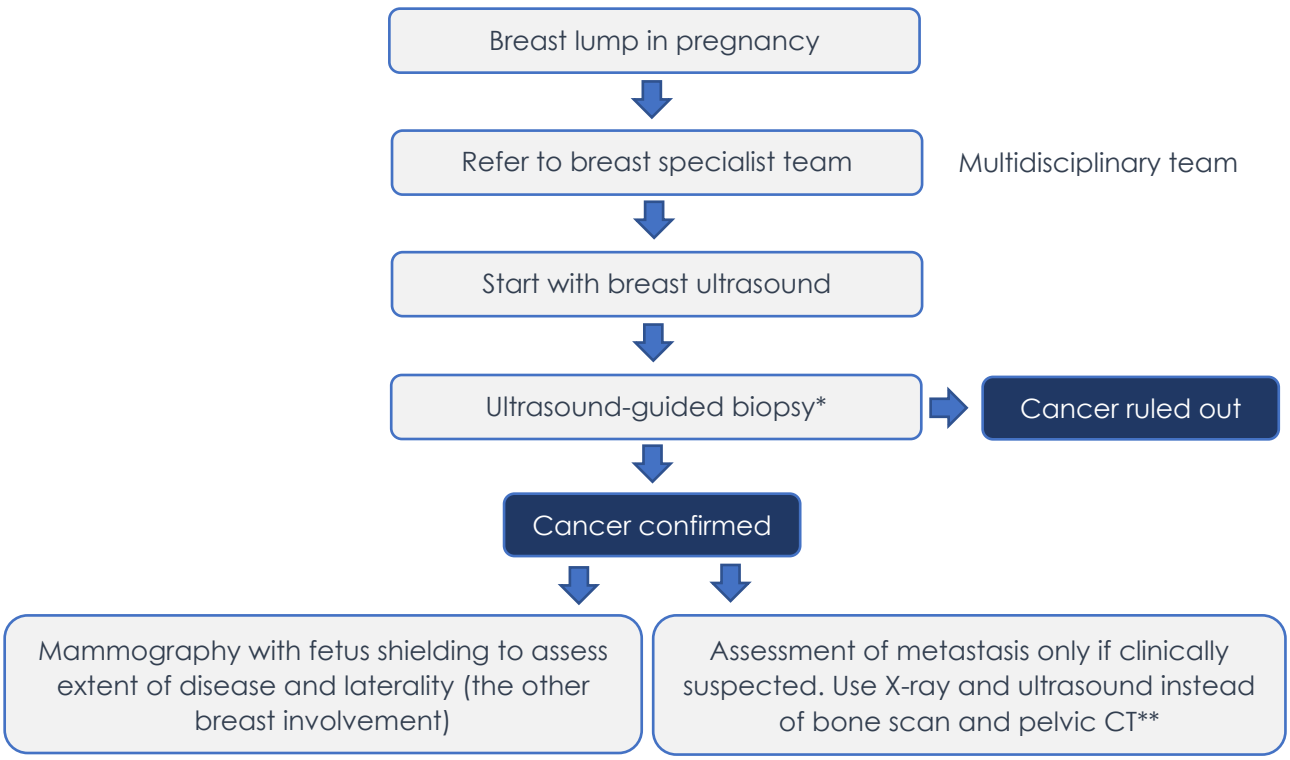
CS = Caesarean section

# Breast Cancer in Pregnancy

## Incidence

- Lifetime risk of breast cancer is 1:9 in UK
- 15% of cases are diagnosed before the age of 45 years. Of these, 10–20% of may coincide with pregnancy or delivery within 1 year
- Less than 10% of women with breast cancer subsequently become pregnant
- Breast cancer is the Leading cancer cause of death in women between 35 and 54 years

## Diagnosis




***** Cytology (aspiration) should not be used in pregnancy (may be inconclusive)

** If bone metastasis is clinically suspected, regional x-ray ± MRI can be used instead of bone scan

## Management of newly diagnosed patients in pregnancy

- **Termination of pregnancy:**

  Decision whether to continue or terminate pregnancy is multidisciplinary and should be discussed with the patient and her family

- **Management of breast cancer:**

### surgery

- Primary surgery can be performed in any trimester
- Axillary lymph node status is assessed with ultrasound:
  - If positive, do axillary clearance,
  - If negative, radioisotope scintigraphy for assessment of sentinel lymph nodes can be used in pregnancy. Blue dye should be avoided.
- Breast reconstruction should be performed after pregnancy

### Systemic chemotherapy

- It can be started after 1st trimester
- Anthracyclines: are safe
- Texans: are an alternative treatment for high risk patients (e.g. positive lymph nodes, metastatic diseases)
- Tamoxifen is contraindicated in pregnancy
- Trastuzumab is contraindicated in pregnancy.
- G-CSF may be used to treat chemotherapy-induced leukopenia if indicated

### Radiotherapy

- Radiotherapy should be postponed to after delivery
- Radiotherapy may be given in pregnancy in certain urgent situations e.g. spinal cord compression
- In urgent situations, shielding or elective early delivery may be considered

* Texans are NOT associated with foetal effects or any known long-term effect and can be used in pregnancy if indicated

- **Timing of delivery:**

  Delivery should be at least 2-3 weeks after the last dose of chemotherapy to permit bone marrow recovery

- **Postpartum management:**
  - Breast feeding:
    - Breast feeding should be avoided if the patient is receiving chemotherapy, Tamoxifen and trastuzumab
    - Breast feeding may be allowed 14 days after the last dose of chemotherapy
  - Contraception: Non-hormonal contraception is generally recommended

## Management of patients with history of breast cancer

### I. Preconception management

- **Pregnancy decision:**
  - Postponing pregnancy for 2 years after completion of treatment is recommended. Thereby, the window of time where recurrence risk is high is avoided
  - Women with metastatic disease should be advised to avoid pregnancy
  - Patients should be advised that pregnancy does not affect cancer prognosis and there is no increased risk of anomalies or foetal loss in women who are not on treatment during pregnancy

- **Pre-pregnancy recommendations:**
  - Women who are treated from breast cancer are recommended to receive Tamoxifen for 5 years to reduce risk of recurrence if the disease is oestrogen receptor positive. Women
  - Women who are planning to get pregnant may discontinue tamoxifen after 2-3 years. It should stop Tamoxifen 3 months before conception. Continuation of Tamoxifen may be considered after delivery
  - Any routine imaging is recommended before conception

## II. Management during pregnancy

- A multidisciplinary team should be involved in patient care (obstetrics consultant, oncologist and breast surgeon)
- If imaging is needed during pregnancy, breast ultrasound is preferred
- Cardiac assessment should be performed in women who were treated previously with anthracycline, echocardiography is used to measure ejection fraction during pregnancy
- Obstetricians should be aware that women with prior history of breast cancer are slightly more likely to experience delivery complications and thereby, to undergo caesarian section
- Breast feeding from the normal breast is allowed if the patient is not currently on treatment. However, lactation is unlikely to succeed in women who received breast/chest radiotherapy

### Fertility after breast cancer

- Chemotherapy is associated with potential gonadotoxicity and permanent amenorrhoea. Effect depends on:
  ① Age: outcome is worse with advanced ages
    - Women younger than 30: risk of amenorrhea is 5%
    - Women older than 35-40: risk of amenorrhea is 50%

  ② Chemotherapeutic agent:
    - Cyclophosphamide, methotrexate, 5-flurouracil regimen is highly gonadotoxic
    - Anthracyclines and Texans are less gonadotoxic.

  ③ Total dose and duration
- Tamoxifen, GnRH and Trastuzumab have no impact on fertility.
- Options for fertility preservation prior to initiation of chemotherapy include:
  ① Embryo cryopreservation: the most popular and well-established technique. Success rate per cycle is approximately 20% per cycle
  Stimulation regimens in women with oestrogen receptor positive breast cancer should include Tamoxifen or letrozole with GnRH

  ② Oocyte cryopreservation: the technique is not yet well-established

  ③ Ovarian tissue preservation: it is currently experimental

  ④ Ovarian suppression with GnRH may be used for fertility preservation during administration of chemotherapy particularly if embryo cryopreservation is not available. However, it may alter response to chemotherapy during its administration

## Prognosis

- 5-year survival rate is approximately 80% in women aged under 50
- Pregnancy does not alter prognosis of breast cancer

# Fibroids with Pregnancy

## Incidence

Uterine fibroids are present in10% of pregnancies in the first trimester

## Fibroids and pregnancy

| Effect of pregnancy on fibroids | Effect of fibroids on pregnancy* | |
|---|---|---|
| | Maternal complications | Foetal complications |
| Effect of pregnancy on fibroid size is inconsistent. If fibroids are to increase in size, this likely occurs in the first trimester | • Pain (associated with fibroids > 5 cm, present in the second and third trimester). It may be caused by:<br>▪ Red degeneration<br>▪ Torsion (if pedunculated)<br>▪ Pressure<br>Risk of placenta praevia (risk is doubled compared to baseline)<br>• Risk of placental abruption<br>• Postpartum haemorrhage<br>• Higher incidence of caesarean section<br>• Risk of retained placenta | • 1st trimester miscarriage, risk is 14% vs. 8% which is the baseline risk<br>• Malpresentation, risk is associated with large, multiple fibroids and lower uterine segment fibroids. External cephalic version is not contraindicated with fibroids<br>• Foetal anomalies may rarely occur due to mechanical "compression" effect (limb reduction, dolichocephaly, torticollis) |

* Incidence of complications is 10-30%, particularly with fibroids larger than 200 $cm^3$

## Fibroids and fertility

- 5-10% of women with fibroids complain of subfertility. This is associated with submucous fibroids. The effect of intramural fibroids is not clear
- In the presence of uterine fibroids and when other causes of infertility are excluded, two thirds of women may get pregnant after myomectomy

## Management in pregnancy

- **Antepartum management:**
  - **Medical treatment:**
    - All medical options are contraindicated during pregnancy and breastfeeding. Therefore, they should be stopped in pregnant women. The only safe options are non-steroidal anti-inflammatory drugs (NSAIDs) prior to 28 weeks and tranexamic acid
    - Ulipristal acetate should be stopped prior to conception due to significant obstetric risks e.g. risk of abortion is 33%, risk of preterm labour is 25%, risk of caesarean section is 90%, and risk of ectopic kidney is 8%

**Consultant led care**

Consultant led care is indicated in women with:

① Fibroids > 3cm

② Fibroids close to the cervix

③ Fibroids present at placental site

  - **Uterine artery embolization (UAE):**
    - UAE is associated with risk of miscarriage, caesarean section, postpartum haemorrhage, and placenta accreta (11%)
    - Because of these risks, UAE should not be recommended in women seeking conception

- **Surgical management:**
  - In women with prior myomectomy, decision of vaginal delivery should be individualized. The size of defect associated with surgery is more significant than endometrial opening. Therefore, operative note should be carefully reviewed
  - Conception should be attempted at least 6 months after surgery (the endometrium heals in 3 months)
  - Antenatal myomectomy is not a standard practice and should be considered only in the following conditions:

    ① Red degeneration after failure of conservative management

    ② Fibroids > 5 cm in the lower uterine segment

    ③ Rapidly growing fibroids

    Surgery is best performed in the first and second trimesters

The risk of uterine rupture after myomectomy:

- 7% after laparoscopic myomectomy (not contraindication)
- 0.4% after open myomectomy

Probability of success of vaginal birth is 90% after myomectomy regardless of the route

- **Imaging:**
  - Serial growth scan is indicated in the presence of large fibroids
  - MRI may be indicated if there are concerns on malignancy

- **Management of red degeneration:**
  - Other causes of pain should be ruled out e.g. preterm labour, placental abruption
  - Women should be admitted
  - Analgesics are used to control pain (paracetamol, opiates). Ibuprofen is the most effective, but it should be used only prior to 28 weeks and for less than 48 hours
  - If there is no response, surgery is indicated

- Ultrasound findings of red degeneration are non-specific e.g. heterogenous echogenic pattern or cystic changes
- However, ultrasound is indicated to confirm viability and rule out other causes of abdominal pain in pregnancy along with clinical assessment

- **Intrapartum management:**
  - **Mode of delivery:**

| Elective caesarean section (CS) | Vaginal delivery |
|---|---|
| • Elective CS should be considered if the endometrium is breached with a large defect due to a previous myomectomy<br>• CS may also be performed for obstetric indications or because fibroids in the lower uterine segment interfere with vaginal delivery. The following measures should be taken at the time of CS:<br>▪ Incision is made away from the fibroids (2 cm is a safe margin)<br>▪ Uterine incision will be likely classic (10 cm)<br>▪ Uterine dextrorotation should be manually corrected before incision is made<br>▪ Uterine artery ligation after delivery of the baby may be considered | If vaginal delivery is not contraindicated in women with prior myomectomy, the following measures should be considered:<br>• Continuous electronic foetal monitoring<br>• Delivery in a high-risk unit.<br>• IV access<br>• Complete blood count<br>• Blood group and screen<br>• Oxytocin may be considered for 24 hours instead of 12 hours after delivery<br>• Ergometrine (if not contraindicated) may be used |

If hysterectomy will be performed in the presence of a broad ligament fibroid, surgery should be started by the more accessible side first

- Myomectomy at the time of CS may be indicated if:
  ① It is essential to provide access to delivery
  ② Uterine incision closure is not possible
  ③ Fibroid is larger than 6 cm
  ④ Subserosal fibroids
  Myomectomy at the time of CS is safe and cost effective. There is no difference in haemoglobin level, transfusion or postoperative fever if it is performed. However, it is associated with risk of incomplete removal

**Outcomes of caesarean myomectomy**

- pregnancy rate is 80% (vs. 45% with interval myomectomy),
- 20% will need fertility treatment
- There is higher risk of previa, talipes, and malpresentation

- **Postpartum management:**
  - In 70% of patients, fibroids shrink in size from early pregnancy to 3-6 months postpartum. This course is less noted in black races and in women using progestin-only contraceptives
  - Postpartum complications are rare and include:
    - Pyomyoma:
      - It is life threatening condition
      - It presents with fever, pain, and septicaemia
      - The most common causative organism is Clostridium
      - Recommended treatment is myomectomy, hysterectomy, or CT guided drainage
    - Rupture of red degeneration:
      - It presents by acute abdominal pain
      - Ultrasound shows a large hyperechoic mass and free fluid
      - Exploratory laparotomy is indicated

# Pregnancy After Bariatric Surgery

## Background

- Bariatric surgery is recommended if body mass index is greater than 40 if other conservative measures fail to reduce weight
- 50% of women who are candidates for bariatric surgery are in their reproductive years
- Obesity in pregnancy is associated with several risks e.g. spontaneous abortion, gestational diabetes, hypertensive disorders

## Types of bariatric surgery

- Bariatric surgery is either restrictive, malabsorptive, or both
- Most common procedures are: Laparoscopic adjustable gastric banding (LAGB) and Roux-en-Y gastric bypass. These procedures are associated with lower complications (5%), adverse maternal, and neonatal outcomes compared to other procedures

## General effects of bariatric surgery

| | Issues |
|---|---|
| **Conception** | • Pregnancy is recommended after 12 months of surgery. By the time, maximum weight loss is likely achieved<br>• It does not seem that conception within or after 12 months of surgery affects birthweight, intrauterine growth restriction (IUGR), hypertension, gestational diabetes or incidence of caesarean section |
| **Fertility** | • Bariatric surgery may improve fertility, which is primarily attributed to restoration of hormonal balance and improvement of ovulation<br>• Less information is available on impact of bariatric surgery on pregnancy rates |
| **Contraception** | • Surgery does not affect contraceptive effectiveness. However, jejunoileal (J-I) bypass may be associated with combined contraceptive pill failure due to decreased plasma concentration<br>• Contraceptive safety after bariatric surgery is not clear |
| **Nutritional deficiencies** | • Malabsorptive procedures lead to vitamin B12, folate and protein deficiency.<br>• These women should be administered iron, calcium, folate, vitamin B 12, protein, fat soluble vitamins<br>• After biliopancreatic diversion (BPD), approximately 20% of women may require parenteral nutrition |

## Management of pregnancy after bariatric surgery

### Preconception

- Contraceptive counselling: discuss the use of reliable contraception, particularly not a pill form, to postpone pregnancy for 12 months after surgery
- Follow-up with nutritionist/dietitian with regular administration of folic acid, vitamin B12, calcium and iron

### Antenatal care

- Multidisciplinary team care (obstetrician, bariatric surgeon, and dietitian)
- Follow-up with micro nutrition status particularly in women who underwent malabsorptive surgery
- Monitoring optimal gestational weight gain (GWG):
  - Ideal GWG is between 7–11 kg.
  - After bariatric surgery, women usually gain significantly less weight than ideal. Weight gain should be carefully monitored
  - LAGB has the advantage of adjusting the band to increase the patient's food intake
- Screening for Neural tubal defects and other malformations
- Serial Ultrasound scans for fetal growth restriction
- Standard 75 or 50 gm glucose tolerance test may cause dumping syndrome. Therefore, screening of gestational diabetes is done by monitoring fasting and postprandial glucose for a week
- Assessment of thromboprophylaxis risk per guidelines
- Risks of surgical complications during pregnancy should be considered

### Surgical complications during pregnancy

- Intestinal hernia (most common), obstruction, perforation and death
- Band slippage and migration (severe vomiting)
- Band leakage (24%)
- gastric prolapse (4%)
- Pouch dilation (rare)

Diagnosis is difficult to make, and CT scan is the standard diagnostic tool. Management may require laparotomy

| | |
|---|---|
| Intrapartum | • Bariatric surgery is not an indication of caesarean delivery and does not increase its risk<br>• Foetal scalp monitoring may be required<br>• Keep anaesthesia and paediatrics informed |
| Postpartum | • Pain control, thromboprophylaxis as indicated, physiotherapy<br>• encourage breast feeding<br>• Follow up with nutritionist.<br>• Cosmetic surgery associated with weight reduction should be postponed till women complete their families |

## Obstetric outcomes of bariatric surgery

| | |
|---|---|
| **Maternal outcomes** | In general, pregnancy is safe, and outcomes are more favourable after bariatric surgery compared to pregnancy with morbid obesity. Risk of gestational diabetes mellitus and pre-eclampsia is significantly reduced. |
| **Perinatal outcomes** | • Risk of congenital anomalies is 1.6% (vs. 0.7% as a baseline). Neural tube defects should be screened for due to folic acid deficiency, which should be adequately replaced<br>• Following biliopancreatic diversion, risk of miscarriage is 4%. There may be increased risk of congenital anomalies e.g. congenital diaphragmatic hernia, intestinal obstruction<br>• Roux-en-Y: may be associated with low birthweight<br>• Following LAGB, there may be elevated homocysteine level in pregnant women post-LAGB, and elevated risk of neural tube defects |

# Pregnancy After Treatment of Cancer

## Effect of cancer treatment

| | Clinical effects | Recommendations |
|---|---|---|
| **Cardio-vascular system** | • Cancer survivors are at increased risk of congestive heart failure, myocardial infarction, pericardial disease, and vulvar abnormalities. Of those, breast cancer survivors suffer high incidence of heart failure and coronary artery disease<br>• Anthracycline is associated with dose-dependent decline in ejection fraction and dilated cardiomyopathy (up to 60% of patients)<br>• Mediastinal Radiotherapy is associated with pericardial disease, vulvar disease, and cardiomyopathy | Women who had history of anthracycline or mediastinal radiotherapy should be screened with regular echocardiography during pregnancy (unless they had normal echocardiography within the last 3 years) |
| **Endocrine system** | • Endocrine system is likely affected with childhood cancer and in women treated with both chemo- and radiotherapy. It is most commonly affected among Hodgkin lymphoma and brain tumour survivors<br>• Thyroid dysfunction is present in 20-30% of women who receive neck radiation | • Women with history of radiation to brain, spine or neck during childhood should be screened for thyroid dysfunction<br>• Women exposed to cranial, abdomen or total body irradiation or alkylating agents should be screened for diabetes |

| | | |
|---|---|---|
| **Respiratory system** | • Patients with history of chest or whole-body radiotherapy are at increased risk of pneumonitis, recurrent pneumonia and fibrosis.<br>• Bleomycin (used for treatment of Hodgkin's lymphoma) can cause pulmonary fibrosis | Pregnant women who have history of chest or whole-body radiotherapy or bleomycin may be offered pulmonary function test |
| **Thrombotic risk** | • Women with previous history of venous thromboembolism are at increased risk of recurrent venous thrombosis during pregnancy. | • Careful risk assessment by an obstetric haematologist during pregnancy<br>• Women may still need thromboprophylaxis even if risk is eliminated |
| **Recurrence** | • Peak incidence of cancer recurrence is usually in the first 2 years following treatment<br>• Survivors of childhood cancer are at risk of a second cancers later in life | Pregnancy should be avoided in the first 2 years following cancer treatment |

## Obstetric outcomes

- **Congenital anomalies:** parental cancer treatment is not associated with increased rate of congenital anomalies
- **Miscarriage:** if there is previous history of pelvic radiation, risk of miscarriage increases by 1.5 times
- **Premature labour:** risk may be limited to women who had prior exposure to abdomen/pelvic Radiotherapy
- **Small for gestational age:** there is no association unless women were exposed to irradiation to the uterus that is greater than 500 cGy. In this case, serial growth scan is recommended
- **Stillbirth:** There is no association unless the uterus was exposed to high dose of irradiation

## Obstetric care

Cancer survivors should be offered the following care during pregnancy:

- Cancer survivors should receive a consultant-led care
- A thorough cancer history should be taken with special consideration to treatment received
- Based on cancer history, screening with echocardiogram, thyroid function tests, glucose tolerance test or respiratory function tests may be indicated
- Genetic counselling should be offered in women with family cancer syndromes

### Imaging during pregnancy

- The accepted cumulative dose of ionizing radiation during pregnancy is 5 rad (50 mGy)
- Natural background radiation during an entire pregnancy is approximately 0.5 - 1.6 mGy
- The commonest teratogenic effects of exposure to high dose radiation are central nervous system changes e.g. microcephaly and severe mental retardation
- This risk is greatest at 10-17 weeks. There is no proven risk before 10 weeks or after 27 weeks
- The greatest risk of foetal growth restriction due to radiation is 3-10 weeks
- A dose of 250 mGy may be associated with a 0.1% risk of foetal malformation

## Surgical disorders with pregnancy

### Abstract

Maternal exposure to viral and parasitic infection carries serious risk to the foetus. Although not all viral infections are transmitted to the foetus, maternal symptoms of viral infection are

indistinguishable, and they should be assessed for possible congenital infection. Clinical suspicion can guide confirmatory investigations that promote early diagnosis of complications, patient counselling, and interventions, if possible. In this chapter, we will discuss congenital infections during pregnancy and how diagnosis and follow-up should be performed.

## Keywords

Appendicitis, fibroids, bariatric surgery, breast cancer

## Further readings

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# Chickenpox in Pregnancy

## Epidemiology

- Risk of primary varicella in pregnancy is 3:1000.
- 90% of reproductive aged women are seropositive to varicella zoster virus (VZV)
- 80% of deaths caused by VZV occur in adult patients

## Transmission

| | |
|---|---|
| **VZV transmission** | • Droplet infection: Significant contact that suggests high risk of transmission includes:<br>▪ Sharing the same room with an infected person for 15 minutes or more<br>▪ Face-to-face contact<br>• Direct contact with vesicle fluid or indirectly e.g. by fomites |
| **Symptoms of primary infection** | • Fever, malaise<br>• Maculopapular rash that becomes vesicular and then crusts over before healing<br>The disease is infectious 2 days before appearance of the rash and till vesicles crust over (usually 5 days after appearance of the rash) |
| **Symptoms of recurrent infection** | • Following primary infection, the virus remains dormant in sensory ganglia<br>• Viral reactivation results in zoster or shingles (erythematous rash which follows dermatomal distribution). |
| **Varicella vaccine** | • Live attenuated vaccine<br>• 2 separate doses 4-8 weeks apart.<br>• Safe in breast feeding |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_17

## Management

- **Preconception:**

  Offer varicella vaccination to seronegative women (Recommend postponing pregnancy for 4 weeks).

- **Prenatal management:**

**Initial antenatal visit**

**If a pregnant woman has no prior chickenpox/shingles infection or is seronegative**

Advise to avoid contact with shingles/chickenpox in pregnancy (vaccine is contraindicated in pregnancy)

**If contact occurs**

Take full history to determine susceptibility of infection and extent of exposure (Previous history of chickenpox predicts seropositivity in 98-100% of cases)

**If the patient has no prior exposure to chickenpox/uncertain**

Blood test to assess immunity status (VZIGs is delayed till sero-negativity is confirmed)

**If the patient is not immune and she had significant exposure**

Check availability of VZ immunoglobulins (VZIG). If available, give VZIG as soon as possible for up to 10 days after exposure. A second dose may be given if another exposure is reported beyond 3 weeks of the first dose

**If VZIG is given**

The patient is considered potentially infectious for 8-21 days

**If VZIG is not given**

The patient is considered potentially infectious for 8-28 days

**Aim**

VZIG may reduce risk of fetal varicella syndrome by attenuating VZV; 50% of women develop normal or attenuated infection

**IVIG**

**Adverse effects**

- Pain and erythema at injection site
- Anaphylaxis (< 0.1%)

**If a pregnant woman develops rash**

**Maternal care**

- Oral acyclovir (800 mg 5 times/day for 7 days) if she presents within 24 hours of appearance of the rash specially if she is 20 weeks or more (IV acyclovir is considered only if severe infection)
- Isolation from other pregnant women/neonates: during the period of infectivity
- VZIG has no role in these patients

**Indications of hospitalization**

- Respiratory or neurological symptoms
- Dense rash Smokers
- Immunocompromised Women
- Women with chronic lung disease
- Infection in the 2nd half of pregnancy

**Fetal care**

- Refer pregnant women with chickenpox to fetal medicine specialist at 16-20 weeks (or 5 weeks after infection). Detailed ultrasound should be performed
- Abnormal ultrasound findings may warrant fetal MRI
- Amniocentesis may be considered to detect varicella DNA. However, it should not be offered before all lesions heals. Amniocentesis has high negative predictive value.

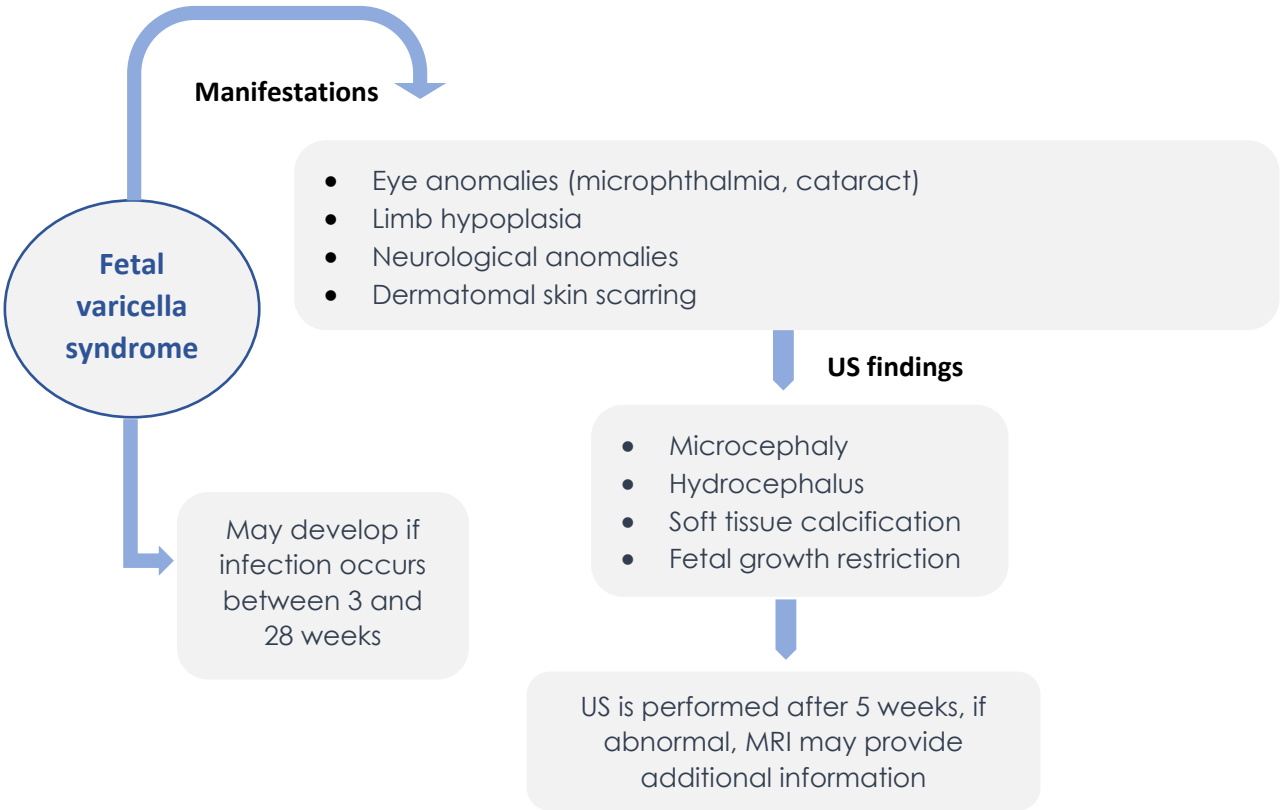
## Maternal risks

- **Chickenpox during pregnancy is associated with maternal risk of:**
  - Pneumonia (5-14% in pregnant women with chickenpox; mortality in this subgroup is 0-14%)
  - Encephalitis

- Hepatitis
- Death (rare)

## Fetal risks

- Maternal infection in the 1st trimester does not increase risk of miscarriage
- Varicella or seroconversion in the first 28 weeks of pregnancy is associated with small risk of fetal varicella syndrome (approximately 1%)




## Neonatal risks

- Varicella infection of the newborn is commonly caused by maternal infection that occurs within 4 weeks of delivery
- Delivery within 1 week of appearance of rash or appearance of rash within 1 week of delivery carries the highest risk. If clinically

In infection occurs within 4 weeks of delivery:

- 50% of newborns will be infected
- 23% develops clinical varicella

appropriate, postponing elective delivery beyond 1 week after appearance of rash may facilitate passive immunity to the newborn

- These newborns should receive VZIG with or without acyclovir

# Cytomegalovirus in Pregnancy

## Epidemiology

- It is the most common virus that causes congenital infection
- It is the most common non-genetic cause of sensorineural hearing loss
- It affects 0.2-2.2% of live births
- 10-15% of infected neonates are symptomatic at birth
- 10-15% of infected neonates develop complications during childhood
- Approximately 2/3 of congenital CMV occurs with secondary infection, if CMV is highly prevalent in the population

## Virology

| | |
|---|---|
| Types of CMV infection | • Primary infection<br>• Secondary infection: which can be either:<br>▪ Reactivation of primary infection (remains dormant primarily in salivary glands) or<br>▪ Infection with a different CMV strain |
| Route of transmission | • Antenatal (transplacental)<br>• intrapartum (through birth canal)<br>• Postnatal (through breast milk) |
| Risk of congenital infection | • Risk of transmission with primary infection: 30-40 % (30% in the first trimester and 47% in third trimester)<br>• Risk of transmission with secondary infection: 1-2%.<br>• Infection in early in pregnancy is associated with lower risk of congenital infection but more severe manifestations, compared to late pregnancy |

## Clinical features

| Maternal | Fetal/neonatal |
|---|---|
| • Majority of cases is asymptomatic<br>• Some has infectious mononucleosis like symptoms (fever, malaise, myalgia, cervical lymphadenopathy)<br>• Few may have hepatitis and pneumonia | • 85-90% are asymptomatic. Of these, 6-23% suffers from some hearing loss<br>• 10-15% is symptomatic. Symptoms include jaundice, petechial rash, hepatosplenomegaly, microcephaly, Small for Gestational Age. |

## Prenatal diagnosis

### Indications of CMV testing

- Routine screening during pregnancy is not recommended.
- Suspicious sonographic findings
- Influenza-like symptoms during pregnancy
- Symptoms of glandular fever after exclusion of Epstein Bar virus
- Hepatitis after exclusion of hepatitis A, B and C

### Investigatory tests

**IgG avidity to diagnose maternal primary infection***

- High avidity index (> 60%) indicates past infection > 3 months
- Low avidity index (< 30%) indicates recent infection within 3 months

For secondary maternal infection, only invasive testing can be used

⬇

**Confirmation of congenital infection**

Amniocentesis and PCR should be done after 20 weeks of gestation (to ensure adequate fetal urine in amniotic fluid)

⬇

**If congenital infection is confirmed**

Fetal cerebral MRI at 28-32 weeks is performed with T1, T2, and diffusion sequences. It may be repeated 3-4 weeks later

* CMV IgM is not used to diagnose primary infection as it persists for months

## Prognosis of congenital CMV

**Prenatal prognostic indicators**

1. Timing of infection during pregnancy
2. Type of infection (primary or secondary)
3. Presence of CNS sonographic abnormalities
4. Fetal CMV IgM and CMV DNAemia (viral markers) by fetal blood sampling
5. Fetal beta-2-microglobulin and platelet count (non-viral markers) by fetal blood sampling

Classification of outcomes of congenital infection

**Asymptomatic fetuses**

- Normal US
- Normal MRI
- Normal markers
- Prognosis is generally good. There may be some hearing loss

**Mild or moderately symptomatic fetuses**

- No CNS abnormalities on ultrasound OR
- Isolated ultrasound abnormalities (mild ventriculomegaly, echogenic bowel)
- Isolated abnormal markers in fetal blood
- Prognosis is unclear. Further follow-up is recommended

**Severely symptomatic fetuses**

- Severe CNS anomalies PLUS
- Fetal thrombocytopenia
- Prognsis is poor and patient should be conuselled on termination

## Management

- **Prenatal treatment:**
  - Antiviral drugs:
    - Anti-viral drugs against CMV are teratogenic except valaciclovir.
    - Valaciclovir administration in moderately infected fetuses may result in more fetuses born asymptomatic. Clinical trials many be needed to support routine treatment for this indication
  - Hyperimmune globulin (HIG):
    HIG is not routinely recommended

- **Neonatal treatment:**
  - Neonatal diagnosis is made by CMV PCR from urine or oral swab within 3 weeks of birth
  - Valganciclovir/ganciclovir treatment may stop disease progression and improve neurodevelopmental outcome if given within the first 4 weeks of birth

## Prevention

- No vaccine available
- Hygiene education is the most effective preventive approach for pregnant women. Incidence of seroconversion is 1% in women who receive such education compared to 8% who do not.

# Rubella in Pregnancy

## Background

- **Type of virus:** Single-stranded RNA togavirus
- **Mode of transmission:** primarily via the respiratory route
- **Incubation period:** It ranges from 12 to 23 days (average 14 days). Viral replication occurs in the nasopharynx and lymph nodes
- **Infective period:** Women are infectious from 7 days before until 7 days after the onset of the rash

## Vertical transmission

- The risk of congenital infection is 90% before 12 weeks, 20% between 12–16 weeks and, thereafter, deafness is a risk up until 20 weeks
- Risk of transmission with congenital infection is approximately 5%.

## Diagnosis

- **Clinical picture of maternal rubella infection:**
  - Maternal rubella infection is usually asymptomatic or associated with mild illness of malaise, headache, flu-like symptoms and lymphadenopathy, followed by a diffuse, fine maculopapular rash
  - This clinical picture is similar to maternal parvovirus B19 infection and any pregnant

woman with rash should be investigated for both types of infection regardless of immunity status (vaccination or antibodies)

- **Investigations of maternal rubella infection:**
  - Primary rubella infection is confirmed by presence of both rubella IgM and rubella IgG seroconversion or presence of low-avidity antibodies
  - Rubella reinfection (or infection in a previously vaccinated woman) is confirmed by the presence of significant increase in baseline rubella IgG titre

- **Diagnosis of congenital rubella syndrome:**
  - ***Sonographic features:***
    - Foetal growth restriction
    - Cardiac defects, primarily pulmonary valvular stenosis and ventricular septal defect
    - peritoneal hyperechogenicity and hyperechogenic foetal bowel

    Neonates may develop cataract and sensorineural hearing loss

  - ***Amniocentesis:***

    Diagnosis can be made by detecting reverse transcriptase PCR (RT-PCR) that is used for the detection of viral nucleic acid in amniotic fluid

## Prevention

A live attenuated virus vaccine is used to prevent rubella infection. This vaccine is contraindicated in pregnancy and therefore, it should be considered postpartum in women who are non-immune

## Management

There is no specific treatment for rubella infection

- **If infection is diagnosed before 12 weeks:** consider termination of pregnancy.
- **If diagnosis is made between 12 and 16-20 weeks:** ultrasound surveillance to identify features of congenital rubella syndrome are considered if invasive testing of the foetus is positive (55% risk of transmission and a 20% risk of congenital rubella syndrome). Specialist foetal echocardiography should be arranged in addition to foetal growth scans
- **If diagnosis is made after 16-20 weeks:** the risks to the foetus are negligible. Therefore, no further action is required

# Toxoplasma in Pregnancy

## Mode of transmission

Transmission of infection occurs by ingesting toxoplasma cysts, which may be present in undercooked meat or food contaminated with soil or cat feces

## Risk of transmission

As with most congenital infections, risk of transmission is lower with early infection. However, severity of infection and risk of congenital abnormalities is higher compared to late pregnancy infection:

| Gestational age | Risk of infection |
|---|---|
| **<4 weeks gestation** | <1% |
| **13 weeks gestation** | 10% |
| **36 weeks gestation** | > 60% |

## Diagnosis

- **Diagnosis of maternal toxoplasmosis:**
  - Clinically, most patients are asymptomatic. Otherwise, they may be present with:
    - Cervical lymphadenopathy
    - low-grade fever
    - muscle ache
    - fatigue
    - headache
  - Maternal infection may be diagnosed by serum IgM and IgG:
    - Both IgM and IgG become positive within 2 weeks of primary infection
    - IgG remains positive for life
    - IgM remains positive for 3 to 18 months
  - IgG avidity may be used to differentiate recent (low avidity) from remote infection (high avidity)

- **Diagnosis of foetal toxoplasmosis (congenital infection):**
  - Amniocentesis for detection of toxoplasma DNA
  - Most common sonographic findings are hydrocephalus, intracranial calcification, and chorioretinitis (the triad is present in approximately 80% of cases)

## Management

If maternal infection is confirmed, spiramycin should be given. Maternal treatment may reduce risk of foetal infection by 60-70%

# Parvovirus B19 in Pregnancy

## Background

- **Type of virus:** Single stranded DNA virus
- **Mode of transmission:** Droplet infection, hand to mouth
- **Incubation period:** 5–7 days following exposure. Women are infectious for 3–10 days post-exposure or until the rash appears.
- **Infectivity period:** 7-10 days before the rash develops to 1 day after the rash appears

## Vertical transmission

- If gestational age is less than 15 weeks, risk of vertical transmission is 15%
- If the gestational age is 15 to 20 weeks, risk of vertical transmission is 25%
- If the foetus is term, risk of vertical transmission is 70%

## Clinical presentation

- Infected children present with diffuse erythematous facial rash 'slapped cheek' after 5 days of prodromal symptoms
- In adults, infected women are asymptomatic in up to 50% of cases. They may present with no non-specific symptoms e.g. transient fever, malaise and arthralgia.

## Investigations

- If a pregnant woman was exposed to Parvovirus or is suspected to have Parvovirus, they should undergo serological testing:

| Results | Interpretation |
|---|---|
| • **IgG positive - IgM negative** | Immune |
| • **IgG negative - IgM negative** | Susceptible to infection |
| • **Positive for IgM (regardless of IgG)** | Recent infection |

- If suspicion is based on clinical symptoms, rubella should be tested in the same time of the patient is not immune or has unknown immunity to rubella as they can cause similar symptoms

## Management

- Urgent referral to a foetal medicine specialist is indicated for serial foetal ultrasound scans and Doppler assessment to detect foetal anaemia, heart failure and hydrops
- The patient should be followed up with serial ultrasound starting 4 weeks after infection and 1- to 2- weekly for up to 12 weeks. This should be combined with middle cerebral artery peak systolic velocity (MCA-PSV) to diagnose anaemia
- If MCA-PSV > 1.5 multiples of the median (MoMs) or if there is ascites or hydrops, Foetal blood sampling and intrauterine blood transfusion may be considered

# Syphilis in Pregnancy

## Background

- Syphilis is the most common congenital infection worldwide.
- Risk factors for syphilis in pregnancy are:
  - Low socioeconomic status
  - Multiparity
  - History of sexually transmitted infections (STIs)
  - Use of illicit drugs before 18 years or illicit drug use by the current partner
  - Poor antenatal care
  - Three or more sexual partners in the previous 12 months
- Transmission of infection:
  - Most common route is via sexual contact
  - Infection through anal, rectal or oral routes
  - Transplacental transmission during any stage of pregnancy.

## Stages of syphilis

| | |
|---|---|
| **Primary syphilis** | 3 weeks following exposure to infection (9-90 days) |
| **Secondary syphilis** | 4-10 weeks after primary chancre |
| **Latent syphilis** | • Early latent syphilis describes infections that occurred within the past year<br>• Late latent syphilis describes infections that occurred > 1 year ago. |
| **Tertiary (late) syphilis** | It can present 20 years later and likely in the obstetric population |

## Syphilis and pregnancy

- Risk of trans-placental transmission starts as early as 14 weeks. This risk increases as the pregnancy progresses towards term
- The stage of syphilis in the mother also influences the risk of transmission to the fetus: it can be as high as 100% in primary syphilis, whereas the risk is much lower in early latent (40%) and late latent syphilis (10%).

### Foetal risks

Foetal infection can result in:

- Foetal growth restriction
- Hepatomegaly and intrahepatic calcifications
- Thrombocytopenia
- Anaemia and ascites
- Distorted fetal long bones or foetal hydrops (in more severe cases)
- Preterm birth
- Stillbirth and neonatal death (risk of foetal loss is 30-40%)

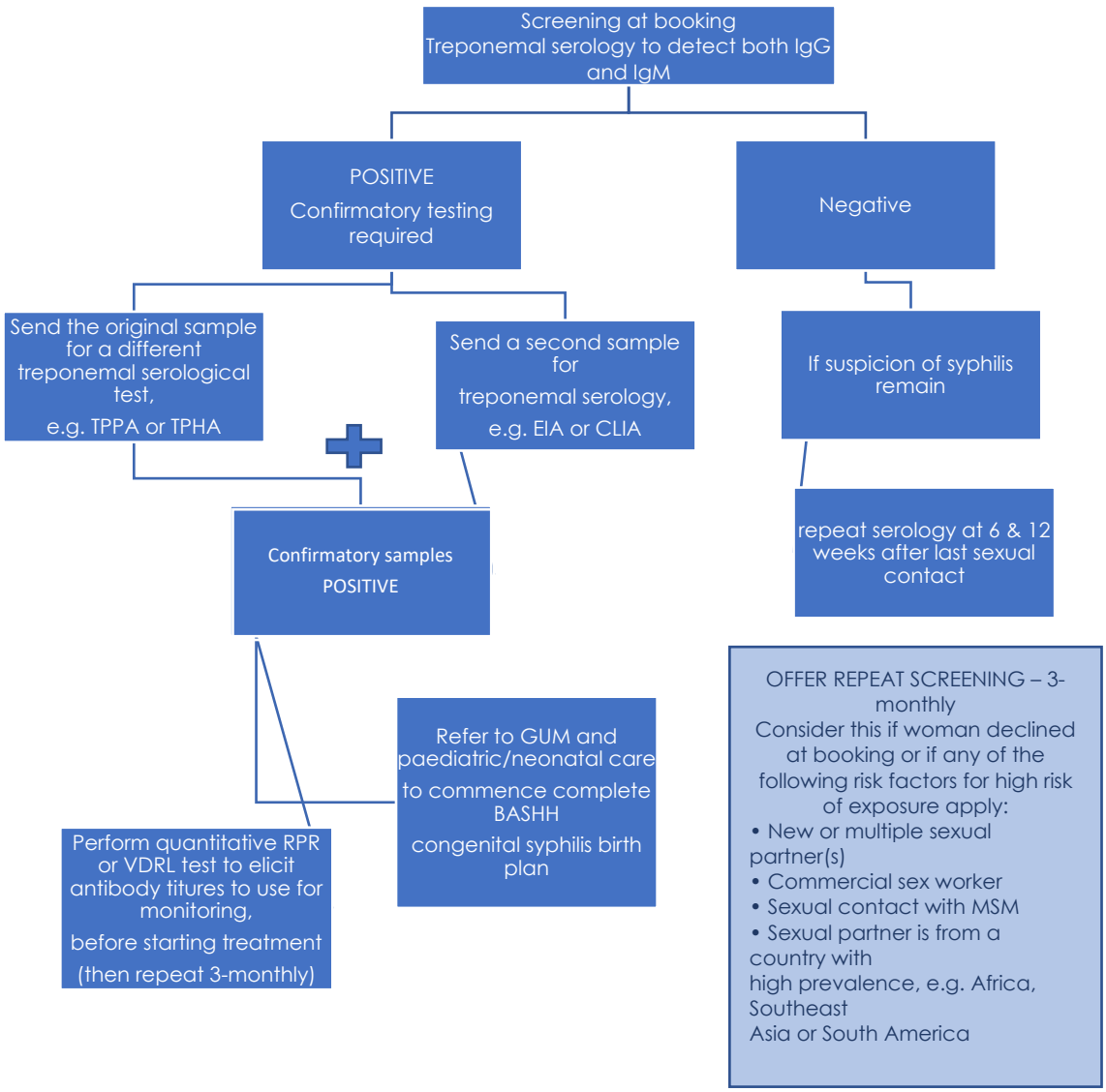
Signs on ultrasound are often general and nonspecific

## Diagnosis

- Direct testing methods include dark-field microscopy and polymerase chain reaction (PCR). They are not widely available, but they detect infection quick and early (before a serological response occurs)
- Indirect testing (Serological tests) detects antibodies (such as enzyme immunoassays and T. pallidum particle agglutination assays, which are the most used)
- NICE Recommendations for diagnosis include:
  - Sending a 10-ml clotted blood sample to obtain a full syphilis screen (serological tests)
  - Sending swab from any active lesions with a 'flock/virology' swab to be tested with syphilis PCR and Herpes Simplex testing
  - Screen for other STIs (e.g., chlamydia, hepatitis B/C and HIV) after obtaining a consent

- Women with suspected disease who decline testing, or with confirmed disease who decline treatment, who may transmit infection to other contacts should be counselled that this could result in legal action against them

**Suggested screening algorithm for syphilis**



## Treatment

- Syphilis in pregnancy should be managed by a multidisciplinary team, which involves genitourinary medicine physicians, neonatologists and microbiologists.
- Management should include antimicrobial therapy, counselling, partner notification and safe sex advice.
- Women should be treated as soon as diagnosis is established, preferably in early gestation
- Treatment of maternal syphilis at least 30 days before delivery is the most important factor influencing the risk of congenital infection and perinatal mortality.
- There is increasing macrolide resistance in T. pallidum and they are no longer considered a treatment option

| Antibiotics used to treat syphilis in each stage of pregnancy | | | | |
|---|---|---|---|---|
| **Trimester** | **Early disease (Primary/secondary or latent <2 years)** | **Late disease (Latent/ unknown duration)** | **Possible sensitivity to penicillin and who can tolerate cephalosporins** | **unable to tolerate an intramuscular regime** |
| **First/second** | Benzathine penicillin 2.4 MU IM; single dose | Benzathine peniciilin 2.4 MU IM; weekly for 3 weeks/doses | ceftriaxone 500 mg IM, daily for 10 days | amoxicillin 500 mg and probenecid 500 mg, both orally, four times per day for 14 days. |
| **Third** | Benzathine penicillin 2.4 mU IM; weekly for 2 weeks/doses | This regimen is used in all stages of pregnancy | | |

### Jarisch–Herxheimer reaction

- It can complicate up to 45% of syphilis treatments in pregnancy.
- Symptoms typically occur within the first 24 hours of treatment and include fever, rigours and a skin rash (or rarely uterine contractions)
- Generally, it is self-limiting; therefore, there is no recommended treatment regimen other than supportive treatment

## Congenital syphilis

| | |
|---|---|
| **Epidemiology** | Congenital syphilis remains rare in the UK |
| **Classification** | • Early disease manifests in the first 2 years of life<br>• Late congenital syphilis is apparent after the age of 2 years |
| **Clinical presentation** | • Around two-thirds are asymptomatic at birth. Two thirds of those demonstrate signs and symptoms from 3–8 weeks of age. Most present before 12 weeks of age<br>• One-third to one-quarter of children presenting over the age of 2 years having asymptomatic neurosyphilis<br>• Clinical manifestations of congenital syphilis include 'Hutchinson's Triad': eighth cranial nerve deafness, interstitial keratitis and 'Hutchinson's Teeth' (notched incisors).<br>• Signs seen in early disease include:<br>▪ Skin rashes<br>▪ Stigmata of meningitis and jaundice<br>▪ Hepatosplenomegaly<br>▪ Anterior bowing of the mid tibia creates the classic 'sabre shins<br>▪ 'Bloody snuffles', caused by syphilitic rhinitis, create a characteristic pink coloured nasal discharge<br>• Late disease typically presents with bony deformities secondary to chronic inflammation. |

| | |
|---|---|
| **Investigations** | • Blood tests: severe anaemia, monocytosis, thrombocytopenia, raised alkaline phosphatase level<br>• X-rays: periostitis, which leads to the development of bone deformity. |
| **Prognosis** | • Congenital syphilis is a multisystem infection that can result in neonatal death and long-term disability<br>• Babies born with congenital syphilis are 10% more likely to die in the first year of life. |

# Zika Virus in Pregnancy

## Background

- Zika virus belongs to the virus family Flaviviridae; genus: Flavivirus. It is a single stranded RNA virus
- Transmission is primarily by Aedes mosquitos. However, it can be sexually transmitted (risk is low)
- Incubation period is 3-12 days

## Clinical picture

- Typical symptoms in adults are fever, maculopapular rash, arthralgia, or conjunctivitis. Many women are asymptomatic
- Rash usually resolves within 2 days but may persist up to 1 week

## Complications

- Guillain Barre syndrome
- Congenital microcephaly (20-fold increase during the pandemic "1:1000 pregnancies"). It may be associated with other congenital abnormalities

## Management

- **Couples planning for conception:**
  - If a male partner has travelled to Zika area, couples should avoid conception for 6 months after return from Zika area

- If a female partner has travelled to Zika area, couples should avoid conception for 8 weeks after return from Zika area if asymptomatic or 8 weeks after recovery if symptomatic

- **Pregnant women:**
  Testing is advised for women who report symptoms suggestive of acute Zika infection within 2 weeks of returning from an area with high or moderate risk of Zika infection transmission OR within 2 weeks of sexual contact with a male sexual partner who has recently visited an area with high or moderate risk of Zika infection

## Congenital infections during pregnancy

### Abstract

Maternal exposure to viral and parasitic infection carries serious risk to the foetus. Although not all viral infections are transmitted to the foetus, maternal symptoms of viral infection are indistinguishable, and they should be assessed for possible congenital infection. Clinical suspicion can guide confirmatory investigations that promote early diagnosis of complications, patient counselling, and interventions, if possible. In this chapter, we will discuss congenital infections during pregnancy and how diagnosis and follow-up should be performed.

### Keywords

CMV, Zika, chickenpox, syphilis, toxoplasma, parvovirus

### Further readings

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# Serum Markers of Obstetric Complications

## Markers of trisomy 21

| Test | Trimester | Components | Diagnostic performance |
|---|---|---|---|
| **Combined test** | First trimester | Pregnancy-associated plasma protein A (PAPP-A), free beta human chorionic gonadotrophin (β-hCG) in combination with nuchal translucency (NT) | Sensitivity is 90% with a false positive rate of 5% |
| **Triple test** | Second trimester | Alpha fetoprotein (AFP), βhCG, unconjugated estriol (uE3) | Sensitivity is 70% with a false positive rate of 5% |
| **Quadruple test** | Second trimester | Alpha fetoprotein (AFP), βhCG, unconjugated estriol (uE3), and inhibin-A | Sensitivity is 75% with a false positive rate of 5% |
| **Integrated test** | First and second trimester | NT, PAPP-A in the first trimester, quadruple screen in the second trimester | Sensitivity is 95% with a false positive rate of 5% |
| **Contingent test** | First and second trimester | Results of first trimester screening determine subsequent second trimester assessment:<br>- Low risk: No further action is required<br>- Intermediate risk: second trimester screening offered<br>- High risk: diagnostic testing is directly offered | Sensitivity is 88-94% with a false positive rate of 5% |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_18

| | AFP | uE3 | hCG | Inhibin A |
|---|---|---|---|---|
| **Trisomy 21 (Down syndrome)** | Low | Low | High | High |
| **Trisomy 18 (Edward syndrome)** | Normal | Low | Very low | Normal |
| **Trisomy 13 (Patau syndrome)** | High | Normal | Normal | Normal |
| **Turner syndrome** | Low | Low | Very high | Very high |

## Markers of adverse obstetric events

### First trimester markers

**Low PAPP-A**

- Spontaneous miscarriage
- Gestational hypertension
- Pre-eclampsia
- Low birthweight
- Preterm labour

**Low hCG**

- Spontaneous miscarriage
- Low birthweight

### Second trimester markers

**High AFP**

- Foetal growth restriction
- Placental abruption
- Miscarriage.
- Foetal demise
- Preterm labour

**High hCG**

- Preterm delivery
- Gestational hypertension
- Pre-eclampsia
- Foetal demise
- Foetal growth restriction

**High inhibin A**

- Preterm labour
- Gestational hypertension
- Pre-eclampsia
- Foetal demise
- Foetal growth restriction

**Low uE3**

- Oligohydramnios
- Miscarriage
- Foetal demise
- Low birth weight

# Noninvasive Prenatal Testing

## Background

- Circulating cell free foetal DNA presents 10% of circulating DNA fragments in maternal plasma
- Assessment of circulating foetal DNA can be used for non-invasive prenatal screening (NIPS) of aneuploidy
- The test should be performed after 10 weeks of gestation

## Accuracy

- The test has high sensitivity and specificity for trisomy 21 and trisomy 18 (99%)
- The test is less sensitive with trisomy 13 (90%) and monosomy X (93%)
- The test is less sensitive for trisomy 21 in twins (94%)

## Advantages

- The test is associated with low risk compared to invasive testing. NIPS reduces need for amniocentesis by 53% and chorionic villus sampling by 77%
- Results are reported in 3-5 days (comparable to PCR invasive testing)

## Disadvantages

- Incidence of non-conclusive results is 2-6%. If these results are repeated, incidence of NIPS failure is 20%
- Most common causes of non-conclusive or false results are:
    - Low foetal DNA fraction
    - Vanishing twin (false positive results)
    - Placental mosaicism (same issue with chorionic villous sampling)
    - Maternal cancers

# Invasive Prenatal Testing

## Introduction

- 5% of the pregnant population are offered invasive prenatal diagnostic tests
- Amniocentesis is the most common invasive prenatal diagnostic procedure in the UK

## Timing

- Amniocenteses are performed to obtain amniotic fluid for karyotyping from 15 weeks ($15^{+0}$) onwards.
- Chorionic villus sampling (CVS) is usually performed between 11 ($11^{+0}$) and 13 ($13^{+6}$) weeks of gestation and involves aspiration or biopsy of placental villi

## Complications

- **Miscarriage:**
  - Additional risk of miscarriage following amniocentesis is around 1%
  - Additional risk of miscarriage following chorionic villus sampling may be slightly higher than amniocentesis
- **Complications associated with improperly timed procedures:**
  - Early amniocentesis (before 14 week) is not recommended. It may be complicated by:
    - Higher fetal loss (1.3 times more)
    - Respiratory morbidity
    - Foetal talipes 5 times more and respiratory morbidity
  - Chorionic villous sampling should never be done before 10 weeks:
    - Technically more difficult
    - Risk of limb reduction defects
    - Risk of mandibular limb hyperplasia

## Consenting

Invasive diagnostic test should be preceded by a written consent which include:

- risk of pregnancy loss (national and local)
- results (limitation, failure, timing, communication of results)
- need for anti D
- indications for seeking medical advice

## Technique

- The procedure should always be done under ultrasound guidance
- Avoid Trans- placental passage whenever possible,
- Needle gauge size 0.9 millimeters (20 gauge) maximum, use local anesthetic if Transplacental

Continuous ultrasound guidance decreases blood staining from 2.4% to 0.8% (blood interferes with amniocyte culture)

Amniocentesis is comparable to venipuncture, so local anesthetic improves pain the angle of the needle insertion does not matter

If trans placental approach is inevitable, go through the thinnest part and avoid cord insertion (it does not increase miscarriage rate)

Needle size of CVS varies (18g, 20g, 17/19, 18/22), varies in aspiration (negative pressure by syringe, vacuum, biopsy forceps depending on preference)

## Good practice

- Competency should be maintained by carrying out at least 30 ultrasound guided invasive procedures per annum
- Operator competence should be reviewed if loss 4% in amniocentesis or 8% for Chorionic villus sampling or 7% second insertion
- Competency is maintained by 30 ultrasound guided procedure per year. If more than 100/year is performed, the practitioner becomes very experienced with less loss. Continuous audit is needed

| Multiple pregnancy consideration |
|---|
| • Invasive diagnostics in Twins need higher level of expertise in selective Termination of pregnancy required<br>• Labelling of twins is greatly assisted if gender is different or in the presence of obvious fetal abnormality |

## Third trimester amniocentesis

- Women should be informed that third-trimester amniocentesis does not appear to be associated with a significant risk of emergency delivery.
- Multiple attempts and bloodstained fluid are more common in third trimester procedures.
- Risk of blood-stained amniotic fluid is 5-10% (10 times higher) and this increases the risk of culture failure (10%)

## Risk of transmission of infection

| Preventing transmission of infection | Source of infection | Important notes |
|---|---|---|
| • US probe sterile bag<br>• Separate sterile gel<br>• Screen for blood borne viruses: if declined, counsel the patient and document risk of vertical transmission<br>• If HIV is positive: check viral load and treat (procedure is delayed till viral load is undetectable viral load. Start treatment if not previously treated)<br>If HIV is inadequately treated or not treated, risk of transmission is 25%, Mono or double treatment only is associated with 6% risk of transmission)<br>• If hepatitis B or C is positive: first and second trimester testing is allowed (very low risk of transmission) | • bowel puncture<br>• skin contamination organism on gel or probe (risk of infection vs. degradation of the probe | • Risk of severe sepsis is 1:1000<br>• Anti-Dis indicated after all procedures |

# Genetic Disorders and Genetic Testing

## Genetic disorders

**Genetic disorders classification**

| Mitochondrial disorders | Chromosomal | Complex diseases | Monogenic disorders |
|---|---|---|---|
| • Incidence: 1:5000-8000.<br>• Mostly commonly linked to inborn errors of metabolism. | Aneuploidy is the most common cause of spontaneous miscarriage and implantation failure | This refers to diseases that are precipitated by polygenic genetic and environmental factors | 1. X-linked dominant<br>2. Y-linked disorder<br>3. Autosomal recessive<br>4. Autosomal dominant<br>5. X-linked recessive |

| | |
|---|---|
| **Mitochondrial disorders** | • Leigh syndrome and MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) syndrome |
| **X-lined dominant disorders** | • Fragile X syndrome<br>• Incontinentia Pigmenti |
| **Y-linked disorders** | • Some cases of Swyer syndrome and Y chromosome related infertility |
| **Autosomal recessive disorders** | • The most common disorder in Europe is cystic fibrosis.<br>• The most common disorder in the UK is sickle cell disease (1 in 2,000).<br>• The most common disorder worldwide is β-thalassemia. |
| **Autosomal dominant disorders** | • BRCA 1 and BRCA2<br>• Marfan and Huntington syndromes |
| **X-linked recessive disorders** | • Duchenne muscular dystrophy<br>• Hemophilia |

## Preimplantation genetic diagnosis

### Definition

- Preimplantation genetic diagnosis (PGD) refers to biopsy and genetic testing of products of conception prior to embryo transfer.

### Applications

- It may be offered to couples undergoing in-vitro fertilization (IVF).
- It is used to assess embryo prior to transfer in couples at high risk of transmitting a genetic disorder.

## Invasive prenatal testing

- **Prevalence:**

  Prenatal diagnostic tests are offered to 5% of the pregnant population. The most common procedure is amniocentesis

- **Timing:**

  - Amniocentesis for karyotyping is performed at or beyond 15 weeks of gestation. Amniocentesis before 14 weeks (early amniocentesis) is not recommended
  - Chorionic villus sampling (CVS) is performed between 11+0 and 13+6 weeks of gestation

- **Risks and complications:**

| | |
|---|---|
| **Miscarriage** | ▪ Amniocentesis is associated with 1% additional risk of miscarriage<br>▪ Chorionic villus sampling is associated with slightly higher risk of miscarriage than amniocentesis<br>▪ Early amniocentesis is associated with 1.3 times higher risk of fetal loss |
| **Fetal defects** | ▪ Early amniocentesis may be associated with respiratory morbidity,<br>▪ Early amniocentesis increases risk of fetal talipes by 5 times |

| | |
|---|---|
| | ▪ CVS before 10 weeks may increase risk of limb reduction defects and mandibular limb hyperplasia |
| **Vertical transmission of infection** | Women should be screened for blood-borne viral infection:<br>▪ If a patient has HIV: viral load should be checked and treated accordingly. Procedure is delayed till viral load is undetectable<br>*Risk of vertical transmission is 25% with no treatment, and 6% with inadequate treatment (monotherapy or double treatment)*<br>▪ If a patient has hepatitis B or C: risk of transmission in the first and second trimester is very low, and procedures can be performed<br>▪ If a patient declines testing, she should be counselled on risk of vertical transmission before the procedure is performed |
| **Severe sepsis** | ▪ Incidence of severe sepsis is 1:1000<br>▪ Infection may originate from bowel puncture, skin contamination, or contamination from the gel or ultrasound probe<br>▪ Measurements that can be taken to prevent infection include using ultrasound probe sterile bag and using separate sterile gel |
| **Multiple attempts and blood-stained amniotic fluid** | ▪ This is more common with third trimester amniocentesis. The risk of blood-stained amniotic fluid is 5-10% (10 times higher than second trimester amniocentesis). This is associated with increased risk of culture failure (10%)*<br>▪ Third-trimester amniocentesis is not associate with risk of emergency delivery |

* Blood staining of amniotic fluid interferes with amniocyte culture

- **Consenting:**

A written consent should be obtained before Invasive diagnostic test is performed. Consent form should include:

- Risk of pregnancy loss
- Test results (limitations and risk of culture failure, timing of testing and results, how results will be communicated)
- need for anti-D immunoglobulin after any procedure in Rh negative women
- Indications for seeking medical advice

- **Technical aspects of amniocentesis or CVS:**

  - The procedure is performed under ultrasound guidance
  - Maximum needle gauge size is 0.9 millimeters (20 gauge)
  - Local anesthetic can be used before entry if Trans placental
  - Avoid trans-placental passage whenever possible

  Continuous ultrasound guidance decreases incidence of blood-stained amniotic fluid from 2.4% to 0.8%

  CVS needle varies in size (18g, 20g, 17/19, 18/22). Sample is obtained by a syringe, vacuum, biopsy forceps (provider's preference)

  If trans-placental passage is inevitable, the needle should pass through the thinnest part and cord insertion should be avoided. Thereby, miscarriage rate is not increased

  Angle of the needle insertion has not significant impact on the procedure

- **Good practice:**
  - Maintenance of operator competency requires at least 30 ultrasound-guided invasive procedures yearly. A highly experienced level with less feta loss is achieved by performing at least 100 procedures/year
  - Operator competency should be reviewed if:
  - Incidence of fetal loss is 4% or more with amniocentesis or
  - Incidence of fetal loss is 8% or more with CVS or
  - Rate of second insertion is 7% or more

# Fetal Growth Restriction

## Background

**Definition**

Small-for-gestational age (SGA) fetus is a fetus that fails to reach a specific biometry or estimated weight threshold by a specific gestational age (the 10th centile for abdominal circumference and estimated birth weight is the commonly used parameter)

**Causes**

- Fetal growth restriction (FGR): 30-50%
- Fetuses that are constitutionally small: 50 – 70%

The lower the centile, the greater the possibility of FGR

**Outcome**

**Immediate**

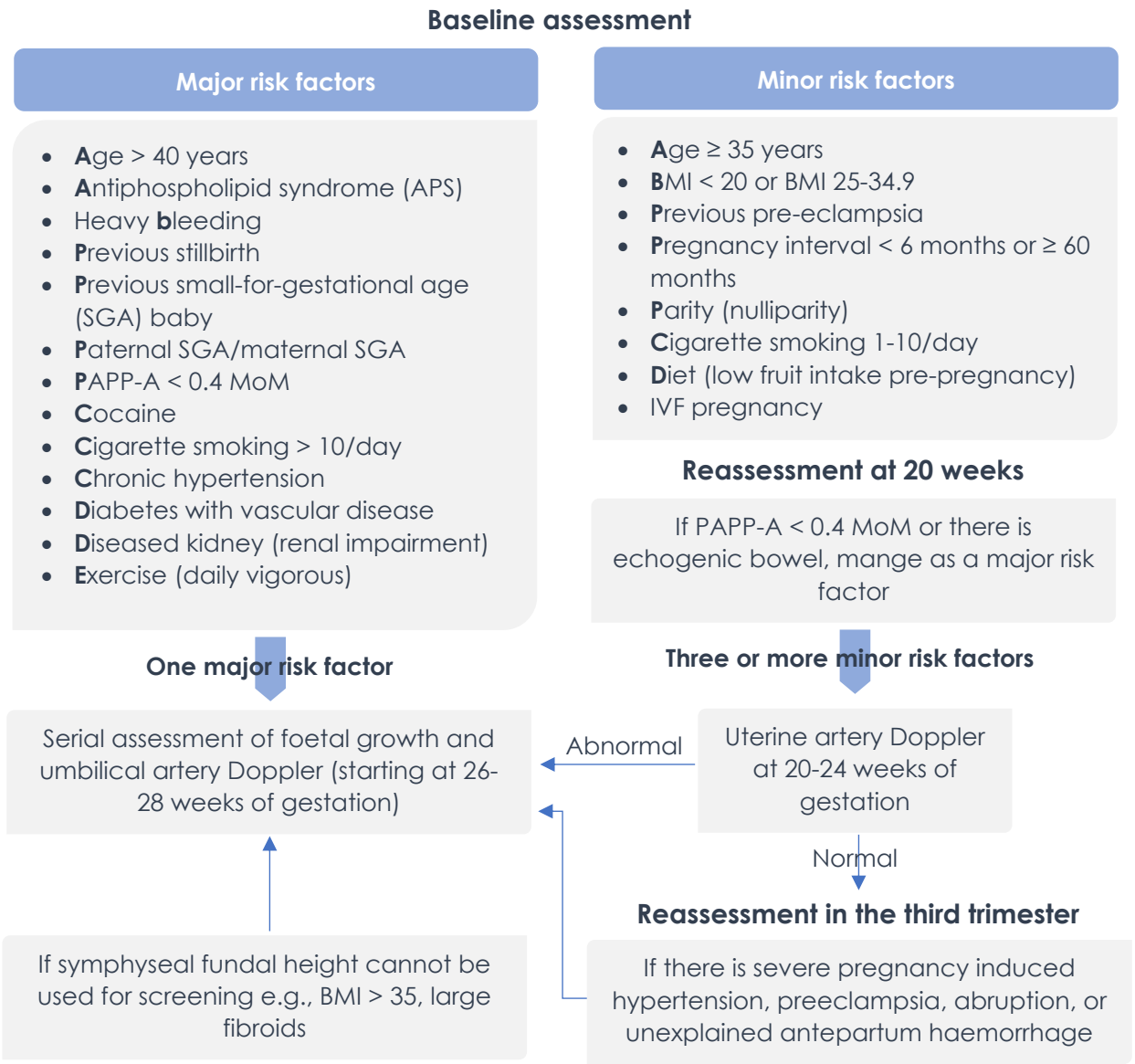
- Risk of stillbirth
- Risk of birth hypoxia
- Risk of neonatal complications & impaired neurodevelopment

**Remote**

- Type 2 (non-insulin-dependent) diabetes in adult life
- Hypertension in adult life

Poor outcome is related to SGA fetuses caused by FGR rather than other cases

## Assessment of high-risk population



## Assessment of low-risk population

- **Symphyseal fundal height (SFH):**
  - SFH is used to screen foetal growth in all low-risk women during antenatal care visits
  - SFH should be plotted on a customized chart, rather than population-based chart, should be considered to improve prediction of SGA neonates
  - If SFH is below the 10$^{th}$ percentile or if it is slow or static over time, ultrasound is indicated
  - SFH may not be feasible in women with body mass index > 35, large fibroids, or polyhydramnios. In this case, foetal growth should be monitored with serial growth ultrasound

- **Ultrasound:**
  - If estimated foetal weight (EFW) or abdominal circumstance (AC) is less than the 10$^{th}$ percentile using customized charts, serial growth ultrasound with umbilical artery Doppler should be performed
  - If ultrasound is serially performed, EFW or AC should be measured at least 3 weeks apart
  - Uterine artery Doppler has a limited role in predicting perinatal outcomes in the third trimester

## Investigations

- **Assessment of the cause:**

  Early onset foetal growth restriction (FGR) "before 23 weeks":
  - Refer to foetal medicine
  - Detailed anatomy scan to rule our structural abnormalities
  - Karyotyping should be considered if there is severe FGR in the presence of normal uterine Doppler
  - Serology testing of cytomegalovirus and toxoplasmosis (± malaria and syphilis in high-risk population) if FGR is severe

- **Foetal surveillance:**

| Method | Assessment |
|---|---|
| **Umbilical artery (UA) Doppler** | ▪ This is the primary tool to reduce perinatal morbidity and mortality in foetuses with FGR<br>▪ It is performed every 2 weeks (1 week if FGR is severe)<br>▪ If UA Doppler is abnormal (pulsatility index [PI] or resistance index [RI] > 2 standard deviations [SD]):<br>□ Ductus venosus (DV) Doppler is performed to time delivery<br>□ If end-diastolic flow is present, it should be repeated twice weekly<br>□ If end-diastolic flow is absent/reversed, it should be repeated daily |
| **Cardiotocography (CTG)** | It is not used alone for foetal surveillance |
| **Amniotic fluid (AF) assessment** | It is not used alone for foetal surveillance. Deep vertical pocket (DVP) is measured |
| **Biophysical profile (BPP)** | Use of BPP is not recommended in women with preterm FGR |
| **Middle cerebral artery (MCA) Doppler** | ▪ It has limited role in foetuses with preterm FGR<br>▪ In foetuses with term FGR, if UA Doppler is normal, MCA Doppler has moderate predictability of acidosis at birth if abnormal (< 5%) and is used to time delivery |

## Prevention

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- Low dose aspirin in women at high risk of preeclampsia may prevent SGA at or before 16 weeks of gestation
- Smoking cessation should be considered
- Anti-thrombotic therapy may yield promising results. However, there is insufficient evidence to support its use and it is associated with serious side effects
- There is no role for diet modifications, calcium or progesterone supplementation

## Management

Symphyseal fundal height < 10th percentile or high risk for FGR

**Foetal biometry**

If AC or EFW is below the 10th percentile, or growth pattern is consistent with FGR

**UA Doppler**

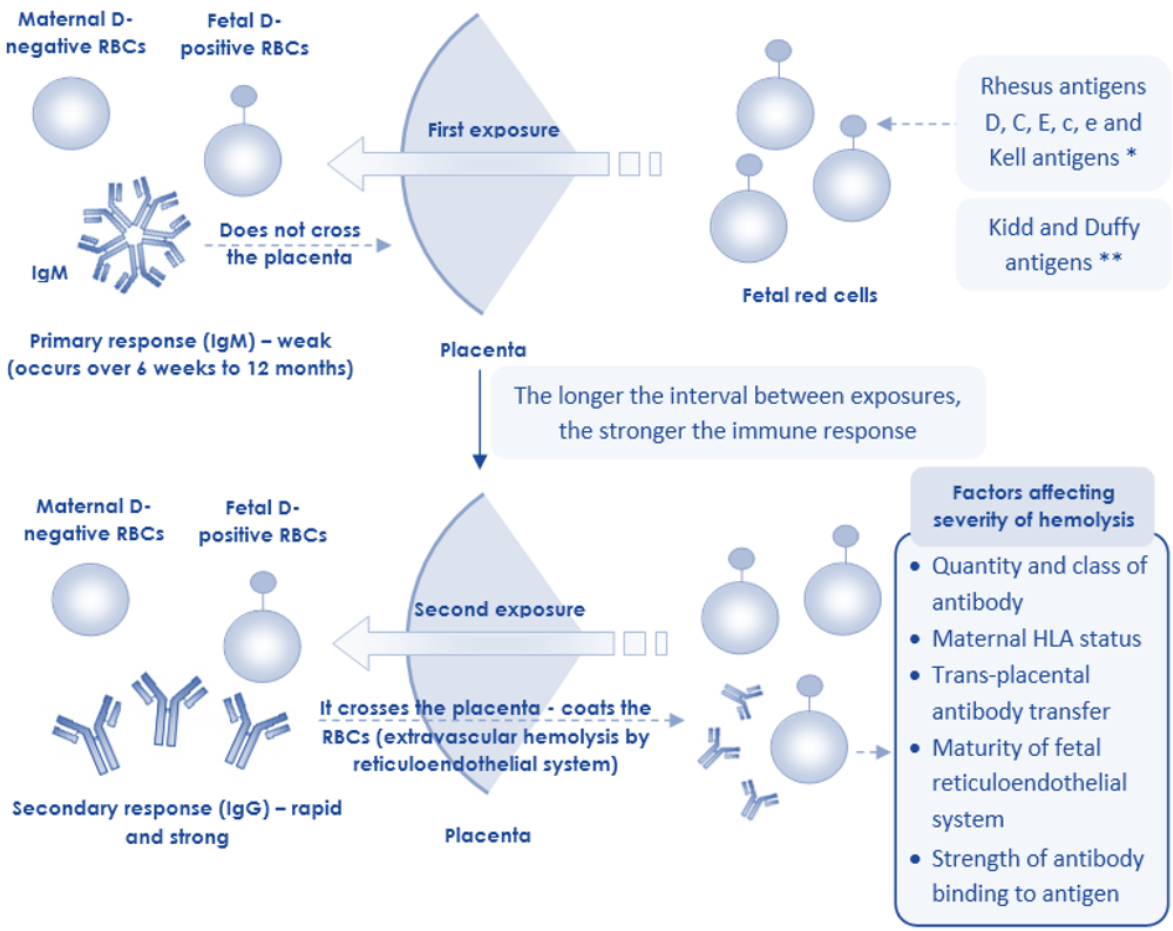
| Normal | EDV present, PI or RI > 2 SDs | Absent or reversed EDV |
|---|---|---|
| Repeat ultrasound every 2 weeks including AC, EFW, UA Doppler, and MCA Doppler (after 32 weeks) | Repeat ultrasound every week including AC and EFW. Twice weekly UA Doppler | Repeat ultrasound every week including AC and EFW. Daily UA, DV Doppler and CTG |
| **Delivery**<br>Offer delivery by 37 weeks (after involving a senior clinician)<br>Recommend delivery at 37 weeks if MCA Doppler PI < 5th centile<br>Consider delivery after 34 weeks if growth is static over 3 weeks<br>Recommend steroids before CS | **Delivery**<br>Recommend delivery at 37 weeks<br>Consider delivery after 34 weeks if growth is static over 3 weeks<br>Consider steroids before CS | **Delivery**<br>Recommend delivery before 32 weeks after completion of steroid course (if gestational age is ≥ 24 weeks and EFW > 500 gram)<br>Recommend delivery by 32 weeks<br>Consider delivery at 30-32 weeks if DV is normal as well |

EDV = End diastolic velocities, CS = Caesarean section

# Red Cell Alloimmunization

## Background

- Incidence of red cell antibodies is 1.2%. Incidence of significant antibodies is 0.4%
- There are no long-term complications to red cell alloimmunization in the mother
- Children to mothers with red cell alloimmunization are at risk of persistent anaemia for few weeks. Anaemia may be delayed in onset



## Antenatal assessment

Women with red cell antibodies who are at risk of fetal anemia or who may have difficulty with availability of compatible blood in case transfusion is indicated

**Pre-pregnancy counseling (but not screening)**

**Screen for alloantibodies at booking appointment and at 28 weeks**

If maternal antibodies (D, C, c, E, e, K) are present

Non-invasive foetal genotype are tested. For other antigens, invasive testing is indicated if there is risk of foetal anaemia

**OR**

Test paternal genotype, if heterozygous, test foetal genotype, if homozygous, consider the foetus at risk

Non-invasive genotype (cell free foetal DNA) is done at 16 weeks for all antigens except K which is done at 20 weeks. If non-conclusive, management is either by repeating the test, considering invasive procedures or manage is as high risk

Invasive testing is not contraindicated if there is alloimmunization

**High risk foetus**

Check antibodies every 4 weeks till 28 weeks of gestation then every 2 weeks till delivery

- If anti-D titre:
  - Moderate risk > 4 - < 15 iu/ml
  - High risk > 15 iu/ml
- If anti-C titre:
  - Moderate risk > 7.5 - < 20 iu/ml
  - High risk >20 iu/ml
- If anti-K Abs:
  Refer immediately regardless of titre
- Anti-E potentiates anti-C:
  Therefore, refer at a lower titre

**Refer to fetal medicine**

- If there are ultrasound finding suggestive of foetal anaemia
- If there is a history of unexplained severe neonatal jaundice or neonatal anaemia requiring transfusion or exchange transfusion
- If there is a history of haemolytic disease of newborn, intrauterine transfusion, or a titre ≥32

**Assessment of risk of haemolytic disease of the fetus and newborn (HDFN)**

Assessment of risk of HDFN is determined by the cause of alloimmunization, past history and prior pregnancy outcomes

If antigens are present, antibody titre is high (see before), or anti-K antibodies are present

If there is history of alloimmunization if a prior pregnancy

Weekly middle cerebral artery peak systolic velocity (MCA-PSV) doppler and ultrasound

If MCA-PSV > 1.5 MOM or there are other signs of anaemia

Intervention (Foetal blood sampling and possible intrauterine transfusion)

**Intrauterine transfusion**

- Group O or identical blood group is used
- It should be negative for antigens that correspond to antibodies

Plasma is removed (increasing hematocrit to 0.7 -0.85)
Blood is irradiated

Foetal blood sampling is associated with 1-3% risk of foetal loss

## Maternal care

Women with alloantibodies and at high risk of transfusion e.g. women with sickle cell anemia and placenta praevia

Blood Crossmatch at least every week

If blood is needed, transfuse blood of the same ABO and Rh group, K and CMV negative

## Intrapartum management

- **Mode of delivery:**
  Mode of delivery is guided by obstetric indications

- **Timing of delivery:**
  It depends on antibody titre, foetal status and need for intervention. If antibody titre is stable with no complications, delivery is scheduled at 37-38 weeks

- **Place of delivery:**
  Women at high risk of transfusion should be delivered in specialized centres

- **Intrapartum measures:**
  - Continuous electronic foetal monitoring is indicated
  - In women with significant antibodies (e.g. anti-D, anti-c, anti-c + anti-E, anti-K) cord blood should be checked for haemoglobin, bilirubin and direct antiglobulin test is done
  - If women with red cell antibodies who need urgent blood transfusion, transfusion of ABO negative, Rh negative, and K-negative (without matching other antibodies) is considered after weighing risk and benefits of this decision

## Neonatal management

- Observe/Follow-up anaemia (haemoglobin), jaundice (bilirubin), and neurobehavioral status
- Early discharge is not recommended
- Encourage breastfeeding (reduces dehydration and risk of jaundice)
- transfusion exchange or phototherapy is considered if bilirubin level becomes high or increasing

### Neonatal exchange transfusion

Given blood should be:

- ABO compatible with the neonate and mother (cross-matched)
- CMV negative and K negative.
- Stored no more than 5 days
- Plasma reduced (Haematocrit is 0.5-0.6)

### Neonatal small value transfusion

Given blood should be:

- ABO compatible with the neonate and mother
- Stored no more than 35 days
- No need to be irradiated (unless there is prior intrauterine transfusion)
- Plasma not reduced

# Reduced Foetal Movements

## Background

**Definition**

Fetal movements should be defined as maternal perception of any discrete kick, flutter, swish or roll.

**Significance**

- Normal perception of fetal movement ensures integrity of the central nervous and musculoskeletal systems.
- Abnormal perception of fetal movement (reduced or absent): may be a warning sign of fetal death (55%). This is significant up to and including the onset of labor.

**Influencing factors**

- **Maternal position:** women may perceive most fetal movements when lying down, fewer when sitting and fewest when standing.
- **Placental position**: an anterior placenta may decrease woman's perception of fetal movements (< 28 weeks).
- **Fetal position** (not presentation): women with anteriorly laid fetal spines may perceive fetal movement less (80% of cases of absent fetal movement despite good fetal movement during ultrasound exam).
- **Sedating drugs:** e.g. alcohol, benzodiazepines and other opioids (transient effect).
- **Blood glucose:** increase in fetal movements following the elevation of glucose concentration in maternal blood (controversial)
- **Carbon dioxide (smoking):** it may be associated with reduced fetal movement and influences fetal respiratory movements (after 30 weeks of gestation).
- **Antenatal corticosteroids:** they may decrease fetal movement and fetal heart rate variability over the 2 days following administration.
- **Major malformations:** e.g.
  - **Anencephaly:** normal or excessive fetal activity.
  - **CNS or musculo-skeletal abnormalities**: a lack of vigorous motion

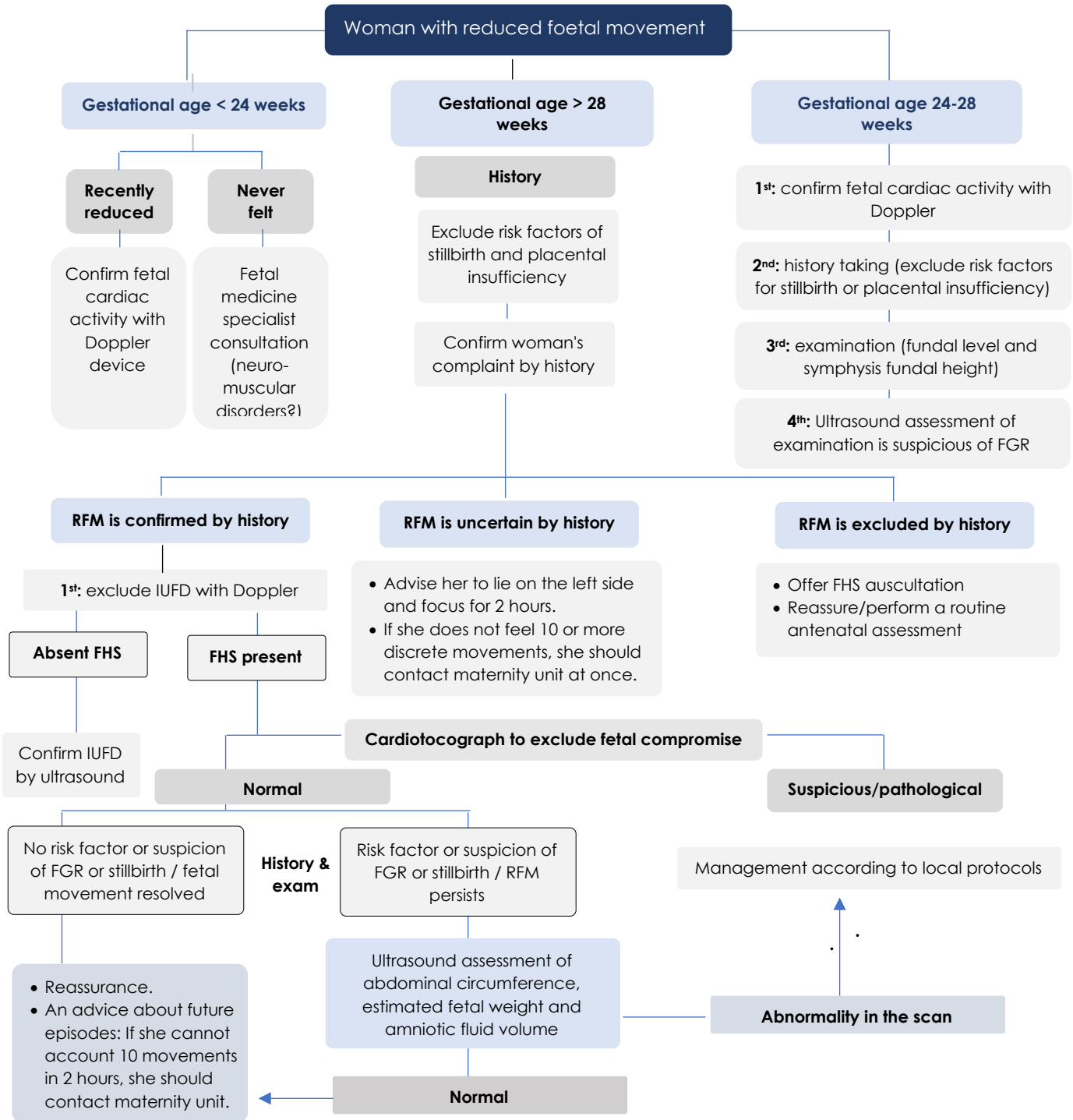
**Normal pattern**

- **Timing of first perception:** between 18 and 20 weeks of gestation (some multipara perceive as early as 16 weeks, some nullipara perceive after 20 weeks).
- **Progress of fetal movement:** The number tends to increase until the 32nd week then to plateau thereafter.
- **Frequency of fetal movement:**
  - The average number at term is 31 (16 - 45) per hour. The longest period between movements is 50 to 75 minutes.
  - The time for counting 10 movements varies between 21 minutes (focused counting) and 162 minutes (unfocused counting).

**Diurnal Variations**

- Diurnal variation is observed as early as 20 weeks of gestation. It is peak in the afternoon and evening periods (may be due to concentration).
- Fetal sleep cycles occur regularly throughout the whole day (20–40 minutes for each, rarely exceed 90 minutes).

## Approach


Woman with reduced foetal movement
Gestational age < 24 weeks
Gestational age > 28 weeks
Gestational age 24-28 weeks
Recently reduced
Never felt
Confirm fetal cardiac activity with Doppler device
Fetal medicine specialist consultation (neuro-muscular disorders?)
History
Exclude risk factors of stillbirth and placental insufficiency
Confirm woman's complaint by history
1st: confirm fetal cardiac activity with Doppler
2nd: history taking (exclude risk factors for stillbirth or placental insufficiency)
3rd: examination (fundal level and symphysis fundal height)
4th: Ultrasound assessment of examination is suspicious of FGR
RFM is confirmed by history
RFM is uncertain by history
RFM is excluded by history
1st: exclude IUFD with Doppler
Absent FHS
FHS present
Confirm IUFD by ultrasound
Advise her to lie on the left side and focus for 2 hours.
If she does not feel 10 or more discrete movements, she should contact maternity unit at once.
Offer FHS auscultation
Reassure/perform a routine antenatal assessment
Cardiotocograph to exclude fetal compromise
Normal
Suspicious/pathological
No risk factor or suspicion of FGR or stillbirth / fetal movement resolved
History & exam
Risk factor or suspicion of FGR or stillbirth / RFM persists
Management according to local protocols
Reassurance.
An advice about future episodes: If she cannot account 10 movements in 2 hours, she should contact maternity unit.
Ultrasound assessment of abdominal circumference, estimated fetal weight and amniotic fluid volume
Abnormality in the scan
Normal

## History

- **Analysis and confirmation of RFM:**
  - Is it reduced or absent?
  - The duration: for how long RFM is observed?
  - Is it the first occasion or recurrent?
- **Risk factors of stillbirth:**
  - Extremes of maternal age.
  - Primiparity.
  - Racial/ethnic factors.
  - Obesity and smoking.
  - Known FGR, hypertension, diabetes, placental insufficiency.
  - Recurrent RFM.
  - Congenital malformation.
  - Poor obstetric history (e.g.FGR and stillbirth).
  - Genetic factors.
- **Risk factors of fetal growth restriction**

## Examination

- **Assessment of blood pressure (and proteinuria):** Pre-eclampsia is associated with placental dysfunction.
- **Auscultation of fetal heart:**
  - Auscultation of the fetal heart using a handheld Doppler device is made to exclude fetal death.
  - The fetal heartbeat is differentiated from the maternal heartbeat by the following:
    - The difference between the fetal heart rate and the maternal pulse rate.
    - Ultrasound assessment of fetal cardiac activity in case of doubt.
- **Assessment of fetal size (SGA):**
  - Clinical detection of SGA fetuses is done by:
    - Abdominal palpation.
    - Measurement of symphysis–fundal height (customized fundal height chart is recommended by RCOG).
    - Ultrasound biometry (particularly when clinical examination is difficult e.g. increased body mass index.

## Investigations

- **Cardiotocograph (CTG):**
  - **Indication**: when history confirms RFM after 28 weeks and Doppler device confirms fetal viability.
  - **The procedure:** CTG monitoring is made initially for at least 20 minutes, computer systems for interpretation of CTG are more accurate than clinical experts.
  - **Normal findings:** The presence of a normal fetal heart rate pattern (fetal heart rate accelerations coinciding with fetal movements) indicates a healthy fetus.
  - **Abnormalities:** No acceleration for more than 80 minutes suggests fetal compromise.

- **Ultrasound assessment:**
  - ***Indication:*** Ultrasound scan assessment in indicated in women with RFM after 28 weeks of gestation if:
    - RFM persists despite a normal CTG or
    - Any additional risk factors for FGR/stillbirth.
  - ***Timing:*** If indicated, it should be performed within 24 hours of initial assessment.
  - ***Procedure:***
    - Assessment of abdominal circumference and/or estimated fetal weight to detect the SGA fetus.
    - Assessment of amniotic fluid volume.
    - Assessment of fetal morphology (if not previously performed). This should be accepted by the woman.

- ***Combined CTG and ultrasound*** are recommended within 2 hours (if women reported no fetal movements) and within 12 hours (if they reported RFM).

- **The biophysical profile (BPP):** the rule of BPP in these cases is controversial.

## Recurrent DFM

Women with recurrent RFM episodes (2 or more) are at increased risk of a poor perinatal outcome (stillbirth, FGR or preterm birth). Ultrasound assessment is essential for evaluation of these cases.

# Polyhydramnios

## Background

- Polyhydramnios refers to the presence of excessive amniotic fluid
- Amniotic fluid increases gradually from the onset of pregnancy till 33 weeks, plateaus between 33 and 38 weeks and starts to decline thereafter
- 50-60% of cases have no identifiable cause. However, perineal mortality increases 2-5 times even if no cause is found

## Causes

| Maternal causes | Foetal causes | Placental causes |
|---|---|---|
| • Uncontrolled diabetes<br>• Rh isoimmunization (causing foetal hydrops)<br>• Drug exposure (lithium causes foetal nephrogenic diabetes insipidus) | • Structural anomalies e.g. oesophageal atresia<br>• Chromosomal abnormalities<br>• Infection e.g. parvo virus, TORCH infection<br>• Foetal tumours e.g. cervical teratoma, neuroblastoma<br>• Macrosomia | • Chorioangioma<br>• Metastatic neuroblastoma |

## Assessment

- Diagnosis is made via ultrasound. Measurement of amniotic fluid is made by the deepest vertical pocket (DVP) if the 4 abdominal quarters. The pocket should be limb free and cord free to take an accurate measurement. Alternatively, amniotic fluid index (AFI) is measured
- Polyhydramnios is diagnosed if DVP is ≥ 8 cm or AFI is ≥ 25
- Once the diagnosis is made, further investigations are made to determine the cause

| | Assessment | Action |
|---|---|---|
| **Foetal causes** | • Foetal anomalies<br>• Foetal movement (ruling out arthrogryposis)<br>• Foetal growth and weight | Urgent referral to foetal medicine if there is concern on foetal anomalies, aneuploidy infection, movement, or growth restriction |
| **Maternal causes** | • Red cell antibodies<br>• TORCH infection, parvovirus<br>• Fasting glucose, HBA1C, glucose tolerance test | Referral to foetal medicine |

## Classification

| | |
|---|---|
| **Mild** | AFI equals 25 to 29.9 cm |
| **Moderate** | AFI equals 30 to 34.9 cm |
| **Severe** | AFI is ≥ 35 cm |

## Complications

- Preterm labour (cervical shortening is assessed, and antenatal steroids onsidered)
- Unstable lie and malpresentation
- Cord prolapse
- Antepartum haemorrhage
- Postpartum haemorrhage
- Higher risk of operative delivery

## Antepartum management

Mild polyhydramnios likely resolves spontaneously and is not associated with higher risk of adverse outcomes except those related to associated macrosomia. Women with severe polyhydramnios may require further treatment

- **Amnioreduction:**
  - **Indications:**
    ① Relieving respiratory symptoms
    ② Reducing the risk of preterm labour if marked cervical shortening is observed
  - **Procedure:**
    - Slow technique (using 50 ml syringe)
    - Rapid technique (using vacuum assisted drainage system)
  - **Target:**
    The procedure should be stopped once symptoms are relieved and AFI is less than 25
  - **Complications: (1.5%)**
    - Preterm labour
    - Rupture of membranes
    - Chorioamnionitis
    - Placental abruption

- **Indomethacin (COX inhibitor) and sulindac (selective COX-2 inhibitor):**
  It should only be performed under strict specialist supervision. Risks associated with these medications are:
  - Gestational age dependent ductus arteriosus closure
  - Impairment of foetal renal function

## Intrapartum management

- Polyhydramnios itself is not an indication of induction of labour
- Close monitoring and anticipation of shoulder dystocia should be considered given the associated risk of macrosomia
- Amniotomy is recommended in the theatre (controlled amniotomy)
- Immediately after delivery, postpartum haemorrhage should be anticipated and actively managed
- A thorough examination of the baby for anomalies should be considered. Upper gastrointestinal patency can be checked by passage of a nasogastric tube

## Outcomes

- In the presence of structural anomalies, mortality risk is 60% versus 4% if no anomalies are detected
- Cases that have no aberrant anomalies may have undiagnosed disorders e.g. Bartter syndrome, West syndrome

# Intrauterine Fetal Death

## Definitions

- **Intrauterine foetal death (IUFD):** babies with no signs of life in utero.
- **Stillbirth:** a baby delivered with no signs of life and is died after 24 completed weeks of pregnancy. One third of stillbirths are small for gestational age fetuses and half are being unexplained.

## Causes

**I. Causes of intrauterine death**

**Maternal**

Maternal diseases e.g. pre-eclampsia and DM

**Foetal**

**Chromosomal anomalies (6%)**

**Trans-placental infection**

- Listeria.
- Cytomegalovirus, parvovirus B19, rubella, herpes simplex, coxsackie.
- Syphilis, leptospira, Q fever, and Lyme disease.
- Toxoplasmosis, malaria parasitemia

**Congenital infection**

**Ascending infection**

- Escherichia coli, Klebsiella.
- Hemophilus influenza.
- Group B Streptococcus, Enterococcus.
- Mycoplasma/ureaplasma
- Chlamydia

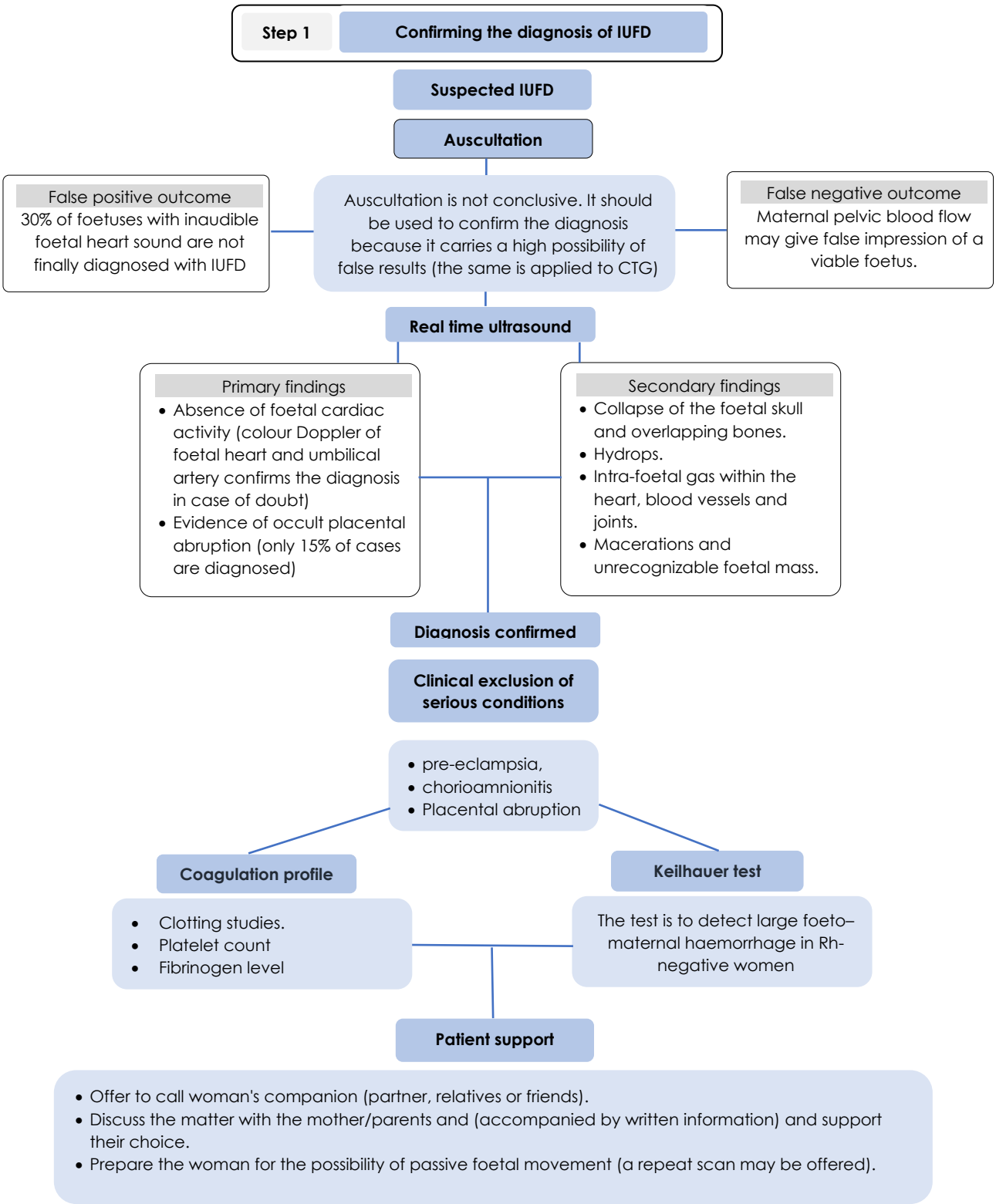
**Combined**

Foeto-maternal causes (antepartum haemorrhage)

**II. Causes of intra-partum death**

- Placental abruption
- Maternal and foetal infection.
- Cord prolapse
- Idiopathic hypoxia–acidosis.
- Uterine rupture.

## Approach

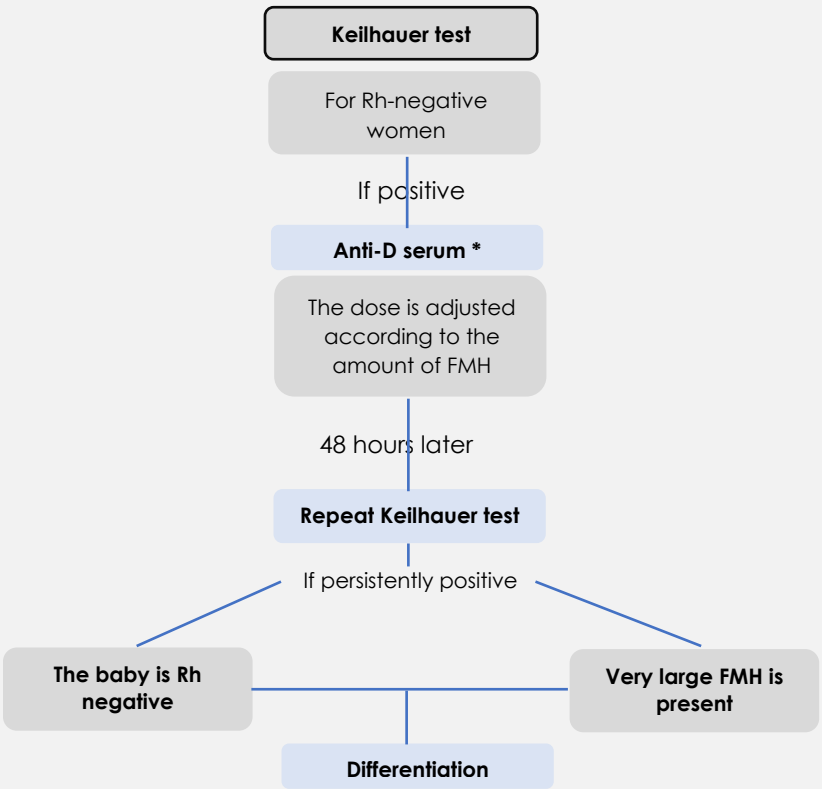

Step 1
Confirming the diagnosis of IUFD
Suspected IUFD
Auscultation
False positive outcome
30% of foetuses with inaudible foetal heart sound are not finally diagnosed with IUFD
Auscultation is not conclusive. It should be used to confirm the diagnosis because it carries a high possibility of false results (the same is applied to CTG)
False negative outcome
Maternal pelvic blood flow may give false impression of a viable foetus.
Real time ultrasound
Primary findings
• Absence of foetal cardiac activity (colour Doppler of foetal heart and umbilical artery confirms the diagnosis in case of doubt)
• Evidence of occult placental abruption (only 15% of cases are diagnosed)
Secondary findings
• Collapse of the foetal skull and overlapping bones.
• Hydrops.
• Intra-foetal gas within the heart, blood vessels and joints.
• Macerations and unrecognizable foetal mass.
Diagnosis confirmed
Clinical exclusion of serious conditions
• pre-eclampsia,
• chorioamnionitis
• Placental abruption
Coagulation profile
• Clotting studies.
• Platelet count
• Fibrinogen level
Keilhauer test
The test is to detect large foeto–maternal haemorrhage in Rh-negative women
Patient support
• Offer to call woman's companion (partner, relatives or friends).
• Discuss the matter with the mother/parents and (accompanied by written information) and support their choice.
• Prepare the woman for the possibility of passive foetal movement (a repeat scan may be offered).

## Coagulation profile

- **Rationale:**
  The risk of DIC after IUFD is 10% within 4 weeks and up to 30% after 4 weeks. The risk is higher with maternal sepsis, placental abruption and pre-eclampsia (cause of IUFD).
- **Frequency:**
  Tests are repeated twice weekly if the patient is managed expectantly.

## Keilhauer test

- **Rationale:**
  It is used to identify large foeto–maternal haemorrhage (FMH) either as a cause or because of IUFD.
- **The immunization approach:**




① Foetal blood grouping using foetal or cord blood

② Free foetal DNA (ffDNA) from maternal blood sample (should be taken shortly after birth)

*Anti-D serum should be given within 72 hours of FMH. However, it is still of some value up to 10 days of the accident. It should be considered that FMH may have occurred days before the diagnosis of IUFD.

**Step 2** **Investigating the cause of IUFD**

**I** **Maternal investigations**

**Standard laboratory tests**

- **Haematology:** platelet count is particularly important in pre-eclampsia and DIC.
- **Chemistry:** it identifies end organ failure in women suffering from sepsis or haemorrhage.
- **Bile salt:** for diagnosis of obstetric cholestasis.

**Keilhauer test**

- **Rationale:** diagnosis of large FMH as a cause of IUFD.
- **Timing:** it should be before birth before foetal RBCs are cleared from the circulation.

**Maternal bacteriology**

- **Indications:**
  Indicated only if there is suspicion of chorioamnionitis including:
  - Maternal fever and flu-like symptoms.
  - Purulent offensive vaginal discharge.
  - Prolonged rupture of membranes before IUFD.
- **The tests:** Blood culture, midstream urine, cervico-vaginal swab.

**Maternal serology**

- **Indications:**
  Indicated for the diagnosis of occult maternal–foetal infection:
  - ***Routinely for all women:*** Parvovirus B19 (hydrops in not necessary), CMV, herpes simplex and Toxoplasma gondii.
  - **For women who are non-immune at booking:** screening for rubella.
  - **For women who are investigated for syphilis at booking:** Treponemal serology.
  - **For women who travelled to endemic areas e.g. Africa:** Malaria.

**Maternal endocrinology**

- **Diabetes mellitus:**
  - ***Maternal random blood glucose:*** for diagnosis of occult diabetes (gestational diabetes may be missed as blood glucose returns to normal few hours after IUFD)
  - ***Maternal HbA1c:*** for diagnosis of gestational diabetes mellitus (gestational diabetes can be also missed because most women have normal HbA1c).
- **Thyroid disease:**
  TSH, FT4 and FT3 are assessed for diagnosis of occult maternal thyroid disease.

**Maternal thrombophilia**

- **Indications:**
  Indicated if there is evidence of foetal growth restriction or placental disease.
  However, the association is weak and further considerations in next pregnancy are still doubtful.
- **Protocol:**
  If the tests are positive, it should be repeated after 6 weeks.

**Maternal thrombophilia**

| *Test* | Indication | Conclusion |
|---|---|---|
| **Anti-red cell antibody serology** | If there is evidence of foetal hydrops | Diagnosis of immune haemolytic disease |
| **Maternal anti-Ro and anti-La antibodies** | If there is evidence of hydrops, endomyocardial fibro-elastosis or AV node calcification (post-mortem examination). | Diagnosis of occult maternal autoimmune disease |
| **Maternal alloimmune antiplatelet antibodies** | If foetal intracranial haemorrhage (post-mortem examination). | Diagnosis of alloimmune thrombocytopenia |

**Maternal urine (metabolites)**

Maternal urine is examined for cocaine metabolites (after consent) if there is suggestive data of occult drug use.

## II Parental investigations

**Parental karyotyping**

- **Indications:**
  - ***If post-mortem examination*** reveals foetal abnormality.
  - ***If foetal genetic testing*** reveals foetal unbalanced translocation or aneuploidy e.g. 45X (Turner syndrome).
  - ***If history is suggestive of aneuploidy (no or failed genetic testing):*** e.g. previous unexplained IUFD, recurrent miscarriage.
- **Conclusion:** Diagnosis of parental balanced translocation and parental mosaicism.

## III Foetal/placental investigations

**Foetal and placental microbiology**

- Under clean conditions, cord or better cardiac blood (consent required) is obtained. Lithium heparin is added.
- This test is more informative than maternal serology in the diagnosis of viral infections.

**Foetal and placental Karyotyping**

Karyotyping helps to diagnose aneuploidy and single gene disorders. This helps in:
- Identification of the cause of IUFD.
- Testing in future pregnancies because some anomalies are possibly recurrent.

This can be achieved by: Tissue culture or QF-PCR

**Post-mortem**

- Parents should be offered post-mortem examination to possibly identify the cause of an IUFD, but they should never be persuaded.

## Delivery

### I Management of labour

#### Time of delivery

**Immediate versus delayed delivery**

**Immediate**

This is indicated in the following conditions:

- Sepsis.
- Preeclampsia.
- Placental abruption.
- Membrane rupture.
- Evidence of DIC.

**Delayed**

**Short delay (48 hours)**
This delay is acceptable. No harm is expected.

**Prolonged delay**
If the woman chooses to be managed conservatively, she should have a 24-hour contact number

**Advantage**
85% of women with IUFD delivers spontaneously within 3 weeks of IUFD

**Disadvantages**
The risk of DIC (see before).
The value of post-mortem is reduced.
Deterioration of foetal appearance.

These points should be covered clearly while counselling the woman for delivery.

#### Mode of delivery

Some women → **I. Caesarean section**

- There is an indication of CS.
- If requested, vaginal delivery of IUFD is emotionally stressful in 47% of women compared with 7% under normal circumstances.

Most women → **II. induction of labour**

90% of women deliver within 24 hours of induction of labour

**Facilities for IUFD labour**

- Facilities for emergency care.
- A special labour wardroom for uncomplicated IUFD (away from the sound of babies) with c nursing team trained to care with these women.
- A double bedroom for the woman and her companion.
- Delivery by experienced midwife

**Intrapartum antibiotic therapy**

- IV broad-spectrum antibiotic therapy (including Chlamydia) is indicated in sepsis.
- Antibiotics are not given routinely or in GBS colonized women.
- Pyrexia secondary to prostaglandin use should be considered and misinterpreted as infection.

**Pain relief during labour**

- Diamorphine is recommended (in preference to pethidine).
- Regional anaesthesia can be offered. However, sepsis and DIC should be excluded before the procedure is offered (sepsis is associated with epidural abscess, DIC is associated with epidural and subdural hematoma).

**Induction regimens for women with IUFD**

**Women with unscarred uterus**

**Mifepristone 200mg single dose ***
**PLUS**

**< 26 weeks**



**100 µg 6 hourly of misoprostol**

**> 26 weeks**



**25–50 µg 4-hourly of misoprostol**

**Misoprostol vs. prostaglandin E2**
Misoprostol is a better choice (less cost, equal safety and efficacy).
**Intra-vaginal misoprostol vs. IV oxytocin**
Misoprostol is more effective than oxytocin.
**Vaginal versus oral misoprostol**
Vaginal misoprostol yields the same efficacy but with less side effects (nausea, vomiting, diarrhea, pyrexia)

**Women with previous 2 CS**

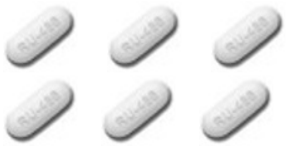
**The risk of induction is slightly higher than in women with previous 1 CS**

**Women with > previous 2 CS**

**The safety of induction is unknown in these women**

Women with previous CS should be monitored for the signs of scar dehiscence (maternal tachycardia, atypical pain, vaginal bleeding, haematuria, and maternal collapse). The decision of oxytocin augmentation is made by the consultant

**Previous 1 lower segment caesarean section (CS)**



**Mifepristone 200mg 3 times for 2 days or 600mg once for 2days ****

**OR**

**Trans-cervical balloon catheter (restricted to clinical trials)**

**Advantages**
- 79% of women achieve vaginal birth.
- Uterine rupture rate (0.58%) is lower than with prostaglandins (like spontaneous labour)

**Disadvantages**
- There is increased risk of ascending infection in the presence of IUFD.

**OR**

**Misoprostol**

NICE recommends the use of lower doses (25–50 µg) for previous CS

**Positives**
No evidence of an increased rate of hysterectomy or maternal death.
Foetal distress risk is of no rule here

**Negatives**
Higher risk of endometritis, blood transfusion and scar dehiscence and rupture (0.7%)

* Mifepristone (when added to misoprostol) reduces the time interval for labour by about 7 hours.
** This regimen increases the chance of labour within 72

## II Postpartum management

**Hospital stay**

- Unless there is associated critical condition that necessitates special care e.g. pre-eclampsia, sepsis, DIC, a woman can return home immediately.
- If a woman does not want to return home immediately, adequate privacy should be provided to the woman with complete separation from the maternity unit.

**Thrombo-prophylaxis**

- IUFD is not a risk factor for thromboembolism. However, many causative conditions (e.g. infection, maternal disease) are themselves risk factors. Assessment of risk should be done according to the usual guidelines.
- Haematological consultation may be necessary if heparin thromboprophylaxis is indicated in a patient with DIC.

**Suppression of lactation**

- **Dopamine agonists:** (90% effective).
  - ***Bromocriptine:*** 2.5 mg twice daily for 14 days.
  - ***Cabergoline:*** 1 mg (a simpler regimen, less rebound activity and side effects than bromocriptine).

  NEVER give these drugs to women with hypertension (including pre-eclampsia) because they may increase blood pressure and may be associated with intracerebral haemorrhage.
- **Other options:** non-pharmacological methods (e.g. support brassière, ice packs and analgesics) and oestrogen are not proper choices for their uncertain effectiveness and adverse effects.

**Fertility - contraception**

- The woman should be counselled about future fertility and contraception choice before leaving the hospital.
- As a health care provider, you should be aware of these 2 points:
  - Early conception following foetal loss experience may predispose to psychological problems.
  - In these women, ovulation may return rapidly (as early as 18 days) due to suppression of lactation and they may conceive before their first menstrual period.

**Psychological support**

- The psychological impact of these women greatly varies but they are generally liable to postnatal depression and post-traumatic stress disorder. There is also 40% higher risk of parental relationship dissolving.
- Accordingly, offer counselling to the woman, her partner and consider family members in this counselling. Advise couples about support groups.

**Follow up**

**Time and frequency of visits**

There is optimal schedule, but the results of different investigations should be available (usually 6-8 weeks)

**Follow up (cont.)**

**Place of visits**

Generally, home visits are not superior to clinical visits. However, it should be offered if possible when the woman finds it distressing to return to the place where she delivered.

**Content of visits**

- **First:** Discuss the results of previous investigations and the possible cause of IUFD. Give information about the chance of recurrence and if applicable, how to avoid further loss.
- **Second:** Discuss delay of conception. The parents should be advised that delaying conception can give time for possible psychological sequences of IUFD to recover. However, both early pregnancy and delayed pregnancy can evoke anxiety.
- **Third:** Offer a pre-pregnancy advice regarding smoke cessation and optimization of body mass index (BMI). A documented plan for the next pregnancy should be agreed in this set.

## III Management in next pregnancy

**During pregnancy**

- Clear documentation of risk (previous IUFD).
- Women with a previous unexplained IUFD should be offered:
  - Obstetric antenatal care.
  - Screening for gestational diabetes.
- Women with previous IUFD (apparently normal but SGA) should be offered serial ultrasound assessment of growth.

**During labour**

- Woman with previous unexplained IUFD should deliver in specialist maternity unit.
- Woman with previous nonrecurrent cause of IUFD requires individual evaluation to choose for the place of birth.
- Scheduled birth should consider the gestational age of the previous IUFD, previous intrapartum events and induction of labor safety.

**After labour**

- After birth, women are at risk of depression. Risk factors for depression include:
  - Depression in the third trimester (risk extends up to 1 year after birth).
  - Women who conceive within < 12 months from a previous IUFD.
- Maternal bonding can be adversely affected.

## Pregnancy following unexplained stillbirth

Women with a history of stillbirth (as a single risk) have:

- A 12-fold increased risk of intrapartum stillbirth.
- An increased risk of pre-eclampsia and placental abruption.
- An increased risk of gestational diabetes (four times).
- An increased risk of ischemic placental disease, foetal distress, chorioamnionitis, extreme preterm birth and early neonatal mortality.

## Appendix - I Foetal and placental karyotyping

**Written consent**

It is necessary for any foetal samples

**I. Tissue**

1. Tissue sampling is taken from the deep foetal skin, cartilage and the placenta. Obtain several specimens to minimize the risk of failure.
2. Preserve in a culture fluid that contains antibiotics to reduce the risk of bacterial contamination (culture failure).
3. Keep culture bottles in the refrigerator away from formalin preservation bottles. They should be thawed slowly before examination.
4. Genetic material should be stored if a single-gene syndrome is suspected.

**Amniocentesis**

A sample from the amniotic fluid may be used in women managed expectantly.

**Disadvantages**
Culture failure rate is ~60% (twice that of other tissues).

**Placental biopsy**

**Technique**
Take approximately 1 cm from the foetal surface near cord insertion (to avoid maternal tissues).

**Advantages**
Placenta is the most viable tissue. It supplies rapid growing cells for tissue culture.

**Disadvantages**
Maternal contamination
Placental pseudo mosaicism

**Cartilage sample**

It is the second choice. However, it is difficult to sample e.g. patella

**Skin sample**

**Technique**
Skin biopsy is taken deep to include underlying muscle (about 1 cm from the upper fleshy part of the thigh).

**If culture fails**

**II. QF-PCR**

Quantitative fluorescent polymerase chain reaction (QF-PCR) can be performed on extracted DNA.

### Tissue culture versus QF-PCR

| Tissue culture | QF-PCR |
|---|---|
| Culture rovides wide range of genetic information (trisomies, monosomies, translocations, major deletions and marker chromosomes). Microdeletions are requested specifically based on postmortem examination findings. | It is reliable (<0.01% failure rate), efficient and cheap for aneuploidies. However, it is unreliable for the detection of translocations and marker chromosomes. |

## Appendix - II Postmortem examination

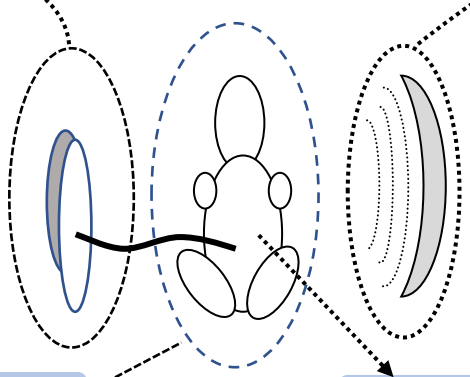
**The consent (cover the following)**

- The purpose of examination.
- The procedure and its extent.
- Possible organ/tissue retention and purpose.

### Methods of postmortem examination

**Placenta/cord**

Pathological examination of the cord/placenta and membranes is recommended (even if not requested).



**Medical**

- **Skeletal X-rays:** can show skeletal defects.
- **MRI:** for the brain and spinal cord (24% adds new information).
- **Ultrasound:** for internal organs (the value is not yet evaluated).

**External examination**

Examiner should report any apparent abnormalities, Weight and height should be reported (consider IUGR).

**Autopsy/microscopy**

Microscopic examination of relevant tissues should be performed (after parent's consent).

### Levels of postmortem examination

The level of postmortem examination goes down according to parent's request. However, the lower the level, the less conclusive the examination.

**Full postmortem examination**
The classic examination in the diagram

**Limited postmortem examination**
Restricted conventional postmortem examination

**Limited postmortem examination**
Minimally invasive examination

**Disadvantages**

- Its value is limited unless there is a specific suspicious organ that the parents agree to be examined.
- It is technically difficult and may need more aggressive dissection than expected by the parents e.g. examination of the heart indicates removal of the lung and the thymus.

**Approach**

- **Minimally invasive surgical methods:** such as transcutaneous tissue biopsy, body-cavity aspiration (less informative).
- **Medical imaging:** ultrasound and magnetic resonance imaging (MRI) are an adjuvant rather than a substitute for conventional postmortem.

# Antenatal Care of Multiple Pregnancy

## Booking visit

First trimester ultrasound should be offered to women with multiple pregnancy for:

- Assessment of viability
- Assessment of gestational age (gestational age is determined by the largest foetus)
- Assessment of chorionicity and amnionicity
- Assignment of nomenclature (assign foetuses as left and right, or upper and lower for consistency)

### Methods of determination of chorionicity and amnionicity

- The number of placental masses
- The presence of amniotic membrane(s) and membrane thickness
- Lambda or T-sign
- Discordant fetal sex (if gestational age is beyond 14 weeks)

| | |
|---|---|
| **Dichorionic diamniotic (DCDA) pregnancy** | ▪ There are 2 chorionic and 2 amniotic layers<br>▪ There is a thick inter-twin membrane (> 2 mm)<br>▪ Lambda sign |
| **Monochorionic diamniotic (MDCA) pregnancy** | ▪ There are 2 amniotic layers only<br>▪ There is a thin inter-twin membrane (< 2 mm)<br>▪ T-sign |
| **Monochorionic monoamniotic (MCMA) pregnancy** | There is no intertwin membrane |

If chorionicity cannot be determined, a second opinion by a senior sonographer or a referral should be considered. If chorionicity remains undetermined, pregnancy should be managed as monochorionic pregnancy

Transvaginal ultrasound may be used as an alternative to transabdominal ultrasound in women with high body mass index and uterine retroversion. 3D ultrasound should not be used

## Antenatal care

- **Care providers:**

Antenatal care is provided to women with multiple pregnancy by a multidisciplinary team

**Core team**

The team consists of specialist obstetricians, specialist midwives and sonographer who have experience with multiple pregnancy

**Role**

They provide emotional support, information and advice on nutrition, risk of preterm labour, time and mode of birth, breastfeeding, and parenting

**Enhanced team**

The team consists of a perinatal mental health professional, women's health physiotherapist, and an infant feeding specialist

**Role**

Enhanced team is available for referral only if indicated (not a routine)

**Dietitian**

Nutritional recommendations are similar to routine antenatal care of singleton pregnancy

- **Antenatal care appointments:**

| Type | Number of appointments | Combined appointments | Appointments without scans |
|---|---|---|---|
| **Dichorionic diamniotic twin pregnancy** | • At least 8 appointments with providers from the core team<br>• At least 2 appointments with a specialist | • Combined appointment (appointment + ultrasound scan) should be offered between $11^{+2}$ and $14^{+1}$ weeks [crown rump length between 45 and 84 mm])<br>• Combined appointment should be offered every 4 weeks between 20 weeks and 36 weeks | Additional appointments (without scan) are offered at 16 and 34 weeks |
| **Monochorionic diamniotic twin pregnancy** | • At least 11 appointments with providers from the core team<br>• At least 2 appointments with a specialist | • Combined appointment (appointment + ultrasound scan) should be offered between $11^{+2}$ and $14^{+1}$ weeks [crown rump length between 45 and 84 mm])<br>• Combined appointment should be offered every 2 weeks between 16 weeks and 34 weeks | None |
| **trichorionic triamniotic triple pregnancy** | • At least 9 appointments with providers from the core team<br>• At least 2 appointments with a specialist | • Combined appointment (appointment + ultrasound scan) should be offered between $11^{+2}$ and $14^{+1}$ weeks [crown rump length between 45 and 84 mm])<br>• Combined appointment should be offered at 20 and 24 weeks and then every 2 weeks between 24 weeks and 34 weeks | Additional appointments (without scan) are offered at 16 weeks |

| | | | |
|---|---|---|---|
| **Dichorionic triamniotic or monochorionic triamniotic triplet pregnancy** | • At least 11 appointments with providers from the core team<br>• At least 5 appointments with a specialist | • Combined appointment (appointment + ultrasound scan) should be offered between $11^{+2}$ and $14^{+1}$ weeks [crown rump length between 45 and 84 mm])<br>• Combined appointment should be offered every 2 weeks between 16 weeks and 34 weeks | None |
| **Twin and triplet pregnancies with a shared amnion** | Individualised care should be offered by a consultant in a tertiary level foetal medicine centre (monochorionic monoamniotic twins, dichorionic diamniotic triplets, monochorionic diamniotic triplets, and monochorionic monoamniotic triplets) | | |

- **Foetal screening:**
  - **Screening for chromosomal abnormalities:**

| | |
|---|---|
| **Twin pregnancy** | ▪ Women are offered screening for Down's syndrome, Edwards' syndrome and Patau's syndrome<br>▪ As routine, screening follows the NHS foetal anomaly screening programme (FASP) |
| **Triple pregnancy** | ▪ Women are offered screening for Down's syndrome, Edwards' syndrome and Patau's syndrome<br>▪ Triplet pregnancy is associated with higher risk of aneuploidy, different screening strategies, higher false positive results and probability of invasive testing, higher risk of complications with invasive testing<br>• Nuchal translucency (between $11^{+2}$ and $14^{+1}$ weeks [crown rump length between 45 and 84 mm]) is used for screening |

| | |
|---|---|
| | ▪ Second trimester serum screening is not recommended<br>▪ Dichorionic and monochorionic triplet pregnancy should be referred to a tertiary level foetal medicine centre if they are interested in screening |

Women are referred to a tertiary-level foetal medicine centre if the risk od any aneuploidy is higher than 1 in 150 at term

- **Screening for structural abnormalities:**

Ultrasound screening is similar to routine antenatal care of a singleton pregnancy. However, it should be offered at a later gestational age. Scheduled scanning time should be 45 minutes for the anomaly scan and 30 minutes for growth scans

- **Screening for preterm labour:**
  - Women with multiple pregnancy are at higher risk of preterm labour
  - Foetal fibronectin alone is not recommended to screen for preterm labour. Home uterine activity monitoring should not be used
  - Routine use of intramuscular progesterone, cerclage, arabin pessary, tocolytics, or bedrest is NOT recommended
  - Antenatal steroids are not used routinely unless otherwise indicated

- **Screening for foetal growth restriction (dichorionic or trichorionic foetuses):**

| **First trimester** | Screening methods should not be offered |
|---|---|
| **Second and third trimester** | • Symphyseal fundal height is not used for screening. Ultrasound should be performed routinely<br>• Starting from 24 weeks, dichorionic or trichorionic foetuses should be screened by 2 biometry measurements and deepest vertical pocket (DVP) at each side (screening interval is 4 weeks in dichorionic twins and 2 weeks in trichorionic triplets)<br>• At each screening, discordance should be calculated |

| | |
|---|---|
| | • If estimated foetal weight (EFW) of any foetus is < 10th percentile or if discordance is > 20%, scans should be scheduled weekly with umbilical artery Doppler<br>• If EFW of any foetus is below the 10th percentile or if discordance is > 25%, consider referral to tertiary level foetal medicine centre (selective foetal growth restriction) |

| Discordance in twins | Discordance in triplets |
|---|---|
| This is calculated by: (estimated foetal weight in the larger twin – estimated foetal weight in the smaller twin)/estimated foetal weight in the larger twin | This is calculated by: (estimated foetal weight in the largest foetus – estimated foetal weight in the smallest foetus)/estimated foetal weight in the largest foetus AND (the largest – the middle foetus)/the largest foetus |

- **Screening for foetal complications of multiple pregnancy:**

| | |
|---|---|
| **Feto-fetal transfusion syndrome** | • A monochorionic twin or triplet pregnancy should be scanned every 2 weeks starting at 16 weeks. Assessment of DVP should be performed<br>• Scanning is performed every 1 week along with Doppler assessment if difference in DVP between sacs is > 4 cm<br>• If one DVP is < 2 cm and the other DVP is > 8 cm (before 20 weeks) or > 10 cm (after 20 weeks), women should be referred to a tertiary level fetal medicine centre<br>• If one DVP is normal and the other is < 2 cm or ≥ 8 cm, women should be referred to their specialist obstetrician |

| | |
|---|---|
| **Foetal growth restriction in monochorionic twins** | • Monochorionic twin or triplet pregnancy is screened every 2 weeks starting at 16 weeks using 2 biometric parameters and DVP at each side. Discordance is calculated at each scan<br>• If discordance is ≥ 20% or EFW of one foetus is < 10th percentile, they should be screened every 1 week including umbilical artery Doppler<br>• Women are referred to a tertiary level foetal medicine centre if discordance is ≥ 25% or EFW is < 10th centile (selective foetal growth restriction) |
| **Twin anaemia polycythaemia sequence (TAPS)** | • Screening for TAPS is indicated if:<br>① Feto-fetal transfusion syndrome after laser photocoagulation<br>② Selective foetal growth restriction<br>• Screening is performed by weekly middle cerebral artery peak systolic velocity (MCA-PSV) assessment starting at 16 weeks<br>• If monochorionic twins show cardiovascular compromise (hydrops or cardiomegaly), unexplained isolated polyhydramnios or abnormal umbilical artery Doppler, women should be assessed by MCA-PSV and referred to a tertiary level foetal medicine |

- **Screening for maternal complications:**
  - **Hypertension:**
    - Blood pressure and proteinuria are screened at each antenatal visit
    - Low dose aspirin should be offered to women who have 2 or more risk factors of preeclampsia

  - **Anaemia:**

    Women with multiple pregnancy are at higher risk of anaemia compared to singleton pregnancy. These women should be offered a complete blood count at 20 to 24 weeks

## Intrapartum management

Intrapartum plan of care should be discussed at 24 weeks (28 weeks is the latest) including place and time of birth, intrapartum foetal monitoring and analgesia, and management of third stage of labour. Intrapartum care should be provided by a multidisciplinary team of obstetricians and midwives

- **Timing of birth:**

| Type | Recommended gestational age of planned delivery* |
|---|---|
| **Uncomplicated dichorionic diamniotic twins** | 37 weeks |
| **Uncomplicated monochorionic diamniotic twins** | 36 weeks (after completion of steroid course) |
| **uncomplicated monochorionic monoamniotic twin** | 32-33$^{+6}$ weeks (after completion of steroid course) |
| **Uncomplicated trichorionic triamniotic or dichorionic triamniotic triplets** | 35 weeks (after completion of steroid course) |

Spontaneous labour occurs in 60% of twins before 37 weeks and 75% of triplets before 35 weeks

* Beyond these gestational ages, women should be informed that there is increased risk of fetoal loss

  - Timing of birth is individualized in women with complicated twin or triplet pregnancy, monochorionic triamniotic triplet pregnancy, or triplet pregnancy with a shared amnion
  - If delivery is declined at the planned date, weekly appointments should be scheduled with the specialist obstetrician with assessment of amniotic fluid level and umbilical artery Doppler at each visit and foetal growth assessment every 2 weeks

- **Mode of birth:**

  One third of Women who are eligible for vaginal delivery eventually undergo caesarean delivery. Of those, a small percentage may undergo caesarean section to deliver the second twin after vaginal delivery of the first twin

| Indications of vaginal delivery | Indications of caesarean section |
|---|---|
| Both vaginal deliveries and caesarean section can be offered if dichorionic diamniotic or monochorionic<br>Diamniotic twins with:<br>① Uncomplicated pregnancy beyond 32 weeks<br>② The first twin is a cephalic presentation<br>③ No significant discordance between the twins<br>④ No obstetric contraindications to vaginal delivery<br>Vaginal birth may be considered in monochorionic monoamniotic twins only if the first twin is close to birth (decision is made by a senior obstetrician) | Women are offered caesarean section if:<br>① The first twin is non-cephalic at the time f planned birth<br>② The first twin is non-cephalic, if preterm labour is established between 26-32 weeks<br>③ Monochorionic monoamniotic twin pregnancy (at time of planned delivery or if there is preterm labour and there is reasonable chance of survival of twins)<br>④ Triplet pregnancy (at time of planned delivery or if there is preterm labour and there is reasonable chance of survival of twins) |

Decision is individualized if preterm labour occurs before 26 weeks

- **Foetal monitoring:**
  - Bedside ultrasound is performed at the onset of labour to assess twin presentation, location, and location of foetal beats
  - Continuous cardiotocography (CTG) should be considered in twin pregnancy at or beyond 26 weeks of gestation who are in labour. Intermittent consultation should not be offered
  - Simultaneous record of twin heart rates and maternal pulse should be made, and they should all be recorded on the same trace. Separating twin heart rates by 20 beats/minute may be considered if differentiation between the 2 heart rates is not feasible
  - Twin pregnancy is a risk factor that should be considered when interpreting traces (abnormal versus non-reassuring)
  - Foetal scalp stimulation should not be used

- If pregnancy is earlier than 26 weeks, a discussion should be made between the patient, her family or carers and the obstetric specialist to decide on foetal monitoring

| Finding | Management |
|---|---|
| **If CTG cannot be achieved or if simultaneous assessment of both heart beats is doubtful** | • A senior obstetrician/senior midwife should be called<br>• A bedside ultrasound is performed to check both heart rates<br>• A foetal scalp electrode is applied to the first twin (if gestational age > 34 weeks). Abdominal monitoring of the second twin is performed<br>• Caesarean section should be considered if all measurements fail |
| **If CTG of the first twin is suspicious** | • The senior obstetrician and senior midwife are called<br>• Possible causes are corrected<br>• A foetal scalp electrode is applied to the first twin (if gestational age ≥ 34 weeks). Abdominal monitoring of the second twin is performed |
| **If CTG of the first twin is pathological in the first stage** | • The senior obstetrician and senior midwife are called<br>• Foetal blood sampling of the first baby (if gestational age ≥ 34 weeks) should be offered after counselling<br>• If foetal blood sampling cannot be obtained, is contraindicated, or is not available within 20 minutes, immediate caesarean section should be considered |
| **If CTG of the first twin is pathological in the second stage** | • The senior obstetrician and senior midwife are called<br>• If feasible, assisted vaginal birth should be offered. However, if delivery cannot be achieved in 20 minutes, an immediate caesarean section should be performed |
| **If CTG of the second twin is suspicious or pathological after delivery of the first twin** | If delivery does not occur within 20 minutes, immediate caesarean section should be considered |

- **Labour analgesia:**
  - Epidural analgesia is offered to women with multiple pregnancy who undergo vaginal delivery
  - Regional anaesthesia is offered to women who will be delivered by caesarean section

- **Management of third stage of labour:**
  - **Umbilical cord clamping:**

    After delivery, cords should be double clamped to sample umbilical cord blood. Samples should be labelled by twin

  - **Prevention of postpartum haemorrhage:**
    - **IV access:**

      IV access should be established in all women with multiple pregnancy when labour is established. Blood products should be available if needed
    - **Active management of the third stage:**

      Women with multiple pregnancy are at higher risk of postpartum haemorrhage. Therefore, active management of the third stage should be offered (rather than conservative management). An additional uterotonic should be added if there are two or more risk factors of postpartum haemorrhage including multiple pregnancy

## Foetal medicine


### Abstract

Diagnosis and management of a silent, non-complaining patient who may be threatened by a serious condition, is the essence of foetal medicine. Unlike other medical specialties, health, and wellbeing of 2 persons, the mother and the foetus, affects clinical outcomes of the patient. The patient cannot be directly examined or seen, making foetal medicine a unique subspeciality.



### Keywords

FGR, IUFD, prenatal testing, alloimmunization

## Further readings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# PART IV

## General gynecology

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# Chronic Pelvic Pain

## Definition

Chronic pelvic pain is an intermittent or constant pain in the lower abdomen or pelvis that is present for at least 6 months. Pain should not be related to or confined to pregnancy, sexual intercourse or menstruation

## Causes

| Origin | Explanation |
|---|---|
| **Neurologic** | • Visceral hyperalgesia and neuropathic pain<br>• Nerve entrapment in scar tissue, fascia or narrow foramen (incidence is 4% after pfannenstiel incision) |
| **Gynaecologic** | • *Endometriosis and adenomyosis:*<br>Pelvic pain which varies markedly over the menstrual cycle is likely to be attributable to a hormonally driven condition<br>• *Adhesions:*<br>▪ Role of adhesions as a cause of pelvic pain is less evident<br>▪ Although division of fine adhesions has no role in women with chronic pelvic pain, division of dense vascular adhesion may be associated with improvement of symptoms |
| **Vascular** | • Pelvic venous congestion (controversial) |
| **Gastrointestinal** | • Irritable bowel syndrome (IBS) is present in 50% of women with chronic pelvic pain (vs. 28% as baseline) |
| **Urinary** | • Interstitial cystitis may be present in 60% of cases of chronic pelvic pain |
| **Musculoskeletal** | • Pain originating from pelvic joints, abdominal or pelvic muscles |
| **Psychological and social issues** | • Depression and sleep problems<br>• Relationship between pelvic pain and sexual/physical abuse is complex |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_19

## Clinical assessment

Initial assessment should be thoroughly made. Chronic pelvic pain may be associated with gynaecologic, gastrointestinal, urological, musculoskeletal, vascular or other causes

- **History taking:**
  - Pattern of pain e.g.
    - Endometriosis/adenomyosis pain is exacerbated around menstruation time
    - Nerve entrapment pain is localized sharp, stabbing, aching, extends for more than 5 weeks or occurs after a period without pain after surgery. Pain is exacerbated by certain movements
  - Exacerbating factors e.g. effect of movement and posture.
  - Bladder symptoms
  - Bowel symptoms including irritable bowel symptoms
  - Psychological symptoms and history of abuse Baseline level of function should be assessed. Daily pain diary for 2-3 cycles may be helpful to reach a diagnosis

**Red flags**

- Bleeding per rectum
- New bowel symptoms in age more than 50
- New pain after menopause
- Pelvic mass
- Suicidal ideation
- Excessive weight loss
- Irregular uterine bleeding in women > 40 years
- Postcoital bleeding

- **Physical examination:**
  - Focal tenderness (abdominal or pelvic)
  - Uterine or ovarian enlargement and tenderness
  - Identifying trigger points (localized muscle tenderness), which may indicate chronic contraction (musculoskeletal pain)
  - Sacroiliac/symphysial tenderness

## Investigations

| | |
|---|---|
| **Screening for infection** | • Chlamydia trachomatis and gonorrhea swabs (if pelvic inflammatory disease "PID" is suspected)<br>• screening for sexually transmitted infections (STIs) |
| **Transvaginal ultrasound (TVUS) and MRI** | • Assessment of adnexal masses<br>• Diagnosis of adenomyosis<br>• Endometriomas<br>Ultrasound predictive signs of identifying pathology in laparoscopy include:<br>① Tenderness<br>② Poor ovarian mobility<br>If they present, likelihood of pathology is 60-70% vs. 20% if these signs are absent |
| **Diagnostic laparoscopy*** | • It may be indicated if therapeutic interventions fail (second-line investigation). It promotes diagnosis of endometriosis<br>• Deeply infiltrating lesions are the most related to pain<br>• 1/3-1/2 of laparoscopies are negative. Micro laparoscopy or conscious pain mapping may be used |
| **Serum CA125** | The test may be indicated if:<br>① Persistent or frequent (> 12 episodes/month) symptoms including one of the following: bloating, early satiety, pelvic pain or urinary urgency or frequency<br>② New IBS symptoms in women older than 50 years |

* Laparoscopy is associated with risk of death (1:10.000), risk of injury bladder, bowel or vascular injury (2.4:1000)

## Management

- **Initial management:**
  - **Anaelgesia:** appropriate anaelgesia should be offered regardless of initial management
  - **Hormonal treatment:** is offered as a trial in women with cyclical pain for 3–6 months. Diagnostic laparoscopy is indicated if this trial fails to relieve symptoms

- **Antispasmodics:** is given to women with IBS along with diet modification as a trial to relieve symptoms

- **Further management:**
  If pain is not adequately controlled after initial management, referral to a pain management team or a specialist pelvic pain clinic is offered

# Pelvic Congestion Syndrome

## Epidemiology

- Chronic pelvic pain accounts for 10-40% of gynaecologic visits
- It affects approximately 4% of women in their reproductive years

## Aetiology

Most cases are multi-factorial. Some of the underlying mechanisms include:

| | |
|---|---|
| **Ovarian varicoceles** | • It refers to absence of valves in cranial portion of ovarian veins<br>• They may be absent in the left vein (15%) or the right vein (6%)<br>• 60% of cases are asymptomatic |
| **Pregnancy** | • Ovarian flow increases 60 times than normal in pregnancy by the relaxing effect of progesterone and gravid uterus pressure<br>• It is more on left side |
| **Nutcracker syndrome** | • This refers to compression of the left renal vein between aorta and superior mesenteric artery |

## Clinical picture

It most commonly presents in premenopausal multiparous women

**Pain**

- Unilateral or bilateral, sharp or dull, acute or chronic pain
- Pain increases premenstrual, after intercourse (throbbing ache) and during pregnancy
- Pain is exacerbated by fatigue and standing, and alleviated by laying down

**Other features**

- Urinary symptoms may be absent or present. Urinary symptoms may be related to varicosities at bladder trigone
- 50% are associated with polycystic changes in ovaries
- Vein insufficiency in lower limb (inner and posterior thigh) may be present

## Investigations

Investigations are necessary to confirm diagnosis:

- **Non-invasive imaging:**
  - **Pelvic ultrasound (1st line):** It is preferable to do ultrasound during **Valsalva manoeuvre**

**Ultrasound diagnostic Criteria**

- Tortuous veins diameter **> 6 mm**
- Slow blood flow **< 3 cm/second** or **reversed** flow in left ovarian vein
- **Dilated, arcuate** veins in myometrium (venous communications between pelvic varicose veins on both sides)
- Polycystic ovarian changes

  - **CT and MRI:**
    - They may show tortuous, dilated tubular enhancing structures near uterus and ovaries
    - These tests are done in a supine position and are likely to miss non-severe cases
  - **MR phase-contrast velocity mapping**: a good diagnostic tool (comparable to venography)

- **Invasive imaging:**
  - **Venography (gold standard):** 1 or more of the following criteria is suggestive of PCS

    1-Ovarian vein diameter **> 10 mm.**
    2-**Uterine** venous engorgement.
    3-Congestion of **ovarian plexus**.
    4-Filling of pelvic veins across the midline &/or filling of vulvovaginal thigh varicosities

  - **Laparoscopy:** may give **false negative** results due to $CO_2$ pressure and supine position. Limited data on its diagnostic role are available.

## Treatment

- **Medical treatment:**
  - **Non-steroidal anti-inflammatory drugs (NSAIDs):**
    It is the first line treatment. It is associated with short term efficacy and it can be offered while assessment is undergoing
  - **Medroxyprogesterone acetate (MPA):** 30 mg for 6 months
    - It provides **subjective enhancement** in pain perception (60% vs 30% of placebo)
    - It achieves **objective improvement** (detected via venography)
    - Long-term use of progestins may be associated with **reversible bone loss**
  - **GnRH (goserelin):**
    It is associated with better outcome at 12 months. Treatment may be used for 6 months without add back therapy and up to 2 years with add-back therapy (to reduce risk of osteoporosis)
  - **Daflon:**
    500 mg twice daily may improve pain

- **Surgical treatment:**
  - **Extraperitoneal resection of left ovarian vein:** response to surgery is approximately **75%**
  - **Laparoscopic transperitoneal ligation of ovarian veins**
  - **Hysterectomy and bilateral salpingo-oophorectomy**

- **Transcatheter embolotherapy:**
  - Response rate is 60-80% relief (superior to hysterectomy and bilateral salpingo-oophorectomy)
  - Complications:
    - Coil migration (main complication, easily retrieved)
    - Ovarian vein perforation
    - Puncture site hematoma

- **Psychotherapy:**

  MPA and psychotherapy show greater than 50% pain reduction compared to MPA alone

# Endometriosis

## Diagnosis

- **Clinical diagnosis:**

| Symptoms | signs |
|---|---|
| Chronic pelvic pain | Abdominal mass |
| Dysmenorrhea | Decrease mobility |
| Deep dyspareunia | Tender nodularity |
| Urinary symptoms | Visible lesions |
| Infertility | |

- **Investigations:**

**Imaging**

**MRI**

- Not used as a first line imaging
- Used only to determine the extent of deep endometriosis

**TVUS**

- Indicated in women with suspected endometriosis even if examination is negative
- Used to detect endometriomas or deep endometriosis of bladder, ureter, and bowel

**Laparoscopy**

Indicated in women with suspected endometriosis even if imaging is negative

**Consider biopsy**

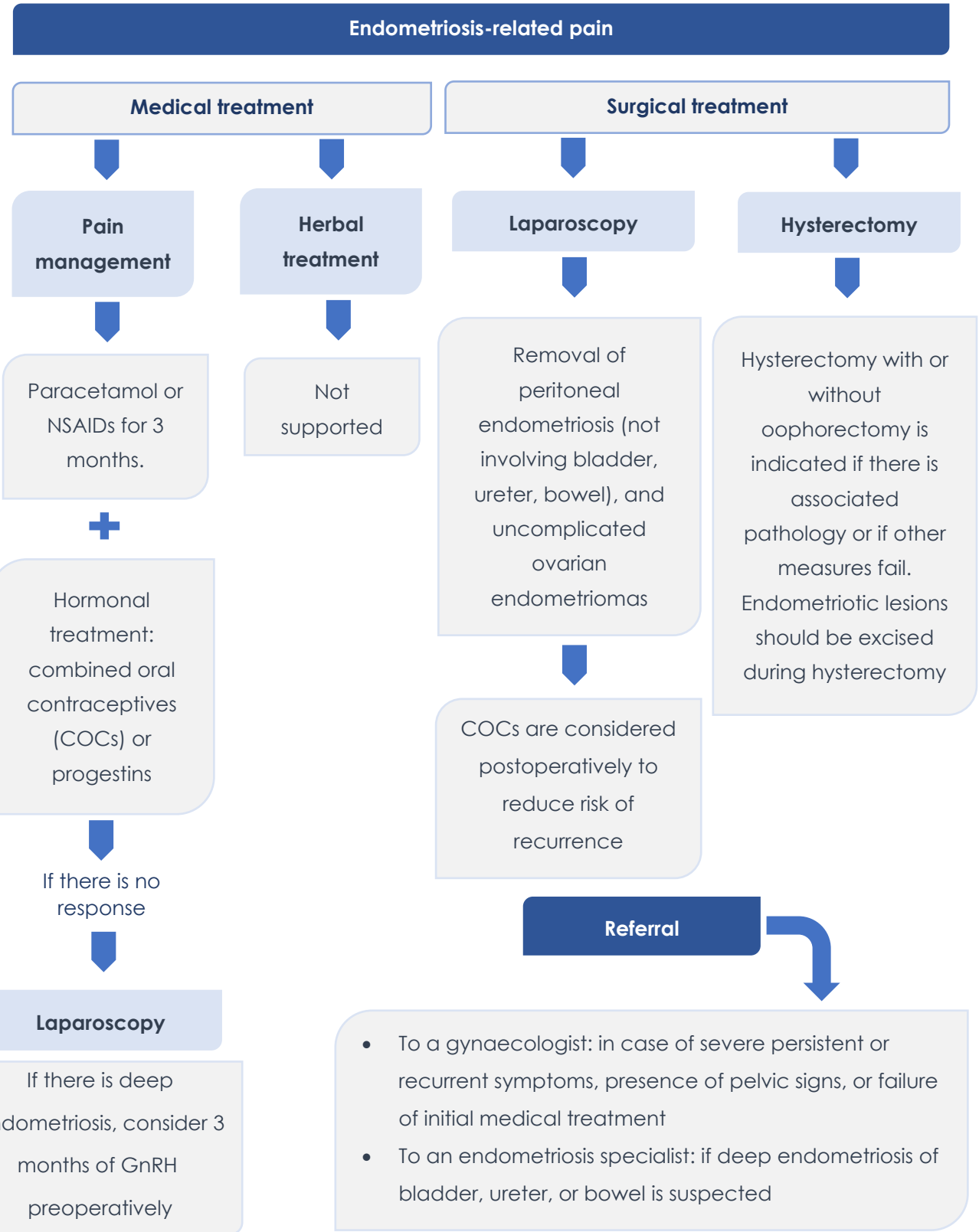
- To confirm diagnosis
- To exclude malignancy (if endometriomas are not excised)

**CA125**

- Endometriosis may be associated with CA 125 if more than 35 IU/ml
- Not diagnostic.

TVUS: transvaginal ultrasound

## Management


Endometriosis-related pain
Medical treatment
Surgical treatment
Pain management
Herbal treatment
Laparoscopy
Hysterectomy
Paracetamol or NSAIDs for 3 months.
+
Hormonal treatment: combined oral contraceptives (COCs) or progestins
If there is no response
Laparoscopy
If there is deep endometriosis, consider 3 months of GnRH preoperatively
Not supported
Removal of peritoneal endometriosis (not involving bladder, ureter, bowel), and uncomplicated ovarian endometriomas
COCs are considered postoperatively to reduce risk of recurrence
Hysterectomy with or without oophorectomy is indicated if there is associated pathology or if other measures fail. Endometriotic lesions should be excised during hysterectomy
Referral
• To a gynaecologist: in case of severe persistent or recurrent symptoms, presence of pelvic signs, or failure of initial medical treatment
• To an endometriosis specialist: if deep endometriosis of bladder, ureter, or bowel is suspected

**Outpatient follow up**

It is indicated in women with confirmed endometriosis, who declined surgery in the presence of:

① Deep endometriosis of bladder, ureter, or bowel

② One or more endometrioma more than 3 cm

## Endometriosis-related infertility

- **Management of endometriomas:**

6-10% of all women in reproductive age have endometriosis, 20-45% of them have endometriomas

**If endometrioma is larger than 3 cm**

**Laparoscopy**

- Symptomatic endometriomas
- Large unilateral endometrioma
- Suspicious endometrioma
- Ovarian reserve is normal

**Cystectomy**

- Increases pregnancy rate
- Decreases recurrence
- Decreases ovarian reserve

**Drainage**

- Recurrence is high
- Ablation of cyst wall decreases recurrence but increases ovarian damage

**Surgically treated endometrioma**

- Same cancellation rate.
- Higher dose of gonadotrophins for ovulation induction
- Decrease in antral follicle count
- Decrease in retrieved oocytes

**Indications**

**In-vitro fertilization (IVF)**

- Asymptomatic women.
- Low ovarian reserve.
- Previous history of ovarian surgery
- Bilateral endometriomas

- Increase the cancellation rate.
- Decrease ovarian response.
- Same pregnancy and miscarriage rate.
- Peritoneal endometriosis and endometrioma are comparable.

**Risks**

- Egg retrieval is associated with
- risk of infection (<2%), follicular fluid contamination (3-6%)
- Lifetime risk of ovarian cancer is higher (1-2%)

- **Management of endometriosis:**

  Excision or ablation of endometriosis (not involving the bowel, bladder or ureter) plus adhesiolysis improve the rate of spontaneous pregnancy

Genital infections

# Pelvic Inflammatory Disease

## Aetiology

- Pelvic inflammatory disease (PID) is commonly an ascending infection from the lower genital tract
- The most common causative organism is Chlamydia (15-35%), other bacteria include gonorrhoea (< 3%), Gardnerella Vaginalis, anaerobes, and mycoplasma

## Risk factors

- Younger age (< 25 years)
- Non-use of barrier contraception
- New sexual partner
- Immediately after intrauterine device insertion (the first 4-6 weeks)

## Clinical presentation

| Symptoms | Signs |
|---|---|
| • Bilateral lower abdominal pain (may be unilateral)<br>• Vaginal discharge (usually purulent)<br>• Deep dyspareunia<br>• Secondary dysmenorrhea<br>• Abnormal uterine bleeding | • Lower abdominal tenderness (bilateral)<br>• Adnexal tenderness +/- mass<br>• Cervical motion tenderness<br>• Fever > 38$^{o}$c in moderate to severe cases |

## assessment

- Symptoms may be present, but they lack sensitivity and specificity. Examples of differential diagnosis Include:
  - Ectopic pregnancy: pregnancy test should be performed
  - Acute appendicitis: most patients complain of nausea and vomiting (vs. 50% of patients with PID). Cervical motion tenderness in present in only 25%
  - Endometriosis: relation of symptoms to menstrual cycle should be considered
  - Torsion or rupture of ovarian cyst: pain is likely of acute onset
  - Urinary tract infection: urinary symptoms are prominent
  - Irritable bowel syndrome: symptoms are long standing and are associated with bowel symptoms
- Lower genital tract testing for infection:
  - Chlamydia, gonorrhea, M. genitalium culture: Positive testing supports diagnosis but is not used for exclusion
  - Endocervical/vaginal pus cells in gram stained exam: this test yields good negative predictive value (95%). However, a positive test has no specific significance
- Blood tests:
  CRP, ESR, WBC count may support diagnosis. However, they lack specificity and they are abnormal in moderate-severe PID only
- Ultrasound:
  There is no role for ultrasound unless there is an adnexal mass

## Complications

- **Fitz-Hugh Curtis syndrome:** perihepatitis and perihepatic adhesions following PID, usually caused by Chlamydia infection
- **Tubo-ovarian abscess:** suspected if the patient develops severe pain, adnexal mass, and appears unwell and not responsive to treatment
  In these patients, ultrasound and CT scan should be consider and they should be admitted and treated with parenteral antibiotics that have anaerobic cover
- **Tubal damage:** with subsequent tubal factor infertility

## Treatment

- Empirical treatment should be started immediately. Delaying treatment increases risk of ectopic pregnancy, infertility, pelvic pain
- Intercourse should be avoided till treatment of the couple is complete. Screening of sexual contacts should be considered
- Current and recent partners (ideally within 6 months) should be contacted and offered screening for chlamydia, gonorrhoea, mycoplasma. If negative, empirical treatment with doxycycline 100 twice daily for 1 week should be considered

| | Outpatient treatment | Inpatient treatment |
|---|---|---|
| **Indications** | Mild to moderate cases (outpatient is comparable to inpatient treatment) | • Failure or intolerance to oral treatment<br>• Severe disease<br>• Tubo-ovarian abscess<br>• Pregnancy<br>IV antibiotics are indicated if there is fever, tubo-ovarian abscess or pelvic peritonitis |
| **Treatment** | • Intramuscular ceftriaxone 500 single dose then doxycycline (100mg twice daily) and metronidazole (400mg twice daily) for 14 days<br>• Alternatively, ceftriaxone may be followed by azithromycin 1g/weekly for 2 weeks<br>• Oral quinolones may be used if gonorrhoea is unlikely | • IV Ceftriaxone 2g/day PLUS IV doxycycline 100mg twice daily followed by oral doxycycline 100 twice daily PLUS metronidazole 400mg twice daily for 2 weeks total<br>• Alternatively, IV clindamycin PLUS gentamicin may be used followed by an oral regimen<br>• IV treatment should continue for 24 hours after clinical improvement |

| Management during pregnancy |
|---|
| • IV antibiotics should be used<br>• Ceftriaxone, erythromycin and metronidazole are safe to be used in pregnancy<br>• Non-pregnancy regimens may be used before pregnancy test is positive |

| Surgical management of PID |
| --- |
| • Ultrasound-guided aspiration is comparable to laparoscopy for treatment of tubo-ovarian abscess<br>• Laparotomy may be required in severe disease |

## Special considerations

- **Women with IUD in place:**
  - IUD may be left in place if there is mild/moderate PID
  - After 48-72 hours of treatment, it may be removed if there is no response to treatment
  - If removed, emergency contraception should be considered if intercourse occurs in the last 7 days
- **PID in HIV patients:**
  Infection is typically severe. However, it responds well to the standard regimen of antibiotics
- **PID with positive M. Genitalium:**
  - Treatment with Moxifloxacin is required
  - Retest after 4 weeks of treatment

## Follow-up

- Follow-up is indicated after 72 hours in severe disease, then after 2-4 weeks to assess response to treatment
- Cure test for gonorrhoea should be considered after 2-4 weeks, and after 3-5 weeks for chlamydia

## Tubo-ovarian abscess (TOA)

| | |
|---|---|
| **Incidence** | • 15-35% of women treated for PID<br>• 60% of patients are nulliparous |
| **Aetiology** | • It develops as a complication of untreated PID<br>• 30-40% of cases of PID is polymicrobial |
| **Complications** | • Infertility<br>• Higher risk of ectopic pregnancy<br>• Chronic pelvic pain |
| **Management** | • Ultrasound is usually used for diagnosis<br>• Standard management is through antibiotic therapy ± surgical intervention |

## Pelvic pain


### Abstract

Pelvic pain is a complex symptom of several underlying mechanisms. Diagnosing and treating pelvic pain may be challenging since pelvic anatomical region is shared by genital organs, intestine, urinary tract, blood vessels, and nerves. All these organs can originate pelvic pain, and anatomical discrimination is essential to determine management strategy. In addition, disorders, such as, endometriosis may be difficult to treat. In this chapter, we will discuss causes of pelvic pain, diagnosis, and management according to the cause.



### Keywords

Endometriosis, pelvic infection, irritable bowel disease


### Further readings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# Heavy Menstrual Bleeding

## Definition

Heavy menstrual bleeding (HMB) is defined menstrual blood loss ≥ 80ml, or menstrual bleeding longer than 7 days, or both

## Clinical assessment

| | |
|---|---|
| **History** | • Bleeding pattern and whether it is considered abnormal<br>• History of associated symptoms, such as persistent intermenstrual bleeding, pelvic pain and/or pressure symptoms<br>These symptoms may indicate uterine cavity abnormality, adenomyosis or uterine fibroids<br>• Factors that may alter treatment choice e.g. medical comorbidities, prior failed treatment |
| **Examination** | • If associated symptoms are present, physical examination is indicated to assess pelvic pathology |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_20

## Investigations

### Laboratory tests

- Complete blood count: for all women with HMB
- Coagulation profile: when coagulation disorders are clinically suspected e.g. HMB with menarche
- Thyroid function test: if signs and symptoms of thyroid disease are present

*Routine assessment of serum ferritin, hormonal profile, or thyroid function is not indicated*

### Offer office hysteroscopy

- It is indicated if fibroids or endometrial pathology is suspected e.g.
  ① Persistent intermenstrual bleeding
  ② Risk factors of endometrial pathology
- Office hysteroscopy is the standard using vaginoscopy approach (the scope is 3.5 mm or less). Oral analgesia is administered prior to the procedure.
- If declined, hysteroscopy under regional or general anaesthesia may be offered. If both declined, pelvic Ultrasound may be offered after discussing limitations

### Endometrial biopsy

- It is indicated at time of hysteroscopy in women at high risk of endometrial pathology:
  ① Persistent Intermenstrual bleeding, irregular bleeding, infrequent bleeding with obesity and poly cystic ovary syndrome
  ② Women on Tamoxifen
  ③ Unsuccessful treatment
- No blind endometrial biopsy offered with HMB

### Pelvic ultrasound

Pelvic ultrasound is indicated if:

- Fibroids are suspected:
  ① Uterus is felt abdominally
  ② Pelvic mass
  ③ Inconclusive examinations e.g. obese patients
- Adenomyosis is suspected:
  ① Significant dysmenorrhea
  ② Bulky tender uterus

## Treatment

- Treatment decision depends on:
  ① Patient preference and conception plans
  ② Presence of comorbidities
  ③ Presence of fibroids
  ④ Other symptoms e.g. pressure, pain
- Women with HMB without associated symptoms are initially treated medically. Physical examination and imaging are not necessary

If no pathology, fibroid less than 3 cm, suspected adenomyosis

Levonorgestrel releasing intrauterine system (LNG-IUS) is the first line

If LNG-IUS is declined

- Non-hormonal treatment: tranexamic acid and non-steroidal anti-inflammatory drugs
- Hormonal treatment: combined hormonal contraception, cyclic Progestins

If declined, no response, or severe symptoms

- Refer to a specialist for further assessment
- Alternative pharmacologic treatment (GnRH or Ulipristal)
- Hysteroscopic myomectomy if Submucosal fibroid
- Endometrial ablation
- Hysterectomy

If fibroids is 3 cm or more in diameter are present

- Refer to specialist.
- Non-hormonal treatment: tranexamic acid and Non-steroidal anti-inflammatory drugs
- Hormonal treatment: Ulipristal, LNG-IUS, combined oral contraception, cyclic Progestins

Medical treatment may be offered temporarily to reduce bleeding while preparing for surgery. Their role is otherwise limited in this fibroid size

- Uterine artery embolization
- Surgical management: myomectomy or hysterectomy

Before any treatment is opted and initiated, its impact on fertility and future conception should be discussed

| Method | Precautions and instructions |
|---|---|
| **LNG-IUS** | Patients should be advised that the first few cycles may be associated with abnormal bleeding patterns. They should be advised that this may continue for up to 6 months and that they should give LNG-IUS up to 6 cycles to appraise benefits of this method |
| **Ulipristal acetate** | • Ulipristal acetate 5 mg is given for up to 4 courses in the presence of:<br>① Heavy menstrual bleeding<br>② Fibroids ≥ 3 cm in diameter<br>③ Haemoglobin ≤ 102 g/L<br>Ulipristal may serve as a preoperative treatment for large fibroids<br>• Liver function should be monitored during administration (liver injury is rare, but serious with ulipristal) |
| **GnRH analogue** | Like ulipristal, it may be considered as a preoperative for large fibroids |
| **Uterine artery embolization** | • Uterus and fibroids should be assessed by ultrasound prior to the procedure. MRI may be required<br>• Patients should be informed that fertility is retained |
| **Endometrial ablation** | • "Dilation and curettage" is not offered as a treatment. However, it is performed preoperatively to assess endometrial pathology since endometrial assessment after endometrial ablation is limited<br>• Endometrial ablation is not a contraception. Pregnancy following endometrial ablation is not safe and therefore, a good contraceptive method should be used |
| **Myomectomy** | Ultrasound is the standard method of assessment. MRI may be needed to better delineate these fibroids |
| **Hysterectomy** | Before hysterectomy is selected, discuss impact on fertility, sexual function, ovarian function, bladder function, and surgical complications |

# Uterine Fibroids

## Definition

Uterine fibroids (leiomyomas) are benign neoplasms arising from the smooth muscle fibres of the myometrium

## Prevalence

Lifetime incidence is 30%

## Risk factors

- Age: the risk increases with age before the menopause
- Nulliparity or low parity
- Race: more common in black women
- Obesity
- Hypertension
- Family history and genetic predisposition

## Clinical picture

Approximately 30% of patients are asymptomatic, and fibroids may be incidentally diagnosed. Symptoms include abnormal uterine bleeding, pelvic pain and pressure and abdominal distension

## Investigations

- Standard imaging modality is pelvic and abdominal ultrasound
- Saline infusion sonography or hysteroscopy may be considered in submucous fibroids to determine treatment plan
- MRI: it may be considered in certain clinical situations:

  ① Surgical decision for challenging fibroids (e.g. interstitial fibroids)

  ② Differentiating leiomyomas from leiomyosarcomas if malignancy is suspicious (suggestive but not conclusive)

  ③ Prior to uterine artery embolization

## Classification

| Grade | Description (FIGO classification) |
|---|---|
| **Grade 0** | • Pedunculated intracavitary leiomyoma |
| **Grade 1** | • Leiomyoma is less than 50% intramural |
| **Grade 2** | • Leiomyoma is 50% or more intramural |
| **Grade 3** | • Leiomyoma is 100% intramural, contact the endometrium. |
| **Grade 4** | • Leiomyoma is 100% intramural, no endometrial contact |
| **Grade 5** | • Leiomyoma is subserosal, 50% or more intramural |
| **Grade 6** | • Leiomyoma is subserosal, less than 50% intramural |
| **Grade 7** | • Leiomyoma is subserosal, pedunculated |
| **Grade 8** | • Other types (e.g., cervical, parasitic) |

## Treatment

- **Pharmacological treatment:**
  - **Indications:**

    Medical treatment is a short-term option that is appropriate for:

    ① Premenopausal women

    ② Women who are unsuitable for or decline surgery

    ③ Prior to surgery (GnRH or ulipristal)

    ④ some women with infertility

  - **Treatment lines:**

| | |
|---|---|
| **Oral hormonal treatment** | • Effect on fibroids is inconclusive<br>• These drugs act by inducing endometrial atrophy, thus, decrease mensural blood loss |
| **Levonorgestrel-releasing intrauterine system (LNG-IUS)** | • This option is suitable if contraception is desired as well<br>• This option is superior to oral hormonal treatment in reducing menstrual blood loss and improving haemoglobin level |
| **Tranexamic acid** | • It decreases both menstrual blood loss and perioperative blood loss in women undergoing surgery<br>• It may induce necrosis and infarctions in large fibroids |
| **Medroxyprogesterone injectables** | • They may decrease menstrual blood loss and fibroid size after 6 months of treatment |
| **GnRH analogues** | • It should be limited to 6 months of treatment. Add-back therapy is given in conjugation<br>• Its use for 3 months is associated with significant improvement of symptoms and 36% reduction in fibroid<br>• Following cessation, menstruation returns in 1-2 months and fibroid size is restored in 4-6 months<br>• Preoperative administration may allow vaginal hysterectomy, decrease perioperative blood loss and hospital stay.<br>• Its use may cause loss of fibroid plane and missing small fibroids during surgery |

| | |
|---|---|
| **Selective progesterone receptor modulators (SPRMs)** | • These agents may be clinically useful e.g. ulipristal, mifepristone, telapristone<br>• Ulipristal:<br>▪ It induces 40% reduction in size that is maintained for 6 months after discontinuation<br>▪ It decreases menstrual blood loss in 90% of patients<br>▪ It is comparable to GnRH but is more tolerated<br>▪ Endometrial changes are observed in 2/3 of patients and they resolve within 6 months. These changes are not prevented by progestins<br>▪ Liver damage is a rare complication<br>• Mifepristone: It is still under research |
| **Aromatase inhibitors** | ▪ Treatment is still experimental. It may be comparable to GnRH in initial results |

- **Uterine artery embolization:**

| | **Uterine artery embolization** | **Surgical management** |
|---|---|---|
| **Satisfaction rate** | No significant difference in both options | |
| **Major complications** | Less common | More common |
| **Minor complications** | More common | Less common |
| **Hospital stay** | Shorter | Longer |
| **Readmission** | More (pain and vaginal discharge) | Less common |
| **Post-treatment Intervention** | More common (5-fold increase in the first 2-5 days) | Less common |
| **Ovarian failure** | No significant difference in both options | |
| **Maternal mortality** | 1:10.000 | 3:10.000 |

- **MRI-guided focused ultrasonography:**
  - This approach is associated with 90% satisfaction rate
  - Less vascular fibroids with low signal intensity are more likely to respond to treatment
  - 25% may require further intervention (specially with Hyperdense fibroids)
  - The procedure is generally safe and is associated with minor side effects:

    ① Mild skin burn

② Nausea

③ Transient buttock or leg pain

④ Transient sciatic nerve palsy

- Compared to uterine artery embolization:
  - It achieves similar relief of symptoms.
  - Risk of intervention is 7-folds higher in the first year

- **Surgical treatment:**
  - **Myomectomy:**

    it may be indicated in women with heavy menstrual bleeding, recurrent miscarriage or infertility (after exclusion of all other possible causes

| | |
|---|---|
| **Hysteroscopic myomectomy** | • This approach is indicated for grade 0 and 1 fibroids:<br>▪ Grade 0 fibroid: it is managed by resectoscope and slicing<br>▪ Grade 1 and 2 fibroid: there is no standard approach. Myolysis and cryomyolysis may be used. However, they do not provide a sample for histopathology, and they may be associated with higher risk of adhesions and reintervention<br>• Safety of this procedure with grade 2 fibroids depends on uterine thickness between the fibroid and the serosa<br>• The procedure may be combined with endometrial ablation (90% of patients experience significant reduction in blood loss within 1 year of treatment) |
| **Laparoscopic myomectomy** | • Compared to open surgery, laparoscopic surgery is associated with:<br>▪ Longer surgical time<br>▪ Less blood loss<br>▪ Less postoperative pain, fever, and hospital stay<br>• It is superior to open surgery in women who want to retain fertility |

Techniques to decrease blood loss include preoperative GnRH or SPRM, intraoperative use vasopressin and uterine tourniquet

- **Laparoscopic uterine artery occlusion:** It is generally **less effective** than myomectomy or uterine artery embolization

- **Endometrial ablation:** it may be used to treat heavy menstrual bleeding in the presence of **small fibroids that do not significantly distort the cavity**

- **Hysterectomy:**
  - It is the last resort if other methods fail or inappropriate
  - One third of hysterectomies are indicated of uterine fibroids

# Premenstrual Syndrome

## Definition

Premenstrual syndrome (PMS) is a spectrum of cyclic physical and psychologic symptoms that occur in the second half of the menstrual cycle and impact life quality

## Epidemiology

PMS affects **40%** of women in; **5-8%** suffers from severe PMS

## Clinical picture

Patients report recurrent symptoms in the last week of each cycle. These symptoms are most significant within 4 days prior to menstruation and in the first 2 days of the cycle

- **Psychological symptoms:** e.g. depression, anxiety, irritability, mood swings
- **Physical symptoms:** e.g. mastalgia, bloating

## Diagnosis

- Diagnosis should be made by prospective recording of symptoms using a menstrual diary for 2 successive cycles
- If the menstrual dairy is inconclusive, GnRH analogues should be tried for 3 months to reach a definitive diagnosis. A good response to GnRH is diagnostic

## Classification

| | |
|---|---|
| **Physiological premenstrual disorder (mild)** | • Cyclic symptoms relieved by menses with symptom-free week<br>• No interference with quality of life |
| **Core premenstrual disorder (premenstrual syndrome, premenstrual dysmorphic disorder)** | • Cyclic symptoms relieved by menses with symptom-free week<br>• Symptoms should include depression and fulfill at least 5 out of 11 criteria of PMS |
| **Progestogen-induced PMD** | • Clinical features of core premenstrual disorder are associated with progestins in hormonal therapy or with combined oral contraceptives (COCs) |
| **Premenstrual disorder with absent menstruation** | • PMS features associated with functioning ovaries. However, menses are absent due to endometrial ablation, hysterectomy, levonorgestrel releasing intrauterine system |
| **Premenstrual exacerbation of underlying condition** | • Cyclic symptoms relieved by menses with NO symptom-free week,<br>• It is associated with an underlying condition e.g. diabetes, epilepsy, migraine, depression, asthma |

If the symptoms are not cyclic and not associated with a symptom-free week, it is unlikely PMS and psychiatric referral is indicated

## Management

- **Complementary medicine:**
  - The role of these medications is controversial. They may be helpful. However, they may be associated with drug interactions
  - Examples include calcium, magnesium, vitamin D, Primrose oil and Ginkgo
- **Integrated holistic approach:** it is recommended in all women with PMS
- **Cognitive behavioural therapy (CBT):** should be considered routinely in **severe PMS**

- **Medical treatment:**
  - **Drospirenone-containing COCs:**
    - It is the first line of treatment and the most effective in women with PMS
    - It should be given continuously not cyclically
    - The lowest dose of progestogen is used to reduce side effects (PMS-type side effects).
    - Alternative to oral route, percutaneous oestrogen with cyclic progestogen may be used
    - Micronized progesterone is less likely to produce PMS-like symptoms
    - Progesterone alone should not be used to treat PMS

  - **Selective serotonin reuptake inhibitors (SSRIs):**
    - One of the first line treatments of severe PMS
    - *Dose:* sertraline 25 mg and 50 mg
    - *Regimen:*

| Luteal regimen | Continuous regimen |
|---|---|
| • lower total premenstrual score while higher mood swings and tension effects than continuous.<br>• Luteal regimen is associated with fewer SEs & higher efficacy using newer agents | • It should be withdrawn gradually<br>• Nausea, insomnia, somnolence, fatigue, reduction in libido |

Symptoms typically improve in pregnancy, therefore: these medications should be discontinued if pregnancy is confirmed. If pregnancy occurs while the patient is on these medications, congenital malformation risk is small, if any

Patients are referred to a gynaecologist if Refer if Failed COCs, vit B6, SSRIs and /or severe symptoms

  - **Danazol**:
    - It improves physical symptoms, particularly breast tenderness
    - It may be used in a low dose (200mg)
    - It induces irreversible virilization and therefore, an effective contraception should be used to prevent female foetus virilization if unintentional pregnancy occurs

- **Spironolactone:**
  It may be used to treat physical symptoms

- **GnRH analogue**:
  - It is reserved to the most severe symptoms
  - Treatment should be limited to 6 months. If treatment must extend beyond 6 months: add-back therapy should be given (continuous hormonal therapy OR tibolone)
  - If long-term treatment is decided, DEXA bone scan should be done every year
  - If bone marrow density declines significantly, treatment should be stopped immediately

- **Surgical treatment:**
  - If all options fail, or if long term GnRH is considered, or if there are other indications of surgery, surgery should be considered
  - In women with PMS, who are younger than 45 years, and who do not have any other indications of surgery, preoperative GnRH should always be given to predict response of surgery
  - Preferred surgery is total hysterectomy and bilateral salpingectomy. Preservation of the ovaries is not recommended as symptoms will likely continue and preservation of the uterus is not recommended because hormonal replacement therapy should include progestins to protect the endometrium, which are likely to cause PMS-like symptoms
  - Women should receive hormonal replacement after surgery particularly if younger than 45 years

## Menstrual disorders

### Abstract

Menstrual disorders are the most common cause of outpatient gynaecologic visits worldwide. They significantly impact quality of life and they may result in significant health sequalae. Menstrual disorders may be caused by alternation of endogenous hormonal regulation or may result from structural abnormalities. Therefore, management spectrum is wide, ranging from simple treatment,

such as non-steroidal anti-inflammatory drugs, to hysterectomy. In this chapter, we will discuss types and causes of menstrual disorders and outline diagnosis and management approaches.

## Keywords

Abnormal uterine bleeding, fibroids, hysterectomy, endometrial ablation, myomectomy

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# Postmenopausal Bleeding

## Definition

- Postmenopausal bleeding (PMB) refers to genital bleeding that occurs after at least 1 year of cessation of menstruation
- Most common causes of PMB are benign in origin

## Causes of PMB

| | |
|---|---|
| Atrophic endometritis and vaginitis | 60- 80 % |
| Exogenous estrogens | 15 – 25 % |
| Endometrial carcinoma | 10 % (1% if younger than 50 years) |
| Endometrial hyperplasia | 5 – 15 % |
| Endometrial polyps | 12 % (vs. 6% in premenopausal women, 45% in women taking Tamoxifen) |
| Cervical polyps | 13 % |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_21

## Endometrial polyps

| | |
|---|---|
| **Epidemiology** | • 25% of PMB cases are associated with endometrial and cervical polyps |
| **Risk factors** | • Elevated oestrone e.g. obesity (polyps have greater oestrogen receptors)<br>• Genetic causes (associated with chromosome 6 and 12 anomalies)<br>• Treatment with Tamoxifen (30-60% of patients)<br>• Hypertension |
| **Malignant potential** | • Most polyps are benign<br>• Incidence of precancerous and cancerous pathology is increased in symptomatic patients:<br>▪ In asymptomatic polyps:<br>□ Risk of atypical hyperplasia is 1.2%<br>□ Risk of endometrial cancer is 0.3%<br>▪ In symptomatic polyps:<br>□ Risk of atypical hyperplasia is 2.2%<br>□ Risk of endometrial cancer is 2.3% (10 times greater than asymptomatic polyps)<br>• Other than symptoms, polyp size is the only predictor of an abnormal histology, if polyp size is greater than 18 mm, the risk is 7 times higher |
| **Diagnosis** | • *Transvaginal ultrasound:*<br>▪ It has 97% sensitivity and 74% specificity<br>▪ Presence of a single feeding vessel has a specificity 95% for diagnosis<br>• *Saline infusion sonography:*<br>▪ Incidence of procedure failure is higher in postmenopausal women (14%) than premenopausal women (5%)<br>▪ Experience in performing the procedure may reduce failure by 10%<br>• *Hysteroscopy:*<br>▪ It is the gold standard test.<br>▪ Sensitivity of hysteroscopy is 100% and specificity is 97% |
| **Management** | • Symptomatic polyps should be removed<br>• Asymptomatic polyps smaller than18 mm are unlikely malignant, and risk of perforation form hysteroscopy in postmenopausal women is high |

## Endometrial hyperplasia

| | |
|---|---|
| **Epidemiology** | • In the 50s, incidence of simple hyperplasia is 140:100.000 and complex hyperplasia 213:100 000.<br>• In the 60s, incidence of atypical hyperplasia is 56:100,000<br>• Age-adjusted incidence decreases over time, especially for atypical hyperplasia |
| **Malignant potential** | The risk of progression to carcinoma:<br>• Hyperplasia without atypia is 2%.<br>• Hyperplasia with atypia is 23%.<br>• Complex hyperplasia with atypia is 29%. |
| **Diagnosis** | • *Ultrasonography:*<br>Endometrial thickness is used to assess women with PMB. However, it should not be used as a screening test in asymptomatic women.<br>• *Pipelle biopsy:*<br>▪ It has a 99% sensitivity in diagnosing endometrial cancer. However, it is less sensitive for hyperplasia<br>▪ It is associated with slightly increased rate of insufficient biopsy<br>• *Hysteroscopy:*<br>▪ Routine screening is not indicated in women with Tamoxifen who are asymptomatic<br>▪ Symptomatic women on Tamoxifen should be assessed by hysteroscopy and biopsy, rather than pipelle biopsy because Tamoxifen may cause subepithelial stromal hypertrophy |
| **Management** | • Definitive treatment: is hysterectomy<br>• Conservative management: treatment with progestins or GnRH and follow-up biopsy after 3 months. Hyperplasia will persist or progress in only 25% of cases<br>Risk of cancer is reduced by 3-5 folds in women with complex or atypical hyperplasia who receive progestins |

## Endometrial carcinoma

- 90% of women with endometrial carcinoma present with PMB
- In women with PMB, risk of endometrial carcinoma is 10%. Risk is higher if associated with other risk factors:
  - Age: risk is 25% in women older than 80
  - Obesity: cancer risk is 18%
  - Diabetes mellitus: risk is 21%
  - Obesity and diabetes: risk is 29%
- Doppler has a sensitivity of 80% and specificity of 100% for endometrial cancer.

## Hormonal replacement

- 15% of patients taking unopposed estrogen may develop endometrial hyperplasia
- Continuous combined therapy is associated with less than 1% risk of endometrial hyperplasia

## Selective estrogen receptor modulators

| Tamoxifen | Raloxifene |
|---|---|
| • it increases endometrial thickness by 0.75 mm/year (12 mm in 5 years). After 1 year of treatment, 80% of women will have endometrial thickness > 5 mm<br>• It decreases by 1.3 mm/year after discontinuation<br>• Incidence of atypical hyperplasia with Tamoxifen is 15% | • It is used for prevention of osteoporosis in postmenopausal women<br>• Although its use is associated with greater risk of endometrial thickness > 5 mm, there is no increased risk of endometrial hyperplasia or carcinoma |

## Atrophic endometritis

| | |
|---|---|
| **Aetiology** | • Chronic endometritis of low resistant endometrium<br>• Chemotherapy<br>• Radiotherapy<br>• Tuberculosis |
| **Symptoms** | • Asymptomatic<br>• PMB<br>• Vaginal itching and discharge<br>It may be complicated by pyometra |
| **Investigations** | • *Transvaginal ultrasound:*<br>Endometrium appears thin and normal. In advanced stage, endometrium may be thickened and heterogenous with intracavitary fluid ± gas<br>• *Endometrial biopsy:*<br>In conjugation with genital swabs, it is diagnostic<br>• *Hysteroscopy and biopsy:*<br>It may be necessary to rule out underlying endometrial cancer |
| **Management** | • Local oestrogen can be used in symptomatic women with genital atrophy<br>• Antibiotics may be used if an infectious cause is detected |

## Assessment

- All women with PMB should be thoroughly assessed
- If endometrial thickness is less than 4 mm with transvaginal sonography, endometrial carcinoma is unlikely, and no further assessment is usually required
- If endometrial thickness is 4 mm or more, office endometrial biopsy is warranted. If biopsy is inconclusive, diagnostic hysteroscopy is indicated

- Women with hormonal replacement therapy have a thicker endometrium. In these patients, hysteroscopy and biopsy is indicated in symptomatic patients with endometrial thickness is > 8 mm

# Hormone Replacement Therapy

## Benefits

- **Vasomotor symptoms:**
  - Vasomotor symptoms are present in 70% of women after menopause and are severe in 20% of cases
  - Although median duration is 5 years, 10% women experience these symptoms for longer duration
- **Cardiovascular benefits:**

  Oestrogen provide the following benefits which overall reduces risk of cardiovascular disease and cardiovascular-related mortality:
  - Lowers risk of atherosclerosis
  - Reduces LDL-cholesterol level and lipoprotein-A
  - Inhibits LDL-cholesterol oxidation
  - Raises HDL-cholesterol level
  - Causes coronary artery vasodilation
  - Prevents platelet aggregation
- **Other benefits of hormone replacement therapy (HRT):**
  - Improves mood
  - Protects against bone loss/osteoporosis including vertebrae and hips
  - Protects against connective tissue loss
  - Reduces risk of colorectal cancer,
  - May be protective of cognitive function including dementia and parkinsonism particularly if given early
- **Topical oestrogen:**

  It is superior to systemic oestrogen in improving vaginal symptoms (e.g. vaginal dryness), and reducing incidence of recurrent urinary tract infection and urgency, with limited side effects

## Risks

- **Breast cancer:**
  - HRT causes slight increase in the risk of breast cancer. It does not increase cancer-related mortality
  - With HRT, 6 additional cases in every 1000 women after 5 years of use
  - The risk returns to baseline 5 years after discontinuation
- **Venous thromboembolism (VTE):**
  - Compared to baseline risk (5:1000), oestrogen alone slightly increases the risk to 7:1000, while oestrogen and progestins increase the risk to 12:1000
  - Maximum risk is present at initiation of HRT and then starts to decline after 12 months
  - Transdermal associated with lowest risk
- **Common side effects:**
  - Headache, breast tenderness, bloating, and cramps
  - HRT is not associated with weight gain
  - Symptoms commonly resolve within 3 months of initiation
  - Any unscheduled bleeding should be investigated
  - HRT does not increase blood pressure. Therefore, blood pressure follow-up is indicated

If side effects develop specifically during progestin administration, progestin type may be changed or levonorgestrel releasing intrauterine system may be considered

## Contraindications

The following conditions are relative contraindications to HRT:

- Cardiac disease
- Systemic lupus erythematosus
- Active liver disease
- History of breast cancer, ovarian or endometrial cancer
- Undiagnosed vaginal bleeding
- Personal or family history of VTE (consider referral to a specialist)

Family history of breast cancer is not a contraindication to HRT. Carriers of BRCA mutations can safely receive HRT after risk-reducing surgery. Risk of breast cancer does not increase specially if oestrogen only preparation is given

## Initiation of HRT

- **Pre-treatment assessment:**
  - Medical history, family history of cardiovascular disease and cancer should be discussed
  - Current symptoms including breast and abdominal symptoms should be reviewed
  - Blood pressure and body mass index should be checked. No examination or screening are indicated
  - Women should be counselled on benefits and risks of HRT. Perimenopausal women should be counselled that HRT not a contraception

- **Administration:**

| Perimenopausal women | Postmenopausal women |
|---|---|
| ▪ Cyclic regimen should be considered<br>▪ HRT starts with the next cycle if menstrual cycles are frequent. It may start any time if cycles are more than 3 months apart<br>▪ Women should switch to continuous combined regimen if treatment continues for more than 5 years to reduce risk of hyperplasia. Changing to combined continuous regimen should be done after a withdrawal bleed<br>▪ Switching to continuous combined regimen should start after menopause. Age 54 may be used as a landmark since 80% will be menopausal by then | ▪ Combined continuous regimen should be considered (or tibolone) after menopause<br>▪ HRT is given initially at a low dose. Dose is increased after 3 months if indicated<br>▪ Breakthrough bleeding is common safter initiation of HRT and it resolves shortly after. However, persistent bleeding beyond 6 months requires assessment with transvaginal ultrasound ± endometrial biopsy<br>▪ Similarly, bleeding episode after a period of absence of bleeding should be investigated even if there is an apparent cause e.g. non-compliance |

- **Follow-up:**
  Women should be assessed 3 months after initiation of HRT to determine effect of treatment on symptoms' improvement and quality of life. Women can decide by then whether she is interested in continuing treatment

**Indications of transdermal HRT**

- Migraine headache
- Diabetes
- Controlled hypertension
- Existing gall bladder disease
- Hyperlipidaemia
- Obesity
- Smoking
- Personal history of VTE

If women are treated with HRT, aromatase inhibitors are not effective, and they should switch to tamoxifen

## Alternatives to HRT

In women who do not want to use hormonal treatment or in the presence of a contraindication to HRT, other alternatives could be:

- **General measures:**
  - Avoiding sudden temperature changes, hot drinks, and spicy food
  - Reducing caffeine and alcohol intake, avoid spicy food
  - Exercise
  - Relaxation techniques
  - Cooling devices
- **Medications:**
  - Clonidine
  - Selective serotonin reuptake inhibitors (SSRI) if women are not on tamoxifen
  - Serotonin and norepinephrine reuptake inhibitors (SNRIs) (unlicensed indication)
  - Gabapentin

## Unscheduled bleeding with HRT

- **Prevalence:**
  - With combined HRT, up to 80% of women will experience unscheduled bleeding or spotting in the first 6 months of treatment
  - Continuous combined regimens usually lead to amenorrhoea and should not cause cyclical or breakthrough bleeding

| Combined continuous regimen | Sequential regimen |
|---|---|
| Irregular bleeding is expected in 0–77% in the first few months. After 9 months, only 3–10% of women will still experience it. | Irregular bleeding is experienced by 8–40% of users |

  - Due to unscheduled bleeding on HRT, 25–50% of women discontinue HRT

- **Assessment:**
  - **Indications:**

    ① If there is breakthrough bleeding on continuous combined HRT regimens that:
    - Occurs after 6 months of therapy or
    - Occurs after amenorrhoea has been established

    ② If there is heavy, prolonged or breakthrough bleeding on sequential HRT regimen for more than 2 cycles
  - **Evaluation process:**
    - A full detailed history including a drug history and a clinical examination.
    - Menstrual diaries should be used to assess bleeding episodes and pattern.
    - Pregnancy and sexually transmitted infections should be excluded, and compliance with medication should be checked.

      **❶ Hysteroscopy:**
      - Hysteroscopy with endometrial sampling remains the gold standard for uterine cavity evaluation in the UK.
      - Criteria for hysteroscopy:

        ① Multiple bleeding episodes

        ② Focal lesions on transvaginal ultrasound

③ Endometrial thickness (ET) >5 mm on continuous combined HRT and ET >7 mm on sequential combined HRT

④ Incomplete visualisation of endometrial echo or fragmentation of endometrial echo on ultrasound scan

⑤ High-risk group with risk factors for endometrial disease or cancer (e.g., raised BMI, familial cancer syndromes)

– Disadvantages:

① Invasive, expensive and can lead to postoperative morbidity such as infection or pain.

② Intraoperative complications as uterine perforation with injury to abdomino-pelvic structures.

③ May facilitate spreading of malignant cells into the peritoneal cavity

**❷ Transvaginal ultrasound:**

– It is an initial tool in the investigation and evaluation of women with postmenopausal bleeding and not on HRT is safe and cost effective.
– Among women with postmenopausal bleeding, a thin endometrium (<5 mm) reasonably excludes endometrial pathology.
– Referral criteria for ultrasound to check endometrial thickness:

① Any bleeding after 6 months of continuous combined HRT even in low-risk women

② Bleeding after amenorrhoea has been established

③ Any bleeding in the first 6 months if any significant risk factors present

**❸ Pipelle endometrial sampling:**

– Pipelle sampling is useful where resources and access to TVS or hysteroscopy is limited. However, its use alone in detecting or ruling out endometrial cancer and other pathologies is debatable.
– Moreover, endometrial biopsy can miss up to 20% of focal lesions like endometrial polyps.

**❹ Further imaging:**

CT or MRI may be needed in the event of the presence of adnexal pathologies or a suspected primary malignancy elsewhere.

- **Management:**
  - **General rules:**
    - Appropriate counselling at the outset
    - On continuous combined HRT, bleeding in the first 6 months is usually acceptable if no other risk factors, but it needs investigating if any risk factors or bleeding after amenorrhoea has been established
    - Sequential HRT is the preferred option in perimenopausal women
    - If on sequential combined HRT, ideally check ET using transvaginal ultrasound within a week of the last progestogen pill
    - Expert opinion in refractory cases

  - **Treatment for unscheduled bleeding on HRT**

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| **Sequential HRT** | ▪ Prolonged or heavy withdrawal bleed: increase dose/change type of progestogen or reduce estrogen<br>▪ Bleeding occurs early in progestogen phase: increase the dose/change type of progestogen<br>▪ Spotting before withdrawal period: increase estrogen dose<br>▪ Irregular bleeding: change regimen or increase progestogen dose<br>▪ Painful bleeding: change type of progestogen |
| **Continuous combined HRT** | ▪ Lower estrogen dose preparations preferable<br>▪ Increase the dose or change the type of progestogen<br>▪ Convert to sequential HRT and have a regular bleed if other options fail |
| **Other options** | ▪ Stop HRT by gradually phasing it out may be appropriate once vasomotor symptoms cease<br>▪ Switch to non-oral HRT<br>▪ Significant urogenital symptoms: vaginal estrogen preparations<br>▪ Offer Mirena (for those who continue to continue their estrogen only preparations)<br>▪ Offer surgery (endometrial ablation, resection, or hysterectomy) in refractory cases |

# Vulval Dermatoses and Skin Conditions

## Vulval dermatoses

| | Vulval lichen sclerosis | Vulval lichen planus | Lichen simplex |
|---|---|---|---|
| **Aetiology** | Unknown aetiology, likely autoimmune in origin (associated with other autoimmune disorders) | Inflammatory disorder, most likely autoimmune in origin | • Underlying dermatoses, i.e. atopic dermatitis<br>• Systemic pruritic conditions i.e. renal failure, Hodgkin's lymphoma<br>• Environmental factors e.g. sweating, rubbing of clothing, local irritants<br>• Psychiatric disorders e.g. anxiety |
| **Symptoms** | • Asymptomatic (uncommon)<br>• Vulval itching<br>• Soreness<br>• Dyspareunia<br>• Urinary symptoms<br>• Constipation (if there is perianal involvement) | • Asymptomatic<br>• Vulval itching/irritation<br>• Soreness<br>• Dyspareunia<br>• Urinary symptoms<br>• Vaginal discharge | • Vulval itching<br>• Soreness |

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| **Signs** | • Pale atrophic areas affecting the vulva<br>• Purpura (ecchymosis)<br>• Fissuring<br>• Erosions<br>• Hyperkeratosis<br>• Loss of architecture (loss of labia minora, midline fusion, introital stenosis)<br>Changes may be localized, or may take a 'figure of eight' distribution with involvement of the perianal area | • **Classical type:** papules on keratinized anogenital skin, with or without striae or hyperpigmentation<br>• **Hypertrophic type:** (rare) thick warty plaques, with or without ulcerations or infecting (mimic malignancy)<br>• **Erosive type:** eroded mucosa, pale epithelium at the edges forming pale network (Wickham striae), friable telangiectasia, patchy erythema, scarring and synaechiae<br>Vulvo-vaginal gingival syndrome is diagnosed if these sites are involved | • Lichenification (thickened, scaly, pale skin with accentuated markings)<br>• Erosions and fissuring<br>• Excoriations<br>• Pubic hair is often lost |
| **Complications** | • Squamous cell carcinoma (< 5%)<br>• Clitoral pseudocyst<br>• Sexual dysfunction<br>• Dysesthesia | • Vulvovaginal scarring and synaechiae<br>• Squamous cell carcinoma (3%) | Secondary infection |
| **Diagnosis** | Diagnosis is made by:<br>• Characteristic clinical appearance<br>• Histopathology: epidermal atrophy, hyperkeratosis, sub-epidermal hyalinization of collagen, and lichenoid infiltrate | Diagnosis is made by:<br>• Clinical appearance.<br>• Histopathology: irregular saw-toothed acanthosis, granular and basal cell liquefaction, band-like dermal infiltrate mainly by lymphocytes | Diagnosis is made by clinical presentation<br>History including mental state assessment is required to identify underlying causes<br>Psoriasis or lichen simplex in other parts of the body should be ruled out |

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| **Investigations** | • Biopsy is used to confirm diagnosis, and rule out premalignant or malignant changes<br>• Assessment of autoimmune diseases if clinically indicated e.g. thyroid dysfunction<br>• Skin swab: to rule out co-existing infection if clinically suspected<br>• Patch testing: may be requested by a dermatologist if allergy is suspected | • Biopsy is used to confirm diagnosis, and rule out premalignant or malignant changes<br>• Assessment of autoimmune disease if clinically indicated<br>• Skin swab: to rule out infection if clinically suspected<br>• Patch testing: if allergy is suspected<br>• Hepatitis C screening is not needed | • Screening for infection (e.g. Staphylococcus aureus, Candida albicans)<br>• Patch testing<br>• Serum ferritin<br>• Biopsy |
| **Treatment** | • Ultra-potent topical steroids e.g. clobetasol<br>It is given daily for 1 month, on alternate days for 1 month, twice weekly for 1 month and then on demand<br>Ointment form is preferred (less irritant)<br>• Short term clobetasol, neomycin and nystatin are used if secondary infection is suspected<br>• For resistant cases, topical calcineurin, tacrolimus (local irritation), oral retinoid, ultraviolet phototherapy may be used<br>• No role for surgery (except for management of labial fusion if needed) | • Ultra-potent topical steroids e.g. clobetasol (75% of women experience improvement, 50% are symptom-free, and 10% have resolution of signs)<br>• Maintenance treatment with weak steroids or less frequent potent steroids can be considered<br>• Vaginal steroids or suppositories may be used for severe cases<br>• Antibiotics may be added if infection is suspected<br>• Vulvo-vaginal-gingival syndrome is treated with oral cyclosporine, retinoids (for hypertrophic type), oral steroids, basiliximab | • Precipitating factors should be avoided<br>• Use of emollient soap institutes<br>• Topical corticosteroids with or without antifungal and antibiotic.<br>Steroids can be gradually withdrawn after 3-4 months to treat Lichenification<br>• Mildly anxiolytic antihistamine such as hydroxyzine or doxepin may be used at night<br>• Cognitive behavioral therapy may be considered if there are underlying psychiatric disorders |

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| **Follow-up** | • Follow-up should be scheduled after 3 months to assess response to treatment<br>• Women should be followed-up annually thereafter (by their general practitioner)<br>• Women should be referred if there is no response to treatment or if they develop precancerous or cancerous pathology<br>• Topical steroids are safe in pregnancy, breastfeeding<br>• Topical calcineurin inhibitors are contraindicated in pregnancy and breastfeeding<br>• If retinoids are used, pregnancy should be avoided for 2 years | • Follow-up should be scheduled after 3 months then annually (unless she is well controlled and properly counselled)<br>• Erosive lichen is an indication of long-term specialized follow-up | • Mild disease is followed-up as clinically required<br>• Severe disease is followed-up after 1 month and then as required |

## Other vulval conditions

| | **Vulval eczema** | **Vulval psoriasis** | **Vulval intraepithelial neoplasia** |
|---|---|---|---|
| **Symptoms** | • Vulval itching<br>• Soreness | • Vulval itching<br>• Soreness<br>• Burning sensation | • Asymptomatic (common)<br>• Lumps<br>• Erosions<br>• Burning and itching<br>• Vulval pain |

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| **Signs** | • Erythema<br>• Lichenification and excoriation<br>• Fissuring<br>• Pallor or hyperpigmentation | • Plaques (well-demarcated and brightly erythematous) with no scaling<br>• It frequently affects natal cleft. Other areas may be also involved e.g. scalp | • Variable lesions<br>• Warty, raised, or eroded lesions<br>• White, erythematous, or pigmented lesions<br>• Multifocal lesions are common |
| **Complications** | Secondary infection | • Koebner effect (caused by irritation from urine, tight-fitting clothes, or sexual intercourse), which causes worsening of symptoms | • Squamous cell carcinoma (9-19%)<br>• Recurrence |
| **Diagnosis** | • Clinical signs<br>• Patch testing<br>• Biopsy is indicated only if there are atypical features | • Clinical signs<br>• General examination of other signs of psoriasis (skin and nails)<br>• Punch biopsy is indicated if diagnosis is doubtful | • Biopsy |
| **Treatment** | • Avoid precipitating factors<br>• Recommend emollient soap institutes<br>• Topical corticosteroids: 1% Hydrocortisone for mild cases, or Betamethasone valerate 0.025% for severe cases<br>• Antifungal and/or antibiotics may be added | • Avoid irritating factors<br>• Recommend emollient soap institutes<br>• Topical corticosteroids: weak to moderate steroids intensive<br>• Antifungals and/or antibiotic may be added<br>• Weak coal-tar preparations may be used<br>• Vitamin D analogues such as Talcalcitol may be used | • **Cervical cytology:** should be followed-up and kept up to date<br>• **Refer to colposcopy:** to rule out CIN and VIN<br>• **Local excision:** is the standard management (lowest risk of recurrence)<br>• **Imiquimod cream 5%:** limited by side effects, and lack of long-term data (unlicensed indication)<br>• **Vulvectomy**: effective. However, it affects function and cosmesis<br>• **5-fluorouracil cream:** side effects are common |

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| **Follow-up** | • As clinically required Long-term follow-up and psychological support may be indicated | • Mild disease: as clinically required<br>• Severe disease: follow-up is scheduled after 1 month and then as indicated | • Close and continuous follow-up is mandatory<br>• Imiquimod and 5 fluorouracil cream are not licensed for use in in pregnancy |

CIN: cervical intraepithelial neoplasia, VIN: vulval intraepithelial neoplasia

## Vulval pain

| | **Localized provoked vulvodynia** | **Unprovoked vulvodynia** |
|---|---|---|
| **Aetiology** | Multifactorial, usually associated with recurrent candidiasis | Unknown, managed as a part of chronic pain syndrome |
| **Symptoms** | Long history of vulval pain at penetration during sexual intercourse | Long standing vulval pain<br>Pain may be associated with other unexplained symptoms including urinary symptoms, irritable bowel syndrome and fibromyalgia |
| **Signs** | Focal tenderness is elicited by gentle application of a cotton swab at introitus or around clitoris<br>No signs of inflammation. Normal vestibular erythema may be noticed and should not be mistaken with inflammation | The vulva appears normal |
| **Complications** | Sexual dysfunction<br>Psychological morbidity | |
| **diagnosis** | Clinical diagnosis made on history and examination | Clinical diagnosis made on history and examination after exclusion of other causes of vulval symptoms |
| **Investigations** | Biopsy only if underlying dermatosis is suspected | |
| **Treatment** | • Avoidance of irritating factors<br>• Use of emollient soap substitutes<br>• Topical local anesthetics (5% lidocaine ointment, 2% lidocaine | • Use of emollient soap substitutes<br>• Pain modifiers e.g. tricyclic antidepressant (10-100mg of amitriptyline) |

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| | gel). They should be applied 15-20 minutes prior to sex. They should be washed off or condoms should be used to avoid penile numbness<br>• Physical therapy: pelvic floor muscle biofeedback<br>• Vaginal transcutaneous electrical nerve stimulation<br>• Vaginal trainers<br>• Cognitive therapy<br>• Psychosocial counselling<br>• Pain modifiers: amitriptyline 10-75 mg may be used<br>• Surgery: modified vestibulectomy may be considered if all other measures fail<br>Surgery is likely effective in women who are responsive to topical lidocaine | • If unresponsive: gabapentin, pregabalin may be used<br>• Alternatives: topical local anesthetics<br>• Cognitive behavioral therapy<br>• Acupuncture<br>• Physical therapy |
| **Follow-up** | Only when clinically indicated | |

## General recommendations

- In all women with vulval skin conditions, the following recommendations should be considered:
  - Avoid skin contact with shampoos, soaps, bubble bath. Simple emollients may be used instead
  - Avoid tight-fitting garments and spermicidal lubricated condoms
- Sexually transmitted infection (STI) screening should be considered in all patients with vulvar symptoms. However, Partner tracing is not required unless screening is positive for STI
- Vulvovaginal candidiasis should be excluded if the patient presents with vulval itching
- All patients should be assessed for sexual dysfunction

# Menopause

## Abstract

Menopause is just a new stage of women life that starts after cessation of menstrual cycle. Transitioning to menopause presents a new experience and women should be aware of the expectations. As gynaecologists, our role is to secure a smooth transition to menopause to all women and to address gynaecologic issues that are associated with this stage of life. In this chapter, we will discuss clinical care of menopausal women and important gynaecologic disorders associated with menopausal transition and after menopause.

## Keywords

Postmenopausal bleeding, HRT, vulvar dystrophy, vulvar conditions

## Further readings

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# PART V

## Reproductive endocrinology and gynecologic oncology

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# Contraception

## Combined hormonal contraception

- **Administration:**
  - Before initiation of combined hormonal contraception (CHC), complete medical history, medications and family history are reviewed. Recent blood pressure and body mass index are checked. However, no pelvic examination, labs or screening are needed
  - Standard preparation to start with is combined oral contraceptives containing ethinyl oestradiol ≤ 30 mcg, and levonorgestrel or norethisterone
  - CHC can be given in the first 5 days of the cycle without additional contraception
  - If given after day 5 of the cycle, additional contraception for 7 days OR pregnancy test may be done immediately and after 21 days
  - CHCs are prescribed for 12 months, routine annual review is recommended to assess blood pressure, body mass index, change to medical history or medications and compliance

- **Regimen:**
  - Tailored (combined hormonal contraception) CHC regimens may be superior to traditional cyclic regimen:
    - **Advantages:** Tailored regimens reduce withdrawal bleeding frequency and side effects
    - **Disadvantages:** unscheduled bleeding is common with tailored regimens
  - Examples to tailored regimens are shortened hormone-free interval, extended 9 weeks, continuous, and flexible extended




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_22

- **Side effects:**

  Breakthrough bleeding is indicative for low oestrogen dose in CHC formula. Therefore, preparations with high oestrogen may be used. Up to 70 mcg may be used for a short term after expert advice is obtained

- **Effectiveness:**
  - **Overall effectiveness:**
    - All CHCs are comparable in effectiveness and are less effective than long acting reversible contraceptives (LARC) specially with typical use
    - Perfect-use failure rates are less than 1% (0.3%). However, typical-use failure rate of combined oral contraceptives is 9%
  - **Effect of obesity:**
    - Oral contraceptives are not affected by weight. However, effectiveness may be reduced by bariatric surgery (absorptive effect)
    - Contraceptive patches are less effective if women weight is 90 kg or above
  - **Effect of enzyme inducing drugs:**
    - Enzyme inducing drugs reduce CHC effectiveness for up to 28 days after stopping these drugs. An effective alternative should be used during this window
    - Use of lamotrigine with CHC should be avoided as it impacts seizure control and increases the risk of lamotrigine toxicity
    - Non-enzyme inducing antibiotics → no precaution
  - **Effect of ulipristal:**

    If ulipristal is used for emergency contraception, use of CHCs should be postponed for 5 days and another contraception is used till CHC is effective
  - **Effect of gastrointestinal symptoms:**

    Effectiveness of COC is reduced by vomiting or severe diarrhea

- **Non-contraceptive benefits:**
  - CHC improves heavy menstrual bleeding, dysmenorrhea, and premenstrual syndrome
  - CHCs reduce the risk of recurrence of endometriosis postoperatively (continuous regimen)
  - CHC improves polycystic ovary syndrome-related symptoms (acne, hirsutism, menstrual irregularities)
  - CHC reduces risk of certain cancers:
    - Endometrial cancer

- Ovarian cancer (risk is reduced by 40-50% after 10 years of use, the benefit persists for 30 years) and colorectal cancer (20%)
- Up to the age of 50, CHCs can be used for contraception, management of menopausal symptoms and prevention of bone loss

- **Side effects:**
  - Headache and dizziness
  - Nausea
  - Breast tenderness
  - Bloating. Better with tailored regimen
  - Unscheduled bleeding
    - These women should be advised to wait for 3 months before seeking medical advice
    - It is less observed with transdermal or vaginal preparations
    - It is less observed with oestradiol dose of 30 compared to 20 mcg
    - It is not related to progestin type
  - Mood changes

    In these cases, an alternative may be used or another CHC with a different progestin may be tried
  - Decrease in libido (unlikely with 20 mcg of oestradiol)
  - Slight delay in return of fertility

    However, return of ovulation occurs within 1 month in most women

- **Adverse effects:**
  - **Venous thromboembolism (VTE):**
    - CHCs increase the risk of VTE. Magnitude of risk is related to oestrogen dose & progestin type (the risk is least with first and second generation progestins and norgestimate)
    - Absolute risk of VTE is very small (5-12:10000 vs 2:10000 as a baseline)
    - Reduce immobility during travelling while on CHCs is associated with significant risk (VTE is 1:500 after an 8-hour flight)
    - Because of the risk of VTE, women should be switched to another contraception 4 weeks prior to surgery
    - The risk is the highest after initiation, and then decreases after 1 year of use

- **Vascular occlusion:**
  - CHCs are associated with very small increase in risk of myocardial infarction (1:10,000) and ischemic stroke (2:10,000) but not haemorrhagic stroke
  - The risk is greater with higher doses of oestrogen
- **Gynaecologic cancers:**
  - CHCs is associated with small increase in breast cancer risk (relative risk is 1.2). The risk decreases after discontinuation and normalizes after 10 years
  - CHC is associated with small increase in cervical cancer risk after 5 years of use (relative risk is 2). Risk is normalized after 10 years of use

- **Absolute contraindications (UKMEC category 4):**
  - Smoking (≥15 cigarettes/day) in women aged ≥35 years
  - Uncontrolled hypertension
  - Multiple risk factors of atherosclerotic cardiovascular disease
  - Current or history of venous thromboembolism/pulmonary embolism
  - Major surgery with prolonged immobilization
  - History of or current ischemic heart disease
  - Known thrombophilia
  - History of cerebrovascular accident
  - Complicated valvular heart disease, e.g., pulmonary hypertension, atrial fibrillation, or subacute bacterial endocarditis
  - Migraine with aura
  - Systemic lupus erythematosus with positive or unknown antiphospholipid antibodies
  - Current breast cancer
  - Complicated or uncontrolled diabetes (with nephropathy, neuropathy, retinopathy)
  - Viral hepatitis (active or flare)
  - Severe (decompensated) cirrhosis
  - Hepatocellular adenoma and hepatoma

  Family history of breast cancer or positive BRCA are not contraindications to CHC

- **Incorrect use:**

  Incorrect use or missed pills more than 24 hours from the due time should be managed by:
  - If one pill is missed (> 24 hrs of due time), missed pill should be taken and the rest of pills are taken as scheduled (patch effect extends for 3 days, ring effect extends for 2 days)

- If 2 or more pills (72 hours since last pill) are missed, the last pill is taken, a backup method is used for 7 days and if a pill is missed in the first week, emergency contraception is used, while if the pill is missed in the third week of the cycle, pill free interval should be cancelled

## Progestin only pills (POPs)

POPs are commonly used during breastfeeding or when oral contraception is preferred and there is a contraindication to oestrogen

- **Types of POPs:**
  - **Conventional POPs:** containing levonorgestrel. They act primarily by affecting cervical mucous permeability, endometrial changes and alteration of tubal mobility. Their effect on ovulation is variable
  - **New POPs:** containing desogestrel. These pills prevent ovulation more reliably (97%) and thereby, they are more effective than old-type POPs

- **Contraindications:**

  The only absolute contraindication (category 4) to POPs is current breast cancer

- **Side effects:**
  - Menstrual disorders: complete amenorrhea to unpredictable bleeding (main cause of discontinuation)
  - Development of functional ovarian cysts
  - Headache, dizziness, nausea, weight gain, bloating, acne, and mood changes

- **Incorrect use:**
  - **Older-type POPs:**

    A pill is considered missed if it is not taken within 3 hours of the due time, women should take the missed POP as soon as possible, take the next POP as scheduled, use additional contraception, or abstain from intercourse for 48 hours
  - **Desogestrel-containing POP:**

    A pill is considered missed if it is not taken within 12 hours of the due time, women should take the missed POP as soon as possible, take the next POP as scheduled, use additional contraception, or abstain from intercourse for 48 hours If the woman is breastfeeding

## Long acting reversible contraception (LARC)

- **Methods:**

  LARC refers to intrauterine device (IUD), levonorgestrel-releasing intrauterine system (LNG-IUS) subdermal implants (Nexplanon), and contraceptive injectables

- **Mode of action:**
  - IUD is the only non-hormonal LARC and it acts mainly be alteration of the endometrium, tubal motility, and uterine contractions
  - Hormonal methods act by inhibition of ovulation through suppression of the hypothalamic/pituitary/ovarian axis. Secondary mechanisms of action include endometrial suppression and increased cervical mucus thickness

- **Effectiveness:**
  - LARC is more cost effectiveness even after 1 year of use compared to COCs
  - LARC reduces the rate of unintended pregnancy
  - IUD and LNG-IUS are more cost effective than injectables
  - Implants are highly effective. Failure rate is 0.1%

- **Administration:**
  - Pregnancy should be excluded before initiation of these methods
  - Informed consent is required. If a woman has difficulties with counselling, discussion should be made with the careers/other parties
  - For girls younger than 16, consider child protection issues and Fraser guidelines before initiation
  - For IUDs and LNG-IUSs, provider skills should be maintained by placing at least one IUD/month

- **Contraindications:**

  The only absolute contraindication (category 4) to POPs is current breast cancer

| | |
|---|---|
| **Intrauterine device (IUD)** | ▪ **Side effects:**<br>□ Heavy menstrual bleeding<br>□ Dysmenorrhea<br>□ Increased vaginal discharge<br>▪ **Complications:**<br>□ Vasovagal reaction<br>□ Uterine perforation (1:1000)<br>□ Failure of insertion<br>□ Contraceptive failure (0.5%)<br>□ Ectopic pregnancy (IUD prevents intrauterine pregnancy rather than extrauterine pregnancy because it does not prevent ovulation. Therefore, it does not increase risk of ectopic pregnancy but if pregnancy occurs, it is likely ectopic pregnancy)<br>□ Pelvic inflammatory disease: the risk increases by 6 folds in the first 3 weeks after insertion. IUD has been linked actinomycosis infection, which is generally rare<br>□ Expulsion (risk is 5%, mainly in the first 3 months)<br>□ IUD displacement<br>▪ **Contraindications (category 4):**<br>□ Pregnancy<br>□ Current pelvic inflammatory disease<br>□ Gestational trophoblastic disease with persistently elevated β-hCG<br>□ Pelvic tuberculosis<br>□ Immediate post-septic abortion<br>□ Postpartum genital infection<br>□ Unexplained vaginal bleeding before assessment<br>□ Endometrial cancer<br>□ Cervical cancer awaiting treatment<br>□ Distorted uterine cavity<br>▪ **Follow-up:**<br>A 3-6 week visit is recommended after insertion to confirm correct placement and absence of infection. No further follow-up is required if there are no concerns |

| | |
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| **levonorgestrel-releasing intrauterine system (LNG-IUS)** | ▪ **Indications:**<br>□ Long term reversible contraception<br>□ Treatment of heavy menstrual bleeding<br>□ Treatment of dysmenorrhea<br>□ Treatment of endometriosis-related pain<br>□ Treatment of endometrial hyperplasia<br>□ As a progestin component of hormonal replacement therapy (endometrial protection)<br>▪ **Contraindications:**<br>□ Pregnancy<br>□ Current breast cancer<br>□ Distorted uterine cavity<br>□ Current pelvic inflammatory disease<br>□ Current purulent cervicitis/pelvic inflammatory disease<br>□ Gestational trophoblastic disease with persistently elevated β-hCG<br>□ Pelvic tuberculosis<br>□ Immediate post-septic abortion<br>□ Postpartum genital infection<br>□ Unexplained vaginal bleeding<br>□ Cervical cancer |
| **subdermal implants (Nexplanon)** | ▪ **Failure rate:** is 0.1%<br>▪ **Duration of action:** Nexplanon is effective for 3 years<br>▪ **Side effects and complications:**<br>□ Complications of insertion and removal e.g. broken or damaged implant, and difficult localization, difficult removal (formation of a fibrous band)<br>*Nexplanon can be visualized by X-ray (radio-opaque) or ultrasound if not palpable*<br>□ Abnormal bleeding patterns e.g., prolonged irregular bleeding<br>□ Weight gain |
| **contraceptive injectables** | ▪ **Failure rate:** is 0.3% with perfect use, 4% with typical use<br>▪ **Non-contraceptive advantages:**<br>□ It may improve premenstrual symptoms and dysmenorrhea<br>□ It reduces frequency of sickle cell crisis in affected women |

| | |
|---|---|
| | ◻ It reduces frequency of epileptic seizures<br>◻ It may relieve endometriosis-related pain<br>▪ **Side effects:**<br>◻ Disturbances in menstrual pattern<br>◻ Weight gain<br>◻ Bone loss (reversible)<br>◻ Progestogenic side effects, e.g., bloating, breast pain, headaches, acne, and decrease in libido<br>◻ Delay in return of fertility (up to 9 months from the last injection)<br>▪ **Incorrect use:**<br>Injectables should be given every 13 weeks. If the next dose is not given within 1 week of the due date, pregnancy should be ruled out, injection is given, and an additional method should be used for 7 days |

## Emergency contraception

- **Indications:**
  - Unprotected intercourse at any day of the cycle
  - Unprotected intercourse 21 days or more postpartum, 5 days or more after miscarriage, ectopic pregnancy, or gestational trophoblastic disease (GTD)

  Emergency contraception does not protect against further unprotected intercourse, and it should be repeated if necessary

- **Administration:**

  Oral levonorgestrel (1.5 mg), IUD, and ulipristal can be used:
  - IUD and ulipristal can be used up to 5 days. Levonorgestrel is used for up to 72 hours
  - Unlike IUD, oral medications do not work if ovulation occurred
  - In women who had unprotected intercourse early in the cycle, and recently has a second unprotected intercourse, levonorgestrel or ulipristal can be offered. They will not result in pregnancy disruption or foetal anomalies
  - IUD can be offered to adolescents if indicated

- After emergency contraception is administered, discuss immediate use of maintenance contraception with these women. If ulipristal was used, combined hormonal contraceptives should be delayed for 5 days and abstinence or barrier method is used for 7 days

- **Effectiveness:**
  - IUD is the most effective, followed by ulipristal and then oral levonorgestrel
  - Women weight affects effectiveness of levonorgestrel
  - Enzyme inducing drugs may reduce effectiveness of ulipristal and levonorgestrel. Therefore, IUD should be considered. The use of higher doses of levonorgestrel (3 mg) is of uncertain effectiveness. Do no repeat the course
  - Ulipristal effectiveness may be reduced if:
    - Progestin is given in the first 5 days after ulipristal administration
    - Progestin is given in the last 7 days before ulipristal administration

    Therefore, if emergency contraception needs to be repeated within the same cycle, levonorgestrel should not be used within 5 days of ulipristal use and ulipristal should not be used if levonorgestrel was used in the last 7 days

- **Contraindications:**
  - IUD contraindications are the same regardless of the indication (see before)
  - Ulipristal is contraindicated in women with severe asthma (managed by oral steroids)

- **Precautions:**
  - Breastfeeding increases the risk of IUD perforation. However, the absolute risk is remains low
  - Ulipristal should not be used with breastfeeding. If ulipristal is given, breastfeeding should be stopped, and breast milk should be discarded for 1 week after administration
  - Levonorgestrel can be used safely with breastfeeding

## Postpartum contraception

- **Initiation of contraception:**
  - Contraception should be initiated by day 21 postpartum
  - Although it is not indicated in the first 3 weeks postpartum, contraceptive methods can be started safely immediately after birth if desired except COCs

- Immediate postpartum placement of intrauterine contraceptive methods or subdermal implants is recommended because it is associated with high acceptance and continuation rate and lower risk of unintended pregnancy
- Contraception should be available to provide to women prior to discharge. If the woman-preferred method cannot be provided immediately, a bridging method should be provided
- Women who start LARC immediately after abortion have lower chance to have another abortion within 2 years versus other methods

**Back-up plans**

- Additional method (barrier methods or abstinence) is required if hormonal contraception is started at or after 21 days postpartum (or 5 days after abortion, methotrexate treatment or treatment of gestational trophoblastic disease 'GTD')
- If unprotected intercourse occurred beyond 21 days postpartum, emergency contraception using levonorgestrel 1.5mg or ulipristal 30mg can be used after 21 days, or copper IUD can be used safely after 28 days

- **Contraceptives options:**
  - **Progestin only contraception:**
    - These options are safe to use at any time postpartum and has no adverse effects on lactation
    - In women receiving mifepristone for medical management of abortion, Implants can be used safely initiated at time of mifepristone administration. However, administration of injectables at time of mifepristone administration may increase incidence of failed abortion and the decision should be discussed with the patient
    - If there is absent or scant bleeding with medical management of abortion, this should not be attributed to hormonal contraception
  - **Combined hormonal contraception (CHC):**
    - In breastfeeding women, it should not be started earlier than 6 weeks postpartum
    - In non-breastfeeding women, CHC can be initiated 3 weeks postpartum if there is no increased risk of venous thromboembolism (VTE)
    - Regardless of breastfeeding status, CHC should not be used within 6 weeks postpartum if there is higher risk of VTE e.g. immobility, transfusion, body mass index ≥ 30, postpartum haemorrhage, caesarean delivery, preeclampsia, smoking

- CHC can start immediately after abortion. In women with recurrent miscarriage, antiphospholipid antibody syndrome should be ruled out before CHC is initiated. Otherwise, contraception should not be postponed to complete work-up
- Hormonal contraception may start immediately after treatment of GTD
- **Lactational amenorrhea method (LAM):**
  - LAM is efficient in the first 6 months if women are amenorrheic and exclusively breastfeed
  - Under these circumstances, LAM success if 98%
- **Intrauterine device (IUD):**
  - IUD can be placed either immediately after birth (10 minutes after delivery of the placenta) or within 48 hours postpartum. Otherwise, IUD placement should be delayed after 4 weeks
  - IUD can be placed immediately after expulsion of products of conception following medical treatment of abortion or at the time of surgical evacuation
- **Permanent sterilization:**
  - Both Flishie clips and modified pomeroy techniques may be used
  - This method should not be decided at delivery because there is high risk of regret
  - Consent of elective sterilization at time of caesarean delivery should be signed at least 2 weeks in advance
  - In case of abortion, an immediate decision of sterilization may be associated with high risk of regret. The procedure can be done at the same time of surgical abortion
  - Sterilization may start immediately after treatment of GTD
- **Barrier methods:**
  - Male and female condoms can be used safely immediately postpartum or after abortion
  - Diaphragm use should be delayed to 6 weeks postpartum after delivery, second trimester abortion or GTD to allow genital involution
- **Fertility awareness methods:**

  These methods may be difficult to use due to bleeding irregularities and breastfeeding

- **Special considerations:**
  - Women who are interested in conception after abortion, should be recommended to try to conceive immediately. Pregnancy outcomes are more Outcomes are more favourable if pregnancy occurs within 6 months of miscarriage compared to more than 6 months

- Women treated with methotrexate should receive highly effective contraception for at least 3 months. If unprotected intercourse occurred after 5 days of treatment, emergency contraception should be considered
- After complete molar pregnancy is surgically managed, pregnancy should be avoided for at least 6 months to allow HCG monitoring
- After partial mole is treated, contraception should continue until 2 monthly consecutive hCG levels are normal

## Contraception in older age groups

20% of pregnancies in women aged > 40 are unplanned and 28% of these pregnancies end in termination

| Method of contraception | Time of discontinuation |
|---|---|
| **Non-hormonal methods** | • Women aged >50 can stop contraception 1 year after cessation of menstruation<br>• Women aged <50 can stop contraception 2 years after cessation of menstruation |
| **Oral progesterone only contraception** | • Contraception should be discontinued 1 year after reporting 2 FSH levels >30 IU/l taken at least 6 weeks apart<br>• It is not recommended to use FSH for the purpose of discontinuation of contraception in women <50 years |
| **Combined hormonal contraception** | Combined hormonal contraception should be discontinued 2 weeks before serum FSH is checked |
| **Progestin injectables** | Combined hormonal contraception should be discontinued 12 months before serum FSH is checked |

Alternatively, contraception can be continued until the age of 55

## Contraception in teenagers

Prescription of contraception to girls younger than 16 years should follow Fraser Guidelines:

- The girl can understand doctor's advice

- The girl does not have to tell her parents and the doctor should not tell her parents against her will. No parental consent is required

Reproductive endocrinology

# Infertility Overview

## Background

- **Definition:**

  Failure of a couple to conceive within one year of regular unprotected sexual intercourse without the use of contraception

- **Incidence:**
  - 80% of couples will conceive within 1 year and 90% within 2 years if a woman age less than 40, does not use any contraception, and has regular sexual intercourse
  - Regular Sexual intercourse every 2-3 days increases pregnancy chance
  - Fertility of females and to a lesser extent male fertility decline with age

- **Risk factors:**
  - **Alcohol:**
    - For women seeking conception, alcohol intoxication should be avoided, and should not exceed 1-2 units of alcohol once or twice weekly
    - For men, 3-4 units/day of alcohol unlikely affects sperm quality. Excess alcohol intake should be avoided
  - **Smoking:**
    - In women, passive and active smoking affects fertility
    - In men, it may decrease sperm quality. However, clinical impact of smoking is not clear
  - **Occupation, over the counter (OTC), and recreational Drugs:**

    These factors may have a negative effect on fertility
  - **Underwear in males:**

    It increases scrotal temperature, which may reduce semen quality

- **Body mass index (BMI):**
  - In women:
    - Women with BMI > 30 take a longer time to conceive. If there is ovulatory dysfunction, weight reduction is recommended to increase probability of conception. Engagement in a group program is more effective
    - Women with BMI < 19 and irregular menstruation or no menstruation should be advised on weight gain
  - In men: BMI > 30 in males reduces fertility and weight reduction is recommended

## Assessment

- **History:**

| | |
|---|---|
| **Personal history** | ▪ Couple's age and duration of relation<br>▪ Occupation e.g. some men occupations may affect semen quality and scrotal temperature<br>▪ Special habits for the couple e.g. smoking, alcohol, recreational drugs |
| **menstrual history** | ▪ Menstrual pattern (regularity of menses is indicative of ovulatory cycles)<br>▪ Date of last menstrual period<br>▪ Presence of dysmenorrhea and premenstrual syndrome<br>▪ Symptoms of hyperandrogenism e.g. acne, hirsutism |
| **obstetric history** | ▪ Number of pregnancies and abortions<br>▪ Type of delivery, indications of caesarean section if applicable, and any obstetric complications<br>▪ Type and management of previous abortions<br>▪ Number of living children, use of any contraception methods, and duration of use |
| **Sexual history** | ▪ Sexual history including frequency of intercourse<br>▪ History of sexual abuse |
| **Family history** | ▪ Couple consanguinity<br>▪ History of infertility in the family |
| **Medical history** | ▪ History of diseases and medications<br>▪ Time and results of the last cervical cancer screening |

- **Investigations:**

**Initiation of investigations**

- Investigations are considered after one year of no conception despite unprotected intercourse OR After 6 months of failed intrauterine insemination
- Earlier evaluation is needed if women are 36 years or older OR if there is known infertility cause or risk factors of infertility

- **Male investigations:**
  - Semen analysis is the first step in assessment of a couple with infertility
  - If the semen analysis is abnormal, it should be repeated after 3 months. However, it should be repeated as soon as possible if there are severe abnormalities e.g. azoospermia, severe oligospermia. Testing anti-sperm antibodies is not recommended

- **Female investigations:**

**❶ Ovarian factor assessment:**

**① Assessment of ovarian reserve:**

- Ovarian reserve indicates ovarian response to ovarian stimulation
- Age is the initial and most important predictor of ovarian reserve and success of natural or in-vitro fertilization (IVF) conception. Other predictors of ovarian reserve include:

| | Antral follicle count (AFC) | Anti-Müllerian hormone (AMH) | Follicle stimulating hormone (FSH) |
|---|---|---|---|
| **Low response** | AFC ≤ 4 | AMH ≤ 5.4 pmol/l | FSH > 8.9 IU/l |
| **High response** | AFC > 16 | AMH ≥ 25 pmol/l | FSH < 4 IU/l |

- There is no role for ovarian volume, ovarian blood flow, inhibin B, Estradiol E2 in assessment of ovarian reserve

② **Assessment of ovulation and ovulatory dysfunction:**

| Diagnosis of ovulation | Diagnosis of causes of anovulation |
|---|---|
| □ Mid-luteal serum progesterone (day 21 of the 28-day cycle) should be considered in all women even if the cycle is regular<br>If the cycle is irregular, the test needs to be delayed (e.g. day 28 if cycle length is 35 days) and should be repeated weekly till next menses.<br>□ Serum FSH and LH: should be considered in women with irregular cycles<br>□ Basal body temperature (BBT): is not reliable, and should not be used | □ Serum prolactin: should be considered in women with ovulatory dysfunction, agalactorrhea, or possible pituitary tumor<br>□ Thyroid Function Test: should not be considered routinely except if there are symptoms of thyroid disease<br>□ Luteal phase defect (LPD): should not be investigated with endometrial biopsy (no evidence that the treatment of LPD improves pregnancy rate) |

❷ **Tubal factor assessment:**

**Assessment of risk of comorbidities should be assessed first:**
(pelvic inflammatory diseases (PID), previous ectopic pregnancy, and endometriosis)

Present → Direct assessment with laparoscopy and chromotubation (dye test) to test tubal patency and assess tubal pathology

Absent → Hysterosalpingography or Hysterosalpingo-contrast ultrasonography

**❸ Uterine factor assessment:**

- Uterine cavity can be assessed along with tubal patency using hysterosalpingography or Hysterosalpingo-contrast ultrasonography
- Hysteroscopy is not offered for screening unless clinically indicated

**❹ Uterine factor assessment:**

Post-coital testing of cervical mucus is not recommended

**❺ Pre-treatment investigations:**

- Rubella antibodies should be tested. Non-immune women should be offered rubella vaccine and pregnancy should be delayed for 1 month after vaccination
- If intrauterine insemination (IUI) is planned, screening for chlamydia trachomatis should be considered:
  - If it tests positive, the couple should be treated
  - If screening was not done, consider prophylactic antibiotics prior to the procedure
- Before IVF, women should be tested for HIV, hepatitis B, and C

## Management

- **Couple counselling:**

**Couple counselling in the first visit**

- Counsel both partners in the same setting
- Counsel couples to wait for one year if their age is younger than 36
- Counseling throughout the process of management should be offered by a person not involved in fertility medical care
- Counsel couples that infertility is stressful, and it may affect relation, libido, frequency of intercourse and offer fertility support group
- Counsel the couple regarding side effects and risks associated with infertility management
- Counsel on lifestyle modification e.g. weight reduction and smoking cessation

- **Couple preparation and initial management:**
  - **Folic acid:**
    - Folic acid should be considered before conception and for 12 weeks
    - Standard dose is 0.4 mg/day. A higher dose (5mg/day) should be considered in the following indications:
      ① Previous history of neural tube defect
      ② Diabetes
      ③ Women treated with antiepileptics
      ④ Haemoglobinopathies
  - **Lifestyle modifications:**
    Smoking cessation, weight reduction, cessation of alcohol and recreational drugs should be considered prior to conception
  - **Management of chronic viral infection:**
    Women with hepatitis B, C, or HIV should be referred to centres with appropriate experience
    - **HIV:**
      - If a man is infected with HIV, a discussion should be held between the couple, fertility specialist and HIV specialist regarding risk of transmission with unprotected sexual intercourse, risks to the mother and foetus, and risks with lactation
      - Risk of sexual transmission is negligible if:
        ① The patient is compliant with Highly Active Antiretroviral Therapy (HAART)
        ② Viral load < 50 for more than 6 months
        ③ HIV is not associated with other infections
        ④ Unprotected intercourse is limited to ovulation time only

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| **If these criteria are present** | Sperm washing is not preferred (it does not decrease risk of transmission and it may decrease likelihood of pregnancy. However, it may be done if requested by the couple<br>Pre-exposure prophylaxis to women is not indicated |
| **If these criteria are absent** | Sperm washing should be offered (it reduces but does not eliminate risk of transmission) |

    - **Hepatitis B:**
      Partners of hepatitis B patients should be offered the vaccine. Sperm washing is not indicated for hepatitis B men

- **Hepatitis C:**
  Hepatitis C infection should be discussed with the couple, IVF specialist, and hepatitis specialist. Treatment options to eradicate hepatitis C should be considered before conception

- **Management of male factor infertility:**
  - **Medical management:**

| | |
|---|---|
| **Hypo gonadotrophic hypogonadism** | Gonadotrophins may be offered to improve fertility of males Medications (e.g. androgens, bromocriptine) has not role to treat semen abnormalities |
| **Genital infection** | Antibiotics are offered to treat infection. However, it should not be offered for" leukocytes in semen" without identified infection |

  - **surgical treatment:**
    - **Obstructive azoospermia:** surgical correction of epididymal blockage can be offered by an experienced surgeon. Otherwise, sperm surgical retrieval is offered
    - **Varicocele:** surgery for varicocele is not recommended (does not improve pregnancy rate)

- **Management of female factor infertility:**
  - **Ovarian factor infertility:**
    - **WHO group I (hypothalamic-pituitary failure):**
      - If BMI is below 19, advise women to gain weight and to practice moderate exercise instead of high exercise level
      - Induction of ovulation is achieved using pulsatile gonadotrophins releasing hormone (GnRH) or gonadotrophins with luteinizing hormone (LH) activity

    - **WHO group II (hypothalamic-pituitary-ovarian dysfunction, polycystic ovary syndrome):**
      - If BMI is above 30, women should be advised on weight reduction. Weight reduction may restore ovulation, improve response to ovulation Induction, and improve obstetric outcomes

– Ovulation induction:

| | Treatment | Monitoring |
|---|---|---|
| **First line** | Clomiphene Citrate (CC) or metformin or combination of both for a maximum of 6 months | Ultrasound monitoring should be considered at least during the first cycle to determine the dose and minimize the risk of multiple pregnancies |
| **Second line** | Gonadotrophins or ovarian drilling is offered to women with CC resistance If gonadotrophins are used, concomitant use of GnRH agonist should be avoided as it provides no improvement in pregnancy rate and it increases the risk of ovarian hyperstimulation syndrome (OHSS) | If gonadotrophins are used, ovarian ultrasound monitoring is mandatory in all cycles to avoid multiple pregnancy and OHSS |

Adjuvant treatment e.g. growth factor or pulsatile GnRH are not recommended

- **Tubal factor infertility:**
  - IVF is the standard management in women with tubal factor infertility. However, surgical treatment may be considered in mild tubal disease and is superior to no surgery
  - Laparoscopic salpingectomy is recommended prior to IVF in women with hydrosalpinges. It increases likelihood of livebirth

- **Uterine factor infertility:**

  Women with amenorrhea secondary to intrauterine adhesions, may be offered hysteroscopic adhesiolysis. It may restore menses and improve likelihood of pregnancy

- **Unexplained infertility:**
  - Couples with infertility are advised to try to get pregnant spontaneously for 1 more year (a total of 2 years)
  - If no conception happened after 2 years of regular unprotected intercourse, IVF should be offered (no role for IUI or ovulation induction)

## Intra-uterine insemination (IUI)

| Indications | Outcomes |
|---|---|
| • Couple who are unable to have intercourse<br>• Same sex couples<br>• Need for sperm washing e.g. HIV infected men<br>IUI has not role in unexplained infertility, mild male factor, or mild endometriosis | • 50% of couples will conceive within 6 cycles if the couple is younger than 40<br>• 75% of couples will conceive after 12 cycles<br>• Fresh sperms are superior to frozen-thawed sperms. IUI is superior to intracervical insemination in both cases |

IUI is offered for 6 cycles. However, couples may be counselled, and its use may be extended to 6 more cycles

## In-vitro fertilization (IVF)

- **Criteria of referral to IVF:**

① Women younger than 40 who:

- Has not conceived after 2 years of unprotected intercourse or
- Underwent 12 cycles (or at least 6 cycles) of IUI

For these women, 3 cycles of IVF with or without ICSI are offered. However, if the patient reaches the age of 40, no more cycles should be offered

② Women aged between 40-42 years who:

- Has not conceived after 2 years of unprotected intercourse or
- Underwent 12 cycles (or at least 6 cycles) of IUI

For these women, one cycle of IVF should be offered with or without ICSI if:

- The patient has never had previous IVF
- Ovarian reserve is not low

These women should be counselled on risk of pregnancy in this age group

③ Women who are not possible to conceive with expectant management should be referred immediately to an IVF specialist

If women had a previous cycle of IVF and they are younger than 40, it counts as one of the 3 cycles that should be offered. The next 2 cycles should be by provided by NHS. Cancelled cycles due to low ovarian reserve should be considered

- **Predictors of IVF success:**

  ① Female age: success rate is higher among younger women

  ② Number of previous cycles: rate of success decreases with increased number of trials

  ③ Previous pregnancy: it increases likelihood of success

  ④ Women BMI: BMI should be ideally between 19 and 30

  ⑤ Alcohol consumption: alcohol consumption > 1 unit/day decreases IVF success rate

  ⑥ Maternal and paternal smoking: decrease likelihood of success of IVF

  ⑦ Caffeine consumption: it decreases likelihood of success of IVF

- **IVF protocol:**
  - **Pre-treatment:**
    - IVF pre-treatment with combined oral contraceptives (COCs) or progestin preparations does not affect the chance of live birth
    - Pre-treatment is only considered to facilitate scheduling of IVF treatment in women not treated with long down-regulation protocol
  - **Controlled ovarian stimulation:**
    - Natural IVF cycles are not recommended. Both CC stimulated and gonadotrophin stimulated IVF cycles are superior to natural cycles
    - Either urinary or recombinant gonadotrophins preparations can be used
    - The starting dose of FSH depends on certain factors:

      ① Age

      ② BMI

      ③ PCOS

      ④ Ovarian reserve

      The maximum dose of gonadotrophins is 450 IU/day
    - Response should be monitored with ultrasound with or without oestradiol level
  - **Down regulation:**

    Down-regulation with GnRH antagonist or agonist (long protocol) regimen is considered to avoid premature LH surge. GnRH agonist protocol is only offered if risk of OHSS is low

- **Ovulation triggering:**

  HCG (urinary or recombinant) is used to trigger ovulation

- **Retrieval of oocytes:**
  - Transvaginal retrieval of oocytes is done under conscious sedation
  - If at least 3 follicles are seen before oocyte retrieval, follicle flushing is not indicated (does not increase the number of retrieved oocytes and it increases duration of retrieval and procedure pain)
  - Assisted hatching is not recommended as it does not increase pregnancy rate
- **Embryo transfer:**
  - Ultrasound-guided embryo transfer improves pregnancy rate
  - If endometrial thickness is less than 5 mm, embryo transfer is not recommended as it is unlikely to result in pregnancy
  - Frozen-thawed embryos are comparable to fresh embryos
  - Number of transferred embryos is related to age:

| Age | First cycle | Second cycle | Third cycle |
|---|---|---|---|
| **< 37 years** | 1 embryo | 1 embryo (or 2 embryos if embryos are not top-quality) | 2 embryos |
| **37 – 39 years** | 1 embryo (or 2 embryos if embryos are not top-quality) | 1 embryo (or 2 embryos if embryos are not top-quality) | 2 embryos |
| **40-42 years** | 2 embryos | | |

If a donated oocyte is used, age depends on donor's age

  - Bed rest after embryo transfer does not improve IVF outcome
- **Luteal phase support:**
  - Progesterone should be offered for luteal phase support
  - HCG should not be offered due to the risk of OHSS
  - Duration of luteal phase support is 8 weeks

## Intracytoplasmic sperm insemination (ICSI)

- **Indications of ICSI:**

  ① Azoospermia either obstructive or non-obstructive

  ② Severe semen abnormalities

  ③ Failure of previous IVF treatment due to failed or very poor fertilization

  ICSI is known to improve fertilization over IVF. Otherwise, it is not superior to conventional IVF in pregnancy rate

- **Pre-procedure investigations:**
  - ICSI should be preceded by appropriate investigations to detect genetic deficits
  - If severe deficits in semen quality or non-obstructive azoospermia is present, male karyotyping should be offered
  - Y chromosome microdeletions are not tested routinely before ICSI

## Gamete donation

| Indications of donor insemination | Indications of oocyte donation |
|---|---|
| • Poor semen parameters: donor insemination may be offered to men with obstructive azoospermia, non-obstructive azoospermia, and severe deficits if ICSI is declined<br>• High risk of transmitting a genetic disorder to offspring<br>• High risk of transmission of infection to women or offspring<br>• Severe Rh iso-immunization<br>Before donor insemination, assess ovarian and tubal factors in women with risk factors before donor insemination<br>If donor insemination fails after 3 cycles, tubes should be assessed even in absence of risk factors | • Premature ovarian failure<br>• Gonadal dysgenesis<br>• Bilateral oophorectomy<br>• Ovarian failure<br>• Certain cases of IVF failure<br>• High risk of transmission of genetic diseases |

## Cryopreservation

- Cryopreservation (including embryos, sperms, or oocytes) is considered for fertility preservation. No lower age limit is considered in cancer patients
  - **Sperms:** freezing of sperms in liquid nitrogen vapor is the preferred way
  - **Oocyte and embryo cryopreservation:**
    This is offered to women who can tolerate ovarian stimulation and oocyte retrieval without affecting her general condition provided that this step will not postpone cancer treatment. Vitrification is preferred for preservation if possible
- Gametes are stored for an initial period of 10 years. Men at risk are offered continued storage
- There is no association between cryopreservation and maternal invasive cancer, childhood cancers, or other children adverse effects on the short and medium-term. There may be a small increase in borderline ovarian tumours

# Male Factor Infertility

## Background

- Male factor infertility represents 30% of cases of infertility
- Normal male reproductive function us managed by pituitary gonadotrophins:
  - FSH: it binds to Sertoli cells in the testes and stimulate production of spermatogonia and maturation of spermatocytes
  - LH: binds to Leydig cells and stimulates secretion of testosterone which is responsible for spermatid maturation and male secondary sexual characters

## Causes

Approximately 50% of cases of male factor infertility are unexplained. The following factors contribute to or cause male factor infertility:

- **General causes:**
  - **Male age:** Sperm quality starts to decline significantly after the age of 50
  - **Endocrine disorders:** e.g. hyperprolactinemia, thyroid disorders
  - **Environmental factors:**
    - Heat and radiation
    - Lead and mercury
    - Sedentary life
    - Obesity
    - Heavy alcohol intake and smoking
    - Administration of anabolic-androgenic steroids (it can cause azoospermia, which may be reversed within 4-12 months, and may be treated with use HCG or HMG)
    - Recreational drugs (decrease libido and erectile dysfunction)

- **Pre-testicular causes (hypogonadotropic hypogonadism):**
  - Rare (< 1%)
  - Examples of causes include Kallmann syndrome, Prader-Willi syndrome, Laurance-Moon-Biedl syndrome, craniopharyngioma, and pituitary surgery.

- **Testicular causes (hypergonadotropic hypogonadism):**
  - Testicular failure is associated with azoospermia and low testosterone with subsequent rise in FSH and LH. Elevation of FSH only is seen in patients with isolated Sertoli failure
  - Examples of causes include bilateral cryptorchidism, radiotherapy, and chemotherapy

**Varicocele**

- Clinical significance is doubtful
- 25% of women with varicocele have abnormal semen parameters
- 11% of women with varicocele have normal semen parameters

- **Post-testicular causes (obstructive azoospermia):**
  - 40% of cases
  - Diagnosis is made by the triad of:
    ① Normal testicular size
    ② Normal FSH
    ③ Normal spermatogenesis on biopsy despite azoospermia
  - Examples of causes are surgical trauma, vasectomy, infection, and bilateral congenital absence of vas deferens

## Clinical assessment

### History

- History of pubertal development
- Sexual history
- History of genital and hernial surgery
- history of genitourinary infection
- History of prior diagnosis of infertility and treatment history

### Examination

- General examination including height, weight, body mass index and blood pressure
- Assessment of secondary sexual characters e.g. hair growth and distribution
- Assessment of gynecomastia
- Assessment of testicular size and consistency (normal volume is 20 ml and normal consistency is firm
- Assessment penile and prostatic abnormalities
- Assessment of varicocele (using Valsalva maneuver)

## Investigations

- **Semen analysis:**
  - **Prerequisites of semen analysis:**

    It should be done after 3 days of abstinence

    It should be tested within 1 hour of sample collection

  - **Normal parameters:**

| | |
|---|---|
| **Sperm volume** | > 1.5 ml * |
| **Sperm concentration** | > 15 million/ml |
| **Total sperm count** | > 39 million |
| **Sperm motility** | > 32% progressive motility (A + B sperms) |
| **Sperm morphology** | > 4% |

* A low volume < 1.5 may indicate retrograde ejaculation, post-testicular obstruction, androgen deficiency or incomplete sample collection

- **Hormonal profile:**
  - Serum FSH and LH
  - Testosterone level
  - Serum prolactin

- **Genetic testing:**
  - **Indications:**

    Non-obstructive azoospermia or severe oligospermia
  - **Tests:**
    - Karyotyping: most common genetic cause is Klinefelter syndrome (XXY)
    - Y chromosome microdeletion (Yq): it accounts for 10-15% of cases of azoospermia and 5-10% cases of severe oligospermia:
      - Azoospermia Factor a (AZFa), Azoospermia factor b (AZFb) microdeletion are associated with poor prognosis. Surgical retrieval should not be offered

- Azoospermia factor-c (AFZc) is associated with good prognosis and surgical retrieval is recommended

- **Ultrasound:**
  - **Scrotal ultrasound:**
    It is only indicated if testicular mass or varicocele is suspected during clinical assessment

  - **Renal ultrasound:**
    Renal ultrasound is indicated if vas deferens is absent to rule out renal anomalies (association is present in 30% of cases)

- **Testicular biopsy:**
  - **Indications:**
    Azoospermia, severe oligospermia
  - **Approach:**
    Percutaneous or open needle biopsy
  - **Results:**
    - Normal findings: normal cells, complete spermatogenesis
    - hypo-spermatogenesis: all cells are present in normal ratio but a small number
    - Maturation arrest: failure of spermatogenesis at a certain stage
    - Sertoli cell-only syndrome (Del Castiollo syndrome): no germ cells

## Management

- **Medical treatment:**
  - Treatment of the cause: e.g. hyperprolactinemia, thyroid dysfunction, congenital adrenal hyperplasia (CAH)
  - Hormonal therapy: gonadotrophin injections in patients with hypogonadism

  Antioxidants may improve fertility. However, medical treatment should not be offered in idiopathic cases

- **Sperm retrieval, donor sperm or cryopreservation:**
  - These options are offered to patients with primary testicular failure
  - Sperm retrieval e.g. Microscopic testicular sperm extraction (microTESE) is associated with:
    - 100% success rate with obstructive cases (with better fertilization and clinical pregnancy rate)
    - 50% success rate with non-obstructive cases

- **Surgical management:**

| Reversal of vasectomy | Varicocelectomy |
|---|---|
| • Outcomes of reversal are variable since restoration of anatomy may not restore fertility. Examples include development of anti-sperm antibodies and secondary epididymal obstruction<br>• Technique and skills, and time since surgery affects outcomes of reversal | • Although it may improve sperm parameters if it is large enough to be clinically palpable and in the presence of low testosterone, impact of surgery on pregnancy rate is not clear<br>• It is currently not recommended by NICE guidelines |

- **Assisted reproduction:**

| Procedure | Indication | Outcome |
|---|---|---|
| Intrauterine insemination | It may be offered in cases of mild male factor infertility (mild oligozoospermia)<br>It may be tried for up to 6 cycles | Pregnancy rate is 8-16% per cycle |
| In-vitro fertilization with intracytoplasmic sperm injection (ICSI) | Severe male factor infertility | Pregnancy rate is 33% per embryo transfer (ET) |

# Polycystic Ovary Syndrome

## Definition

Diagnosis of polycystic ovary syndrome (PCOS) is made by Rotterdam criteria. To meet diagnostic criteria, two of the three following criteria should be present:

- Hyperandrogenism or hyperandrogenaemia (clinical or biochemical)
- Ovulatory dysfunction
- Polycystic ovaries on ultrasound

| | |
|---|---|
| **Hyperandrogenism or hyperandrogenaemia** | • Clinical hyperandrogenism:<br>▪ Features of clinical hyperandrogenism include acne, alopecia, and hirsutism<br>▪ Modified Ferriman Gallway is used to to assess hirsutism (a score ≥ 4-6 is consistent with hirsutism). Hirsutism is determined by terminal hair which should be differentiated from vellus hair (terminal hair is pigmented, thicker than 5mm)<br>▪ Ludwig visual scale is used to assess alopecia<br>▪ There is no scoring system for acne<br>• Biochemical hyperandrogenism:<br>▪ Biochemical testing is indicated if clinical signs are unclear or absent. This feature is diagnosed by:<br>① Calculated free testosterone (Direct free testosterone is not used)<br>② Free androgen index **(the best test)**<br>It equals (total testosterone/sex hormone binding globulin) X 100<br>③ Calculated bioavailable testosterone |

| | |
|---|---|
| | ▪ Women should be tested while on hormonal contraception. They should be stopped 3 months before testing<br>▪ Serum androstenedione and DHEAS may be tested if testosterone is not elevated in the presence of clinical hyperandrogenism (limited role in diagnosis of PCOS itself)<br>▪ If there is significant rise in androgen levels, androgen secreting tumours should be ruled out |
| **Ovulatory dysfunction** | • Irregular menstrual cycles are indicative of ovulatory dysfunction. Menstrual irregularities are related to age:<br>▪ Within 1 year of menarche: menstrual irregularities are normal<br>▪ Within 1-3 years of menarche: cycles are abnormal if shorter than 21 or longer than 45 days<br>▪ Beyond 3 years post-menarche (or perimenopausal): cycles are abnormal if shorter than 21 or longer than 35 days OR if cycle frequency is fewer than 8/year<br>▪ Primary amenorrhea is considered if there are no menses by 3 years after thelarche OR by age of 15<br>• Ovulatory dysfunction may occur with regular cycles. In these cases, anovulation is diagnosed by mid-luteal serum progesterone |
| **Polycystic ovaries on ultrasound** | • Ultrasound diagnosis should not be used within 8 years of menarche<br>• Sonographic features include:<br>▪ Follicle number > 12 or ovarian volume >= 10 $cm^3$ with no corpus luteum, cysts or dominant follicles<br>▪ Each follicle is 2-9 mm in diameter (dominant follicle is 10 mm or more diameter)<br>• Transvaginal ultrasound is the standard. If transabdominal ultrasound is used, only ovarian volume feature is used |

**Racial variations**

caucasians have mild phenotype, but higher body mass index (BMI), Asians have lower BMI and less hirsutism, while Africans have higher BMI and metabolic features. Hirsutism is more prominent in Middle Eastern and Hispanics

## Assessment

- In women in their reproductive years, PCOS is assessed if they complain of menstrual irregularities or infertility
- Adolescents with features suggestive of PCOS should be assessed 8 years after menarche. This includes those who experience significant weight gain in adolescence, PCOS features before using COCs, or if persistent symptoms of PCOS are present
- In postmenopausal women, PCOS is considered if there is long-term history of PCOS or PCOS symptoms, or continuous evidence of hyperandrogenism
  However, new onset or severe symptoms should be carefully assessed to rule out androgen secreting tumours or ovarian hyperthecosis
- Congenital adrenal hyperplasia (CAH) and androgen secreting tumours should be ruled out if:
  ① Hyperandrogenism symptoms are acute (less than 1 year between onset and consultation)
  ② Total testosterone is significantly elevated (> 5 nmol/l)
- CAH should be ruled out if there is family history of CAH or in Ashkenazi Jews. In these women, serum 17 hydroxyprogesterone is measured. If results are inconclusive, ACTH stimulation test cn be performed

## Complications

- **Cardiovascular disease:**

  Cardiovascular risk should be assessed in women with PCOS. Women are at high risk of in the presence of other risk factors e.g. obesity, smoking, hypertension, impaired glucose tolerance, hyperlipidaemia, sedentary lifestyle. Conventional cardiovascular calculators are not validated in women with PCOS

  - **Weight monitoring:**
    Weight should be monitored every 6-12 months, this includes monitoring of body mass index (BMI) and waist circumstance (specially in Asian women and high-risk group)
  - **Lipid profile screen:**
    - Women with PCOS and high BMI (overweight or obese) should have lipid profile screen regardless of age. Lipid lowering medications are not offered as a routine

- Statins improve lipid profile if findings are abnormal. They also improve hyperandrogenaemia. However, they should not be used solely for this indication

- **Blood pressure monitoring:**
  - Blood pressure should be assessed at diagnosis, during treatment with combined hormonal contraceptives, and should be followed-up at least annually
  - Hypertension should be treated if:
    - Blood pressure is persistently higher than 140/90 despite lifestyle measures
    - Blood pressure is higher than 30/80 in the presence of diabetes (or other significant risk factors of cardiovascular disease)

- **Diabetes mellitus:**

Women with PCOS are at higher risk of type 2 diabetes, gestational diabetes, and glucose intolerance regardless of age and BMI. Obesity exacerbates the risk. Insulin resistance is present in 70-75% of patients with PCOS

- **Screening for type 2 diabetes:**
  - Screening is indicated every 1-3 years depending on the presence of other risk factors
  - Screening can be done using oral 75 gram 2-hour glucose tolerance test (GTT), fasting glucose or HgbA1C
  - Oral GTT is specifically used in women who have other risk factors of diabetes:
    ① Family history of diabetes
    ② Overweight or obesity (BMI > 25 or 23 in Asians)
    ③ History of glucose intolerance or impaired fasting glucose
    ④ Personal history of gestational diabetes or hypertension
    ⑤ Age > 40 years
  - Women with impaired fasting glucose (6.1-6.9 mmol/L) or impaired glucose tolerance (7.8-11.1 mmol/L) should be followed-up with annual GTT
- **Screening in pregnancy:**
  - Women who are planning to get pregnant or in early pregnancy should undergo 75 g oral GTT before conception or earlier than 20 weeks of gestation to rule out pregestational diabetes

- Women should be rescreened for gestational diabetes between 24 and 28 weeks of gestation (risk of gestational diabetes is doubled in women with PCOS)

- **Obstructive sleep apnoea (OSA):**
  - Women with PCOS are assessed for OSA only if clinically indicated (i.e. symptomatic) and treated to alleviate symptoms. There is inadequate evidence that management of OSA improves CVD risk
  - Screening is performed using Berlin tool. If findings are positive, women should be referred to a specialist for management

- **Endometrial cancer:**

PCOS increases risk of endometrial cancer by 3 folds. Endometrial cancer associated with PCOS often presents before menopause

  - Routine screening not recommended
  - Assessment using transvaginal ultrasound if there is prolonged amenorrhoea, abnormal uterine bleeding, or excess weight gain:
    - Endometrial thickness < 7 mm makes diagnosis of hyperplasia unlikely (sensitivity 100%, specificity 56%). In general, risk of hyperplasia increases by 1.5 folds with each 1mm
    - If there is increased endometria thickness, biopsy and/or hysteroscopy should be considered
  - Prevention may be achieved by administering combined oral contraceptives or progestins to PCOS patients whose cycles extend beyond 90 days (higher risk of endometrial hyperplasia). Progestins are recommended to induce bleeding at least every 3-4 months if patients remain amenorrheic
  - PCOS is not associated with higher risk of breast or ovarian cancer and no screening is required

- **Impaired quality of life:**
  - **Anxiety and depression:**
    - These disorders are common in PCOS patients specially adolescents
    - Depression/anxiety screening should be considered in each clinical visit

- If depression or anxiety is a concern on direct questions, PHQ or GAD7 screening tool should be used and referral should be considered if screening tests are positive

- **Psychosexual disorders:**
  - PCOS women may be at risk of psychosexual disorders
  - Female sexual function index may be used if suspected e.g. negative body image
- **Eating disorders:**

  If there is a concern, SCOFF screening tool may be used

## Management

- **Lifestyle modifications:**

5-10% of weight reduction within 6 months may result in significant clinical improvement. This can be achieved through diet, exercise, and management of other related issues e.g. anxiety, depression, negative body image. In addition, lifestyle modifications are associated with improved long-term outcomes

- **Diet:**
  - Dietary regimens are similar to those used with general population
  - Target caloric intake is 1.200-1500 kcal/day (30% energy deficit)
- **Exercise:**

| Goal | Requirement |
|---|---|
| **Preventing weight gain** | • 150 min/week of moderate exercise OR<br>• 75 min/week of vigorous exercise<br>For Adolescents, it should be 60 minutes/day |
| **Modest weight loss** | • 250 min/week moderate exercise OR<br>• 150 min/week of vigorous exercise |

Activity can be increased by 5% weekly

- **Behavioural strategies:**

They may improve outcomes by managing associated issues

- **Bariatric surgery:**
  It may be considered in women with BMI > 40 or > 35 in the presence of other risk factors after failure of other measures. Risk of mortality is 0.1-1% with these surgeries

- **Medical treatment:**

| | |
|---|---|
| **Combined oral contraceptives (COCs)** | • COCs is given to adult women with PCOS to improve irregular bleeding, hyperandrogenism symptoms and to provide endometrial protection<br>• COCs may be considered in adolescents with diagnosed or high risk of PCOS for the same indications<br>• All COC types are comparable and can be used in treatment of PCOS symptoms including hirsutism (no specific type is recommended)<br>• Combined use of 35 mcg of ethinyl oestradiol and cyproterone should be avoided because of venous thromboembolism risk with this combination |
| **Metformin** | • Metformin may be used in combination with COCs for metabolic benefits in women with BMI > 25<br>• Treatment is most beneficial among high metabolic risk group (e.g. glucose intolerance)<br>• Metformin reduces androgen levels by approximately 10%<br>• Gastrointestinal side effects are dose dependent and they are a common cause of drug discontinuation. Therefore, medication should start by 500mg, and increase every 1-2 weeks. Extended release forms are better tolerated |
| **Anti-androgen drugs** | • They may be added to COCs if hirsutism is not responsive after 6 months of COCs and cosmetic therapy<br>• It may be used to treat alopecia<br>• Their use should be combined to a contraception to avoid male under-virilization |
| **Anti-obesity medications** | They may be used as per general population in women with high BMI |

- **Treatment of infertility:**
  - **Complete assessment:**
    Before commencing ovulation induction for PCOS, semen analysis of the partner and tubal assessment should be done
  - **Lifestyle modifications:**
    Similar to other symptoms, ovulation function and menstrual pattern improves with weight reduction and lifestyle modification
  - **Ovulation induction:**
    Pregnancy should be excluded prior to ovulation induction

| | |
|---|---|
| **Letrozole** | • Letrozole is the first line of ovulation induction in women with PCOS and is superior to clomiphene citrate.<br>• Letrozole is associated with lower risk of multiple pregnancy compared to clomiphene citrate |
| **Clomiphene citrate (CC)** | • CC may be used for ovulation induction<br>• It may be combined to metformin in women with CC-resistance |
| **Metformin** | Metformin may be used to induction regimen to improve ovulation, pregnancy rate and live birth rate specially in women with BMI > 30 |
| **Gonado-trophins** | • Gonadotrophins are the second line of ovulation induction (unless otherwise opted by the couple as a first line after explaining risks)<br>• It is used in women with CC resistance and is superior to combined CC and metformin in these women<br>• Gonadotrophins may be combined with metformin in the presence of CC resistance<br>• Trigger of ovulation should be done only if 2 mature follicles are available and should be avoided if > 2 are present |
| **Laparoscopic drilling** | • Laparoscopic drilling: may be offered as a second line treatment to CC-resistant patients as an alternative to gonadotrophins<br>• It may be offered as a first line if laparoscopy is performed for another indication<br>• Laparoscopic drilling is particularly beneficial in women with normal BMI. In this group, 60% will have persistent ovulation and normalization of androgen for up to 20 years after treatment<br>• Ovarian drilling is associated with risk of periaxial adhesions, small risk of diminishing ovarian reserve, and loss of ovarian function |

- **Invitro fertilisation (IVF):**

  IVF is offered as a third line treatment

  - **Controlled ovarian hyperstimulation:**
    - Urinary or recombinant FSH without LH should be used
    - GnRH antagonist protocol is superior to long GnRH agonist protocol and is associated with shorter induction, fewer doses, and lower risk of ovarian hyperstimulation (OHSS)
    - Metformin (1000-2250 mg daily) may be used before and/or during FSH stimulation to improve pregnancy rate and reduce risk of OHSS. Treatment stops if pregnancy test is positive or with menses
  - **Trigger of ovulation:**
    - The lowest HCG dose should be used to trigger ovulation
    - Alternatively, GnRH agonist should be used specially in women at high risk of OHSS if they received GnRH antagonist protocol for stimulation and fresh embryo transfer is not planned
  - **Embryo transfer:** Single embryo transfer is used to minimize risk of multiple pregnancy

Anti-obesity medication and bariatric surgery are experimental in management of PCOS-related infertility

Once pregnancy occurs, women should be monitored closely during pregnancy because of increased risk of maternal and foetal complications

# Ovarian Hyperstimulation Syndrome

## Incidence

- After conventional in-vitro fertilization (IVF), 1/3 develop mild ovarian hyperstimulation syndrome (OHSS), 3-8% develop moderate to severe OHSS
- Incidence of hospitalization due to OHSS 0.3%

## Protocols

- Women undergoing IVF should be counselled on risk of OHSS
- Verbal and written information should be provided including a 24-hour contact information for medical assistance
- All Infertility units should have local protocols for management of OHSS
- OHSS should be reported according to HEFA (Human Fertilisation and Embryology Authority) regulations. It should be reported within 12 hours verbally, and within 24 hours in a written form. OHSS should be reported to the initial infertility centre

### Risk factors

- History of OHSS
- Polycystic ovary syndrome
- High antral follicle count
- High anti-Mullerian hormone

### Protective factors

- GnRH antagonist regimen (compared to agonist regimens)
- Trigger with GnRH agonist (compared to hCG trigger)

## Diagnosis

- OHSS is a clinical diagnosis
- Women should be seen and assessed if diagnosis is doubtful or if OHSS severity is likely more than mild

- Initial assessment should include haematocrit value, serum electrolytes, osmolality, and pelvic ultrasound. Elevated haematocrit, low sodium and osmolality are indicative of OHSS

| Assessment of OHSS | |
|---|---|
| **History** | • Relation of symptoms to trigger time<br>• Medications used for triggering<br>• Number of follicles on the last scan and number of collected ova<br>• Number of embryo transfer<br>• History of polycystic ovary syndrome (PCOS) |
| **Symptoms** | • Abdominal bloating, distension, and pain<br>• Nausea and vomiting<br>• Shortness of breath<br>• Diminished urine output<br>• Leg and vulvar swelling<br>• Venous thrombosis |
| **Examination** | • Assessment of vital signs<br>• Assessment of dehydration<br>• Assessment of oedema and body weight<br>• Assessment of ascites, peritonism, and palpable mass<br>• Measurement of abdominal girth<br>• Assessment of pleural effusion and pulmonary oedema |
| **Work-up** | • Complete blood count (CBC) and haematocrit value<br>• C-reactive protein (may be used monitor severity)<br>• Serum urea and electrolytes<br>• Serum osmolality<br>• Liver function test<br>• Coagulation profile<br>• Serum hCG<br>• Abdominal ultrasound |

- In the presence of severe abdominal pain and pyrexia, other causes should be ruled out e.g.
  - Pelvic infection or abscess
  - Appendicitis
  - Ovarian torsion or cyst rupture
  - Bowel perforation

## Classification

| | Clinical features | Sonographic features | Laboratory features |
|---|---|---|---|
| **Mild** | Bloating and mild abdominal pain | Ovarian size < 8 cm | |
| **Moderate** | Moderate pain<br>Nausea and vomiting | Ovarian size 8-12 cm | |
| **Severe** | Clinical ascites/hydrothorax<br>Oliguria (< 30ml/hour, < 300ml/day) | ovarian size > 12 cm | haematocrit > 0.45<br>Serum sodium < 135 mmol/L<br>Serum potassium > 5 mmol/L<br>Serum osmolality < 282 mosm/kg<br>hypoproteinaemia < 35 g/l |
| **Critical** | Tense ascites/severe hydrothorax<br>Oliguria/anuria<br>Thromboembolism<br>Acute respiratory distress syndrome (ARDS) | | Serum haematocrit > 0.55<br>White blood cell count > 25000/µl |

Early onset OHSS occurs within 7 days of ovulation trigger and is caused by exogenous hormones

Late onset OHSS: occurs after 10 days, and is caused by endogenous hCG of pregnancy

## Management

- **Outpatient management:**
  - **Indications:**
    Mild to moderate (some selected severe cases)
  - **Management:**
    - Women should be educated on monitoring fluid intake and output

- Women are encouraged to drink in response to thirst
- Paracetamol or codeine are safe for pain. Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided (risk of renal function compromise)

In severe cases treated as outpatient, low molecular weight heparin should be considered. Paracentesis can be done as an outpatient procedure abdominally or vaginally under ultrasound guidance

- **Follow-up:**
  - Patients should be followed up every 2-3 days
  - Immediate assessment is indicated if:
    - Symptoms and signs of worsening OHSS develop e.g. worsening abdominal distension or pain, weight gain, shortness of birth
    - Urine output is less than 1000 ml/day or if fluid balance is positive by 1000 ml

    In these cases, labs should be repeated (haematocrit is the most important investigation)

- **Inpatient management:**
  - **Indications of hospitalization:**

    ① Failure of pain control
    ② Failure of hydration due to persistent nausea and vomiting
    ③ Unable to follow-up as outpatient
    ④ Worsening symptoms
    ⑤ Critical OHSS

  - **Management:**
    - **Setting:**

      Women with critical OHSS should be admitted to the intensive care unit
    - **Clinical assessment:**

      Daily assessment of body weight, abdominal girth, fluid chart and labs should be performed. More frequent assessment is required in critical and complicated cases
    - **Symptomatic treatment:**
      - Treatment includes antiemetics and analgesia
      - NSAIDs and any medications contraindicated in pregnancy should be avoided
    - **Hydration:**
      - Oral hydration is preferred, and I should be guided by thirst

- Persistent haemoconcentration despite volume replacement with IV colloids is an indication of invasive fluid input and anaesthetic management

- **Diuretics:**
  - Diuretics should not be used to treat oliguria in women with OHSS
  - Diuretics are only indicated if oliguria is present despite adequate fluid replacement and drainage of ascites
- **Paracentesis:**

| Indications of paracentesis | Fluid replacement after paracentesis |
|---|---|
| • Ascites causing severe abdominal pain and distension, or respiratory compromise<br>• Oliguria despite volume replacement (2 litres are usually aspirated) | If large fluid volume is removed by paracentesis, IV colloids are given (e.g. human albumin solution 25% 50-100g) over 4 hours. It can be repeated every 4-12 hours |

- **Low molecular weight heparin (LMWH):**
  - LMWH should be considered in women with severe OHSS, critical OHSS or any admitted OHSS
  - Women with moderate OHSS may be managed with anti-embolic stocking or LMWH if indicated (depending on risk factors)

In women who develop unusual neurologic symptoms after several weeks of apparent improvement of OHSS, venous thrombosis should be suspected

- **Surgery:**

Surgery is only indicated if ovarian torsion, ovarian rupture, or ectopic pregnancy is diagnosed

Women with OHSS are at high risk of preterm labour and preeclampsia

# Premature Ovarian Insufficiency

## Definition

Premature ovarian insufficiency (POI) refers to the loss of ovarian function, which is manifested by amenorrhoea, oligomenorrhoea, decrease in oestradiol, and increase in gonadotropins, before the age of 40

## Epidemiology

Incidence of POI is **1%**

## Diagnosis

- **Establishment of diagnosis: (diagnostic criteria):**
  Diagnosis of POI is made by the following criteria:
  ① Oligomenorrhea/amenorrhea for at least 4 months AND
  ② Serum FSH > 25 IU/l on two occasions 4 weeks apart

- **Assessment of underlying causes and associations:**
  - **Chromosomal analysis:**
    It should be evaluated in all women with non-iatrogenic POI
    - **Turner syndrome:**

| Positive cases | Negative cases |
|---|---|
| • Refer to endocrinologist, cardiologist, and geneticist<br>• If Y chromosome is detected, gonadectomy is indicated (risk of malignancy) | Second analysis of epithelial cells is indicated if there is high clinical suspicion |

- **Fragile-X syndrome:**
  - Refer to geneticists
  - Before testing for fragile X pre-mutation, patients should be counselled on sequences of a positive test result
  - If testing is positive, relatives should be offered genetic counselling and testing

  No autosomal genetic testing is indicated, except when specific mutations are suspected

- **Testing for autoantibodies:**

  They are checked, where POI cause is unknown or when immune disorders are suspected

  - **21OH-ab (or adrenocortical antibodies)**

    If antibodies are positive, patients should be referred to an endocrinologist to check cortical function
  - **(TPO-Abs):**

    If antibodies are positive, serum TSH should be checked annually

If these antibodies are negative, DO NOT repeat the test unless new relevant symptoms develop

**Relatives of women with non-iatrogenic POI**

- No testing is indicated unless genetic mutation is detected in the patient
- No preventive measures are indicated
- Potential risk of early menopause should be considered and discussed
- When planning for a family, fertility preservation may be a promising option. However, evidence is still lacking

## Complications

- **Life expectancy:**
  - Life expectancy may be reduced significantly due to cardiovascular disease if not treated
  - Women should be advised on regular exercise, cessation of smoking, and maintaining healthy weight

- **Fertility:**

  Fertility is significantly reduced. However, there is a small chance of conception. Therefore, if pregnancy is not desired, contraception is advised

- **Obstetric outcomes:**
  - Spontaneous pregnancy after idiopathic POI or chemotherapy is NOT associated with higher obstetric or neonatal risks
  - Risk assessment and management should be individualized based on underlying cause e.g. cardiac risk in women treated with anthracycline

- **Bone loss:**
  - POI is associated with decreased Bone Mineral Density (BMD)
  - Bone protection may be achieved by:
    - Lifestyle measures: regular exercise, avoidance of smoking, maintaining normal weight, balanced diet with adequate calcium and vitamin D intake
    - Oestrogen replacement (combined oral contraceptives may be used instead of hormone replacement therapy but are generally less effective)
    - Bisphosphonate (only prescribed by osteoporosis specialist). They should not be taken if a woman is trying to conceive
  - Check BMD at time of diagnosis of POI in all women especially those with additional risk factors of osteoporosis:

| | |
|---|---|
| **If BMD is normal** | Consider oestrogen replacement, no need to repeat DEXA scan |
| **If there is osteoporosis** | Start treatment and repeat DEXA scan every 5 years |

- **Cardiovascular risks:**
  - When POI is diagnosed, CV risk is required with annual monitoring of blood pressure, weight, smoking status, lipid profile, fasting glucose, and HbA1c
  - Patients with cardiovascular risk should be advised on exercise, healthy weight, and cessation of smoking
  - Women with Turner syndrome should be evaluated by an experienced cardiologist. Oestrogen may be cardioprotective, and it should continue till the average age of menopause

- **Psychological and sexual dysfunction:**
  - Lifestyle and psychological support should be available
  - Routine screening on sexual function and sexual wellbeing is indicated
  - Hormonal replacement therapy improves these symptoms. If systemic oestrogen is not enough, local oestrogen is required to control dyspareunia. Lubricants can be used in women not using hormonal therapy
  - Patients should be adequately counselled on using testosterone for sexual dysfunction. Safety of this treatment is unknown. If androgen therapy is initiated, treatment should be evaluated after 3-6 months and should be limited to 24 months

- **Cognitive impairment:**
  - There is risk of cognitive deterioration after hysterectomy and/or oophorectomy in women younger than 50
  - Hormonal therapy should be considered till the natural age of menopause

## Hormonal replacement therapy (HRT)

- **Treatment regimen:**
  - **Oestrogen:** 17β-oestradiol is superior to oethinyl-oestradiol or conjugated equine oestrogens
  - **Progestins:** Progestins should be used for endometrial protection. Oral cyclical combined treatment should be used if the uterus is present

- **Indications for HRT:**
  - Menopausal symptoms
  - Primary prevention of cardiovascular disease and bone protection

- **Contraindications:**
  - Breast cancer survivors
  - Using combined oral contraceptives instead of HRT for puberty induction is contraindicated

> - Migraine is not a contraindication to HRT. Change dose or use transdermal route if it becomes worse. I
> - Hypertension is not a contraindication to HRT. However, transdermal patch is preferred in hypertensive patients
> - Fibroid is not a contraindication to HRT
> - BRCA carrier status is not a contraindication to HRT
> - HRT does not increase risk of breast cancer if given prior to natural age of menopause
> - Women with prior venous thromboembolism requires referral to haematologist before starting HRT. Transdermal route is preferred

- **Follow-up:**

  HRT requires annual monitoring for assessment of symptoms, new risk factors and compliance

- **HRT in special situations:**
  - **Turner syndrome:**
    - HRT should be considered throughout reproductive lifespan till the natural age of the menopause
    - Puberty induction is achieved by 17 β-oestradiol starting with a low dose at age 12 with gradual increase of dose over 2-3 years. Cyclical progestogens are started after at least 2 years of oestrogen treatment or when breakthrough bleeding occurs

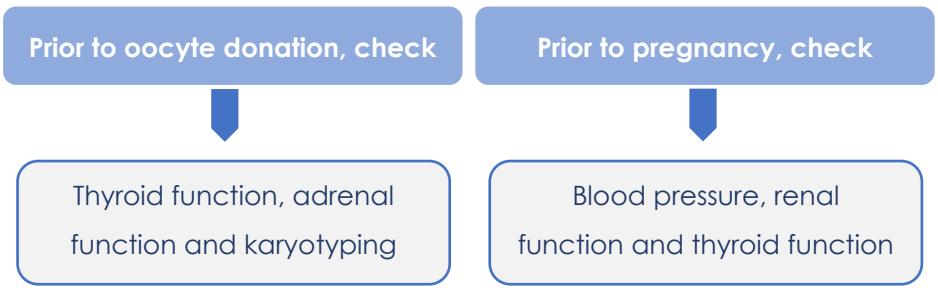
> Transdermal route achieves physiologic hormonal levels and it may be superior to oral route

- **Endometriosis:**
  - Combined oestrogen/progestin is indicated after oophorectomy for endometriosis
  - Treatment prevents/improves potential vasomotor symptoms and reduces disease recurrence
- **Obesity:**

  Transdermal route is preferred in obese and overweight

## Management of infertility

- There is no intervention to raise chance of spontaneous pregnancy. Fertility preservation is not an option in women with diagnosed POI
- Oocyte donation should be offered to women interested in pregnancy
  - Counsel the patient that oocyte donation from sisters is associated with higher risk of cycle cancellation
  - Women who have medical risk of pregnancy may not be an appropriate candidate for oocyte donation




If there is history of high dose cyclophosphamide, mediastinal irradiation or anthracycline treatment, consider echocardiography before pregnancy and referral to a cardiologist

# Tubal Factor Infertility

## Assessment of tubal patency

Tubal factor infertility accounts for 11-30% of cases of infertility

- **Medical history:**
  If the following history is present, laparoscopy will be offered:
  ① History of pelvic inflammatory disease (PID) or sexually transmitted infections (STIs)
  ② History of complicated appendicitis
  ③ History of pelvic surgery

- **Laboratory assessment:**
  - Chlamydia antibody testing (C. trachomatis is the most common cause of acquired tubal pathology)
  - Micro-immunofluorescence is superior to ELISA and immunofluorescence assay.

- **Imaging assessment:**

| | Procedure | Advantages | Disadvantages |
|---|---|---|---|
| **Hystero-salpingography (HSG)** | • The test is done between day 7-12 of the cycle.<br>• It identifies site and laterality of tubal block.<br>• Bilateral tubal block is associated with | • Good screening test for tubal block (53% sensitivity and 87% specificity)<br>• Oil soluble contrast medium may have therapeutic effect (restores tubal | • Technical failure may occur due to failed catheterization or poor seal around cervix<br>• False positive findings may |

| | | | |
|---|---|---|---|
| | 72% decrease in fecundity rate | patency). However, it is not usually used because of risk of oil embolism, granulomas and reduced image quality | occur due to tubal spasm and debris<br>• Risk of pelvic infection (1-3%)<br>• Exposure to radiation |
| **Hystero-salpingo-contrast-sonography (HyCoSy)** | • Patient is placed in a semi-lithotomy position. Water soluble contrast medium is injected through the cervix using 5F or 7F catheter<br>• Visualization of the uterus is best obtained by normal saline. Tubes are best visualized by hysterosalpingo-foam sonography | • Higher sensitivity, specificity compared to HSG<br>• Higher tolerability than HSG | • Possibility of uncertain findings is higher (9%) compared to HSG (0.5%)<br>• Intra-observer reliability is less specially on left side<br>• Technical difficulties with obese women, acute retroversion, or high ovaries |
| **Selective salpingography and tubal catheterization** | The procedure is performed by passing a catheter under fluoroscopic control and direct injection of radio-opaque dye into tubal ostium | • It is a second line test to improve diagnostic accuracy of proximal tubal obstruction.<br>• It decreases false positive results associated with HSG (due to tubal spasm or debris)<br>• It can be used to measure tubal perfusion pressure (a prognostic factor) | With tubal catheterization:<br>• Risk of tubal perforation is 2%<br>• Risk of ectopic is 3% |

- **Endoscopic assessment:**

| | |
|---|---|
| **Conventional laparoscopy** | • It is the standard test for diagnosis of endometriosis and adhesions. Furthermore, it plays a therapeutic role in women with mild endometriosis and peri-adnexal adhesions<br>• Laparoscopy may require general anaesthesia. The procedure is associated with risk of visceral and/or vascular injury (0.13%) |
| **Transvaginal hydro-laparoscopy** | • A fluid is instilled via a Veress needle that passes through the posterior fornix and a small diameter angled rigid scope is inserted. A dye is injected into the uterus and the scope is used to assess whether the dye comes out from the tube<br>• Minor procedures may be performed through this approach e.g. drilling, adhesiolysis<br>• The procedure can be performed in an outpatient setting with local anesthesia<br>• Risk of bowel injury (0.61% rectosigmoid) is higher than conventional laparoscopy. The procedure should be avoided with obliterated Douglas pouch, fibroids, or endometriosis |
| **Salpingoscopy** | • The procedure is done during laparoscopy<br>• An endoscopy is used to visualize lateral endosalpinx and tubal ampulla |
| **Falloposcopy** | • The procedure is done during hysteroscopy<br>• It is used to visualize all endosalpinx |
| **Fertiloscopy** | • It is an outpatient procedure that combines hysteroscopy, Transvaginal hydro-laparoscopy and salpingoscopy<br>• Findings are highly concordant with laparoscopic findings |

## Tubal surgery

- Standard management of tubal factor infertility is in-vitro fertilization
- Tubal surgery for infertility includes the following:
  - **Destructive tubal surgery:**
    - Salpingectomy and tubal occlusion are indicated in women with hydrosalpinx cases prior to IVF.
    - Best candidates are those with severe disease (bilateral hydrosalpinx, hydrosalpinx visualized by ultrasound)
    - Salpingectomy may double chance of pregnancy. However, patient will be dependent on IVF in future pregnancy

**Diagnosis of hydrosalpinx**

- 2D ultrasound is the standard method (sensitivity is 85%, specificity is 99%)
- Assessment if uterine cavity within 2 cycles prior to IVF may be performed using HyCoSy to assess tubal patency in the same setting
- Invasive methods to diagnose hydrosalpinx not detectable by ultrasound are not recommended unless there is recurrent implantation failure of high-quality blastocyst transfer

Primary salpingectomy vs interim salpingectomy (after failed IVF)

Outcomes are similar after a maximum of 3 IVF cycles

- **Reconstructive tubal surgery:** tubal pathology may be proximal, distal or combined

| Site | Procedure | Success rate | Risk of ectopic |
|---|---|---|---|
| **Proximal tubal disease (15%)** | • Resection anastomosis | 44% | 7% |
| | • Hysteroscopic/fluoroscopic tubal catheterization (for less common causes e.g. tubal debris, intraluminal adhesions) | 60–90% (30% pregnancy rate) | |
| **Distal tubal disease (85%)** | • Salpingo-ovariolysis | 50% | 5% |
| | • Fimbrioplasty | 50% | 7% |
| | • Salpingostomy | 30% | 9% |
| **Reversal of tubal sterilization** | • Re-anastomosis using microsurgical techniques (via laparotomy or laparoscopy)<br>• Predictors are of success are age < 35 years and residual length > 4 cm | 50% | 5% |

* Most common cause is salpingitis isthmica nodosa (SIN)

# Unexplained Infertility

## Contributing factors

Unexplained infertility is considered when no clear cause is detected after routine infertility investigations. Some underlying causes or contributing factors of infertility are suggested in this group of patients. However, these factors are not typically investigated, and management should be the same:

| Factor | Risk factor | Effect |
|---|---|---|
| **Age** | Advanced maternal age | It adversely impacts number and quality of oocytes and is associated with increased risk of aneuploidy. These factors may result in failure of implantation and subsequent infertility |
| **Body mass index** | BMI > 30 or BMI < 19 (for both partners) | • In women: Abnormal weight adversely affects follicular development. Therefore, it affects embryo quality and implantation rate.<br>• In men: it may cause erectile dysfunction, damage to sperm DNA |
| **Smoking** | Cigarette smoking (for both partners) | • In women, it affects ovarian reserve, tubal function, and uterine environment.<br>• In men, it may affect sperm quality (affects sperm DNA, mitochondria, and fertilisation capacity) |

| | | |
|---|---|---|
| **Alcohol intake** | Excessive alcohol intake especially in women | • In women, it may cause luteal phase defects, failure of implantation, and poor development of the embryo<br>• In men, although it may affect sperm quality, clinical impact is unclear |
| **Tubal dysfunction** | Defective tubal function despite patency as a sequence of mild pelvic infection | Failure of oocyte and zygote transport |
| **Fertilisation defects** | Defects in the gametes that results in failure of proper fertilisation e.g. sperm DNA fragmentation | These defects may result in failure of fertilisation or high risk of miscarriage |
| **Pelvic pathology** | Endometriosis, adenomyosis, uterine fibroids | The role of these diseases is not clear. Although 30% of women with unexplained infertility may have mild endometriosis, it should still be treated similarly as outcomes are comparable. Ablation of endometriosis minimally alters live birth rate |

## Investigations

If there is no cause identified after basic investigations were performed, the following advanced investigations are recommended before diagnosis of unexplained infertility is made:

- **Assessment of ovulation:** if a woman has regular cycles, possibility of anovulation is low
- **Assessment of tubal patency**: these tests do not provide information on anatomical but not functional patency
- **Ovarian reserve tests**
- **Laparoscopy:**
  Laparoscopy is considered if 3-6 cycles of ovarian stimulation and timed intercourse fail
- **Assessment of uterine cavity**:
  Hysteroscopy (or saline Infusion Sonography, 3-dimensional ultrasound) is used to assess to assess polyps, septum, and adhesions. Treatment of these lesions may increase pregnancy rate

## treatment

| Expectant management | Tubal flushing or perturbation | In-vitro fertilisation (IVF) | Intracytoplasmic sperm injection (ICSI) |
|---|---|---|---|
| 75% of couples with unexplained infertility may conceive spontaneously | Tubal flushing with oil or water-soluble media may increase pregnancy chance by 3 times<br>This effect may be attributed to both mechanical and immunological action | IVF success rate is 30% per cycle in women younger than 37 years* | ICSI is indicated If IVF pregnancy fails due to failure of fertilisation (5-25% of cases). Every 5 ICSI procedures prevent 1 fertilisation failure ** |

* Intrauterine insemination (IUI) with or without ovarian stimulation is NOT recommended if regular intercourse is possible. Success rate is 9% per cycle and has similar multiple pregnancy rate to IVF

** Split IVF-ICSI may be considered to detect fertilisation defects and reduce risk of IVF failure

# Recurrent Pregnancy Loss

## Background

**Definitions**

Recurrent miscarriage describes 3 or more consecutive pregnancy losses. This obstetric problem affects 1% of all women.

**Risk factors**

**Epidemiologic factors**

- **Advanced maternal and paternal age:** women ≥ 35 years of age and men ≥40 years of age are at higher risk
- **Previous miscarriage:** the risk is 40% after 3 consecutive miscarriages (particularly in elderly women)

**Environmental factors**

- **Dose dependent smoking and caffeine:** insufficient evidence.
- **Heavy alcohol consumption:** it may increase the risk of sporadic miscarriage even if consumed in moderation (5 units or more/week)
- **Obesity:** increases the risk of sporadic and recurrent miscarriage

**Anti-phospholipid syndrome**

- It is the most important treatable cause of recurrent miscarriage
- Antiphospholipid antibodies are present in 15% of women with recurrent miscarriage versus < 2% in low risk women

**Genetic factors**

| | |
|---|---|
| **Parental chromosomal rearrangements** | In 2-5% of cases of recurrent miscarriage (mostly balanced reciprocal or Robertsonian translocation). |
| **Embryonic chromosomal abnormalities** | The risk of miscarriage in related to advancing maternal age. if present, the risk is 30-57% in next miscarriages |

**Anatomical factors**

**Uterine malformation**

- More common in second rather than first trimester miscarriage
- Arcuate uteri are associated with second trimester miscarriage, while septate uteri are associated with the first trimester miscarriage

| | | |
|---|---|---|
| | **Cervical weakness** | It is typically characterized by recurrent second-trimester miscarriage preceded by spontaneous rupture of membranes or painless cervical dilatation |
| **Endocrine factors** | **Diabetes mellitus** | • Uncontrolled diabetes (indicated by high HBA1c) is at risk of first trimester miscarriage<br>• Controlled diabetes is not a risk factor |
| | **Thyroid dysfunction** | • Anti-thyroid antibodies are a possible cause of recurrent miscarriage<br>• Treated thyroid dysfunction is not a risk factor |
| | **Polycystic ovary syndrome** | • Insulin resistance, hyperinsulinemia and hyperandrogenemia may explain the risk<br>• Elevated free androgen index predicts the risk of subsequent miscarriage in women with recurrent miscarriage |
| **Immune factors** | **HLA incompatibility** | There is no evidence to support a causal relationship between these factors and recurrent miscarriage |
| | **Natural killer cells** | • Uterine natural killer (uNK) cells differ in function and shape from peripheral natural killer (NK) cells<br>• Altered peripheral NK cells may be related to recurrent miscarriage. However, this is not supported by evidence and should not be investigated routinely |
| | **Cytokines** | • The normal shift to T-helper-2 cell response (which produces anti-inflammatory cytokines e.g. IL 4, 6, 10) over T-helper-1 cell response (produces inflammatory cytokines e.g. IL2, IFN γ, TNF α) occurs during pregnancy.<br>• Shift towards TH-1 response is suspected in recurrent miscarriage (needs further research) |
| **Infective factors** | | • **TORCH and Listeria:** should not be accused or routinely screened<br>• **Bacterial vaginosis:** first trimester infection predisposes to second trimester miscarriage/preterm labour. Oral clindamycin in early in the second trimester reduces the risk |
| **Inherited thrombophilia** | | They are suggested causes of recurrent miscarriage and late pregnancy complications (possibly due to thrombosis of uteroplacental circulation) |

## Management

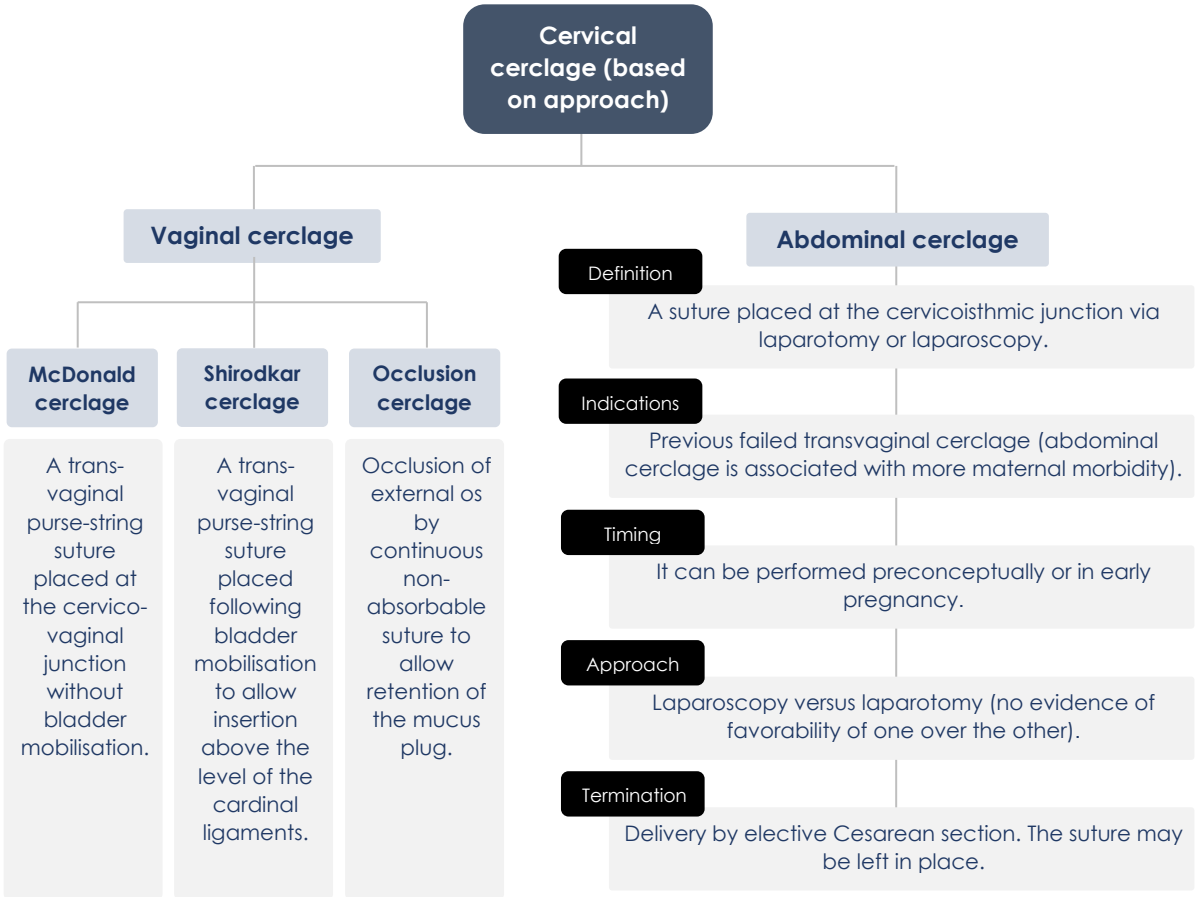
| | Indications of testing | Assessment | Treatment |
|---|---|---|---|
| **Anti-phospholipid syndrome** | • Women with recurrent 1st trimester miscarriage<br>• Women with 1 or more 2nd trimester miscarriage | Diagnosis is made by 2 positive tests at least 12 weeks apart of lupus anticoagulant or anti-cardiolipin antibodies (IgG and/or IgM, medium or high titre over 40 ml/l or > the 99th percentile) | Low-dose aspirin plus heparin (to prevent further miscarriage). This is no rule for steroids or immunoglobulin |
| **Cytogenetic (genetic) analysis** | Third and subsequent consecutive miscarriage(s) are indication for genetic analysis. This provides data about the prognosis. | Cytogenetic analysis of the products of conception. This may reveal:<br>• **Fetal aneuploidy:** the risk of miscarriage decreases with increasing number of miscarriages (better prognosis in next the pregnancy).<br>• **Unbalanced structural chromosomal abnormality:** if present, parental peripheral blood karyotyping of both partners is indicated. Referral to a clinical geneticist is indicated | Management of chromosomal rearrangements includes:<br>• Trying another natural pregnancy with or without prenatal diagnosis test<br>• Gamete donation.<br>• Preimplantation genetic screening<br>• Adoption. |
| **Anatomical factors** | All women with recurrent 1st trimester miscarriage and all women with 1 or more 2nd trimester miscarriages | • **Initial screening tests:** 2D pelvic ultrasound and/or HSG.<br>• **Tests for definitive diagnosis:** combined hysteroscopy and laparoscopy ± 3D ultrasound scanning.<br>The rule of MRI is controversial. | • **Congenital uterine malformations:** septum resection may be done (not supported by sufficient evidence)<br>• **Cervical weakness:** cerclage (see later) |
| **Thrombophilias** | Women with second-trimester miscarriage (evidence on testing is conflicting) | screened for inherited thrombophilias including factor V Leiden, factor II (prothrombin) gene mutation and protein S. | Heparin therapy during pregnancy may improve the live birth rate (insufficient evidence) |
| **Endocrine** | All women with recurrent miscarriage (particularly first trimester) | Testing for diabetes, thyroid function test, polycystic ovary syndrome | Control of diabetes and thyroid function Progesterone, hCG, LH suppression, and metformin are not supported by evidence |
| **Immune factors** | These should not be routinely investigated or treated (only for research) | | |
| **Unexplained** | Unexplained recurrent miscarriage has an excellent prognosis for future pregnancy without treatment. Only supportive care in early pregnancy assessment unit is needed. IVF and Preimplantation genetic screening do not improve outcome in unexplained miscarriage | | |

**Fact Box: Anti-phospholipid syndrome**

Antiphospholipid antibody syndrome is related to anti-phospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies and anti-B2 glycoprotein-I antibodies).

- **For assessment of Antiphospholipid syndrome:** lupus anticoagulant, anticardiolipin antibodies are assessed by:
  - ***For lupus anticoagulant:*** the dilute Russell's viper venom time test and platelet neutralisation procedure are more sensitive and specific than activated partial thromboplastin time test or the kaolin clotting time test.
  - ***For anticardiolipin antibodies:*** detected using a standardised ELISA.
- **Percussions and problems:**
  - Temporal fluctuation of antibody titres in individual women.
  - Transient positivity with infections.
  - Suboptimal sample collection and preparation and lack of standardization of laboratory tests can influence the results.


Cervical cerclage (based on indication)
History induced cerclage
Definition
Insertion of a cerclage based on woman's obstetric or gynaecological history.
Indications
• 3 or more previous preterm births and/or second-trimester losses.
• Suggestive features (e.g. painless dilatation of the cervix or rupture of the membranes before the onset of contractions) or history of cervical surgery are not evident to indicate cerclage.
• The use of prepregnancy diagnostic techniques for cervical weakness in suspected women (e.g. Cervical resistance index, hysterography or insertion of cervical dilators) is not evident as an indication of history induced cerclage.
Timing
A history-indicated suture is performed as prophylaxis in asymptomatic women at 12–14 weeks of gestation.
Ultrasound induced
Definition
Insertion of a cerclage based on cervical length shortening as diagnosed by transvaginal ultrasound
Indications
• Women with a history of 1 or more spontaneous mid-trimester losses or preterm births should be followed with transvaginal Sonography of cervical length. Cerclage is indicated if the cervix is 25 mm or less and before 24 weeks
• There is no indication if there is cervical funneling without shortening or shortening without history of spontaneous pregnancy loss or preterm labour.
• Women candidate for a history-indicated cerclage who have undergone the procedure can be followed up by sonographic surveillance for cervical shortening.
Timing
Whenever the cervix is shortened while the cervix is followed up between 14 and 24 weeks
Rescue cerclage
Definition
Insertion of cerclage as a salvage for premature cervical dilatation with exposed fetal membranes in the vagina.
Indications
A senior obstetrician-based decision is made for women with premature cervical dilatation and exposed fetal membranes in the vagina (diagnosed clinically or by ultrasound in response to specific complains e.g. vaginal bleeding, discharge, heaviness). The decision depends on 2 arms:
• The advantage of delaying labour for ± 5 weeks with 2-fold reduction in delivery < 34 weeks
• The high risk of severe preterm delivery and neonatal mortality and morbidity even with cerclage. There is also high failure rate of cerclage with > 4 cm cervical dilation and membrane prolapse beyond the external os
Timing
No evidence of superiority of immediate versus delayed procedure in either rescue or ultrasound indicated cerclage (however, delayed procedure may increase the risk of infection).

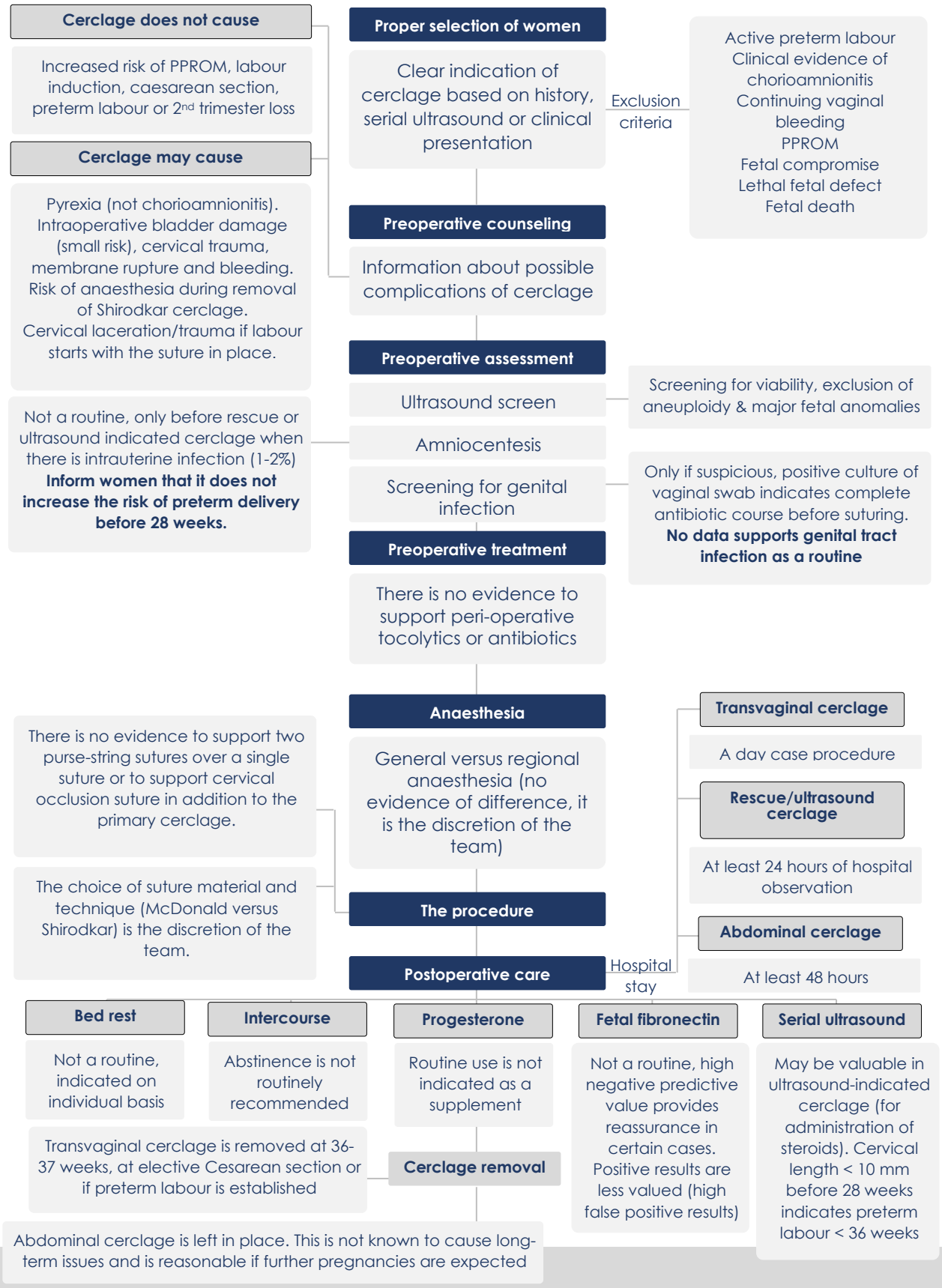



**Fact Box: Special situations with abdominal cerclage**

Delayed miscarriage or fetal death in women with an abdominal cerclage is a challenging situation that needs a senior obstetrician with adequate skill in this procedure to take a decision. Options include:

- Suction curettage or dilatation and evacuation (up to 18 weeks of gestation) through the stitch.
- Cutting the suture via a posterior colpotomy.
- Hysterotomy or caesarean section if other measures fail.

## Management of cerclage



**Fact Box: Management of cervical cerclage**

- Preoperative white blood count and C-reactive protein before rescue cerclage (to diagnose infection) are not recommended unless clinically indicated.
- The value of amnioreduction before rescue cerclage is controversial.
- Postoperative upper cervical length (closed cervix above cerclage) is detected by transvaginal ultrasound following ultrasound indicated cerclage.

**Appendix** **Cerclage in certain obstetric situations**

**Multiple pregnancy**

The insertion of a history- or ultrasound-indicated cerclage in women with multiple pregnancies is not recommended because it may be associated with an increase in preterm delivery and pregnancy loss.

**Uterine anomalies**

History- or ultrasound-indicated cerclage is not recommended in women with müllerian anomalies.

**Cervical trauma**

History- or ultrasound-indicated cerclage is not recommended in women with previous cervical surgery (cone biopsy, large loop excision of the transformation zone or destructive procedures (laser ablation or diathermy) or multiple dilatation and evacuation.
The decision to place a cerclage in women who had radical trachelectomy should be individualized.

**PPROM**

- **In women with PPROM between 24 and 34 weeks of gestation:** if there is no evidence of infection or preterm labour, delayed removal of the cerclage (for 48 hours) may be beneficial for a course of prophylactic steroids to be completed and/or in utero transfer to be arranged.
  However, delayed suture removal until labour or until delivery is indicated not recommended because it is associated with an increased risk of maternal/fetal sepsis
- **In women with PPROM before 23 and after 34 weeks of gestation:** the risk of neonatal and/or maternal sepsis is considerable and the benefit of 48 hours of latency is minimal. Immediate removal of the cerclage is recommended.

**Post-cerclage cervical shortening**

- An ultrasound-indicated cerclage due to cervical length shortening is not recommended over expectant management because this may be associated with an increase in both pregnancy loss and delivery before 35 weeks of gestation.
- A rescue cerclage following history or ultrasound-indicated cerclage is an individualized decision according to circumstances.

# Outflow Tract Disorders

## Background

- The urogenital system develops from intermediate mesothelium of the peritoneal cavity and the endoderm of the urogenital sinus
- Incidence of congenital anomalies of the genital tract is 3%
- Abnormalities of uterine fusion with septate uteri constituting 90% of cases

## Disorders

### ❶ Mayer–Rokitansky–Küster–Hauser (MRKH) syndrome (Müllerian agenesis)

- Incidence is approximately 1:5000 female births
- Patients present as teenagers with primary amenorrhoea (absent uterus and vagina)
- There are normal secondary sexual characteristics due to functioning ovaries
- 40% of cases have associated renal abnormalities
- Treatment consists of psychological support and use of vaginal dilators to dilate the vaginal dimple to allow sexual intercourse
- Surgical treatment is also an option

### ❷ Imperforate Hymen

- The hymen is a thin membrane that occurs at the junction of the sinovaginal bulb with the urogenital sinus. It usually perforates during fetal life
- An imperforate hymen results in haematocolpos (blood collection in the vagina proximal to the hymen) forms after menstruation starts. It presents with primary amenorrhoea and severe cyclic abdominal pain
- Treatment involves a cruciate incision to relieve the obstruction and drain old blood. Hymen tissue can be excised or left

### ❸ Transverse vaginal septum

- Incidence is approximately 1:40,000
- Typical symptoms are increasing cyclical abdominal pain and primary amenorrhoea secondary to haematocolpos
- Treatment involves the excision of the septum and end to end vaginal anastomosis
- Vaginal mould is inserted for 10 days after surgery and use of vaginal dilators reduce the risk of stenosis
- Pregnancy rates are 100% with lower third obstruction, 40% with middle third and 20% with upper third obstruction

### ❹ Longitudinal vaginal septum

- These fusion defects may occur in the presence of two hemi-uteri and two hemi-cervices. Each cervix fuses with the urogenital sinus to create two hemi-vaginas
- Symptoms include difficulty in inserting tampons and painful sexual intercourse. It is sometimes diagnosed in pregnancy
- It may present with a mass if one hemi-vagina is obstructed forming a haematocolpos. In this case, there is no amenorrhoea since menses flow via the other hemi-vagina
- Excision of the septum is advised to treat symptoms, improve chance of conception, and reduce complications associated with vaginal delivery

# Hirsutism

## Background

- Hirsutism is the presence of coarse terminal hairs in a male pattern distribution in women
- Incidence is 5–15%
- Hirsutism is diagnosed by the presence of terminal hair only. Other types of hair (lanugo or vellus) do not indicate hirsutism
- Hair growth is influenced by circulating androgens:
  - Testosterone is converted within hair follicle to its more potent form dihydrotestosterone (by the enzyme, 5 alfa-reductase), which stimulates hair growth
  - Weaker androgens (e.g. androstenedione) are metabolized to testosterone and dihydrotestosterone in the skin
- Deficiency in thyroid or growth hormones alters anagen: telogen ratio.

**Phases of hair growth**

Anagen (active growing)

Catagen (involuting phase)

Telogen (resting, shedding)

## Aetiology

### Androgen excess

- Polycystic ovary syndrome (PCOS):
  - It is the most common cause of chronic anovulation
  - It accounts for 70-80% of cases
- Androgen-secreting tumours:
  - Incidence is 1 in 300 and 1 in 1000 of cases of hirsutism
  - Diagnosis is suspected clinically rather than laboratory. Diagnosis is considered if:
    ① Symptoms are rapid in onset and progression
    ② Hirsutism is associated with virilization
    ③ Cushingoid features are present
  - It is suspected if there are rapid symptoms, virilizing or associated with cushingoid.
- Non-classic congenital adrenal hyperplasia:
  - It accounts for 2% of cases
  - It is caused by 21-hydroxylase deficiency
  - It is associated with high level of 17 - hydroxyprogesterone
- Other endocrine cause: e.g. Thyroid dysfunction, acromegaly, Cushing syndrome, hyperprolactinemia.
- HAIRAN syndrome
- Medications: e.g. testosterone, danazol, anabolic steroids.

### Non-androgen causes

Medications e.g. phenytoin, minoxidil, diazoxide, streptomycin, psoralen, penicillamine

### Idiopathic

No cause is identified in 7% of cases

## Clinical classification

| Mild hirsutism | Moderate to severe hirsutism |
|---|---|
| • Ferryman Galloway score 8-15 | • Ferryman Galloway score >15 |
| • Treatment can be started based on clinical findings. Investigations are indicated if hirsutism is not responsive to treatment or is getting worse. | • Investigations are recommended to determine the cause:<br>▪ If testosterone is extremely high (>1.5–2 ng/ml), an underlying androgen-secreting tumour is likely. Pelviabdominal imaging may help to determine diagnosis<br>▪ 17-hydroxyprogesterone > 200 ng/dl is suggestive of non-classical congenital adrenal hyperplasia. |

## Treatment

**Life-style changes**

Weight reduction (5-10% of total weight) may improve hirsutism by 40-55% within 6 months

**Physical methods**

- Laser photo thermolysis is more appropriate for white women. After 3 sessions, it decreases hair density by approximately 30%
- Electrolysis, waxing, and shaving are not recommended

## Hormonal treatment

Hormonal treatment provides the best effect after 9-12 months
Patients should be counselled that treatment needs time to get a response

| | |
|---|---|
| **Combined oral contraceptives** | • It acts by reducing production of LH and increasing production of sex hormone-binding globulin, which binds to, and decreases level of free androgens<br>• Drospirenone-containing pills have additional anti-androgen effect |
| **Spironolactone** | • It is superior to Finasteride and cyproterone<br>• Its effect is better if combined with combined oral contraceptives |
| **Cyproterone** | • It reduces LH level and has peripheral antiandrogenic effect<br>• It improves hirsutism by 15-40% after 6 months<br>• Side effects include weight gain, depression, fatigue, and sexual dysfunction<br>• Because of the low, bur serious risk of liver impairment, liver function tests should be checked before treatment and after 6 months |
| **Finasteride** | • It is a 5a-reductase inhibitor<br>• It is superior to cyproterone (comparable efficacy with less side effects)<br>• Combined oral contraceptives should be used with Finasteride to prevent pregnancy. Otherwise, there is risk of feminization of male foetuses |
| **Flutamide** | • It is an androgen receptor blocker<br>• It is inferior to spironolactone (comparable efficacy with more side effects e.g. greenish urine, dry skin, liver impairment can be fatal) |

| | |
|---|---|
| **Metformin** | • In patients with PCOS, it may protect against type2 diabetes and cardiovascular disease<br>• It decreases androgen level by 20% |
| **Eflornithine** | • It is an irreversible inhibitor of ornithine decarboxylase<br>• It should be applied topically to the skin and face for 4 months. If no response, a longer trial is not recommended. Improvement is reported in 60% of cases |

# Antenatal Care Following Assisted Reproduction

## Early pregnancy complications

During antenatal care of women who conceived by assisted reproductive technology (ART), obstetricians should be aware and recognize the risks associated with ART and adjust obstetric care to diagnose and manage these risks

| Condition | Incidence/risk | Recommendations |
|---|---|---|
| **Ovarian hyperstimulation syndrome (OHSS)** | Mild: incidence ~33%<br>Moderate - severe: incidence 3.1–8% | • Establish evidence-based protocols for assessment and management of OHSS<br>• Admitting centre to inform fertility clinic about admission and diagnosis<br>• Fertility clinic to report all cases of severe/critical OHSS to Human Fertilisation and Embryology Authority (HEFA) |
| **Miscarriage** | Incidence ~15–20% | • Manage as per spontaneous conception<br>• Women should have access to specialist counsellors before, during and after ART |
| **Ectopic pregnancy** | Incidence ~1.4% | • Manage as per spontaneous conception<br>• Women should have access to specialist counsellors before, during and after ART<br>• In women who are reliant on ART to conceive, a salpingectomy may be preferential to salpingotomy |
| **Subclinical Hypothyroidism (SCH)** | - | • Current guidelines recommend treatment with levothyroxine in pregnant women with SCH but there is insufficient evidence that it improves clinical outcomes |

## Advanced pregnancy complications

| Maternal complications | | |
|---|---|---|
| **Condition** | Incidence/risk | Recommendations |
| **Pregnancy-induced hypertension/pre-eclampsia** | RR 1.49<br>Absolute increase in risk ~2% | Risk assessment as per local and national guidelines<br>ART is not an indication for aspirin prophylaxis in the absence of other risk factors (which may be more common in women requiring ART to conceive) |
| **Gestational diabetes mellitus** | RR 1.48<br>Absolute increase in risk ~1% | Risk assessment as per local and national guidelines<br>In the UK, ART is not an indication for a glucose tolerance test in the absence of other risk factors |
| **Venous thromboembolism** | Highest in first trimester | Risk assessment as per local and national guidelines<br>In the absence of other risk factors, no need for anticoagulation |

| Foetal complications | | |
|---|---|---|
| **Condition** | **Incidence/risk** | **Recommendations** |
| **Structural abnormalities** | 30–40% increased incidence<br>Absolute risk still low: 6.5–7% | No additional surveillance recommended |
| **Fetal growth restriction** | Odds ratio is 1.6 | No additional surveillance in absence of other risk factors (which may be more common in women requiring ART to conceive) |
| **Stillbirth** | Odds ratio is 2.4 | Consider induction of labour at term<br>Elective caesarean section is more common in assisted conceptions (as per patients' request) |
| **Preterm labour** | Incidence of preterm labour is 11.2%. Incidence of very preterm labour is 2.6% | No additional surveillance recommended |

- Congenital abnormalities may be more common in children conceived following intracytoplasmic sperm injection than standard IVF
- Unrecognised chromosomal abnormalities are more common in those requiring ART than in the general population
- Minor anomalies of the male genitalia as hypospadias may be related to subtle Y chromosomal genetic defects. The incidence of autosomal translocations or inversions is 4.6–13.7% and the incidence of Y chromosome microdeletions is 5–15% in oligozoospermic men
- Incidence of reciprocal balanced translocations is 7 times higher following ART
- There are concerns on foetal imprinting disorders such as Angelman and Beckwith–Weidermann syndromes following ART. However, the risk is extremely rare

| **Placental complications** | | |
|---|---|---|
| **Condition** | Incidence/risk | Recommendations |
| **Placenta praevia** | Odds ratio is 3.8 | No additional surveillance recommended |
| **Placenta accreta** | Odds ratio is 2.3 | No additional surveillance recommended |
| **Placental abruption** | Odds ratio is 1.9 | No additional surveillance recommended |
| **Vasa praevia** | - | If low lying placenta diagnosed during anomaly scan, transvaginal ultrasound with colour Doppler to exclude vasa praevia should be undertaken |

- Placental complications are likely related to ART itself rather than underlying maternal causes of infertility
- ART using a cryopreserved embryo is associated with lower risk of placenta praevia compared to fresh embryos

# Reproductive endocrinology

## Abstract

Although infertility presents a single symptom in gynaecology, the symptom is worthy of a complete subspecialty in the field. Fertility issues may be a sequalae of a spectrum of hormonal and structural abnormalities. Such abnormalities could be easily corrected with medical treatment or could require complex interventions including surgery and in vitro fertilization. In this chapter, we will discuss major causes of infertility and other related problems and how to diagnose and manage these disorders

## Keywords

Infertility, PCOS, contraception, ovulation induction, IVF

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# Ovarian Cysts

## Ovarian cysts in neonates

- Ovarian cysts are the most common cause of abdominal cysts in female fetuses and neonates, usually presenting in the third trimester.
- Most are unilateral and simple in nature
- The cause is usually fetal gonadotrophins, maternal oestrogen or placental human chorionic gonadotrophin (hCG).
- Management is often conservative and may involve serial scans, but if the cyst is very large or if torsion is suspected, then surgical management is considered

## Ovarian cysts in children and adolescents

### Types

| Benign (majority) | Malignant (4–16%) |
|---|---|
| • Simple cyst (60%, risk of malignancy is < 1%)<br>• Complex cyst (mature cystic teratoma, endometrioma, gonadoblastoma, serous cytadneoma, mucinous cystadenoma, cystadenofibroma)<br>• Ovarian torsion<br>• Tubo-ovarian abscess<br>• Paratubal and paraovarian cysts | • Sex cord-stromal tumours:<br>Juvenile granulosa cell tumour (most common), Sertoli–Leydig cell tumour<br>• Germ cell tumours:<br>Dysgerminoma, yolk sac tumour, embryonal carcinoma, polyembryoma, immature teratoma<br>• Epithelial tumours:<br>Serous adenocarcinoma, mucinous adenocarcinoma |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_23

**Benign ovarian tumours:**

- **Functional cysts:**
  - Most functional cysts resolve spontaneously.
  - Functional haemorrhagic cysts may result in midcycle pain in postmenarchal girls and there may be some free fluid or haemoperitoneum. Most cases resolve spontaneously

- **Paratubal cysts:**

  They can grow and do not tend to resolve. If the cyst is large or causing pain, It should be managed laparoscopically.

- **Mature cystic teratomas (dermoid cysts):**
  - Germ cell tumours are the most common in children and adolescents (55–70% are dermoid cysts)
  - 10% may be bilateral.
  - Usually asymptomatic and discovered incidentally. 15% of dermoid cysts can present with abdominal pain and torsion.
  - Spontaneous rupture occurs in less than 1%
  - Malignant transformation occurs in 1.7%.
  - Rare complications include carcinoid tumours, struma ovarii, haemolytic anaemia and anti-NMDA receptor encephalitis.

- **Gonadoblastoma:**
  - It is a mixed germ cell tumour that develops in girls with gonadal dysgenesis, when there is a Y chromosome
  - It is benign. However, it can evolve into a dysgerminoma with malignant features.

**Malignant ovarian tumours**

- **Juvenile granulosa cell tumours (JGCTs):**
  - It accounts for almost 50% malignant ovarian tumours in children and adolescents
  - They are the most common sex cord-stromal tumours
  - Usually, solid tumours
  - 50% are diagnosed between the ages of 6 and 13 years, and one-third are diagnosed between the ages of 14 and 19 years.
  - 2–5% of tumours are bilateral

- The most common presenting feature of is pseudoprecocious puberty (breast enlargement, vaginal discharge and pubic hair growth)
- Although JGCTs are mainly oestrogen-secreting tumours, they may present with excessive androgenism (clitoral enlargement, hirsutism, deep voice, irregular periods or amenorrhoea)
- Prognosis is good. Over 95% of tumours are limited to the ovary at diagnosis. Survival rate is greater than 90% with surgical resection alone

- **Malignant ovarian germ cell tumours (MOGCTs):**
  - They account for 1.5% of ovarian cancers
  - Most occur in the first two decades of life
  - One-third of cases are dysgerminomas and one-third are immature teratomas
  - Early diagnosis and multi-agent chemotherapy are associated with high cure rate. Risk of premature ovarian insufficiency is low (3%)

- **Immature teratomas:**
  - Most are unilateral. Mature teratomas may present in the contralateral ovary
  - They may be isolated or within a mixed germ cell tumour

## Clinical presentation

- Asymptomatic or incidental
- Pain (30%)
- Abdominal distension or effects of abdominal mass
- Weight loss
- Polymenorrhoea and menorrhagia
- Precocious puberty, hyperandrogenism
- Dysuria, constipation
- Leg pain
- Acute tubo-ovarian torsion (acute unilateral constant or intermittent non-migrating pain associated with vomiting and tachycardia). Pain here has longer duration compared to appendicitis (> 48 hours)
- Non-malignant ascites (Meigs' syndrome) is a rare complication of fibromas, thecomas and granulosa cell tumours

## Investigations

- **Ultrasound:**
  - Transabdominal pelvic ultrasound is easy, cost effective and requires full bladder
  - If an adolescent has been sexually active, then she could have a transvaginal ultrasound scan

**Sonographic findings of torsion**

- Unilateral ovarian enlargement and oedema are the most consistent sonographic findings in ovarian torsion.
- Abnormal Doppler signals in the ovarian vessels are seen in almost all cases, with either absent peripheral blood flow or coiling of ovarian vessels in subacute ovarian torsion.

- **Pelvic MRI:**

  If a complex ovarian cyst is diagnosed on an ultrasound, Pelvic MRI should be requested.

- **CT scan with contrast:**

  If there are any complex features with suspicion of malignancy, CT with contrast is indicated to identify the bowel, and identify metastasis in the chest, abdomen, and pelvis.

- **Tumour markers:**

  Tumour markers are indicated in the presence of complex cysts or large persistent simple cysts

| Tumour marker | Ovarian neoplasm |
|---|---|
| **AFP** | Immature teratoma, Sertoli–Leydig cell tumour, Yolk sac tumour, Embryonal carcinoma |
| **HCG** | Dysgerminoma, Embryonal carcinoma |
| **LDH** | Dysgerminoma, Immature teratoma |
| **CA-125** | Epithelial tumours |
| **CEA** | Epithelial tumours |
| **Oestradiol** | Juvenile granulosa cell tumour |
| **Testosterone** | Sertoli–Leydig cell tumours |

- **Hormonal profile:**
  - It is indicated if there are any signs of precocious puberty
  - A hormone profile (including follicle-stimulating hormone, luteinizing hormone, oestradiol and thyroid function) should also be performed

Sterile pyuria has been observed in the presence of ovarian torsion and often mimics a urinary tract infection

## Management

- Multidisciplinary approach is recommended and priority to minimally invasive ovarian preserving surgery whenever possible
- With laparoscopic ovarian cystectomy, the main risk is intraoperative cyst rupture which includes:
  - Risk of dissemination of potential malignancy: to avoid any spill in a potentially malignant tumour, a tissue bag can be used to collect cyst contents, or laparotomy can be considered
  - Chemical peritonitis with dermoid cysts (< 0.2%): pelvic lavage with warm saline is indicated in any intraperitoneal rupture

### Laparoscopic surgery in adolescents

- Catheterisation can cause urethral trauma in children < 10 years
- Caution with umbilical incision since the aorta is just beneath the skin
- Smaller scopes (2–5 mm) and smaller trocars should be used
- Pneumoperitoneum should be adjusted to 12–15 mmHg for thin adolescents and 8-10 mmHg for younger children
- Keep the camera in the port when umbilical port is removed
- Keep the port open while removing it

- If adnexal torsion is suspected, immediate intervention is indicated. Detorsion with or without cystectomy should be performed even if the ovary looks necrotic
- Gonadopexy (oophoropexy) after detorsion can be considered, especially with previous oophorectomy and the presence of unilateral torted ovary
- There is no risk of thromboembolism following untwisting of the ovarian pedicle in detorsion

- Recurrence risk must be considered with laparoscopic surgery for mature cystic teratoma (10%). Young age, large cyst size and bilaterality are predictive factors for recurrence

| | |
|---|---|
| **Simple cyst 3-5 cm** | Rescan in 3 months for reassurance |
| **Simple cyst 5-7 cm** | • If asymptomatic, rescan in 3months. If persistent, tumour markers and MRI should be considered<br>• If symptomatic, consider tumour markers and MRI |
| **Simple cyst > 7 cm** | • Laparoscopic ovarian cystectomy OR<br>• Rescan in 3months if asymptomatic |
| **Complex cysts** | • If there is no suspicion of cancer, size is > 5cm, symptomatic: perform laparoscopic ovarian cystectomy<br>• If cancer is suspected, a multidisciplinary team should discuss management plan |

# Ovarian cysts in adult premenopausal women

## Epidemiology

- Lifetime incidence of surgery for ovarian mass is 10%
- 10% of suspected ovarian masses are found to be non-ovarian
- Risk of malignancy in the presence of symptomatic premenopausal ovarian cyst is 1:1000. The risk increase to 3:1000 by the age of 50

## Diagnosis

- **History:**
  - History of risk factors and protective factors
  - Family history of breast or ovarian cancer
  - Symptoms of endometriosis
  - Symptoms suggestive of malignancy i.e. persistent abdominal distension, change in appetite, abdominal and pelvic pain, urgency, and frequency

- **Physical examination:**

  Physical examination yields poor sensitivity in differentiating benign from malignant ovarian masses (15-51%)

- **Ultrasound:**
  - Pelvic ultrasound is the most effective diagnostic tool
  - Doppler assessment does not increase diagnostic accuracy. However, transvaginal ultrasound in combination with colour flow mapping and 3D imaging may improve sensitivity
  - Assessment of the endometrium is indicated in women with oestrogen secreting tumours
  - Up to 20% of borderline ovarian tumours may appear as simple cysts in ultrasound. However, the majority have suspicious findings

- **Tumour markers:**
  - **Indications:**
    - CA 125 is tested in women with suspected ovarian cysts e.g. complex ovarian cysts
    - Premenopausal women younger than 40 with complex ovarian cyst should be tested for LDH, APF, and hCG
    - Premenstrual women with simple ovarian cyst do not have to be tested for CA 125

  - **Value and interpretation:**
    - Preoperative differentiation between benign and malignant tumours in premenopausal women is challenging with tumour markers. An exception is germ cell tumours which can be suspected by hCG and AFP
    - CA 125 is not reliable particularly in this age group because:
      - It is associated with high false positive results e.g. pelvic inflammatory disease, endometriosis
      - It is confined to epithelial tumours
      - It is only raised in 50% of early cases

    If CA125 is < 200, it may be reasonable to rule out cancer and anticipate other causes However, if CA 125 is high, follow-up may verify diagnosis since rapid rise in CA 125 is suggestive of malignancy compared to a high plateaued level. A level above 200 should be discussed with an oncologist

- HE4 is a new tumour marker that does not increase in endometriosis and is associated with lower false positive results with benign conditions

## Risk assessment

- Risk of malignancy index (RMI) I is the most effective tool to identify suspected ovarian cancer
- In addition, since CA 125 has a poor specificity in this age group. An alternative to CA 125 is IOTA group ultrasound rules: B-rules and M-rules (sensitivity 95%, specificity 91%)

| B-rules | M-rules |
|---|---|
| ▪ Unilocular cysts<br>▪ Presence of acoustic shadowing<br>▪ Solid components with the largest component < 7 mm<br>▪ No blood flow<br>▪ Smooth multilocular tumour<br>▪ Largest diameter < 10 cm | ▪ Irregular solid tumour<br>▪ Ascites<br>▪ At least 4 papillary structures<br>▪ Irregular multilocular solid tumour<br>▪ The largest diameter > 10 cm<br>▪ Very strong blood flow |

If any of M-rule features are present, women should be referred to gynaecologic oncology service

## Management

- **Management decision:**

Management of asymptomatic simple ovarian cysts depends on cyst size:

| | |
|---|---|
| **Simple ovarian cyst < 5 cm** | There is no need for follow-up (likely physiologic) |
| **Cyst size between 5-7 cm** | yearly follow-up is recommended<br>If the cyst persists or increases in size, it is unlikely functional and surgical intervention is recommended. In this case, RMI I or US rules should be considered |
| **Cyst size > 7 cm** | MRI or surgical intervention should be considered |

Combined oral contraceptives (COCs) do not promote resolution of functional cysts

- **Surgical intervention:**
  - **Approach:**
    - Laparoscopy is the standard approach (cost effective)
    - Laparotomy may be considered for large ovarian masses with solid components. Risk of cyst rupture with laparoscopy is high with cysts larger than 7 cm
  - **Procedure:**
    - Ovarian cystectomy is the standard procedure if possible
    - Laparoscopic or vaginal aspiration of cyst is less effective and is associated with high rate of recurrence (50-85%)
    - Removal of benign cysts should be done through the umbilical port (less pain, quicker retrieval time)
  - **Precautions:**
    - Spillage of cyst contents should be avoided as much as possible specially if preoperative diagnosis is suspicious. However, preoperative and intraoperative assessment cannot preclude malignancy. Tissue retrieval bag is recommended
    - Risk of chemical peritonitis after spillage of dermoid contents is < 0.2%
      In these cases, irrigation with large amount of warm fluid is recommended. Avoid cold irrigation, which may cause hypothermia and solidification of fat-rich contents
    - In the presence of endometriomas larger than 3 cm, histology should be obtained to rule out malignancy
    - Possibility of oophorectomy should be discussed with women prior to surgery

## Ovarian cysts in postmenopausal women

### Epidemiology

- Incidence of ovarian cysts in postmenopausal women is 5-17%
- Any ovarian cyst that is 1 cm or larger in diameter is considered significant in this age group

## Diagnosis

- **History:**
  - **Risk factors of ovarian cancer:**
    Women are at high risk of ovarian cancer there is known history of BRCA 1, BRCA 2 or mismatch repair mutations OR if they are not tested but they are first or second degree relative to individuals with known mutation
  - **Symptoms suggestive of malignancy:**
    Postmenopausal women with symptoms suggestive of irritable bowel syndrome in the last 12 months (especially if older than 50 or in the presence of significant family history of cancer) should be investigated
  - **Family history of ovarian, breast or bowel cancer:**
    Women with significant family history should be referred to a regional cancer genetics service

Acute abdominal pain in postmenopausal women may be caused by ovarian cyst accident (haemorrhage, torsion, rupture)

**Significant family history**

- 2 or more first degree relatives of each other with ovarian cancer
- 1 member with ovarian cancer (any age) + 1 member with breast cancer < 50 years who are first degree relatives
- 1 member with ovarian cancer (any age) + 2 member with breast cancers < 60 years who are first degree relatives
- 3 members with colon cancer OR 2 with colon cancer + 1 member with ovarian/endometrial/urinary tract/small bowel cancer in 2 generations who are first degree relatives of each other
- 1 member with ovarian and breast cancer

- **Physical examination:**
  - Physical examination includes assessment of body mass index, abdominal examination for ascites, and vaginal/abdominal for palpable pelvic masses
  - Physical examination yields poor sensitivity

- **Investigations:**

  Any postmenopausal women with ovarian cysts should be assessed by CA 125 and transvaginal ultrasound

  - **CA 125:**
    - CA 125 is the only tumour marker used for primary evaluation. CA 125 is not used in isolation (sensitivity and specificity is approximately 80%)
    - Factors that increases CA 125 (false positive results): fibroids, pelvic inflammatory disease, torsion, cyst haemorrhage, endometriosis, cirrhosis, ascites, hepatitis, pancreatitis, peritonitis, pleuritis, breast, pancreatic, lung, colon cancer
    - Factors that may decrease CA 125: caffeine intake, hysterectomy, and smoking

  - **Imaging:**
    - **Transvaginal ultrasound:**

      it is the single most effective evaluation tool. Transabdominal ultrasound may be used in conjugation with transvaginal ultrasound if the cyst is large

| Features of simple cysts | Features of complex cysts |
|---|---|
| • Round or oval shaped<br>• Thin walled<br>• Posterior acoustic enhancement<br>• Anechoic fluid<br>• Absence of septations or nodules<br>Diagnostic accuracy of ultrasound is 95-99% | • Multilocular (malignancy risk is 8%)<br>• Solid nodules (malignancy risk is 36-39%)<br>• Papillary projects |

    - **Colour Doppler:**

      It should not be used as a routine. It does not improve diagnostic accuracy of malignancy
    - **3D ultrasound:**

      It should not be used as a routine. It does not improve diagnostic accuracy of malignancy
    - **Magnetic resonance imaging (MRI):**

      MRI is not a primary evaluation tool. It is considered for characterization of indeterminate ovarian cysts when ultrasound is inconclusive

- **Computerized tomography (CT) scan:**
  - CT scan is not recommended during initial evaluation
  - If clinical picture, ultrasound, and CA 125 are suspicious of malignancy, CT abdomen/pelvis should be considered to assess potential disease metastasis and women are referred to a gynaecologic oncology multidisciplinary team

## Risk assessment

- RMI I is the most validated and utilized triaging system of suspected ovarian cancer
- If RMI I ≥ 200, CT scan and referral to gynaecologic oncology team should be considered (some authors use a threshold of 250). Sensitivity of RMI I ≥ 200 is 78% and specificity is 87
- Other scoring systems may be less practical. IOTA has a classification based on US expertise that is comparable to RMI I

## Management

- **Management decision:**
  - Postmenopausal women with simple unilateral unilocular cyst < 5cm, and normal CA125 can be managed conservatively

    In this case, women are followed up after 4-6 months. If cyst size is the same or less, follow-up can be stopped after 1 year
  - If the cyst is symptomatic or complex, surgical evaluation is indicated

- **Procedure:**
  - **Laparoscopic bilateral salpingo-oophorectomy:**
    - The procedure is indicated if RMI I < 200
    - Bilateral salpingo-oophorectomy is performed. Ovarian cystectomy is not recommended
    - Intraperitoneal spillage should be avoided by using tissue retrieval bag through the umbilical port
    - If malignancy is suspected, full staging will be required, and the patient should be referred to a cancer centre (this scenario should be included in preoperative counselling)
  - **Staging laparotomy:**

    Staging laparotomy is indicated if RMI > 200, preoperative CT or laparoscopy is suspicious

- **Aspiration:**

  Aspiration is contraindicated in postmenopausal women unless the procedure is indicated for symptom relief in advanced cancer stages

- **Manging team:**
  - Ovarian cysts associated with RMI I < 200 are manage by general gynaecology or cancer unit
  - Ovarian cysts associated with RMI I > 200 should be managed by cancer unit

# Ovarian Cancer

## Epidemiology

- Ovarian cancer is the sixth most common cancer in women. It accounts for 4% of all new cases of cancer in women
- Lifetime cancer risk 1.3%
- It is associated with the highest rate of mortality among all gynaecologic cancer; it accounts for 6% of all cancer deaths in women
- Approximately 70% of all cases are diagnosed at stage 3 or 4. One third of patients are diagnosed in emergency department; 75% of them are not eligible for active treatment

## Risk factors

- BRCA1 (risk of ovarian cancer is 40%) and BRCA2 (risk of ovarian cancer is 10-15%) mutations
- Mismatch repair genes (LYNCH syndrome)
- Nulliparity
- First birth after 35 years
- Early menarche
- Late menopause

## Protective factors

- Combined oral contraceptives (COCs)
- Pregnancy
- Sterilization and tubal ligation
- Hysterectomy

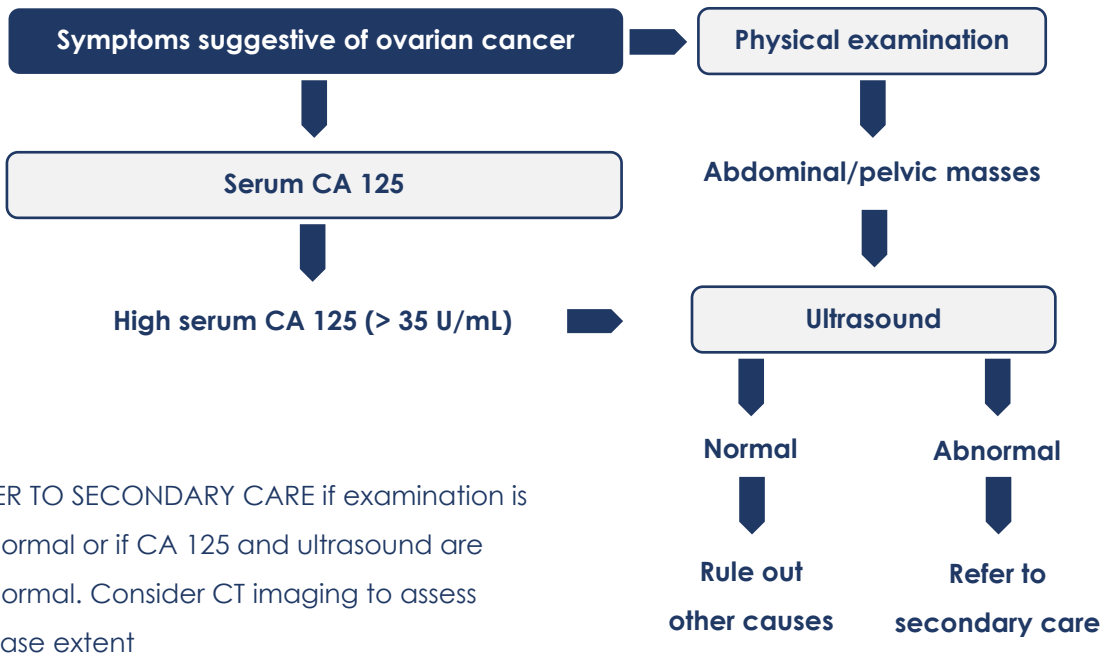
## Diagnosis

- **Symptoms:**
  - 12 episodes per month or more than 1 year of persistent abdominal distension, bloating, early satiety, loss of appetite, pelviabdominal pain, and urinary urgency (particularly in women above the age of 50)
  - Unexplained weight loss
  - Fatigue
  - Change in bowel habits
  - Postmenopausal bleeding

- **Physical examination:**
  - Examination is performed to assess pelvic and abdominal masses
  - Examination is always recommended prior to surgery

- **Investigations:**
  - **Ultrasound and CA 125:**

    Postmenopausal women with symptoms or signs of ovarian cancer should be assessed by CA125 and transvaginal ultrasound




REFER TO SECONDARY CARE if examination is abnormal or if CA 125 and ultrasound are abnormal. Consider CT imaging to assess disease extent

If risk of malignancy index (RMI) > 250, consider further investigations and referral to a specialist

- **Other tumour markers:**

| | |
|---|---|
| **AFP, hCG, and inhibin** | In women with suspected ovarian cancer who are younger than 40 years, AFP, hCG, and inhibin should be added to CA 125 (tumour markers of germ cell and sex cord-stromal tumours) |
| **CEA and CA 19-9** | ▪ If CA125 is elevated, CA 125: CEA ratio should be assessed<br>▪ If this ratio is < 25 specially with elevated CA19-9, peritoneal carcinomatosis with gastrointestinal cancer should be suspected, and bidirectional gastrointestinal endoscopy should be performed prior to primary debulking surgery |
| **HE4** | HE4 is promising diagnostic and prognostic marker in younger as it is associated with fewer false positive results compared to CA 125 e.g. not elevated in women with endometriosis or pelvic infection |

- **Computerized tomography (CT):**
  - CT scan is performed at referral to assess distant macroscopic disease (liver, lung, and lymph node metastasis) synchronous cancers, and thromboembolic events
  - Ability of CT to predict suboptimal debulking is insufficiently reliable and is not used alone to make the final decision

- **Magnetic resonance imaging (MRI):**
  - MRI is not routinely used
  - MRI is considered in young women with a solitary mass who want to preserve their fertility

- **Histopathology:**
  - Histopathology is crucial to confirm diagnosis, determine pathological type, and grade
  - If primary chemotherapy is considered to manage suspected ovarian cancer, tissue diagnosis should be made before treatment via image guided biopsy or laparoscopy
  - if tissue sampling is not feasible e.g. poor performance status, imaging **OR** CA125: CEA ratio > 25 **PLUS** positive cytology is used as an alternative to allow chemotherapy
  - Negative cytology does not exclude cancer specially in the presence of inflammation
  - Routine use of laparoscopy for assessment or tissue biopsy is not recommended
  - Intraoperative frozen section assessment may be used if it may alter intraoperative management. This technique has many limitation

- **Genetic testing:**

  High grade serous carcinoma and G3 endometroid adenocarcinoma are associated with 18% risk of germline BRCA mutation (45% of these patients have no family history)

**Advantages of BRCA testing**

- Testing provides prognostic information (longer remission period)
- A positive test promotes counselling of other family members
- BRCA positive women are eligible for PARP inhibitor treatment. Treatment may provide better response and longer remission in some of these patients Therefore, Olaparib can be offered to BRCA carriers, who responded to platinum-based chemotherapy after 3 or more courses.

## Risk assessment

- Risk of malignancy index (RMI) = U X M X CA125
- U = 0 (no sonographic features) ,1 (1 feature), or 3 (2-5 features)

  Ultrasound features: multilocular cyst, solid areas, metastasis, ascites, bilateral lesions
- M = 1 (premenopausal), or 3 (if menopausal or older than 50 years with hysterectomy)
- If RMI > 250, women should be referred to a specialist

## Prevention

- **Screening:**
  - No screening is recommended for low risk women
  - Ovarian cancer screening for high risk group is not well established

- **Preventive interventions:**
  - When ovarian cancer risk is above 10%, risk reducing salpingo-oophorectomy should be considered. It reduces cancer risk by 98%. However, there is 2% risk of peritoneal cancer
  - If risk-reducing surgery is declined, annual ultrasound and CA125 surveillance should be offered (positive predictive value is 25%, negative predictive factor is 100%)

## Management

30% of apparently early ovarian cancer are upstaged in surgery

**Treatment**

**Surgical treatment**

**Early stage**

Surgery should be performed at cancer center by a specialist multidisciplinary team (MDT)

Complete macroscopic resection and adequate surgical staging if fertility sparing surgery is not planned

If disease is unexpectedly malignant by postoperative histopathology, restaging procedure by an oncologist should be performed

Second look surgery is not recommended

**Late stage**

Primary cytoreductive surgery followed by adjuvant chemotherapy is the standard treatment

Neoadjuvant chemotherapy followed by interval cytoreductive surgery is not inferior to primary debulking and adjuvant chemotherapy and is appropriate if disease burden is extensive or if resectability of the disease is uncertain (yields less morbidity)

Neoadjuvant chemotherapy for 3 cycles followed by interval debulking is superior to no surgery (prolongs progress free interval and improves overall survival)

Bulky lymph nodes should be removed as a part of debulking surgery (prolongs survival)

**Systemic treatment**

**Early stage**

Adjuvant platinum-based chemotherapy should be offered to women with ovarian cancers except low grade (1 or 2) stage 1A or 1B disease

Grade 3 or stage 1C should receive 6 cycles of carboplatin

There is no role for targeted therapy in early ovarian cancer

**Systemic treatment**

**Late stage**

Intraperitoneal chemotherapy may be offered within clinical trials

Targeted therapy (bevacizumab) PLUS chemotherapy and then alone for 12-15 months as a maintenance therapy. It prolongs progress free survival but not overall survival

Anti-angiogenic therapy increases toxicity, increase progress free interval but not overall survival (e.g. pazopanib)

Adjuvant chemotherapy for all stages consists of carboplatin and paclitaxel every 3 weeks for 6 cycles

If there is allergy or intolerance to paclitaxel, consider protein-bound paclitaxel or pegylated liposomal doxorubicin as an alternative

Recurrence-related symptoms are reviewed, and examination is performed. CA 125 is not mandatory (no survival benefit). Visits are scheduled every 3 months for 2 year then every 6 months for up to 5 years

**Surgical staging of ovarian cancer**

- Peritoneal washing/ascitic sampling
- Total hysterectomy and bilateral salpingo-oophorectomy
- multiple peritoneal biopsies from paracolic spaces and subdiaphragmatic spaces bilaterally.
- Infracolic omentectomy
- Pelvic and paraaortic lymph node assessment up to level of origin of ovarian vessels in absence of peritoneal dissemination
- Appendectomy if the tumour is mucinous

Systemic retroperitoneal lymphadenectomy in absence of enlarged lymph nodes is not warranted

## Recurrent disease

| Types of recurrent disease | |
|---|---|
| **Platinum sensitive** | Disease progresses after 12 months of completion of treatment |
| **partially platinum sensitive** | Disease progresses after 6-12 of completion of treatment |
| **Platinum resistant** | Disease progresses after < 6 months of completion of treatment |
| **Platinum refractory** | Disease progresses during or within 4 weeks of completion of treatment |

- Cytoreductive surgery is indicated if the disease is resectable, platinum sensitive, and the patient is eligible for surgery (good performance status). Surgery improves progress free survival and overall survival
- If chemotherapy is considered, combination therapy is considered if disease free interval is more than 6 months. A single agent is used to managed recurrence if disease free interval is less than 6 months (less toxic and similarly effective)

## Type-specific considerations

| | |
|---|---|
| **Low grade serous ovarian cancer** | • 5% of serous tumours<br>• Surgery is the most effective treatment<br>• Low grade tumours are less responsive compared to high grade serous cancer. Response to combined regimen is 25%. However, there is no superior regimen |
| **Endometroid ovarian cancer** | • The second most common type of epithelial ovarian cancers (10-15%)<br>• 15% of cases are associated with synchronous ovarian cancer<br>• Grade 3 endometrial ovarian cancer management is similar to high grade serous cancer, adenofibromatous pattern and squamous metaplasia |
| **Mucinous tumour** | • 3-5% of all ovarian cancers<br>• Primary advanced primary tumour is rare. Secondaries from primary gastrointestinal tumour should be excluded<br>Primary ovarian tumours exhibit CK7+\CK2-\CDX2- immunoprofile |
| **Small cell carcinoma of the ovary** | • It includes hypercalcaemic, pulmonary, and large cell variant<br>• Treatment protocol is comparable to serous tumours |
| **Wolffian tumour** | • Usually begin<br>• It consists of cysts of different size, solid and spindled areas |
| **Clear cell carcinoma** | • It is most frequently associated with pelvic endometriosis, paraneoplastic hypercalcaemia, and venous thromboembolism<br>• This type is characterised by clear (hobnail) cells in papillary, glandular, or solid pattern<br>• Management is similar to high grade serous carcinoma. However, it lacks hormonal receptors and is less responsive to chemotherapy |
| **Carcinosarcoma** | • 2% of all ovarian cancers (rare)<br>• Characterised by epithelial and mesenchymal component<br>• It is associated with aberrant p53 expression, occasionally germline mutation BRCA2<br>• Prognosis is worse than high grade ovarian cancer and 90% of cases are diagnosed at advanced stage |

## Prognosis

- Average 5-year survival rate of ovarian cancer is 35%
- Disease Stage is the most prognostic factor

# Borderline Ovarian Tumours

## Epidemiology

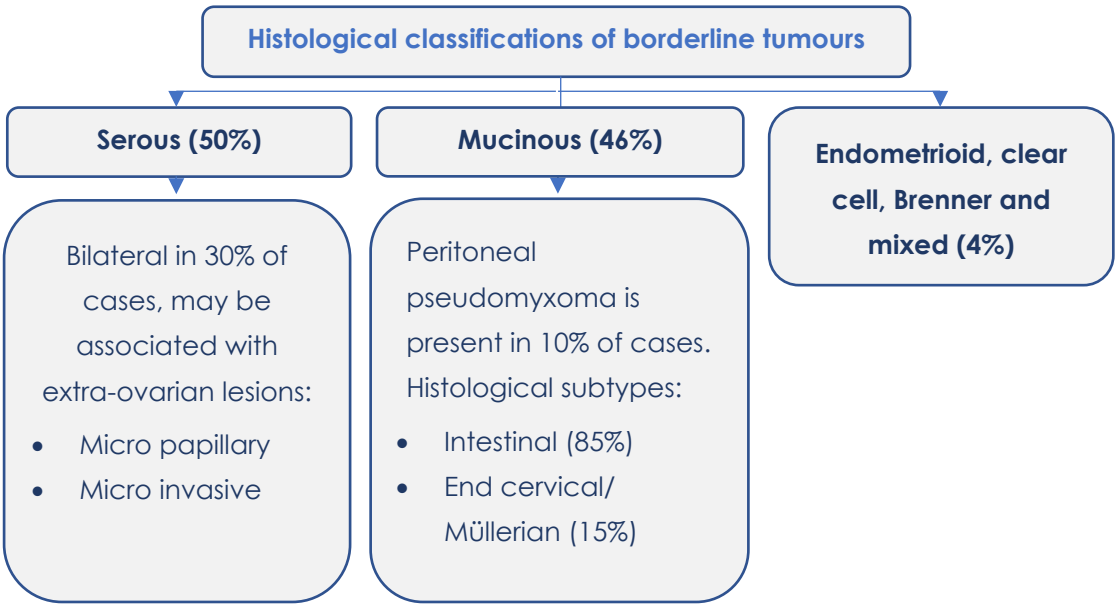
- They account for 10–15% of all epithelial ovarian neoplasms
- Unlike ovarian cancer, borderline tumours are characterized by presence of atypical epithelial proliferation without stromal invasion

## Risk factors

- Younger age (40 years vs. 60 years for ovarian cancer)
- Nulliparity (multiparty and breast feeding are protective factors)
- Hormonal contraception is not protective (unlike ovarian cancer)

## Classification

- Ovarian cancer is classified to either high grade serous cancer (associated with high rate of P53 mutation) and low-grade cancer including borderline tumours, mutation of BRAF/KRAS pathway
- Because low grade cancer does not progress to high grade cancer, if borderline tumours progress, they will behave as low-grade cancer (which is uncommon)



## Diagnosis

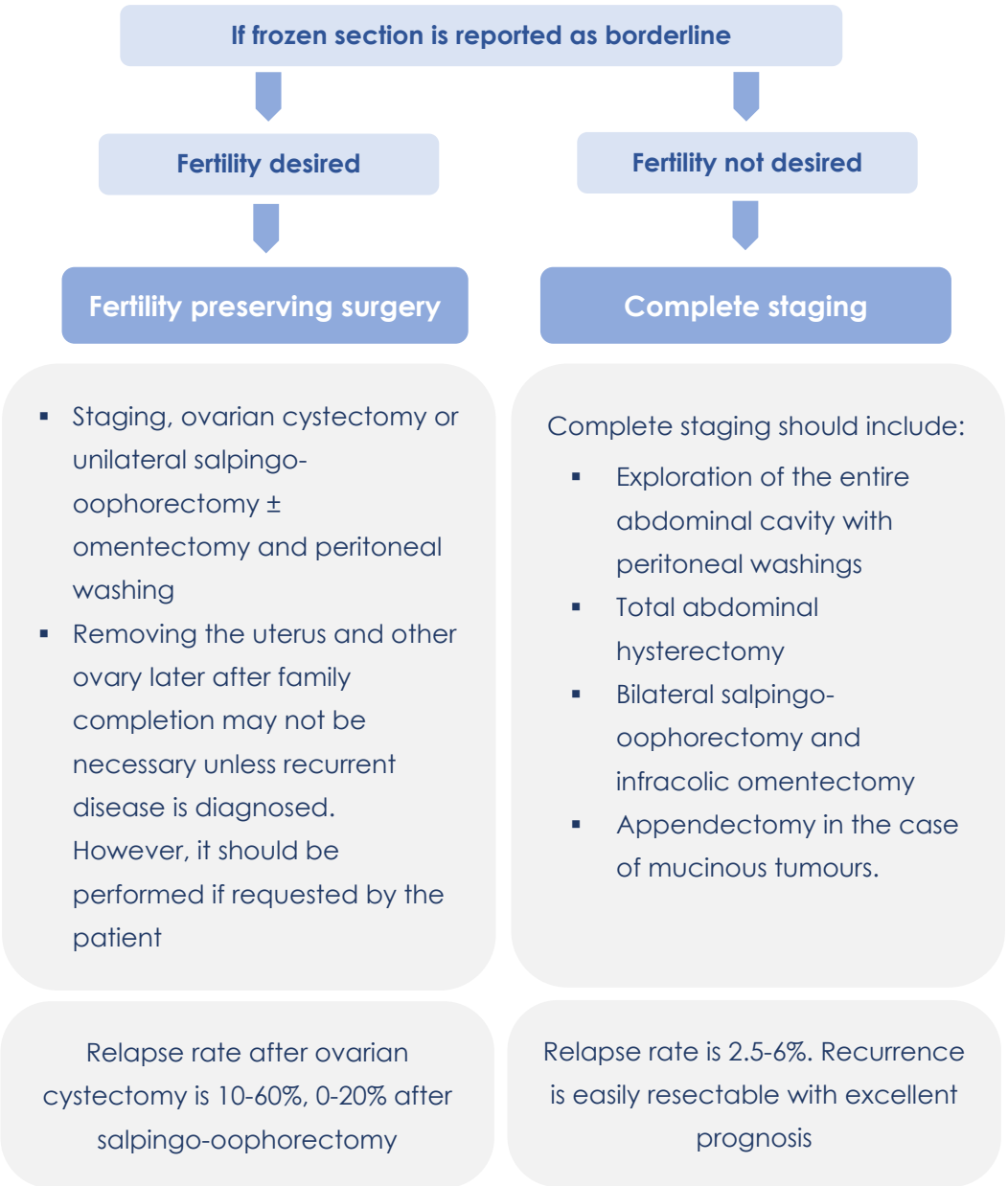
Most patients are asymptomatic. Diagnosis is commonly incidental during physical examination or pelviabdominal imaging for other indications

| Symptoms | Investigations |
|---|---|
| • Pelvic pain<br>• Bloating<br>• Dyspareunia<br>• Menstrual irregularities<br>• Pressure symptoms<br>• Frequency of micturition<br>• constipation | • **CA 125:**<br>▪ CA 125 is elevated in 75% of serous tumours<br>▪ CA 125 is elevated in only 30% with mucinous tumours (elevated CA 19-9 is more common with mucinous tumours)<br>• **Transvaginal ultrasound:**<br>▪ Ultrasound is the standard modality to assess cyst features<br>▪ Presence of intra-cystic blood flow is a sensitive finding for ovarian cancer |

## Management

- **Determinants of management:**
  - Patient age
  - Disease stage
  - Desire of fertility preservation
  - Peritoneal implants

- **Standard management:**
  - Standard surgery is accurate staging and cytoreductive surgery via laparotomy
  - If available, frozen section testing should be performed. However, diagnostic accuracy of frozen section to borderline ovarian tumours is low; 33% of cases will be reclassified as invasive cancer on final histopathology




- After fertility preserving management, 50% of women conceive spontaneously. If fertility treatment is indicated, it should be confined to stage I and number of cycles should be limited. Recurrence rate following fertility treatment 13-30%
- Lymphadenectomy has no role in borderline ovarian tumours. However, it may be considered in women with invasive disease
- Chemotherapy has no role unless the disease is recurrent and is irresectable

- **Restaging and completion of surgery:**

| | |
|---|---|
| **Indications of restaging *** | • Micropapillary tumours<br>• Invasive implants (5-year risk of recurrence is 31% vs. 21% with non-invasive implants).<br>• Tumour DNA aneuploidy (19-fold increased risk of mortality compared to diploid tumour) |
| **Restaging procedure** | • Peritoneal washings<br>• Omentectomy<br>• Complete examination of the peritoneum<br>• Hysterectomy and oophorectomy (only if there is no fertility desire)<br>• No role of lymphadenectomy |

* Restaging is unlikely indicated if a woman has undergone full laparotomy with inspection of all surfaces (including contralateral ovary, momentum and peritoneal surfaces) during primary surgery. Therefore, these steps are indicated as a routine during primary surgery

## Follow-up

- After treatment, patients should be followed-up every 3 months for 2 years
- After 2 years, follow-up visits are scheduled every 6 months for another 2 years and then annually

## Prognosis

- 5-year survival rate of stage I borderline ovarian tumours is excellent (95–97%)
- Women with stage III disease also have a good prognosis; 5-year survival rate is 50–86%
- Overall 10-year survival rates range from 70–80%, due to late recurrence

# Ovarian Cancer Prevention

## Epidemiology

- Ovarian cancer is the second most common gynaecologic malignancy
- 90% of ovarian tumours are epithelial in origin
- Lifetime risk of ovarian cancer in the general population is 1.4%
- Overall 5-year survival is less than 45%.
- Spread of cancer beyond ovaries at time of diagnosis occurs 75% of cases

## Risk factors

Family history of ovarian cancer is the strongest risk factor (10-15% of all cases)

| | |
|---|---|
| **Family history** | Risk of ovarian cancer increases even it occurs in sporadically. However, hereditary cancer syndrome is associated with significant increase in cancer risk:<br>• If 1 family member has ovarian cancer: risk is 5%<br>• If 2 family members have ovarian cancer: risk is 7%<br>• Family history consistent with hereditary cancer syndrome: risk is 15-50% |
| **Breast ovarian cancer syndrome** | • Women with BRCA gene mutations have significantly increased risk of ovarian and breast cancers<br>• BRCA mutations may account for up to 90% of hereditary ovarian cancers<br>• The estimated risk of ovarian cancer is:<br>  ▪ 35–46% in BRCA1 mutation carriers<br>  ▪ 13–23% in BRCA2 mutation carriers<br>• BRCA2 carriers have a better cancer prognosis than non-carriers |

| | |
|---|---|
| **Other high-risk genetic syndromes** | • Lynch syndrome (hereditary non-polyposis colorectal cancer, HNPCC):<br>▪ It accounts for 1% of ovarian cancers<br>▪ Risk of ovarian cancer in women with Lynch syndrome is 4-14%<br>• Peutz-Jeghers syndrome:<br>▪ Risk of ovarian cancer is 20%<br>▪ Tumours are likely sex-cord stromal tumours |
| **Non-genetic risk factors** | • Endometriosis:<br>▪ Risk of malignant transformation is 2.5%<br>▪ Developing cancer is likely well differentiated, low stage carcinoma (good prognosis)<br>• PCOS and obesity:<br>There may be small increase in risk of ovarian cancer in women with PCOS and obesity<br>• Ovulation induction:<br>It does not increase risk of ovarian carcinoma. However, it may be associated with increased risk of borderline ovarian tumours |
| **Protective factors** | These factors may reduce the risk of ovarian cancer:<br>• Pregnancy<br>• Breast feeding for more than 12 months (risk reduction is 0.7)<br>• Combined oral contraceptives (COCs) decrease risk by 20% every 5 years, reaching approximately 50% after 15 years. The effect extends for 30 years. Risk reduction is 30% within 10 years of cessation and 15% 30 years after cessation<br>• Tubal ligation decreases risk by 60% among BRCA 1 patients<br>Risk reduction is 72% if COCs are used<br>• Hysterectomy decreases risk by 34% |

## Screening of ovarian cancer

Screening is not recommended in low risk. Combined screening is associated with anxiety and unnecessary interventions and it does not improve mortality

| | High risk women | Low risk women |
|---|---|---|
| **Risk factors** | • Family history suggestive of a hereditary cancer syndrome<br>• BRCA1 carrier<br>• BRCA2 carrier<br>• Lynch syndrome (HNPCC) | • Positive family history, single member affected<br>• not suggestive of a hereditary cancer syndrome<br>• Risk of ovarian cancer: 4–5% |
| **Management** | • Offer risk-reducing bilateral salpingo-oophorectomy (BSO) after age 35 when childbearing is complete<br>• If surgery is declined, women can be offered screening with transvaginal ultrasound and CA 125 every 6 months starting at the age of 35 or 5-10 years earlier than the youngest age at diagnosis in the family. COCs should be offered if not given before | • No evidence to support screening in this group<br>• Risk-reducing bilateral salpingo-oophorectomy (BSO) may be considered based on individual considerations after thorough counselling |

## Prevention of ovarian cancer

- **Chemoprevention:**
  COCs are found to reduce yield long-term reduction in ovarian cancer risk including women who are BRCA carriers

- **Risk-reducing surgery:**

  Patients should be counselled that risk-reducing surgery is not completely protective; risk of cancer is 2% after surgery owing to peritoneal cancer

| | |
|---|---|
| **Time of surgery** | ▪ BRCA 1 carriers:<br>55% diagnosed before age of 50 while 2-3% are diagnosed before age of 40. Therefore, surgery should be considered at age 35<br>▪ BRCA 2 carriers:<br>Age of cancer diagnosis is later than BRCA 1 carriers (2-3% at age of 50). Therefore, surgery may be delayed to the age of 45. Nevertheless, this delay precludes benefit of reducing breast cancer<br>▪ If women have not completed their family, embryo cryopreservation or surrogacy may be discussed |
| **Preoperative measures** | • Perform Transvaginal ultrasound and CA 125 prior to surgery<br>• Counsel women on possible need for full staging at time of surgery since incidence of occult malignancy is 4-8%, reaching up to 20% above the age of 45 |
| **Surgical procedure** | • BSO with removal of all ovarian tissues and all ovarian adhesions<br>• Ovarian vessels are clamped at least 2 cm proximal to ovary or ideally at pelvic brim to ensure removal of all ovarian tissue<br>• Tubes should be completely removed. The interstitial part does not have to be removed as it is not associated with cancer development<br>• Concurrent hysterectomy:<br>▪ It should be considered in women with Lynch syndrome since the risk of endometrial cancer is 40-60%<br>▪ Some BRCA carrier who receive tamoxifen for chemoprophylaxis may be offered hysterectomy<br>▪ It may be considered in women who will receive hormone replacement therapy so they can use oestrogen only (which is not associated with significant increase in breast cancer risk in postmenopausal compared to combined therapy) |

- Oophorectomy at time of hysterectomy for benign indications decrease risk of breast and ovarian cancer. However, it increases the risk of all-cause mortality and mortality related to coronary heart disease.

## Premature menopause

- Surgical menopause is associated with abrupt decrease in sex hormones
- Hormone replacement therapy does not interfere with benefit of risk-reducing surgery in reducing risk of breast cancer
- Hormone replacement therapy is associated with small increase in breast cancer risk. However, if breast cancer develops, it is typically low grade. There is no increase in breast cancer mortality with hormone replacement therapy
- BRCA 1 is typically oestrogen/progesterone receptor negative. BRCA 2 is typically receptor positive. Hormone replacement therapy is contraindicated if there is personal history of breast cancer.

# Endometrial Hyperplasia

## Risk factors

- High body mass index (peripheral conversion of androgen to oestrogen)
- Perimenopausal anovulation, polycystic ovary syndrome (PCOS)
- Oestrogen secreting ovarian tumours e.g. granulosa cell tumour (up to 40%)
- Long term tamoxifen
- Systemic oestrogen replacement therapy
- Immunosuppression: e.g. renal graft patients with abnormal uterine bleeding (70%)

## Assessment

- **Outpatient endometrial sampling:**
  - Endometrial surveillance for endometrial hyperplasia is performed using outpatient endometrial biopsy and the diagnosis is made by histological examination
  - Up to 10% of endometrial pathology may be missed even if inpatient endometrial sampling is performed
- **Hysteroscopy:**
  - If outpatient sampling fails or is non-diagnostic, diagnostic hysteroscopy should be performed
  - Hysteroscopy is also indicated if hyperplasia is diagnosed within a polyp or other discrete focal lesion
- **Transvaginal ultrasound:**
  - It may have a role in diagnosing endometrial hyperplasia in pre- and postmenopausal women

- Endometrial thickness ≤ 4mm is associated with cancer risk < 1%. Endometrial thickness with PCOS is unlikely hyperplasia if < 7mm

- **CT and MRI:**
  They are not routinely recommended

## Management

Reversible risk factors should be identified and managed e.g. obesity, hormone replacement therapy (HRT)

- **Endometrial hyperplasia without atypia:**
  - **Indications of treatment:**
    ① In all women, progestin treatment is superior to observation alone in regression rate
    ② Failure of observation
    ③ Symptomatic patients with abnormal uterine bleeding

    Risk of progression to cancer is < 5%. The majority regress spontaneously
  - **Treatment options:**
    - First line treatment is levonorgestrel-releasing intrauterine system (LNG-IUS) since it is the most effective form of progestin therapy, and is associated with fewer side effects
    - If LNG-IUS is declined, continuous progestin (medroxyprogesterone acetate [MPA] 10-20 mg/day or norethisterone 10-15 mg/day) is used
    - Cyclic progestin treatment is not recommended (less effective)
  - **Treatment duration:**
    - A minimum of 6 months is required to allow disease regression
    - Women who are not interested in pregnancy should be counselled on keeping LNG-IUS for 5 years to reduce the risk of relapse
  - **Follow-up:**
    - Endometrial surveillance should be performed every 6 months. At least, two successive negative samples should be obtained prior to discharge
    - Women at higher risk of relapse e.g. BMI ≥ 35 should be followed up every 6 months, till 2 negative results are obtained and then annually
    - If abnormal bleeding recurs after treatment, referral and reassessment should be considered
    - Risk of relapse is maximum in the first 2 years after treatment

- **Hysterectomy:**
  - **Indications of hysterectomy:**
    ① Progression to atypical hyperplasia
    ② Failure of regression after 12 months of treatment
    ③ Relapse after progestin therapy
    ④ Persistence of bleeding symptoms
    ⑤ Patients declining or not compliant to surveillance
  - **Procedure:**
    - Total hysterectomy with bilateral salpingo-oophorectomy is considered in postmenopausal women
    - In premenopausal women, hysterectomy with bilateral salpingectomy should be performed. Decision of oophorectomy should be individualized

- **Atypical hyperplasia:**
  - **Definitive management:**
    - Total hysterectomy is the standard management
    - Intraoperative frozen section or routine lymphadenectomy is not recommended
  - **Fertility sparing management:**
    - Women who wish to retain fertility should be counselled on risk of malignancy progression, rule out invasive cancer or coexisting ovarian cancer
    - Before fertility sparing treatment is discussed, transvaginal ultrasound/MRI and CA125 should be considered (risk of coexisting ovarian cancer is up to 4%)
    - First line of management is LNG-IUS. Second line is oral progestins followed by hysterectomy after completing her family
    - Follow-up after treatment consists of endometrial surveillance every 3 months till 2 consecutive negative biopsies are obtained then every 6-12 months until hysterectomy is performed

Assisted reproductive technology (ART) may be considered since it is associated with higher pregnancy rate. It may prevent relapse compared to attempting natural conception

- At least one sample should show regression before trying to conceive. Women are referred to fertility specialist. Regression of endometrial hyperplasia is associated with higher implantation and clinical pregnancy rate

- **Hyperplastic polyps:**

  In presence of hyperplasia within a polyp, polyps should be removed, and background endometrium should be sampled

- **Hormonal treatment and endometrial hyperplasia:**

| | |
|---|---|
| **Hormone replacement therapy (HRT)** | ▪ Unscheduled bleeding should be assessed<br>▪ Women with endometrial hyperplasia on sequential HRT should be switched to combined continuous HRT or start using LNG-IUS<br>▪ If endometrial hyperplasia develops while using continuous HRT, treatment may continue, progestin treatment (dose is not well defined or LNG-IUS should be considered |
| **Tamoxifen** | • Women taking Tamoxifen are at high risk of hyperplasia or cancer<br>• Any abnormal vaginal bleeding or discharge should be assessed promptly<br>• LNG-IUS is not recommended for prophylaxis<br>• If hyperplasia develops on Tamoxifen, management should be discussed with an oncologist |
| **Aromatase inhibitors** | • Aromatase inhibitors e.g. letrozole do not increase risk of hyperplasia or cancer |

# Uterine Cancer

## Incidence

- Uterine cancer is the 6th most common cancer worldwide in women and the 14th most common cancer overall
- It accounts for 5% of female cancer cases. Mean age at diagnosis is 60 years
- 2-5% of endometrial cancer cases are genetic

## Cancer screening

### Screening in low-risk women

- There is **NO** role of screening in low risk asymptomatic women
- Only symptomatic women with postmenopausal bleeding/abnormal uterine bleeding should be assessed by transvaginal ultrasound (TVUS).
- If endometrial thickness (ET) by transvaginal sonography is ≤ 4mm, risk of endometrial carcinoma (EC) is unlikely (<1%)

### Screening in high-risk women (selective screening)

- **Lynch syndrome:**
  - Lynch syndrome is an autosomal dominant disorder of mismatch repair genes, that results in colon, endometrial and ovarian cancer. Life-time risk of EC is 40-60%.
  - Women with Lynch Syndrome and their first-degree relatives are offered annual screening with TVUS and endometrial biopsy starting at the age of 35 years or if they are symptomatic
  - Mean age at diagnosis is 47 years
- **Tamoxifen therapy:**
  - Routine screening is not recommended
  - Symptomatic patients should be evaluated by TVUS, hysteroscopy and biopsy

## Cancer Prevention

### Prevention in the general population

A normal body mass index (BMI) reduces risk of EC. Lifetime risk in obese is women is 9-10% (vs. 3% in general population)

Every 5 kg/m$^2$ increase body weight is associated with 1.6-fold increase in EC risk

80% of EC are overweight (BMI 25-29.9) and 50% are obese (BMI is 30 or more)

Sustained weight loss decreases risk by 25%.

Loss of wright either by bariatric surgery or lifestyle modification may reduce EC risk

If BMI in later life is less than BMI at age 20, these women are 50% less likely to develop EC compared to other women

### Prevention in high-risk group

Prevention in high risk population

- Risk reducing surgery is effective in preventing EC in high risk women
- Prophylactic hysterectomy and bilateral salpingo-oophorectomy when family is completed prevents endometrial and ovarian cancer in high-risk women
- Non-invasive procedures e.g. levonorgestrel-releasing intrauterine system and weight loss may play a role. However, their role has not been established yet

## diagnosis

- **Presenting symptoms:**
  - postmenopausal bleeding (PMB). EC represents 5-10% of patient with PMB
  - intermenstrual or prolonged bleeding in premenopausal women

- **Examination:**
  - Women with any of the above symptoms should undergo abdominal, speculum and pelvic examination
  - Endometrial sampling is indicated in women with:
    ① Abnormal uterine bleeding at or above 45 years
    ② Women with irregular bleeding or bleeding unresponsive to treatment in younger age group

- **Diagnostic investigations:**

**TVUS**

- It is the first investigation in women with PMB
- If endometrial thickness ≤ 4 mm with no other abnormalities, EC is unlikely, and no further management is needed

**Endometrial biopsy**

- If endometrial thickness is more than 4 mm, outpatient endometrial biopsy is indicated
- Recurrent PMB, regardless of TVUS, warrants endometrial biopsy

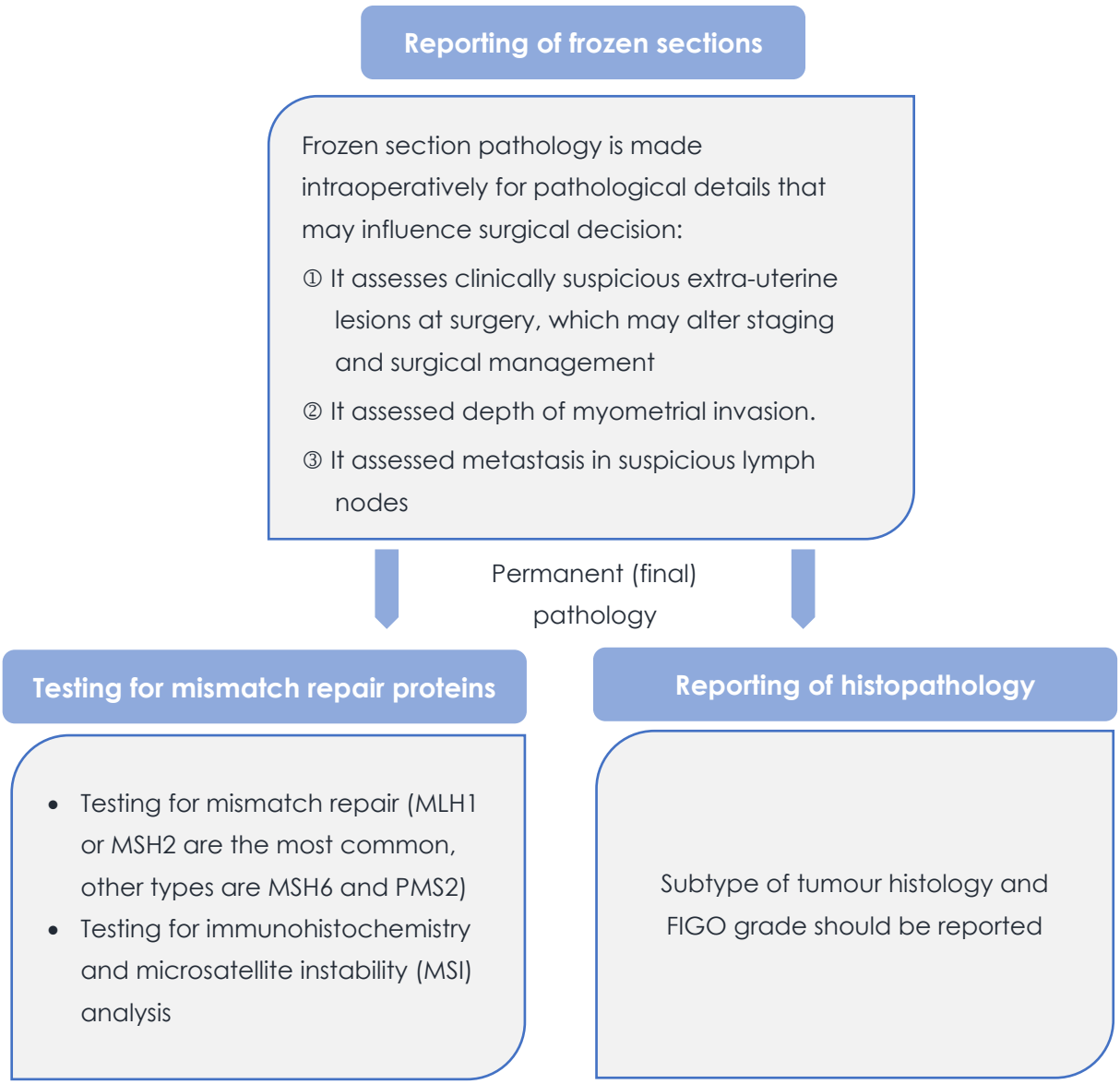
**Hysteroscopy**

- Outpatient hysteroscopy is performed if office endometrial biopsy is not available, in women at high risk of EC or recurrent PMB
- Suspicious findings are associated with 70% risk of EC
- Negative findings are associated with 0.6% risk of EC

**Hysterectomy**

- Hysterectomy is indicated in women with hyperplasia specially in the presence of atypia due to risk of coexisting cancer foci and risk of conversion to EC
- Hysterectomy is offered to women with recurrent PMB when no cause is identified

- **Metastatic investigations:**
  - Chest radiology (chest x-ray or CT): should be performed in all women with diagnosis of EC
  - Abdomino-pelvic MRI or CT abdomen and pelvis: in women with high-risk histological subtype (non-endometroid EC). If histological subtype was not known prior to surgery, these tests should be performed postoperatively to determine adjuvant therapy. MRI is superior to CT in assessment of lymph nodes
  - PET scan and CA-125 are not recommended.



- **Clinical information required on the specimen request form:**
  - Patient demographics
  - Clinical presentation
  - Previous biopsies and imaging investigations
  - Surgical procedure in details
  - Family history of cancer
  - Hormonal therapy
  - Careful report of site of origin and orientation of the specimen

## Surgical management

### Where to treat women with endometrial caner

- Women with stage 1A G1 or 2: surgery can be done in a diagnostic centre by a gynaecologist who is member of specialist gynaecological cancer multidisciplinary team meeting.
- Women with papillary, serous, clear, carcinosarcoma, G3, or 1B: surgery is done in a cancer centre by a specialized surgeon
- Failsafe mechanisms should be applied to ensure reliable direction and management of patients

- **Management of early disease (FIGO Stage I and II):**
  - Women with stage I-II grade 1 or 2 EC are treated with hysterectomy and bilateral salpingo-oophorectomy. In women with stage II disease, simple hysterectomy with radiotherapy is comparable to radical hysterectomy
  - Lymphadenectomy is not indicated. It does not affect survival or recurrence
  - Laparoscopy and robotic surgery are appropriate approaches

### Sentinel lymph node

- In low risk and intermediate risk patients,10% and 15% positive lymph nodes with sentinel lymph node assessment. Diagnostic performance is promising but routine use has not yet been adopted
- In high risk patients, sentinel lymph nodes are not recommended because 50% may have metastasis. Lymphadenctomy may be considered

- **Management of stage III and IV:**
  - Surgical resection of all visible disease is performed (it may improve survival)
  - Systematic lymphadenectomy is associated with 4-fold increase in detection rate of metastasis compared to selective sampling of enlarged lymph nodes
  - In the presence of irresectable disease, surgery may be considered if disease responds well to neoadjuvant chemotherapy

## Adjuvant therapy

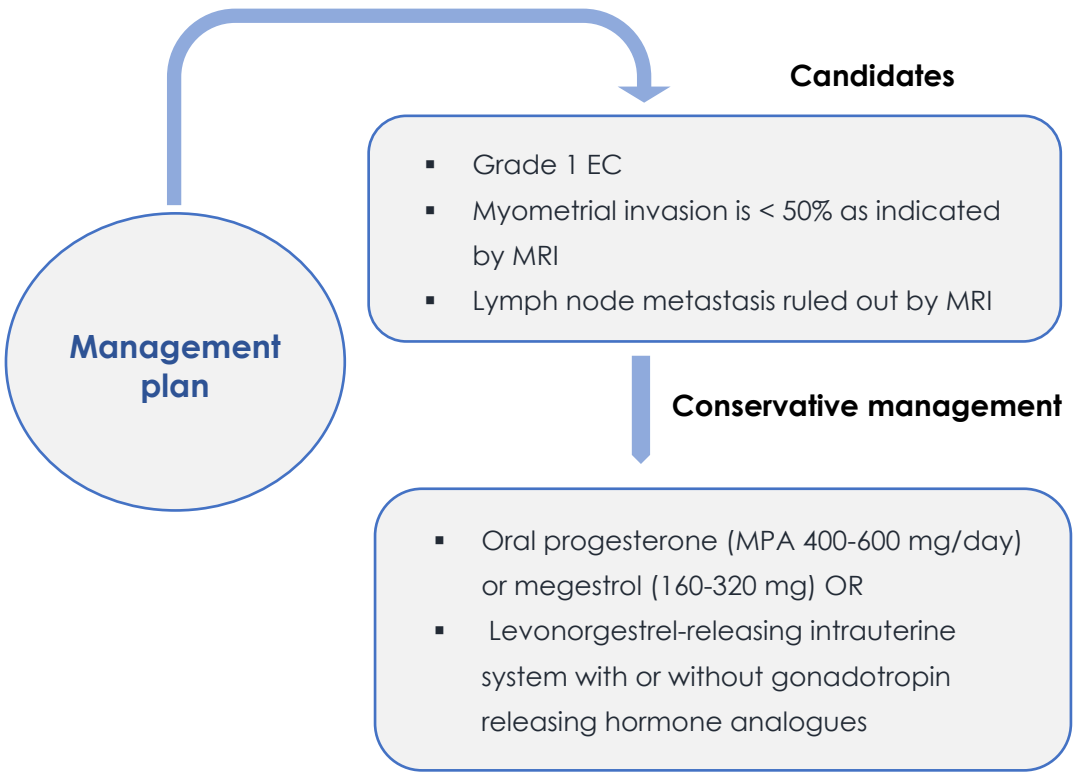
| Classification | Definition | Treatment |
|---|---|---|
| **Low risk** | FIGO grade 1, Stage Ia, Ib, no LVSI<br>FIGO grade 2, Stage Ia, no LVSI | • No adjuvant treatment |
| **Intermediate risk** | FIGO grade 2, Stage Ib, no LVSI<br>FIGO grade 3, Stage Ia, no LVSI | • Vaginal brachytherapy |
| **High-intermediate risk** | FIGO grade 3, Stage 1a, regardless of LVSI<br>FIGO grade 1, grade 2, LVSI unequivocally positive, regardless of depth of invasion | • Consider external beam radiation versus vaginal brachytherapy if nodal status is unknown<br>• Consider adjuvant brachytherapy versus no adjuvant therapy if nodes are negative |
| **High risk** | FIGO grade 3, Stage Ib | • Consider external beam radiation versus vaginal brachytherapy.<br>• Consider adjuvant chemotherapy |

LVSI: lymphovascular space invasion

## Management of unfit patient


## Fertility preserving management

- Less than 5% of endometrioid EC occur in young women (< 45 years)



## Follow-up

- Telephone follow-up may be an alternative to clinic visits in women with grade 1 EC
- Imaging and labs are not routinely indicated

- **Frequency of visits:**

| Low grade endometroid cancer | High grade endometroid cancer |
|---|---|
| • Infrequent visits in the first 2 years or patient-initiated follow-up | • More frequent visits in the first 2 years and up to 5 years after surgery |

## Management of relapsed EC

- PET/CT scan should be considered to rule out distant metastasis prior to treatment
- If recurrent disease is an isolated lesion, it should be managed by surgery and adjuvant chemotherapy
- If residual lesions appear after surgery, external beam radiotherapy or brachytherapy may be considered
- If the patient has not received prior radiotherapy, consider radical radiotherapy

# Vulval Cancer

## Background

- Incidence of vulval cancer is 4:100.000, crude mortality rate is 1:100.000
- 90% of vulval cancers are squamous cell carcinoma (SCC)
- Nodal spread is present in 30% of operable women

| Excisions | | |
|---|---|---|
| **Incisional biopsy** | **Excisional biopsy** | **Radical excision** |
| For securing a diagnosis only | No safety margin | Excision with safety margin at least 1 cm after fixation |

## Screening

- There is no screening strategy for general population
- High grade vulval intraepithelial neoplasia (VIN), high grade VIN with multicentric disease, VIN in immunocompromised women, Paget's disease, and melanoma in situ, needs a specialist multidisciplinary clinic or gynaecologic oncologists for assessment and follow-up
- Women with Paget's disease need prolonged follow-up
- Follow-up of uncomplicated lichen sclerosus does not need to be hospital-based

## Diagnosis

- Diagnosis is made by biopsy. Vulvar cytology should not substitute biopsy
- If the lesion is highly suspicious, do not await biopsy results and consider immediate referral
- Diagnostic biopsies of suspected vulval cancer should be incisional biopsies. Removal of the whole lesion (excisional biopsy) should be avoided

## Treatment

- **Primary treatment:**
  - Surgery is primary treatment
  - The standard surgery is wide radical local excision of the primary tumour with a minimum margin of 15 mm of disease-free tissue (a margin greater than 8 mm is associated with 0% recurrence compared to 50% if the margin is less than 8 mm)
  - Primary radiotherapy is considered only if surgery is not possible even under regional anaesthesia
  - Long saphenous vein preservation decreases groin wound and lower limb complications
  - Plastic surgeons should be involved if large defects are anticipated and when radiotherapy is used
  - Diverting stoma 1-2 weeks before definitive surgery may be considered

**Surgical management of non-squamous vulval cancer**

| Carcinoma of Bartholin gland (SCC or adenocarcinoma) | Basal cell carcinoma/verrucous carcinoma | Malignant melanoma [Breslow classification is preferred) |
|---|---|---|
| Partial resection with reconstruction, defunctioning temporary colostomy and bilateral lymphadenectomy (deeper cancer, likely to metastasize, and close to anal sphincter) | No lymph node dissection needed<br>Basal cell carcinoma can be treated with radiotherapy (if surgery would affect sphincter function) | Wide local excision is preferred.<br>No benefit from block dissection of the groin. Vulval melanomas should be managed by a melanoma multidisciplinary team |

- **Lymph node management:**
  - If there is a unifocal tumour < 4 cm with no evidence of lymph node metastasis, sentinel lymph node biopsy should be considered

**Eligibility for sentinel lymph node biopsy**

① Primary SCC
② Cancer size is less than 4 cm
③ Macroscopic unifocal cancer
④ No clinical or radiological evidence of lymph node metastasis
⑤ No safety issues with use of patent blue dye and/or technetium[99]

If sentinel lymph node biopsy fails, radical lymph-adenectomy is performed

- If there is a lateral tumour, ipsilateral groin node surgery should be considered. If these lymph nodes are positive, contralateral lymphadenectomy should be performed
- Groin lymph node surgery is done through separate incisions (triple incisions) to decrease morbidity (incidence of skin bridge recurrence is low with early stage disease)
- In the presence of a large primary tumour with clinically suspicious lymph nodes, radical vulvectomy with en-bloc groin lymph node dissection should be considered
- If fixed or ulcerated groin nodes, do surgery and/or RT.
- Superficial groin node dissection should not be performed (higher risk of groin recurrence)

| Stage IA (lesion < 2 cm, stromal invasion ≤ 1 mm | Stage ≥ IB (depth of invasion > 1mm or size > 2 cm) | Lesion < 4 cm |
|---|---|---|
| Wide local excision without groin node dissection | Triple incision technique | Bilateral sentinel lymph nodes |

- Groin lymph node dissection is not indicated with:
  - Stage IA SCC
  - Verrucous tumour
  - Basal cell carcinoma
  - Melanoma

- **Reconstructive surgery:**

<table>
<tr><th colspan="4">Reconstructive surgery</th></tr>
<tr><td>Secondary intention</td><td>Split skin grafts (thigh, buttocks)</td><td colspan="2">Flap coverage</td></tr>
<tr><td rowspan="2">Smaller defects can be left to heal if tension-free closure cannot be done</td><td rowspan="2">Only for large areas when no flap options. Less reliable after radiotherapy or with extensive scarring (depends on underlying blood supply)</td><td colspan="2">Thicker, suitable for less vascularized areas and areas that would receive irradiation</td></tr>
<tr><td>Local flaps</td><td>Distant flaps</td></tr>
<tr><td colspan="2"></td><td>Rhomboid flaps, lotus petal flaps, pudendal thigh flaps</td><td>Gracilis, rectus abdominis for larger bulky reconstruction</td></tr>
</table>

- **Radiotherapy:**

**Indications of primary radiotherapy**

- Advanced vulval cancer
- Preoperative treatment to preserve anal sphincters if risk of damage is high with surgery
  In these cases, radiotherapy may be considered primarily or prior to surgery to decrease the risk of functioning stomas. However, radiotherapy increases risk of surgical complications and morbidity and the decision should be carefully made
- Treatment of histologically proven groin lymph node metastasis (post-radiation lymph node dissection is of unknown role)
  Pathological assessment of lymph nodes (fine needle aspiration) prior to radiotherapy is mandatory to confirm metastasis

- **Chemotherapy:**

  Primary and recurrent vulval cancer respond to chemotherapy. However, response is variable, and treatment is associated with risk of toxicity

| Chemotherapy | | |
|---|---|---|
| **Neoadjuvant chemotherapy** | **Adjuvant chemotherapy** | **Chemoradiation** |
| Response of invasive SCC to this approach is variable | May be useful in women with high risk of relapse (cisplatin) | Similar to its use in cervical cancer treatment [Cisplatin (40 mg/m2) alone or with 5-flurouracil |

- **Targeted therapy:**

  Erlotinib (after mutation testing) may improve toxicity benefit ratio

## Complications

### Complications

| Risk factors of short-term complications | Risk factors of long-term complications |
|---|---|
| • Older age<br>• Diabetes<br>• En bloc surgery<br>• Large drain output on last day of drain placement | • Younger age<br>• Lymphocele<br>✹ Dissection of greater number of nodes is protective against long-term complications |

| Surgical complications | |
|---|---|
| • Wound breakdown<br>• Infection<br>• Deep venous thrombosis (DVT), pulmonary embolism (PE)<br>• pressure sores<br>• Introital stenosis<br>• UI, rectocele<br>• Fecal incontinence | • Inguinal lymphocyst<br>• Lymphedema<br>• Hernia<br>• psychosexual complications |

## Follow-up

After treatment, patients should be followed up every 3 months for 1 year, then every 6 months for 1 year, and then annually

## Prognosis

### Recurrence

- Recurrence rate is 15-30%.
- Most common sites of recurrence are:
  - The vulva 70%
  - Groin nodes is 25%
  - Distant recurrence 20%
  - Pelvis 15%
- Groin recurrence: poorer prognosis.
  - If primary management was surgery, radiotherapy is recommended and vice versa. If both methods were done, palliative treatment should be considered

### Survival

- 5-year survival rate is 45%
- Survival rate is significantly influenced by nodal metastasis:
  - Survival rate is 80% if there is no nodal spread
  - Survival rate is < 50% with inguinal lymph node spread
  - Survival rate is 10-15% if iliac or other lymph nodes are involved

- The following factors are associated with poorer prognosis:
- Infiltrative growth pattern
- Lymphovascular space invasion
  Both factors are associated with high local recurrence and poorer prognosis. However, adjuvant treatment is not recommended
- Prominent fibromyxoid stroma at invasive edge

## Staging

| FIGO Classification | |
|---|---|
| ***Stage I*** | ***Tumour confined to vulva*** |
| Stage Ia | Lesions ≤ 2 cm in size, confined to the vulva or perineum and with stromal invasion ≤ 1 mm. No nodal metastasis |
| Stage Ib | Lesions > 2 cm in size, or with stromal invasion > 1 mm confined to the vulva or perineum. No nodal metastasis |
| ***Stage II*** | ***Tumour of any size with extension to adjacent perineal structures (lower 1/3 urethra; lower 1/3 vagina; anus) with negative nodes*** |
| ***Stage III*** | ***Tumour of any size with or without extension to adjacent perineal structures (lower 1/3 urethra; lower 1/3 vagina; anus) with positive inguinofemoral nodes*** |
| Stage IIIa | (i) With 1 lymph node metastasis (≥ 5 mm), or<br>(ii) 1-2 lymph node metastasis(es) (< 5 mm) |
| Stage IIIb | (i) With 2 or more lymph node metastases (≥ 5 mm), or<br>(ii) 3 or more lymph node metastases (< 5 mm) |
| Stage IIIc | With positive nodes with extracapsular spread |
| ***Stage IV*** | ***Tumour invades other regional (upper 2/3 urethra, 2/3 vagina) or distant structures*** |
| Stage IVa | Tumour invades any of the following<br>(i) Upper urethral &/or vaginal mucosa; bladder mucosa; rectal mucosa or fixed to<br>pelvic bone, or<br>(ii) Fixed or ulcerated inguinofemoral lymph nodes |
| Stage IVb | Any distant metastasis including pelvic lymph nodes |

# Gestational Trophoblastic Disease

## Definition

Gestational trophoblastic disease (GTD) is a spectrum of conditions that are associated with elevated hCG after molar, non-molar and live pregnancy

## Incidence

Overall incidence of GTD is 1:700. Incidence is approximately doubled in Asian population (1:380)

## Types

- Hydatidiform mole (complete or partial)
- Invasive mole
- Choriocarcinoma
- Placental-site trophoblastic tumour
- Epithelioid trophoblastic tumour

| Complete mole | Partial mole |
|---|---|
| Paternal origin (sperms only) | Maternal and paternal origin |
| Diploid chromosomes | Triploid (90%), tetraploid or mosaic (10%) |
| No foetal tissues | Foetal tissues/blood cells are present |
| 6% eventually receive chemotherapy | 0.5% eventually receive chemotherapy |

## Diagnosis

- **Clinical presentation:**

| Common presentation | Uncommon presentation |
|---|---|
| • Positive pregnancy test<br>• History of hyperemesis in early pregnancy<br>• Uterine enlargement<br>• Irregular uterine bleeding | • Hyperthyroidism<br>• Early onset pre-eclampsia<br>• Acute respiratory symptoms<br>• Neurological symptoms |

- **Investigations:**

  - **Initial (pre-evacuation) diagnosis:**
    Initial diagnosis is made by ultrasound:
    - ***Complete mole:*** It is diagnosed by the presence of the characteristic "snowstorm" appearance in absence of gestational sac or foetal parts
    - ***Partial mole:*** diagnosis is more challenging. The following clues facilitate diagnosis:
      ① Presence of cystic spaces in the placenta
      ② Ratio of transverse: anteroposterior diameter of the gestational sac is greater than 1.5

    Diagnostic accuracy depends on gestational age (40% if less than 14 weeks of gestation, 60% if more than 14 weeks of gestation)

  - **Definitive diagnosis:**
    Final diagnosis is made by histopathology. Molar pregnancy may be misdiagnosed with an embryonic or delayed miscarriage

## Early detection

GTD may complicate different types of conception. Recommendations to prevent misdiagnosis and delayed diagnosis of GTD include:

- Products of conception from all miscarriages should be tested by histopathology to rule out GTD. Immunohistochemistry stain for P57 and ploidy stains should be used to differentiating between complete and partial mole
- Histopathology examination is not indicated in women who underwent therapeutic termination of pregnancy if ultrasound shows foetal parts
- Pregnancy test should be performed 3 weeks after medical treatment of failed pregnancy with no previous history of GTD to confirm normalization of hCG
- Pregnancy test is indicated if bleeding is persistent after any pregnancy even

The prognosis is worse after non molar pregnancy due to delayed diagnosis

## Management

- **Cervical preparation:**

  Prostaglandins may be used only for cervical ripening and for a short duration

- **Surgical evacuation:**
  - **Complete mole:**

    Treatment of complete mole is achieved by suction evacuation. Medical evacuation with mifepristone and misoprostol is avoided whenever possible because of the theoretical increased risk of embolization and dissemination. These agents increase uterine sensitivity to prostaglandin
  - **Partial mole:**
    - If foetal size is small, treatment is achieved by suction evacuation
    - If foetal size is significant, management with medical evacuation is recommended
  - **Control of bleeding:**
    - Oxytocin should not be used prior to complete evacuation
    - If bleeding is significant, evacuation may be expedited. Oxytocin may be considered if extremely necessary

- **Post-evacuation management:**
  - Anti-D prophylaxis is indicated
  - Patients should be monitored for symptoms after evacuation. If symptoms are persistent, patients should be assessed with ultrasound and hCG. If hCG is below 5000 mIU/ml, evacuation may be repeated

**Indications of registration to trophoblast screening center**

- Complete mole and partial mole
- A twin with complete or partial mole
- Limited molar changes
- Chemotherapy or PSTD
- Atypical placental site nodule

- **hCG Follow-up:**

  hCG is followed-up weekly:
  - If it is negative within 56 days, continue follow-up for 6 months after evacuation
  - If it is negative after 56 days, continue follow-up for 6 months after hCG becomes negative
  - If there is history of GTD, hCG should be followed-up for 6-8 weeks after any future pregnancy

- **Contraception:**
  - Barrier methods are appropriate until HCG is normalised. Combined contraceptive pills should be avoided (because of potential increased risk of neoplasia). Intrauterine devices should be avoided (risk of perforation)
  - Combined contraceptive pills and intrauterine devices can be used after normalisation
  - If combined contraceptive pills started before hCG normalisation, do not stop them (risk is low)

## Twin pregnancy with a complete mole

**Management**

- Prenatal karyotyping to rule out partial mole or suspected mesenchymal hyperplasia
- Referral to foetal medicine

**Outcomes**

- Incidence of live birth is 25%
- Risk of early pregnancy loss is 40%
- Risk of preterm labour is 36%
- Risk of pre-eclampsia is 4-20%
- Risk of GTN or chemotherapy is not increased compared to singleton molar

## Gestational trophoblastic neoplasia

- **Definition:**

Gestational trophoblastic neoplasia (GTN) refers to the subtypes of GTD that have invasion potential e.g. invasive mole, choriocarcinoma, placental site trophoblastic tumour, and epithelioid trophoblastic tumour

- **Modified WHO Prognostic Scoring System (adopted by FIGO):**

| Scores | 0 | 1 | 2 | 4 |
|---|---|---|---|---|
| **Age** | < 40 | ≥ 40 | — | — |
| **Antecedent pregnancy** | Mole | Abortion | Term | — |
| **Interval from antecedent pregnancy (in months)** | <4 | 4–6 | 7–12 | ≥ 13 |
| **Pretreatment serum β-hCG (mIU/mL)** | < 1000 | 1000-10000 | 10000-100000 | ≥ 100000 |
| **Largest tumor size** | — | 3–5 cm | ≥ 5 cm | — |
| **Site of metastases** | Lung | Spleen, kidney | Gastro-intestinal | Liver, brain |
| **Number of metastases** | — | 1–4 | 5–8 | > 8 |
| **Previous failed chemotherapy** | — | — | 1 | ≥ 2 |
| **Blood type** | | O or A | AB or B | |

- If the score is 0-6, patients are classified as low risk, and are eligible for a single agent chemotherapy treatment with 100% cure rate
- If the score is 0-6, patients are classified as high risk, and are eligible for a multiagent chemotherapy treatment with 95% cure rate

- **Management:**
  - Single agent treatment: Methotrexate and folic acid are given. Each cycle is 1 week followed by a 6-day off period
  - Multiagent treatment: it consists of methotrexate plus dactinomycin and vincristine, etoposide, cyclophosphamide. Treatment should continue for 6 weeks after normalisation of hCG. Pregnancy should be avoided for 1 year thereafter

| Long term complications of chemotherapy | |
|---|---|
| **Methotrexate** | It may induce earlier menopause (by 1 year when used as a single agent and 3 years when used as a part of a multiagent protocol) |
| **Etoposide** | There is increased risk of secondary cancers in women who receive combination treatment for longer than 6 months e.g.<br>• Colon cancer (4 times)<br>• Acute myeloid leukemia (16 times)<br>• Melanoma (3 times)<br>• Breast cancer (5 times) |

  - Surgery (hysterectomy): it is the first choice for women with placental site trophoblastic tumour because this histologic subtype is chemo-resistant

## Recurrence

- Recurrence rate of molar pregnancy is 1/80 (less than 2%)
- Same histologic type is found in approximately 75% of cases of recurrence of GTD

# Cervical Cancer Screening

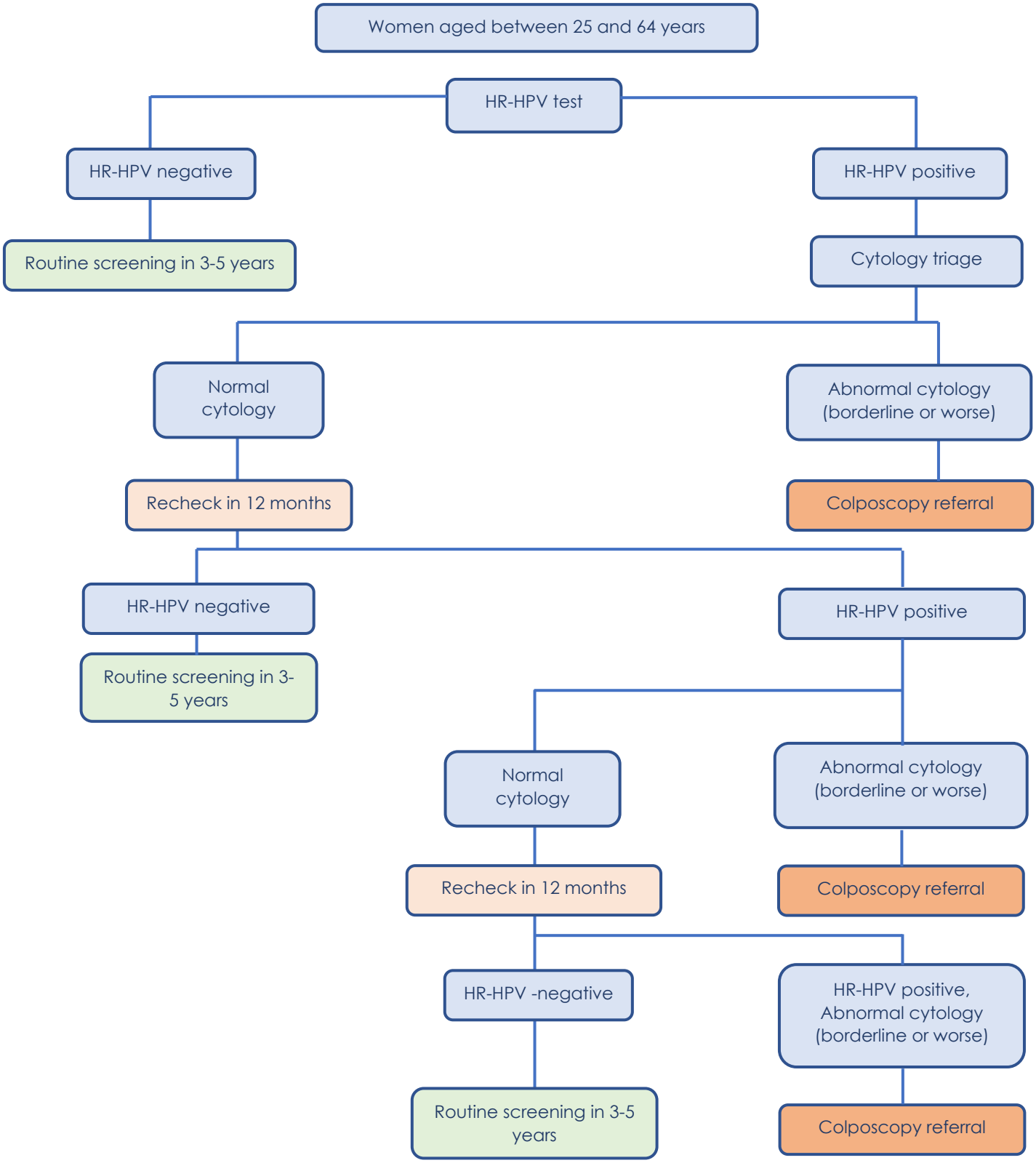
## Screening schedule

| Screening initiation | Screening frequency | Screening termination |
|---|---|---|
| All women should be screened starting at the age of 25 | • Age 25-49 years: screening every 3 years<br>• Age 50-64 years: screening every 5 years | Screening should stop after the age of 64 except if:<br>• No cervical screening is done after the age of 50<br>• A recent cervical cytology is abnormal. |

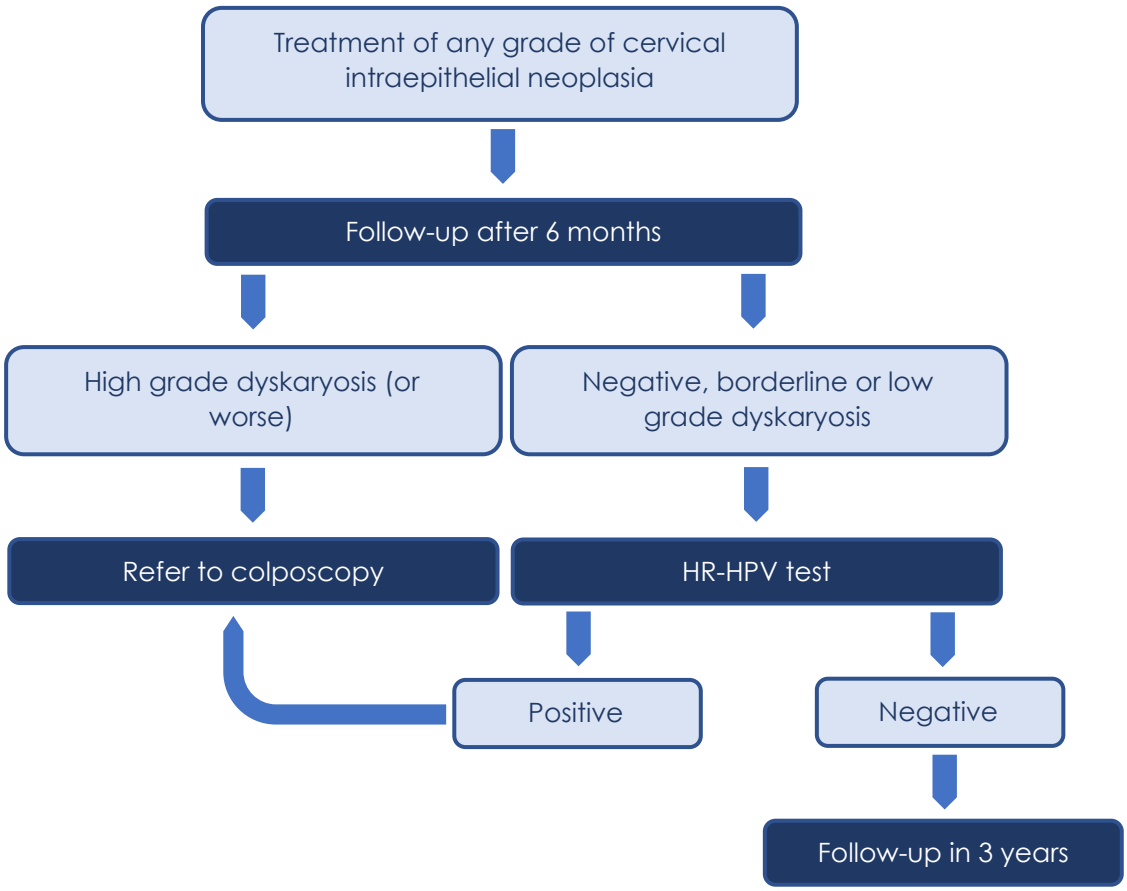
## Screening method

- HR-HPV testing has replaced traditional cervical cytology as an initial screening test for cervical neoplasia cytology as the primary test.
- Cervical cytology is performed on samples obtained from women if their HR-HPV testing is positive

## Management of screening results



## Follow-up after treatment



# Cervical Cancer

## Risk factors

- **Age:** the most common age is between 35 and 44 years.
- **Socioeconomic status:** it is more common among low socioeconomic levels
- **Inadequate cervical cancer screening:** including non-compliance to Pap testing
- **Early coitarche:** due to increased risk of acquiring HPV infection at young age
- **Multiple sexual partners:** due to increased risk of acquiring oncogenic human papillomavirus (HPV) infection
- **Tobacco smoking:** it increases the risk among HPV-positive women
- **Cervical high-risk HPV infection:**
  HPV 16 is most associated with squamous cell cervical cancer. HPV 18 is most associated with adenocarcinoma
- **High parity:** This may be due to the action of hormonal status, and impaired immunity during pregnancy
- **Combined oral contraceptives (COCs):** The risk is related to duration of use

## Diagnosis

- **Symptoms:**
  - **Asymptomatic:**
    Early stages of invasive carcinoma may be asymptomatic

  - **Early symptoms of cervical carcinoma:**
    - Vaginal bleeding: usually starts as postcoital bleeding. Then, bleeding may become spontaneous, irregular, and variable in amount.

- Vaginal discharge
- Dyspareunia
- Vaginal mass

- **Late symptoms of cervical carcinoma:**
  - **Pain:**
    - Deep pelvic pain (parametrial invasion)
    - Flank pain (ureteric obstruction)
    - Dysuria (bladder invasion)
    - Pain with defecation (uterosacral ligaments or rectal invasion)
    - Suprapubic colicky pain (pyometra and cervical obstruction)
    - Sciatic pain or obturator pain (nerve compression)
    - Low back pain (uterosacral ligament infiltration or spinal metastasis)
  - **Urinary/faecal incontinence**
  - **Leg swelling**

- **Physical examination:**
  - Cervical cancer appears as a nodule, cauliflower mass, or an ulcer. Cervix may appear normal or barrel-shaped with infiltrative cancer
  - Parametrium may be indurated due to malignant spread or infection
  - Uterosacral ligaments, and rectal involvement should be assessed with rectal examination

- **Investigations:**
  - Diagnosis is made by biopsy
  - Computerized tomography (CT) scan is essential once the diagnosis is made to assess disease extent, lymph node and organ metastasis
  - Cystoscopy and Sigmoidoscopy: may be performed to rule out bladder and rectal spread, respectively

## Management

- **Fertility sparing surgery:**

| | |
|---|---|
| **Stage IA1** | Conization (cone biopsy) can be considered:<br>• **If margins are negative:** no further treatment is indicated<br>• **If the margins are positive:** repeat conization versus radical trachelectomy should be performed |
| **Stage IA2** | Two options can be performed:<br>• Conization with pelvic lymph node dissection<br>• Radical trachelectomy with pelvic lymph node dissection |
| **Stage IB1** | Radical trachelectomy with pelvic lymph node dissection |

- **Radical surgery:**

Management is determined by disease stage:

| Stage | | Treatment |
|---|---|---|
| Stage I | Stage IA1<br>Tumour confined to the cervix (≤ 3 mm in depth and ≤ 7 mm in width) | • Simple hysterectomy (if there is no lymphovascular invasion)<br>• Radical hysterectomy with pelvic lymphadenectomy (if there is lymphovascular invasion) |
| | Stage IA2<br>Tumour confined to the cervix, stromal invasion 3-5 mm, and ≤ 7 mm in width | • External beam radiation therapy (EBRT) to the pelvis + brachytherapy OR<br>• Radical hysterectomy with pelvic lymph node dissection and sampling of para-aortic lymph nodes |
| | Stage IB1<br>clinical lesions ≤ 4 cm in size | • Same as stage IA2<br>• Chemotherapy may be given with radiation (concurrent chemoradiation). |

| | | |
|---|---|---|
| | Stage IB2<br>clinical lesions greater than 4 cm in size | • Chemoradiation (primary treatment):<br>▪ Chemotherapy: cisplatin or cisplatin plus fluorouracil.<br>▪ Radiation: both external beam radiation and brachytherapy.<br>• Radical hysterectomy with pelvic lymph node dissection and para-aortic lymph node sampling in addition to concurrent chemoradiation if lymph nodes are positive, or in the presence of positive margins |
| Stage II | Stage IIA<br>Involvement of the lower third of the vagina | Same as stage IB1 |
| | Stage IIB<br>parametrial involvement not reaching the pelvic side wall | Chemoradiation |
| Stage III<br>IIIA: no extension to the pelvic wall, but involvement of the lower third of vagina<br>IIIB: extension to the pelvic wall, or hydronephrosis or nonfunctioning kidney due to the tumor | | Chemoradiation |
| Stage IV | Stage IVA<br>spread of growth to adjacent pelvic organs | Chemoradiation |
| | Stage IVB<br>spread to distant organs | Palliative treatment |

# Hormonal Therapy After Gynecologic Cancer Treatment

## Hormone replacement therapy

Hormone replacement therapy (HRT) may be indicated in menopausal women with history of gynaecologic cancer treatment either those who undergo natural menopause or surgical menopause secondary to cancer surgery. The following summarizes safety of HRT in these women:

| Malignancy | Type | Stage | HRT recommendation |
|---|---|---|---|
| **Ovarian** | Epithelial | Any | Limited data |
| | Germ cell | | Avoid |
| | Sex cord stromal | | Avoid |
| | Borderline | | Avoid/use cautiously |
| **Endometrial** | Type 1 (Endometrioid) | I and II | Estrogen only if no concerns of possible occult foci (adequately staged); otherwise, continuous combined regimen is used |
| | | III and IV | Avoid |
| | Type 2 | | Avoid |
| **Cervical** | Squamous cell | I and II | Estrogen only if previous hysterectomy; otherwise, continuous combined regimen is used |
| | | III | Avoid/use cautiously |
| | | IV | Avoid/use cautiously |
| | Adenocarcinoma | Any | Avoid/use cautiously |

| | | | |
|---|---|---|---|
| **Vaginal** | Squamous cell | Any | Estrogen only if previous hysterectomy; otherwise, continuous combined regimen is used |
| | Non-squamous cell | | Avoid |
| **Vulval** | Squamous cell | Any | Oestrogen only if she had previous hysterectomy; otherwise, continuous combined regimen is used |
| | Non-squamous cell | | Avoid |

## Alternatives to hormonal therapy

Women who experience vasomotor symptoms and in whom HRT should be avoided can be offered other options, which are generally similar to options offered when HRT is contraidicated. These options include:

- Lifestyle modifications
- Non-hormonal medications including venlafaxine, fluoxetine, paroxetine, citalopram, clonidine or gabapentin.
- Complementary medicines such as isoflavones, black cohosh or St John's wort should NOT be recommended.
- Acupuncture is generally of poor quality.
- Cognitive behavioural therapy (CBT) can be used to treat low mood or anxiety as a consequence of the menopause.

# Gynaecologic oncology

## Abstract

Despite all ongoing clinical and research efforts, cancer remains the most challenging disease in all medical specialties. Although modern medicine has managed to control some types of cancers such as cervical cancer though effective screening strategies, other types, such as ovarian cancer,

remain frustrating since there is no efficient way to screen or diagnose them early. In this chapter, we will discuss screening, diagnosis, and management of common gynaecologic cancers.

## Keywords

Ovarian cancer, endometrial cancer, cervical cancer, cervical screening

## Further readings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# PART VI

## Urogynecology and gynecologic surgery

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# Female Genital Mutilation

## Definition

Female genital mutilation (FGM) refers to any procedure that involves excision or injury to the external female genitalia in absence of medical indications

## Classification

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| **Type 1** | Clitoridectomy | Partial or total removal of the clitoris ± the prepuce |
| **Type 2** | Excision | Partial or total removal of the clitoris and labia minora ± labia majora |
| **Type 3** | Infibulation | Narrowing of vaginal orifice by cutting and approximating the labia minora ± labia majora |
| **Type 4** | Others | All other procedures e.g. piercing, pricking, incising |

## Complications

- FGM can be associated with dyspareunia, apareunia and impaired sexual function
- FGM is associated with psychological complications e.g. anxiety, post-traumatic stress disorder




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_24

## Management

- **Care team:**
  - A consultant or midwife trained in FGM should be assigned to their care
  - A Specialist multidisciplinary FGM service should be available for care of these patients on self-referral

- **The legal and regulatory responsibilities of health professionals:**
  - FGM Act 2003 in England states that:
    ① FGM is illegal unless medically indicated
    ② Involvement in arrangement of FGM overseas for a UK national or UK resident is illegal
    ③ Diagnosis of FGM in a girl < 18 years should be reported to police
    ④ FGM suspicion in a girl < 18 years indicates referral to social services
  - Female genital cosmetic surgery is prohibited unless medically indicated
  - Re-infibulation is illegal under any circumstances.
  - Responsibilities of health care providers caring of patients with recent FGM:
    - Health care providers should recognize symptoms and signs of recent FGM e.g. pain, infection, haemorrhage, urinary retention
    - If FGM is suspected, examination should be thoroughly documented in conjugation with photography
    - All women and girls with acute or recent FGM require police and social services referral
    - If FGM is diagnosed or suspected in children, they should be referred to child safeguarding service
    - Patients should be informed that they will be documented to HSCIC FGM enhance database

- **Medical management of FGM:**
  - **Gynecological practice:**
    - **Clinical assessment:**
      - ***History:*** All women in communities that practice traditional FGM should be asked directly on history of FGM. Patients may be also referred from a GP or self-referred
      - ***Physical assessment:*** it should include:
        ① Assessment of degree of FGM by inspection of the vulva
        ② Assessment of the need for de-infibulation (e.g. significant narrowing)

③ Assess FGM-related morbidities e.g. epidermoid inclusion cysts.

- ***Psychological assessment:*** should be offered to all women who experienced FGM
- ***Laboratory tests:*** All women with FGM should be tested for hepatitis B, C, HIV along with sexual health screening

- **Management:**
  - ***De-infibulation:***

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| **Indications** | De-infibulation may be indicated in women with type 3 FGM. Significant narrowing may prevent cervical cancer screening, genital infection screening, or other gynaecological procedures |
| **Timing** | If indicated, it should be offered before first intercourse or before pregnancy |
| **Setting** | The procedure may be performed under local anaesthesia in outpatient setting if accepted by the patient |

  - ***Clitoral reconstruction:*** it should not be offered as it is associated with high risk of complications without clear benefit

- **Obstetric practice:**

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| *Antenatal care* | • All women should be directly asked about history of FGM in their first prenatal visit regardless of country of origin. A positive history indicates referral to a consultant or midwife who is responsible for FGM patients who should discuss and document plan of care<br>• Examination is required in the first visit to determine if de-infibulation is indicated. Indications of de-infibulation are:<br>① Invisible urethral meatus<br>② Insufficiently open vagina<br>• Hepatitis C testing should be added to first visit labs<br>• FGM in pregnant women does not need to be reported to police or social service |

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| | • Risk assessment is done using FGM safeguarding risk assessment tool. If there is risk to the unborn child or other children, risk should be reported<br>• Consultant care is generally recommended because of the risk of complications. However, if patients had previous uncomplicated vaginal deliveries, their care can be led by a midwife |
| *Intrapartum care* | • If de-infibulation is necessary, it may be performed antenatally, during 1st stage of labor or at the time of delivery using local anesthesia or perioperatively after caesarean section.<br>• Labial tears are treated in the conventional way |
| *Postpartum care* | • If de-infibulation was not performed for any reason, it should be offered in outpatient gynecological clinic or FGM clinic. If accepted by the patient, it should ideally be performed before next pregnancy |

# Pelvic Organ Prolapse

## Definition

Pelvic organ prolapse (POP) refers to descent of one or more of pelvic organs below its normal anatomical position due to deficiency of pelvic support

## Clinical assessment

- If POP is incidentally found during pelvic assessment by primary care provider, history should be reviewed with the patient, symptoms should be surveys, and examination should be performed to document prolapse and any other associated abnormalities
- If POP is incidentally detected by a secondary care provider, patient should be referred to a specialist with expertise in prolapse
- Specialist evaluation should include:
    - Symptom assessment using validated pelvic floor symptom questionnaire
    - POP-Q classification assessment
    - Assessment of pelvic floor muscles.
    - Assessment of vaginal atrophy
    - Ruling out pelvic masses or other pelvic pathology

  If symptoms are not explained by physical findings, repeat examination at standing or squatting position or at a different time. Imaging is not routinely offered

## Investigations

Investigations are not routinely required, and they may be considered only in the presence of one of these symptoms:

- Bothersome urinary symptoms that may warrant surgery
- Obstructed defecation or faecal incontinence

- Pelvic pain
- Other symptoms not explained by physical findings

## Management

- **Non-surgical management of POP:**

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| **Life-style modification** | • The patient is advised to avoid heavy lifting<br>• Prevention/treatment of constipation<br>• Weight loss if body mass index is above 30 |
| **Topical oestrogen** | • It is considered in women with POP associated with vaginal atrophy<br>• In women with cognitive or physical impairment, oestrogen-releasing ring may be considered |
| **Pelvic floor muscle training** | • Supervised pelvic floor muscle training is the first line of management for stage 1 or 2 prolapse. It should be considered for at least 16 weeks<br>• If it is beneficial, women are advised to continue this management |
| **Pessaries** | • Vaginal pessary is considered for symptomatic POP as a sole management or in conjugation with pelvic floor muscle training<br>• Before placing a pessary, provider should:<br>▪ Consider treatment of vaginal atrophy with topical oestrogen<br>▪ Explain to the patient that more than 1 pessary may be tried to find the most suitable pessary<br>▪ Discuss effect of pessary on sexual intercourse<br>▪ Discuss complications e.g. vaginal discharge, bleeding, difficulty removing pessary, pessary expulsion<br>• Pessary should be removed at least once every 6 months to prevent complications e.g. vaginal erosions<br>• If the patient cannot remove it herself despite education, offer regular appointments in the pessary clinic every 6 months |

- **Surgical management of POP:**
  - **Indications:**

    Surgical treatment is offered, if non-surgical management is declined or fails.

- **Patient counselling:**
  - Women who will have surgery for anterior or apical prolapse, should be counselled on risk of postoperative incontinence which may need further treatment
  - If mesh will be used, you should explain the type of mesh and whether it is permanent and ensure that procedure, as well as short- and long-term outcomes are recorded in national registry

- **Surgical options:**

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| **Uterine prolapse** | ***If the patient is not interested in preserving her uterus:*** offer vaginal hysterectomy with or without vaginal sacrospinous fixation or vaginal sacrospinous hysteropexy with sutures or Manchester repair or Sacrohysteropexy with mesh | ***If the patient is interested in preserving her uterus:*** offer vaginal sacrospinous hysteropexy or Manchester repair, if she is not desiring pregnancy Consider Sacrohysteropexy with mesh |
| **Vault prolapse** | • Offer the patient vaginal sacrospinous fixation or Sacro colpopexy.<br>• If synthetic mesh is to be used, procedures and outcomes should be collected in a national registry. | |
| **Vault or uterine prolapse in high risk patients** | Colpocleisis may be considered in women with vault or uterine prolapse who are not interested in sexual function and at higher surgical risk | |
| **Anterior prolapse** | Anterior repair without mesh | |
| **Posterior prolapse** | Posterior repair without mesh. | |

Do not offer surgery to prevent incontinence in women undergoing prolapse surgery and who do not have incontinence

- **Continence surgery at the time of pelvic organ prolapse repair:**
  - Pelvic floor muscle training (PFMT) is the first-line management for both SUI and mild-to-moderate POP
  - Continence surgeries include:
  - Colposuspension (Burch) at the time of abdominal sacrocolpopexy
  - Synthetic midurethral slings (SMUS) either retropubic tension-free vaginal tape (RP-TVT) or transobturator tension-free vaginal tape (TO-TVT) at the time of vaginal prolapse repair

- Stress urinary incontinence (SUI) affects approximately 1 in 3 women, while POP affects approximately 1in 9 women. SUI being the most prevalent type of UI (approximately 50% of all women with UI
- POP and SUI may coexist in up to 80% of women with prolapse.

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| **Group A: women with POP and asymptomatic for SUI (including occult urinary incontinence OSI)** | ▪ Occult stress incontinence (OSI) is the demonstration of SUI following the reduction of POP in women who are asymptomatic for SUI. Significant prolapse can lead to urethral kinking and preservation of continence or masking of UI.<br>▪ Combined prolapse and continence surgery more likely to treat OSI than prolapse surgery alone.<br>▪ The rate of symptomatic postoperative SUI after combined surgery in women asymptomatic for SUI (including OSI) is almost 30%, raising the debate of whether patients would benefit from interval surgery (treating with POP repair alone and dealing with postoperative SUI if and/or when required.<br>▪ In view of the lower success rate for secondary continence procedures, interval surgery may also be preferable. |
| **Group B: women with POP and coexisting symptomatic SUI** | ▪ women who are symptomatic of SUI and POP, concomitant vaginal POP repair and synthetic midureth eral slings (SMUS) is beneficial for reducing postoperative SUI.<br>▪ However, it must be borne in mind that in women undergoing vaginal POP surgery alone, almost one-third may experience cure of SUI symptoms. |

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| **Group C: women with SUI and asymptomatic POP** | ▪ the limited evidence available indicates that in women with SUI and asymptomatic POP, concomitant repair at the time of SMUS is unlikely to confer a benefit to the continence outcomes and the POP itself is unlikely to progress within 3 years. |

- Whether asymptomatic or symptomatic of SUI, more women are continent following concomitant POP and SUI procedures compared with POP repair only.
- Despite concomitant continence surgery, SUI can still persist in approximately one-third of women especially with the lower success rate of all secondary continence procedures compared with primary procedures.
- In almost one-third of women, prolapse repair alone can improve SUI symptoms.
- Although SUI may persist or develop after POP repair alone, not all women opt for further surgery.

- **Follow-up after surgery:**
  - The patient should be followed up 6 months after surgery
  - During this visit, vaginal examination should be performed to rule out mesh exposure, if a mesh was used

## Mesh-related complications

- **Assessment of complications associated with mesh-related surgery:**
  - **Symptoms related to mesh exposure:**
    - Pain or sensory changes in the back, abdomen, vagina, pelvis, leg, groin or perineum:
      - Unprovoked or provoked e.g. movement or sexual activity
      - Generalized or follows a specific distribution e.g. obturator nerve
    - Vaginal discharge or bleeding
    - Painful intercourse, penile trauma or pain
    - Urinary symptoms e.g. recurrent infection, incontinence, retention, or dysuria
    - Bowel symptoms e.g. difficulty or pain on defecation, incontinence, rectal bleeding
    - Symptoms of infection.

- **Further management:**
  - On suspicion, patients should be referred to a urogynecologist, urologist or colorectal surgeon for specialist assessment
  - Specialist evaluation covers the following points:
    - Full history of past mesh-related surgical procedures
    - Validated pelvic floor symptom questionnaire and pain questionnaire
    - Vaginal examination to determine if the mesh is palpable or exposed, and to localize pain in relationship to the mesh
    - Rectal examination, if necessary, to assess mesh perforation or fistula
    - Neurological assessment is considered to assess pain distribution, sensory affection, and muscle weakness
    - Imaging may be offered if there are signs of infection
  - If symptoms are confirmed to be related to the mesh or if they are otherwise unexplained, patients should be referred to a specialized consultant (unless mesh erosion is asymptomatic and is less than 1 $cm^2$ in size)
  - These complications should be reported in a national registry and to medicines and healthcare products regulatory agency (MHRA)

- **Management of mesh-related complications:**
  - **Mesh removal:**
    - If mesh removal was asked by the patient, decision should involve the patient and a regional multidisciplinary team
    - Counsel the patient that:
      - Benefits of partial or complete removal versus no mesh removal are not clear
      - Mesh removal may be associated with organ injury, worsening pain, urinary, bowel or sexual dysfunction.
      - Mesh removal may not improve symptoms
      - Complete removal of the mesh may not be technically possible
      - Removing a part of mesh may be comparable to complete removal
      - Prolapse or incontinence may recur after removal

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| **Slings for urinary incontinence** | • Complete removal (vs. partial removal) is associated with increased risk of recurrence of incontinence<br>• Partial removal is associated with further mesh extrusion<br>• Complete removal may not be surgically possible |
| **Mesh for vaginal prolapse** | • Complete removal (vs. partial removal) is associated with higher risk of urinary or bowel injury<br>• Removal may be associated with risk of recurrent prolapse<br>• Complete removal may not be surgically possible |
| **Abdominal mesh** | • Removal of mesh is associated with high risk of urinary or bowel injury.<br>• Removal may result in recurrence of the prolapse<br>• Complete removal may not be surgically possible<br>• Removal may require abdominal surgery |

- **Management of vaginal symptoms:**
  - If the patient has pain or painful intercourse, further management is determined by the specialist assessment:
    - If symptoms are related to the mesh, refer to multidisciplinary team for treatment decision
    - If symptoms are not related to the mesh, manage symptoms with oestrogen, dilators and psychosexual counselling
  - Topical oestrogen may be used if there is a single area of erosion less than 1 $cm^2$. Treatment should be reviewed within 3 months.
  - Surgical removal of vaginal portion of the mesh is indicated if:
    ① Denying local oestrogen
    ② Oestrogen fails after 3 months
    ③ There is mesh extrusion
    ④ Vaginal erosion is 1 $cm^2$ or more

- **Managing urinary complications:**
  - If the mesh perforates through the urinary tract, refer to a specialised centre

- If mesh causes voiding difficulty, consider division of the mesh. If excision of the sling is considered for persistent voiding dysfunction, refer to a specialised centre
- Risk of recurrence of incontinence is greater with excision compared to division

- **Managing bowel symptoms:**
  - If symptoms are directly related to mesh complications (e.g. erosion stricture, fistula), Discuss with a regional multidisciplinary team.
  - Patients should be aware that bowel symptoms may persist or recur after surgical removal of the mesh. They may need a temporary or permanent stoma after surgery

# Post-Hysterectomy Vaginal Vault Prolapse

## Incidence

- Post-hysterectomy vaginal vault prolapse (PHVVP) occurs in 11% of patient who had hysterectomy for prolapse
- PHVVP occurs in 2% of patient who had hysterectomy for benign indications

## Diagnosis

- Assessment and management decision should be made by specialists who are a part of pelvic floor multidisciplinary team
- Assessment should include:
  - ① Assessment of symptoms and their impact on quality of life
  - ② Physical examination and documentation of pelvic organ prolapse using standardized classification (POP-Q system)
- Routine urodynamic study is not predictive of postoperative incontinence and is not recommended

## Prevention

| Effective techniques | Unnecessary techniques |
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| • During vaginal hysterectomy:<br>  ▪ McCall Culdoplasty is superior to Moskowitz technique. Within 2 years, 90% of women develop no prolapse and 10% develop stage 1 only. Satisfaction rate is 80%<br>  ▪ Sacrospinous ligament fixation should be considered if vaginal vault descends to introitus during vault closure<br>• During vaginal or abdominal hysterectomy: suturing cardinal ligaments and uterosacral ligaments to vaginal cuff is beneficial | • Subtotal hysterectomy does not prevent PHVVP and is generally not recommended. Subtotal hysterectomy increases risk of urinary incontinence and future prolapse<br>• Use of non-absorbable sutures (permanent) sutures does not provide benefit and it is associated with high suture exposure rate |

## Management

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| **Conservative management** | • **Pelvic floor muscle training:**<br>It is effective in stage I-II vaginal prolapse<br>• **Vaginal pessary:**<br>It may be used as an alternative to surgery in treating stage II to IV vaginal prolapse |
| **Surgical management** | • It is the standard management for symptomatic patients after appropriate counselling<br>• **Surgical options:** |

- Both abdominal sacrocolpopexy (ASC) and vaginal sacrospinous fixation (SSF) are effective in primary treatment
- Colpocleisis is suitable for flail patients who are not interested in retaining sexual function

- **Approach:** Laparoscopic is comparable to abdominal route in selected cases. Evidence on robotic surgery is limited
- **Complications:**
  ① Risk of ureteric injury specially with laparoscopic approach
  ② Mesh-related complications (5-20%)
  ③ Recurrence rate is 15%
  All surgical procedures should be audited and submitted to British society of urogynecology
  Mesh complications should be reported to medicine and health care products regulatory agency
- **Success rate:**
  - Success rate of mesh-related procedures is 90-95%
  - Success rate of colpocleisis is 97%
- **Concomitant procedures:**
  - Concomitant Burch colposuspension with anterior Sacrocolpopexy:
    - In women who were continent before surgery, it decreases post-operative stress incontinence (25% vs 45% if not done)
    - In women with stress incontinence prior to surgery, the procedure is not effective; 55% will still be incontinent after surgery
  - Concomitant mid-urethral sling:
    It is indicated in women with stress incontinence when vaginal surgery is performed to correct PHVVP. Risk of incontinence after surgery is 20%

| | Open abdominal sacrocolpopexy | Vaginal sacrospinous fixation |
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| **Advantages** | • Lower risk of recurrence, dyspareunia and post-operative stress incontinence (compared to sacrospinous fixation)<br>• Despite these advantages, patient satisfaction and reoperation is comparable to sacrospinous fixation<br>• Long-term success rate is 80-100%. | • The procedure is performed vaginally, it is performed by suturing right sacrospinous ligament (1.5-2 cm medial to ischial spines) to vaginal vault<br>• Earlier recovery compared to sacrocolpopexy |
| **Disadvantages** | • Mesh erosion rate is 2-10%.<br>• Incidence of serious complications (bowel injury, sacral myelitis, severe bleeding) is 2% | • The procedure should be avoided in women with a short vagina. Therefore, patients with preexisting dyspareunia should be carefully considered<br>• Risk of post-operative anterior prolapse and stress incontinence is 10-30%<br>• Incidence of buttock pain is 20%. Pain is temporary (resolves within 2-3 months)<br>• Incidence of sciatic nerve irritation is 7.5% (temporary)<br>• Rate of partial ureteric obstruction is 5% (temporary)<br>• Failure rate is 15% |

High uterosacral ligament suspension is associated with 10% risk of complications e.g. bladder injury, and bowel injury. It should not be offered in clinical setting

# Urinary Incontinence

## Background

Urinary incontinence (UI) is defined as involuntary leakage of urine.

## Types

Types of UI include:

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| **Stress incontinence (SUI)** | Urine leakage associated with increased intrabdominal pressure e.g. coughing, sneezing, laughing, exercising |
| **Urge incontinence (UUI)** | Urine leakage preceded by a sudden, intense urge to urinate |
| **Overflow incontinence** | Frequent or constant dribbling of urine due to incomplete emptying of the urinary bladder |
| **Functional incontinence** | Urine leakage due to physical or mental impairment that does not allow the patient to make it to the toilet in time |
| **Mixed incontinence** | The presence of more than one type of urinary incontinence |

## Clinical assessment

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| **History** | • Assessment of type of UI:<br>  ▪ Type of incontinence determines types of treatment<br>  ▪ In the presence of mixed UI, treatment should be primarily directed to the predominant type.<br>• Assessment of predisposing and precipitating factors<br>• Assessment of impact of incontinence on quality of life: treatment is offered to women who report adverse impact on her life activities. Validated urinary incontinence specific symptom and quality of life questionnaire should be used. |
| **Examination** | • Objective assessment of stress UI is performed by asking the patient to cough. The bladder should not be completely empty during the exam. Any prolapsed organs should be reduced before the patient is asked to cough<br>• Pelvic floor muscles are assessed by digital examination to evaluate pelvic floor muscle strength. Weak pelvic floor muscles may warrant the use of supervised pelvic floor training for treatment of urinary incontinence.<br>• Pad testing is not recommended |

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| **Indications of referral to a specialist** | • Persistent bladder or urethral pain<br>• Palpable bladder after voiding<br>• Suspected fistulae<br>• Benign pelvic masses<br>• Fecal incontinence<br>• Suspected neurological disease<br>• Voiding difficulty<br>• Hematuria<br>• Persistent or recurrent unexplained UTI<br>• Previous continence surgery<br>• History of pelvic cancer surgery<br>• History of pelvic radiation |

## Investigations

### ❶ Urine testing

- **Urine dipstick:** for all women with UI to detect blood, glucose, protein, leukocytes and nitrites
- **Urine culture:**
  - If symptoms of urinary tract infection (UTI) AND urine test are positive for both leukocytes and nitrites, a mid-stream urine specimen should be sent for culture and antibiotic sensitivities. Antibiotics should be initiated pending cultures results.
  - If women have symptoms of UTI BUT urine test is negative for either leucocytes or nitrites, a midstream urine specimen is sent for culture and antibiotic sensitivities and consider antibiotics pending culture results
  - If no symptoms BUT urine test is positive for both leukocytes and nitrites, do not give antibiotics unless urine culture results are positive

### ❷ Assessing residual urine

- In women with recurrent UTI or voiding dysfunction, post-void residual volume is measured by bladder scan or catheterization
- Bladder scan is preferred over catheterization for this test

### ❸ Urodynamic testing

- SUI is a clinical diagnosis. If SUI or stress predominant mixed incontinence are diagnosed clinically, multi-channel filling and voiding cystometry are not routinely indicated
- Preoperative multichannel filling and voiding cystometry are indicated if any of the following is present:
  ① Unclear type or urge predominant mixed incontinence.
  ② Symptoms suggestive of voiding dysfunction
  ③ Anterior or apical pelvic organ prolapse
  ④ History of previous surgery for stress urinary incontinence

### ❹ Bladder diaries

Patients should use bladder diaries for at least 3 days to facilitate diagnosis

### ❺ Cystoscopy

Cystoscopy is not used routinely for assessment of UI. It may be indicated in the presence of hematuria or in the presence of acute and severe urgency

## Management

- **Non-surgical management:**

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| **Lifestyle modification** | • Women with overactive bladder (UUI) are advised to reduce caffeine use and fluid intake<br>• Weight loss is recommended for women with body mass index > 30 |
| **Behavioral therapy** | • Women with urgency or mixed incontinence should be offered bladder training for at least 6 weeks (first line treatment)<br>• Medications may be considered in women who do not respond to this management |
| **Pelvic floor muscle training** | • In women with stress or mixed incontinence, supervised pelvic muscle training for 3 months may be offered as a first line management. Treatment may continue if it improves symptoms<br>• Pelvic floor exercise should include at least 8 contractions for 3 times per day |
| **Neurostimulation** | • Percutaneous posterior tibial nerve stimulation is only indicated if:<br>① Non-surgical treatment failed<br>② There is a local multidisciplinary team review<br>③ women decline Botox injection or percutaneous sacral nerve stimulation<br>• do not offer transcutaneous sacral nerve stimulation (TENS) to women with overactive bladder. |
| **Electrical stimulation** | Electrical stimulation and/or biofeedback should be offered only to women with UI who cannot actively contract their pelvic floor muscles and do pelvic floor exercise |
| **Absorbent containment products, urinals, toileting aids** | • It may be used in the following circumstances:<br>① As a temporary option while awaiting definite management<br>② As an adjunct to other options<br>③ As a last option if other options fail or are not possible<br>• If it is used as long term option, yearly assessment of symptoms, skin |

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| | integrity, weight and lifestyle are indicated. Current suitability to other options should be reviewed |
| **Urinary catheters** | Intermittent or indwelling or suprapubic catheters may be offered in women with persistent urinary retention<br>• Intermittent catheter:<br>It is suitable for women who can do self-catheterization or have caregivers that can help her<br>• Long-term indwelling catheter is indicated in:<br>① Chronic urinary infection that cannot be managed by self-catheterization.<br>② Skin wounds, ulcers or irritations<br>③ Distress by pad and clothing frequent changing<br>④ Patient preference<br>Indwelling catheters may not result in continence with UUI (leakage from round the catheter)<br>• Indwelling suprapubic catheter is an alternative to long term urethral catheter as it reduces risk of symptomatic urinary tract infection |

- **Medical treatment (for overactive bladder):**

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| **Patient counselling** | • Before prescribing medications, counsel the patient on:<br>▪ Chance of success of medical treatment and latency before medications are fully effective<br>▪ Anticipated side effects, most commonly dry mouth and constipation (indicators of medication effect)<br>• Evidence on long-term cognitive adverse effect of anti-cholinergic medications is not uncertain |
| **Choosing medicine** | • **Anticholinergic medications:**<br>▪ They are the 1st line of treatment of overactive bladder and mixed urinary incontinence. However, Anticholinergics may not be appropriate for women with:<br>① Dementia and cognitive impairment<br>② Poor bladder emptying<br>③ Current use of drugs that increase cholinergic load<br>▪ Immediate release oxybutynin should be avoided in older women (risk of rapid deterioration of physical or mental status)<br>▪ If first medication is not effective, an alternative medicine of low cost may be offered<br>▪ Transdermal medications are offered if oral medications are not tolerable<br>• **Desmopressin:**<br>▪ It may be offered to patients with troublesome nocturia.<br>▪ It should be used with caution in patients with cystic fibrosis<br>▪ It should be avoided in patients older than 65 years who have cardiovascular disease or hypertension<br>• **Duloxetine:**<br>▪ It should not be offered either as a first or a second line treatment in women with SUI or predominant SUI unless surgery is declined by the patient and she is counselled clearly about medication adverse effects |

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| | • **Hormonal therapy:**<br>▪ Local estrogen may be used in postmenopausal women who complain of UUI in the presence of vaginal atrophy<br>▪ There is no role to systemic hormonal therapy in women with SUI<br>Imipramine, flavoxate, propantheline should not be offered |
| **Follow-up** | • Symptoms should be reviewed after 4 weeks of initiation of treatment<br>▪ *if improvement is optimal:* continue treatment and follow-up with primary care follow-up every 12 months or every 6 months if aged > 75 years<br>▪ *If no or suboptimal improvement or intolerable adverse effects:* change the dose or prescribe an alternative treatment and review again after 4 weeks.<br>• Review earlier, if side effects are intolerable or the treatment stops working.<br>• If medical treatment failed or side effects developed, patient should be referred to secondary care |

- **Invasive treatment for overactive bladder:**

Women who did not respond to non-surgical management and medications should be assessed with urodynamic study:

- If the urodynamic study shows detrusor overactivity, offer invasive options
- If it is negative for detrusor overactivity, further management should be decided by a local multidisciplinary team (MDT)

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| **Botulinum toxin type A injection** | • **Indications:**<br>① Overactive bladder in women with detrusor overactivity after local MDT review<br>② Overactive bladder in absence of evidence of detrusor overactivity in urodynamic study after failure of non-surgical and medical treatment after local MDT review<br>• **Counselling:**<br>▪ Treatment may be associated with complete or partial response. There is no evidence on duration of response and long-term effects<br>▪ Treatment may result in temporary urinary retention and need for intermittent catheterization (patients should not be offered this option if they decline possible intermittent or indwelling catheterization)<br>▪ Increased risk of urinary tract infection<br>• **Treatment protocol:**<br>▪ Initial dose of injection is 100 units. Response is reviewed in 3 months<br>□ If there is good response, patient may self-refer herself if symptoms recur<br>□ If there is good response but is less than 6 months, future doses may be increased to 200 unit and review after 3 months<br>□ If suboptimal response: injection is repeated with as dose of 200 units and symptoms are review after 3 months |

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| | ▪ After the second session, if no response, review with local MDT team |
| **Percutaneous sacral nerve stimulation** | • **Indications:**<br>▪ Failure of botulinum toxin in women with refractory overactive bladder<br>▪ Women who decline botulinum toxin (decline risk of catheterization)<br>• **Counselling:**<br>▪ The procedure is 2-staged, a test stage should be performed before the procedure is completed. Patient should be aware of risk of failure<br>▪ The procedure is associated with long-term commitment and need for surgical revision |
| **Augmentation cystoplasty** | • **Indication:**<br>Women with refractory idiopathic detrusor overactivity after failure of all other measurements if she accepts to self-catheterize<br>• **Counselling:**<br>Counsel on isks of the procedure e.g.<br>▪ Bowel disturbance and mucus production<br>▪ Metabolic acidosis<br>▪ Retention of urine and urinary infection<br>▪ Small risk of malignancy |
| **Urinary diversion** | It is the last resort in women with overactive bladder after all other measurements fail including augmentation cystoplasty |

- **Surgical management of stress incontinence:**

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| **Counselling** | Beside counselling on surgery, surgical risks and postoperative care, mesh use should be discussed including uncertainty of long-term outcomes. Mesh is permanent and if complete removal is requested, it may not be possible. These surgeries are reported to national registry |
| **Surgical options** | • Open or laparoscopic colposuspension<br>• Autologous rectus fascial sling<br>• Mid-urethral mesh sling:<br>  ▪ Coloured mesh with type 1 microporous polypropylene mesh is used<br>  ▪ Retropubic approach is the standard. Trans-obturator approach should not be performed unless there is contraindication to the standard approach e.g. previous pelvic surgery<br>  ▪ Other techniques (e.g. top-down technique, single incision sling) should not be offered except for research purposes |
| **Alternatives to standard surgery** | • **Injection of intramural bulking agents:**<br>  ▪ It may be offered to patients who decline surgery<br>  ▪ The procedure is less effective than surgery<br>  ▪ Effect of injection declines over time and repeat injections may be needed<br>  ▪ Evidence on long term effect and adverse effects is limited. Injection material is permanent<br>• **Artificial urinary sphincters:**<br>It is only offered when other surgical options for treatment of SUI fail |
| **Follow-up** | • Follow-up should be scheduled within 6 months postoperatively<br>• Vaginal examination is indicated if a mesh was placed to rule out exposure or extrusion of mesh sling<br>• If surgery fails, a MDT recommendation is required |

**Procedures that should not be offered:** anterior colporrhaphy, needle suspension, paravaginal defect repair, procaine dermis sling, Marshall-Marchetti-Krantz procedure.

# Recurrent Urinary Tract Infection

## Definition

- Recurrent urinary tract infection (UTI) refers to at least 3 UTIs in a year, or 2 UTIs in 6 months
- The diagnosis of UTI is made by clinical symptoms (dysuria, suprapubic tenderness, urinary urgency and frequency) and presence of bacteria in urine culture (>105 cfu/ml).
- The most common bacterium associated with UTI is Escherichia coli (E. coli).

## Risk factors

The main risk factors for UTI are:

- Female gender
- Use of spermicides
- Sexual intercourse
- Renal tract anomalies

## Management

- Single isolated UTIs are treated with trimethoprim or nitrofurantoin (first line) or gentamicin (second line)
- The use of urinalysis alone is often inaccurate in diagnosing UTI. Treatment should be initiated on the correlation of symptoms and urine culture

### Indications of hospitalization

- If the infection is severe or complicated
- If the infection appears to be ascending into the upper urinary tract

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| **Low-dose antibiotic prophylaxis** | • There are significant concerns with the development of antibiotic resistance<br>• Nitrofurantoin use can cause liver toxicity and in extreme cases liver failure. Also, it can cause acute and chronic pulmonary toxicity which can result in pulmonary fibrosis especially with long term use.<br>• Nearly one-third of E. coli-related UTIs are resistant to the usual first-line antibiotic prescribed. |
| **Chinese herbal medicine** | • There is no robust data to support its use |
| **Methenamine** | • Methenamine is converted to ammonia and formaldehyde (has antimicrobial) in urine<br>• There is no robust data to support its use |
| **Cranberries** | • NICE and RCOG guidelines recommend against the use of cranberry for management of rUTI |
| **D-mannose** | • NICE has recommended that nonpregnant women may wish to try D-mannose as a self-care treatment. |
| **Lactobacilli** | • There is no robust data to support its use. |
| **Urethral dilatation** | • Lack of robust data to support its use. |
| **Oestrogens** | • In postmenopausal women, vaginal oestrogens are effective in preventing recurrent UTI but systemic estrogens are not. |
| **Glycosaminoglycans (GAG)** | • Synthetic hyaluronic acid and chondroitin sulphate has shown promise results. However, results are still not definitive |
| **Sublingual vaccination** | • The sublingual therapeutic vaccination contains a mixture of equal amounts of selected strains of E. coli, Klebsiella pneumoniae, Proteus vulgaris and Enterococcus faecalis.<br>• Data on the efficacy of this sublingual vaccination are currently sparse |

# Bladder Pain Syndrome

## Definition

Bladder pain syndrome (also known as interstitial cystitis) is a chronic bladder pain condition. The underlying aetiology is poorly understood

## Incidence

- It is more common in women and it usually presents for the first time in the 30s or 40s of age. However, it may present at any age
- Prevalence is 2.3–6.5%

## Diagnosis

- Patients present with at least 6 weeks to 6 months of:
  - Pelvic Pain, Pressure or Discomfort
  - At Least one other urinary symptom e.g. frequency or urgency
- Diagnosis is made clinically by exclusion (ruling out other causes)

### Clinical assessment

- Bladder Dairy and Food Diary
- Urinalysis to rule out Infection. If the patient is symptomatic, with negative culture and Pyuria, test for Ureaplasma and Chlamydia
- Cytology and cystoscopy: if cancer Suspected. Refer to a urologist
- Urodynamic study is indicated if there is coexisting disease or overactive bladder not responding to treatment
- Visual analogue scale is used to assess pain. A validated symptom score should be used to assess the severity

- Biopsy and hydrodistension are not recommended for diagnosis
- Cystoscopy is not used for diagnosis. It may be performed to rule out other causes

- **Hunner lesion**
  - The term describes diffuse inflamed/non-blanched glomerulations, in at least three quadrants of the bladder (10 per quadrant) during cystoscopy when bladder is distended to 80-100 cm $H_2O$
  - This feature is long considered diagnostic. It may be present in normal women

## Management

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| **Conservative management** | • Dietary modification (avoid caffeine, alcohol, acidic food and drinks)<br>• Stress management<br>• Regular exercise<br>• Analgesia<br>If there is not response in 3 to 6 months, refer to secondary care |
| **Pharmacological treatment** | • Oral amitriptyline or<br>• Oral cimetidine<br>Hydroxyzine, oral pentosan, long term antibiotics are not recommended<br>If treatment fails, refer to a multidisciplinary team (MDT), pain team ± a psychologist |
| **Intravesical treatment** | If the above measures fail, the following is used:<br>• Lidocaine (30%)<br>• Hyalouronic acid<br>• Botulinum toxin (Botox)<br>• Dimethyl sulfoxide (DMSO)<br>• Heparin<br>• Chondroitin sulfate |

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| | BCG, steroids, and high-pressure long term hydrodistension are not recommended |
| **Interventional management** | • Posterior tibial or sacral neuromodulation<br>If failed, add:<br>• Oral cyclosporin<br>If failed:<br>• Cystoscopy and hydrodistension |
| **Surgery** | If surgery is considered, refer to a tertiary centre:<br>• Transurethral resection of Hunner lesions<br>• Major surgery |

**Pregnant women**

- All treatment options are safe especially oral amitriptyline and IV heparin
- DMSO may be used prior to pregnancy to ensure remission in pregnancy. The medication is teratogenic only in in animals

- Refer to physiotherapist and psychological counselling during the process of treatment to support life quality
- Follow up is recommended by a secondary team (urogynecologist and pain team). Primary team may be involved if symptoms are controlled

# Urethral Diverticulum

## Background

### Definition

- The presence of a sac or a pouch that is connected to the urethra
- This pouch ranges in size from 3 mm to 4 cm

### Incidence

- Incidence is 1-6%
- Incidence is 3 times higher in black women compared to white women
- Age at presentation ranges from 30 to 60 years

### Aetiology

- Congenital e.g. remnants of Gartner duct
- Acquired e.g. repeated infections and obstruction of periurethral glands which eventually rupture and epithelize. Other causes may include traumatic childbirth and transurethral collagen injection.

### Pathology

- The diverticulum may have a single ostium or complex with multiple ostia. It may partially or completely extend around the urethra, thereby, interfere with sphincter function.
- Urethral diverticulum is lined by urothelium. Squamous and glandular metaplasia may occur

## Clinical presentation

Time from presentation to diagnosis is 10 months

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| **Symptoms** | • Lower urinary tract symptoms e.g. urgency, frequency (most common; 40-100% of patients)<br>• Urinary incontinence (35%)<br>• Tender vaginal mass (35%)<br>• Recurrent urinary tract infection (30-50%)<br>• Postmicturition dribble (10-30%)<br>• Dyspareunia (10-25%)<br>• hematuria (10-25%)<br>• vaginal discharge (12%)<br>• retention of urine (4%)<br>The classic triad of dysuria, dyspareunia, postvoiding drippling is not common |
| **Signs** | • Anterior vaginal tender mass 2-3 cm inside the introitus<br>• Purulent discharge is expressed on palpation of the mass (25% of patients)<br>• Presence of induration or hardness, or presence of blood should raise concerns on malignancy or calculi |
| **Differential diagnosis** | • ***Differential diagnosis of lower urinary tract symptoms:***<br>▪ Interstitial cystitis.<br>▪ Carcinoma in situ.<br>▪ Overactive bladder.<br>• ***Differential diagnosis of anterior vaginal wall mass:***<br>▪ Vaginal wall cysts.<br>▪ Urethral caruncle.<br>▪ Mucosa prolapses.<br>▪ Vaginal wall cysts.<br>▪ Urethral caruncle.<br>▪ Skene gland abnormality.<br>▪ Vaginal leiomyoma.<br>▪ Gartner duct cyst.<br>• ***Differential diagnosis of vaginal pain/tender mass:***<br>▪ Endometriosis. |

## Investigations

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| **Urethroscopy** | • It is the first line investigation in women with urethral diverticulum (UD)<br>• It helps to locate UD and to visualize mucosal defect in 70% of cases |
| **Urodynamics** | It is indicated prior to intervention because:<br>• 60% of patients may have associated incontinence and the type of incontinence should be identified prior to treatment (stress, urgency, or postmicturition dribbling)<br>• 17% of patients develop incontinence after surgery. Therefore, baseline assessment is indicated |
| **T2-weighted MRI** | MRI can differentiate solid masses from complex UD |
| **Ultrasound** | • Transvaginal ultrasound: is an excellent alternative to MRI and for UDs that do not fill with a dye. However, they may directly compress the urethra<br>• Transabdominal ultrasound: is insensitive to UD smaller than 2 cm<br>• Trans-perineal ultrasound: is better than TAUS. However, it is still less sensitive to small UDs.<br>• Trans-anal ultrasound: it may improve visualization without compressing the urethra |
| **CT scan** | • It can detect calculi and malignancy if suspected<br>• Detection rate is higher if CT urethrogram is used |
| **Voiding cystourethrogram** | • Detection rate is 85-95%<br>• It can diagnose malignancy |
| **Double balloon urethrogram** | • Detection rate is 90%<br>• However, it is difficult, uncomfortable and may result in urethral injury |

## Complications

- Urinary tract infection: in 30-50% of case. It should be treated before surgery.
- Abscess formation:
    - The presence of extreme tenderness and an anterior vaginal mass is consistent with diagnosis.
    - Treatment is by aspiration and antibiotics. Definitive treatment should be delayed till the abscess resolves. It should not be drained (risk of fistula formation)
- Calculi (1.5% to 10%): They should be removed during excision of UD
- Urinary incontinence: This may be caused by postvoiding dribbling or weakness of the sphincter
- Urethral neoplasm (6-9%):
    - Diagnosis is made by a biopsy of suspicious lesions; 40-60% are adenocarcinoma
    - Management is by partial or complete urethrectomy or anterior exenteration
- Malignant transformation: this cancer is associated with early metastasis, late diagnosis and high incidence of recurrence

## Management

- **Indications of surgery:** persistent symptoms or presence of complications
- **Types of surgery:**

| Surgery | Indication | Principle |
|---|---|---|
| **Diverticulectomy** | Standard surgery. Cure rate is 70% | UD is incised, vaginal wall flap is created, excision of UD is performed with preservation of peri-urethral fascia and sphincter |
| **Marsupialization** | UD in the distal one-third of the urethra in women not fit for diverticulectomy | UD is incised, and urethral and vaginal epithelium are closed<br>This surgery is associated with high risk of fistula formation and splayed stream |
| **Endoscopic re-roofing or transurethral incision** | Recurrent UD in the distal third of the urethra | The procedure widens the neck of the UD to facilitate drainage |

- **Complications:**
  ① Recurrence or incomplete excision (35%)
  ② Damage to urethral sphincter and stress incontinence (17%)
  ③ Urethral stricture
  ④ Urethrovaginal fistula (6%)

# Management of Transgender

## Background

- Gender identity clinics (GIC) provides service to adults
- Gender identity development service (GIDS) provides service to children and adolescents up to 18 years age

| Terminology | |
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| **Gender non-conformity/ gender variant** | • The extent to which a person's gender identity, role or expression differs from the cultural norms prescribed for people of a particular sex. |
| **Gender dysphoria** | • A condition in which there is distress caused by the psychological experience of oneself as a man or a woman, which is incongruent with one's phenotype.<br>• The individual's physical sex is therefore not aligned with their gender identity.<br>• The distress associated with this inconsistency may lead an to seek clinical consultation. |
| **Transgender/ trans** | • An umbrella term to cover a variety of atypical gender experiences, which sometimes lead to the desire for a change of gender role but may not necessarily lead to any hormonal or surgical intervention. Trans and gender variant people are not necessarily gender dysphoric. |
| **Transitioning** | • The process of living according to the gender role that is consistent with gender identity.<br>• During this phase, a person should be addressed by the name, pronoun and style of address that they deem to be correct for them. |
| **Transman** | • A natal female who identifies as male and who lives as a male. |

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| **Transwoman** | • A natal male who identifies as female and lives as a female. |
| **Non-binary/agender** | • Someone whose gender expression does not fit within the gender binary.<br>• There are many different non-binary identities: some feel neither male nor female, some a bit of both; some feel they are a definite fixed 'third thing' that is neither male nor female; and some experience a fluctuating sense of gender identity. |
| **Intersex** | • A general term for several conditions in which a person's reproductive or sexual anatomy does not fit into the typical definition of a man or a woman. |
| **Gender recognition certificate** | • Awarded to individuals who have a demonstrated diagnosis of gender dysphoria and who they lived in a gender role other than that they were assigned at birth for at least 2 years.<br>• These individuals must then be legally identified as 'man' or 'woman' and not 'transman' or 'transwoman'. Thereafter, in law, the person is considered to be someone of their new sex and must be treated exactly as someone born into that new sex. |
| **Gender reassignment surgery (GRS)** | • The surgical procedures by which the physical function and appearance of a person's existing sexual characteristics are altered to resemble that of the other sex. |
| **Cisgender** | • A person whose gender identity matches the gender they were assigned at birth, i.e., someone who is not transgender. |

## Management

- **Pretreatment considerations:**
  - Adolescents may be offered reversible gonadotrophin-releasing hormone analogues (GnRHa). They act as hormone blockers to delay puberty and provide time to continue exploring their gender identity and consider long-term options.
  - Innate sex hormones can be suppressed using GnRHa, which produce a reversible chemical gonadectomy until a surgical gonadectomy is performed.
  - Eligibility criteria for gender treatments:

    ① Persistent and well-documented gender dysphoria.

    ② The patient has the capacity to make informed decisions and give consent.

③ Any significant medical or mental health issues are controlled.

④ The patient has a realistic, achievable plan

- Hormonal suppression and cross-sex hormone supplementation are generally initiated by endocrinologists and long-term monitoring is offered once hormone treatment is established (6 months for 3 years, then yearly if the patient is clinically stable).

- **Cross-sex hormonal treatment:**

| Male-to-female hormone treatment | Female-to-male hormone treatment |
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| • Estrogen therapy aims to:<br>▪ Induce breast formation<br>▪ Promote female-pattern fat distribution and reduce overall lean body mass<br>▪ Male-pattern hair growth<br>▪ Reduce libido and erectile function<br>• Estrogen therapy may be oral (e.g., oestradiol oral tablets; 1–6 mg daily), oestradiol transdermal gel or patches<br>• Oestradiol, testosterone and dihydrotestosterone levels should be monitored during maintenance therapy<br>• If needed, circulating adrenal androgens are blocked by finasteride.<br>• Androgen receptor blockers (cyproterone or spironolactone) may be used if needed<br>• Oestrogen therapy is safe and does not increase risk of venous thromboembolism (VTE). If additional risk factors are present, transdermal estrogen should be used<br>• If liver dysfunction is detected, topical estrogen may be used (oestrogen increases incidence of gallstones)<br>• Transwomen must be screened for breast cancer as appropriate | • Testosterone therapy aims to:<br>▪ Increase muscle mass<br>▪ Decrease fat mass<br>▪ Increase facial hair<br>▪ increases libido<br>▪ Cause hypertrophy of the clitoris<br>• Testosterone therapy may be given intramuscularly (e.g., Testosterone esters 250–500 mg by intramuscular injection every 2–6 weeks), or in the form of gel<br>• The most serious risk is development of polycythaemia that can predispose to a cerebrovascular accident. In refractory cases, venesection can be used.<br>• Hysterectomy should be considered after 4–5 years of testosterone therapy to reduce endometrial cancer risk (unopposed estrogen is produced by the aromatisation of testosterone). Alternatively, an ultrasound assessment of the endometrium is advised every 2 years.<br>• Transmen remain eligible for breast cancer screening if they have breast tissue remaining after bilateral mastectomy. |

- **Gender reassignment surgery**

  For a patient to be approved for this surgery, they must spend a verifiable period of time (usually at least 12 months) living and thriving in a gender role, as well as 12 months of continuous endocrine treatment

| Gender reassignment surgery for transwomen | | Gender reassignment surgery for transmen | |
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| ▪ Penectomy<br>▪ Orchidectomy<br>▪ Vaginoplasty<br>▪ Clitoroplasty<br>▪ Labiaplasty<br>▪ Breast augmentation | ▪ Cricothyroid approximation (phonosurgery)<br>▪ Thyroid cartilage reduction<br>▪ Feminising facial surgery | ▪ Bilateral mastectomy and chest reconstruction<br>▪ Hysterectomy<br>▪ Vaginectomy<br>▪ Salpingo-ophorectomy | ▪ Phalloplasty<br>▪ Urethroplasty<br>▪ Scrotoplasty<br>▪ penile/testicular prosthesis implantation<br>▪ Metoidoplasty |

- **Fertility management:**
  - Future reproductive options should be discussed before initiating medical or surgical treatment
  - Transgender patients must be aware that gender reassignment surgery leads to irreversible sterility
  - Prolonged oestrogen therapy (for cross-sex hormone treatment) causes reduction in testicular volume and poor-quality sperm. These effects may be reversible after treatment discontinuation
  - Testosterone treatment for transmen leads to reversible amenorrhoea and may affect follicular growth. Contraception should be provided since the patient is still fertile and testosterone is teratogenic
  - Ideally, gamete storage should be offered before commencing hormone treatment

- **Surgery:**
  - Guidelines recommend that transmen consider a hysterectomy after 4–5 years of testosterone therapy to reduce the risk of endometrial cancer
  - When opting for surgery, patients almost always also prefer bilateral salpingo-oophorectomy to abolish endogenous estrogen production, which would allow them to discontinue GnRHas and to improve the efficacy of testosterone therapy

- In general, a laparoscopic route is preferred to avoid scarring the abdomen in case this area becomes a donor site for phalloplasty. The vaginal route may be difficult because these patients are typically childless.

- **Pregnancy in transmen:**
  - No clear recommendations about the mode of delivery in this population
  - Many transmen chest-feed their infants, even after chest masculinisation surgery

- **Cervical screening:**
  - It is recommended that any transman who has their cervix should undergo cervical screening. It is the GP responsibility to ensure these patients are offered cervical screening
  - There is a ten-fold increased rate of inadequate cytology found in cervical smears of transmen due to the effects of testosterone on the cervical epithelium.

# Cystoscopy in Gynaecology

## Indications

1. Unexplained hematuria without UTI, or persists after treatment of UTI in women > 45 years
2. Unexplained hematuria with elevated WBCs in women > 60 years
3. Bladder pain syndrome
4. Recurrent UTI
5. Urethral strictures
6. Urinary
7. congenital genital tract anomalies
8. Voiding symptoms
9. Intraoperatively

## Contraindications

untreated UTI

## Complications

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| **Common risks (> 10%)** | ▪ Mild post-procedure burning or bleeding<br>▪ Need for biopsy |
| **Occasional risks (2-10%)** | Bladder infection |
| **Rare (< 2%)** | ▪ Need for catheter insertion (temporary)<br>▪ Delayed bleeding, requiring removal of blood clots or surgery<br>▪ Urethral injury and delayed scar formation |
| **Very rare** | Bladder perforation |

## Procedure

| Rigid cystoscopy | Flexible cystoscopy |
|---|---|
| • A 0 or 30 ° lens is used, and a lubricant is applied.<br>• Irrigation is run outside the body to get rid of bubbles, then the scope is passed while irrigation is running<br>• Overfilling of the bladder should be avoided, otherwise, small lesions would be missed<br>• Bladder examination starts from the base of the bladder towards bladder neck till the trigone is seen (by moving the tip down and withdrawing the scope)<br>• One the trigone is seen, inter-ureteric bar is followed on both sides, to visualize left or right ureteric orifices.<br>• Over distension should be avoided, which may distort the orifices.<br>• The scope is pushed to the front to visualize the dome of the bladder (air bubble) and withdraw towards the bladder neck.<br>• The scope is rotated to the left wall and withdrawn to visualize the whole wall. The right wall is examined in the same way. The anterior wall is examined by pushing the scope up.<br>• Empty bladder at the end of the procedure.<br>• 0 or 12 lenses are used for urethral visualization. | • A local anaesthetic is applied to the urethra<br>• Irrigation is done<br>• The bladder is examined systematically (see under rigid cystoscopy).<br>• Afterwards, the J maneuver is used. It involves pushing the scope inside the bladder while fully deflecting with your thumb. Therefore, bladder neck is visualized. The scope is then rotated to see all around bladder neck.<br>• When finished, deflection is released while withdrawing the scope. |

### Parts of cystoscope

- Telescope (0º, 30 °, 70 °)
- Outer sheath
- Obturator
- Bridge
- Biopsy forceps
- Camera
- Light cable
- irrigation system (normal saline, water, or 1.5% glycine)

### Prophylactic antibiotics

| Indications | Antibiotic |
|---|---|
| • If botulinum toxin.<br>• Recurrent UTI.<br>• Recent mechanical heart valve in the last 6 months. | Single dose IV gentamicin |

# Urinary Catheters in Gynaecology

## Types

- **Types of catheter material:**

  Urinary catheters are classified according to their material and duration of use to:

  - Short term use: plastic and latex catheters (less than 1 week)
  - Intermediate use: polytetrafuroethelene (PTFE) coated catheter (1-3 weeks)
  - Long-term use: silicone or Teflon based catheters (associated with lower risk of encrustation and blockade)

- **Types of catheter use:**
  - **Self-retaining suprapubic catheter (SPC, Add-a-Cath):**

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| **Indications** | ▪ Short term (perioperative, urethral stricture, acute retention, severe pelvic trauma, anorectal surgery)<br>▪ Long term (neurogenic bladder, chronic retention, mobility problems, persistent expulsion of intrauterine catheter, last resort for intractable incontinence) |
| **Contraindications** | ▪ Absolute contraindication: unexplained hematuria<br>▪ Relative contraindications:<br>• Significant obesity<br>• Extensive abdominal adhesions<br>• Bladder reconstruction<br>• Limited capacity of 300 cc<br>• Suspicion of ovarian cyst<br>• Ascites<br>• Anticoagulation treatment |

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| **Type of catheter material** | ▪ Short term: Bonnano (must be fixed with a stitch). Used for 3 weeks<br>▪ Long term: Foley catheter or 100% silicone catheter (add-a-cath), it can be changed every 3 months |
| **Insertion technique** | ▪ Techniques of insertion are either open (rare) and closed<br>▪ A closed technique is performed through a small suprapubic incision, bladder is filled with at least 500cc, patient placed in Trendelenburg position, and then a trocar is inserted 3 cm above SP under cystoscopic guidance into the bladder. The catheter is placed through the trocar. The balloon is inflated, and trocar is removed |
| **Advantages** | ▪ More comfortable to the patient<br>▪ It allows patient-controlled voiding trials and checking postvoiding residual (PVR)<br>▪ It decreased risk of catheter migration and leakage with long term use<br>▪ Less sexual interference<br>▪ Lower risk of bacteriuria |
| **Disadvantages** | ▪ Over granulation<br>▪ Risk of bowel injury<br>▪ Mortality rate is up to 2%<br>▪ Altered body image<br>▪ Ulcers in skin folds particularly in obese women |
| **Care and follow-up** | ▪ SPC should be changed every 8-12 weeks<br>▪ If it comes out spontaneously, immediate replacement is necessary, since the tract closes rapidly and after 2 hours, it will be very difficult to replace<br>▪ First change should be done in acute care setting and then in the community. No dressing is required once the tract is closed<br>▪ Flip flow valve is used to stop free flow. The patient then tries voiding though the urethra and measures PVR.<br>▪ Valves should be released every 3-4 hours to maintain bladder tone |

- **Indwelling catheters:**
  - This method is more appropriate with short term use. The most common indication is perioperative bladder care
  - Time of removal of indwelling catheter postoperatively is variable. However, midnight removal may be associated with shorter time and greater first void volume and shorter hospital stay

- **Clean intermittent self-catheterization (CISC):**

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| **Indications** | ▪ Neurogenic bladder<br>▪ Chronic retention<br>▪ Obstruction<br>▪ Post-surgery:<br>□ Risk of voiding dysfunction is 3-38% after sling placement and anterior repair<br>□ CISC is superior to IUC for 3 days in prolapse surgery in management of high PVR<br>▪ After botulinum injection (risk of retention is 16%)<br>CISC should be used till PVR < 150 cc and voiding volume ≥ 200 cc |
| **Type of catheter used** | ▪ Self-lubricating hydrophilic catheters (less traumatic, more expensive) can be used<br>▪ Catheter size is 10-12 |
| **Advantages** | ▪ Lower risk of infection<br>▪ Lower incidence of catheter blockade and catheter rejection |
| **Complications** | ▪ Urethral bleeding<br>▪ Catheter retention<br>▪ Trauma to urethra<br>▪ Urinary tract infection (UTIs):<br>□ Each catheter use is associated with 3-4% infection risk<br>□ Most women will have bacteriuria after 2-3 weeks: 50% will have asymptomatic bacteriuria).<br>□ Prophylactic antibiotics can be considered |

## Complications

- **Catheter-associated urinary tract infections (CAUTIs):**
  - It is the leading cause of hospital acquired infection (20-40%)
  - There is no evidence that coating with antibiotics or antiseptics reduces the risk
  - It should be treated with antibiotics for 5-21 days
  - Prophylactic low dose antibiotics are not recommended
- **Failure to deflate the balloon:**

  Removing blocked catheters when the balloon does not deflate can be performed by:
  - Cutting the proximal segment of the valve OR
  - Passing a ureteric catheter stylet through inflation channel till it touches the balloon or using needle to rupture the balloon
- **Burst balloon:**
  - In 27% of cases, burst balloon forms fragments that calcify causing irritative symptoms
  - Management is by cystoscopy and bladder irrigation
- **Bladder cancer:**

  Catheterization for > 10 years is associated with risk of bladder cancer

# Urogynecology

## Abstract

Urogynaecology and pelvic floor medicine present a large portion of gynaecologic practice. As average life expectancy tends to rise worldwide, pelvic floor disorders have become more prevalent. Although such disorders do not commonly have morbid sequalae, their impact on life quality may be substantial. In this chapter, we will discuss common urologic disorders in gynaecology and their standard management.

## Keywords

Pelvic organ prolapse, incontinence, mid-urethral sling, pelvic floor

## Further readings


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# Surgical Instruments in Gynaecology

| Instrument | Features | Examples |
|---|---|---|
| Allis forceps | It is used to grasp touch structures | • Holding the cervix during dilation and curettage<br>• Holding edges of the vagina during hysterectomy<br>• Holding rectus sheath during abdominal surgery<br>• Grasping of the ovary and tubo-ovarian masses in case of oophorectomy |
| Babcock Forceps | It is used to grasp delicate structures (e.g. tube, appendix, bowel) | Holding the Fallopian tubes during tubal sterilization and salpingectomy |
| Ramsey forceps | It is used to grasp tissue edges (toothed and non-toothed) | • Non-toothed forceps is used to inside peritoneal cavity<br>• Toothed forceps is used to grasp skin edges during skin closure |
| Tissue holding forceps | It is used to grasp and retract tissues for long period of time (Littlewood and lanes tissue forceps) | Littlewood tissue forceps is used to grasp the edges of the rectus sheath to aid dissection and during closure |
| Green Armytage uterine haemostatic forceps | It is used to hold tissue edges | Holding uterine edges to facilitate closure of hysterotomy incision during caesarean section |
| Polyp forceps | It is used to grasp | Used to grasp and avulse uterine and cervical polyps |




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_25

| | | |
|---|---|---|
| | tissues firmly for removal | (polypectomy) |
| Rampley sponge forceps | It is used to hold a gauze swab for the purpose of cleaning | A swab on a stick is used to prep the skin or to dab blood in tissues without damaging them |
| Doyens retractor | A broad and short abdominal retractor | It is used to retract the bladder during caesarean section |
| Langenbeck retractor | Light and small retractors | It is used to retract the skin during closure of rectus sheath during caesarean section (commonly used in pairs) |
| Morris retractor | Right angle retractors | Used to improve visualization during pelvic surgery |
| Balfour retractor | Self-retaining abdominal retractor | Used during abdominal surgery to provide adequate exposure |
| Auvard speculum | Self-retaining vaginal retractor | It may be used in dilation and curettage and other pelvic procedures |
| Vulsellum forceps | It is used to grasp tissues firmly (single-toothed, double-toothed or multiple toothed) | • Used to grasp the cervix during vaginal hysterectomy<br>• May be used to grasp a fibroid polyp |
| Haemostatic clamps | They are atraumatic causing minimal tissue trauma, and serrated so they prevent slippage (Gwilliams and Rogers) | Used during hysterectomy to clamp vascular pedicles |
| Haemostatic forceps | They have a strong grip and sharp teeth (Kocher, Spencer Wells) | • Used to compress bleeding vessels and help haemostasis (Spencer Wells)<br>• Used to clamp the cord before dividing |

# Office Hysteroscopy

## Prior to procedure

- Patients should be counselled on the procedure, its value and limitations. Written information should be supplied
- Nurse chaperone should be present regardless of provider gender

## Cervical preparation

- Routine cervical preparation is not indicated
- Routine cervical dilation during the procedure should be avoided

## Sedation

- Conscious sedation should not be routinely used

## Anaelgesia

- Non-steroidal anti-inflammatory drugs (NSAIDs): should be given 1 hour before the procedure. Routine preoperative opiate should be avoided
- Local anaesthetics:
    - Instillation into the cervical canal may be associated with lower risk of vasovagal reaction but not pain
    - Application of local anaesthetic into and around the cervix decreases procedure-related pain

These options should be considered particularly in postmenopausal women. In premenopausal women, it may be considered only if cervical dilation is anticipated or if a scope larger than 5 mm should be used. Routine use in premenopausal women to reduce incidence of vasovagal reaction is not indicated

- Topical applications of a local anaesthetic to ectocervix is indicated if a tenaculum will be used during the procedure

## Equipment

| | |
|---|---|
| **scopes** | • Hysteroscope miniature scope has a diameter of 2.7 mm (with 3.5mm sheath)<br>• flexible scopes are associated with less pain, better image, quicker exam, fewer failed procedures, and less cost compared to rigid scopes |
| **lenses** | • They are available at angles zero, 12°, 25° or 30° off-set lenses<br>• There is no evidence of superiority of one lens type (operator choice) |
| **distention media** | • Carbon dioxide versus normal saline<br>• Normal saline is associated with better image quality, less vasovagal attacks, and quicker procedure<br>• Normal saline is used if bipolar electrosurgery will be used for operative procedures |

## Approach

Vaginoscopy is associated with less pain particularly when rigid outpatient hysteroscopy is used. It should be performed routinely specially if:

- Speculum insertion/cervical instrumentation is difficult
- Blind endometrial biopsy is not required

# Laparoscopic Entry Complications

## Incidence

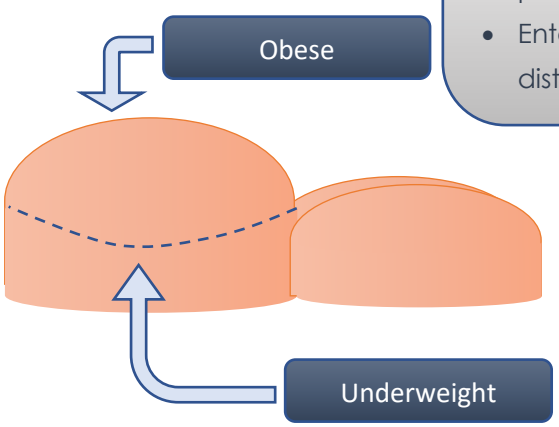
- Incidence of all complications is 1-12:1000
- Incidence of major complications is 1.4/1000:
  - Intestinal injury: 0.6/1000
  - Urologic injury: 0.3/1000
  - Vascular injury: 0.1/1000

## Risk factors

- Obese or underweight
- Midline abdominal incision
- Inflammatory bowel disease
- Peritonitis

## Prevention

- Open technique or palmer's is superior to Veress technique.
- If Veress needle is used, a standard Veress length may be used (the distance between umbilicus to peritoneum is 6 cm
- Entering at 45 degree would result in longer distances to enter the abdomen




- There is high risk of vascular injury. The risk is higher in young and nulliparous women with well-developed musculature.
- If a patient is severely underweight, aorta may be < 2.5 cm deep to umbilicus.
- Hasson technique and Palmer's points are referred

## Safe entry of primary port

### Closed technique

- Small superficial vertical incision at base of the umbilicus.
- Check the spring action of Veress needle.
- Entry is performed while patient is in horizontal position (not Trendelenburg)
- Palpate the abdomen to check for masses and position of the aorta.
- Veress is inserted perpendicularly while lower abdominal wall is stabilized
- Two clicks should be audible (entry of fascia, peritoneal entry).
- To ensure successful entry, initial insufflation pressure should be < 8 mmHg with free flow.
- Excessive lateral movement of the needle should be avoided, otherwise, a potential tear may be expanded.
- Insufflation through the needle should continue till pressure is 20-25mmHg. At this pressure, aorta is 4-8 cm away from the umbilicus (only 0.6 cm if pressure is 10 mmHg).
- Thereafter, primary trocar can be inserted perpendicularly. Once all trocars are placed, pressure should be dropped to 12-15 mmHg (which is ideal for good visualization and proper patient ventilation).
- The scope is inserted through the primary cannula and rotate inside the abdomen (360°) to check any injuries, bleeding or adhesions.
- If adherent bowel at the umbilicus, the trocar may be inserted under vision using 5 mm scope PLUS visual control during removal to ensure no bowel injury.

### Open technique

- An incision is made through the umbilicus till peritoneum is open (as confirmed by visualizing omentum or bowel).
- Lateral stay sutures should be taken at fascial edges
- A blunt-tipped cannula is inserted. Stay sutures are firmly attached to suture holders of the cannula (airtight seal).
- The abdomen is partially distended and then, the trocar is withdrawn.
- At the end of the procedure, fascia is closed using these stay sutures with or without additional stitches to reduce risk of incisional hernia.

### Alternative entry techniques

#### Direct trocar entry

If a surgeon is experienced in this technique, it is not associated with significant difference in major complications compared to closed technique.

#### Optical insertion

The technique is not superior to other techniques

#### Palmer's point

- This technique is recommended in the presence of previous abdominal surgeries. Umbilical adhesions are present in **50%** of patient after midline vertical and **25%** after low transverse
- The point is 3 cm below the left costal margin at midclavicular line.
- A Veress needle is inserted, pressure is raised to to 25 mmHg then a 2-5 mm scope is used to assess periumbilical adhesions
- In no adhesions found, umbilical access is done, otherwise, adhesiolysis is performed first.

**Other entries**

- Entry through fundus **(risk on injury to adherent bowel)**
- Entry through DP **(risk of injury to adherent rectum e.g. deeply infiltrating endometriosis)**
- Suprapubic access **(risk on bladder injury)**

## Safe entry of secondary port

- Secondary ports should be Inserted under direct vision. They should be perpendicularly inserted
- IAP should be 20-25mmHg prior to insertion
- Prior to insertion, IE vessels should be identified prior to entry (lateral to medial umbilical ligaments "obliterated umbilical arteries")
- If IE vessels cannot be seen e.g. obese patients, trocars should be inserted lateral to lateral border of rectus sheath.
- Insertion direction is perpendicular. Once the trocar passes through the peritoneum, trocar should be angled toward anterior pelvis to avoid injury to pelvic sidewall vessels.

## Safe exit of secondary ports

- Ports should be removed under direct vision to rule out bleeding from entry site
- Closure of any midline abdominal incision longer than 10 mm or non-midline incision longer than 7 mm should include fascial closure to reduce risk of incisional hernia

DP: Douglas pouch
IAP: Intra-abdominal pressure.
IE: Inferior epigastric

# Abdominal Incisions and Closure

## Types of abdominal incisions

- Transverse incisions
- vertical incisions
- oblique incisions

- Do not use monopolar electrosurgical device to make abdominal incision
- Scalpel are used to make abdominal incision. Changing scalpel when making superficial and deep incisions is not necessary

| Incision | Advantages | Disadvantages | Types |
|---|---|---|---|
| **Transverse incisions** | • Best cosmetic results<br>• Less postoperative pain painful<br>• Less interference respirations during recovery<br>• Greater strength on healing | • More time-consuming<br>• Associated with more bleeding<br>• Inadequate exposure of upper abdominal cavity<br>• Incision through several layers of fascia and muscle<br>• Possible incision through abdominal wall nerves<br>• May create potential spaces that result in hematomas or seroma | • **Pfannenstiel incision:**<br>▪ Incision is curved<br>▪ 10–15 cm long<br>▪ 2 cm above pubic symphysis<br>▪ Rectus muscles are split but not cut<br>• **Küstner incision:**<br>▪ Incision is slightly curved<br>▪ Incision starts below level of ASIS and passes just below pubic hairline.<br>▪ Incision has limited extensibility<br>▪ It may be associated with superficial branches of the inferior epigastric artery or vein<br>• **Cherney incision:**<br>▪ Rectus muscle is incised at its insertion to pubic symphysis |

| | | | |
|---|---|---|---|
| | | | ▪ It allows access to space of Retzius and is used in urinary incontinence procedures<br>▪ It is also suitable for hypogastric artery ligation<br>• **Maylard incision:**<br>▪ Incision is 3–8 cm above the symphysis<br>▪ All muscle layers of lower abdominal wall are transversely cut<br>▪ Rectus fascia is not dissected free of rectus muscles<br>▪ Peritoneum is incised transversely<br>• **Mouchel incision:**<br>▪ Incision is made at upper limit of pubic hair (below Maylard incision)<br>▪ Abdominal muscles are divided above the openings of the inguinal canals.<br>• **Joel-Cohen incision:**<br>▪ Straight incision 3 cm below the level of ASIS<br>▪ Subcutaneous tissues and fascia are incised transversely in the midline. Incision is bluntly extended laterally with blunt finger dissection.<br>▪ Rectus fascia is dissected bluntly from muscle layer, rectus muscle is split, and peritoneum is opened |

| | | | |
|---|---|---|---|
| **Vertical incisions** | • Excellent abdominal exposure<br>• Easy to extend<br>• Less bleeding<br>• Nerve injury is unlikely<br>• Time saving | • Incidence of wound dehiscence and hernia may be higher<br>• Less favorable cosmetic results | • **Midline (median) incision:**<br>▪ It can be easily extended<br>▪ Perfect exposure<br>▪ Pyramidalis muscle is a landmark to identify the midline<br>• **Paramedian incision:**<br>▪ It is extensible especially on the side of the pelvis<br>▪ No difference in wound infection, dehiscence or postoperative respiratory difficulty with midline and paramedian incisions.<br>▪ Paramedian incisions may be associated with more bleeding, and operative time |
| **Oblique incisions** | • Gridiron incision allows extraperitoneal abscess drainage (no peritoneal contamination) and provides access to appendicectomy in pregnant women | Limited exposure | • **The Gridiron incision:**<br>▪ Incision starts at McBurney point and passes downward and inward<br>▪ Abdominal wall muscles are split along the direction of the fibres.<br>• **Rockey–Davis incision:**<br>▪ Transverse incision<br>▪ It is done at junction of the middle and lower thirds of a line drawn between ASIS and the umbilicus. |

ASIS = anterior superior iliac spine

**Joel-Cohen Vs. Pfannenstiel incision**

**In Caesarean section, Joel-Cohen is superior:**

- It is associated with less postoperative febrile morbidity
- It is associated with less postoperative pain and need for analgesia
- It is time saving
- It is associated with less intraoperative bleeding and adhesion formation
- It is associated with fewer rate of wound infection and shorter hospital stay

- **Electrosurgery:**
  - It should not be used to create skin incision (skin blistering and poor healing due to desiccation effect)
  - Tissues can be incised using electrosurgery. A small/thin electrode is used, with cut current, that should be activated just before the tissue is reached
  - Abdominal fat can be cut using electrosurgery. A coagulation waveform should be used

## Closure of abdominal incision

- **Principles of suturing skin incisions:**
  - Debridement of skin edges must be done whenever necessary
  - Direct tissue trauma should be avoided
  - Skin edges should just touch each other. Skin should not be blanched

- **Closure techniques:**

**Primary suture line**

This refers to continuous or interrupted sutures that approximates wound edges during healing by first intention

- Continuous suture: less foreign body mass in the wound, event distribution of tension.
- Interrupted sutures: better in the presence of infection. Therefore, a suture break does not open the whole incision

No difference in continuous versus interrupted closure in wound breakdown and hernia formation

**Secondary suture line**

- Also known as retention sutures
- Used to reinforce the primary suture line and close any dead space
- Retention sutures are placed 2 inches from wound edge

**Fascial closure**

- The incision is sutured continuously
- If incision extends laterally beyond the edge of rectus muscles into external and internal oblique muscles, this may be associated with injury to ilio-hypogastric and ilioinguinal nerves
- So, if these extensions are present, sutures should be carefully placed so they incorporate external oblique fascia only

## Closure of unclean wounds

**Secondary closure**

- It is used more often to manage contaminated or dirty wounds
- Wound is cleaned first, then, it is allowed to heal by secondary intention without stitches

**Delayed primary closure**

- It is occasionally used for contaminated or dirty wounds
- First, the wound is cleaned, then, it is reassessed after a few days to rule out infection, then the wound is surgically closed
- In this case, staples or monofilament delayed sutures or non-absorbable sutures may be used

### Layered versus mass closure

- Mass closure using looped delayed–absorbable suture is superior to conventional layered closure
- Suture length: wound length ratio should be at least 1:4

### Smead–Jones closure

- Anterior wall mass closure is performed using a far–far (1.5–2 cm from fascial edges), near–near (only anterior fascia) technique
- Sutures are either interrupted or running using delayed absorbable suture.
- Fascial dehiscence rate with this technique is 0.4%.

### Gallup closure

- This technique is used to close midline incisions
- No. 2 polypropylene suture is run 1.5–2 cm from the fascial edge
- The suture includes peritoneum, fascial layers and the intervening muscles.
- One suture run from each end of the wound and they are tied in the middle where they meet. The knot consists of 3 square knots

## Incisions and closure in obese patients

Morbid obesity is associated with 7-fold increased risk of wound infection

- Skin incision:
  - Transverse incision: should be made away from the moist subpannicular fold to reduce risk of infection
  - Midline vertical incision: panniculus should be retracted inferiorly to avoid the moist area
- Abdominal wall closure:
  - Smead–Jones closure
  - Running mass closure
- Intra-fascial drain:
  A drain is placed and monitored for drain output. The drain is removed if output is <50 ml/24 hours
- Skin closure: staples are superior to subcuticular sutures

## Laparoscopic incisions and closure

- **Primary incision:**
  - Incision is made below vertically in the midline
  - Incision is made from the base of the umbilicus, and not below it

- **Closure:**
  - Laparoscopic incisions require skin closure
  - Non-midline incisions > 7 mm and midline incisions >10 mm require deep sheath closure to reduce risk of port site hernia

## Wound closure materials

The following options are available for closure

### Sutures

Suture materials used for closure are:

- non-absorbable sutures: e.g. polypropylene suture
- Slowly absorbable sutures: e.g. Poliglecaprone 25 suture
- rapidly absorbable sutures e.g. polyglactin 910 suture

Monofilament sutures are associated with less risk of infection (less likelihood of bacterial overgrowth) e.g. Poliglecaprone 25

### Staples

Types of staples are:

- **Non-absorbable staples:** stainless steel staples (high tensile length and tissue reaction)
- **Absorbable staples:** Associated with low risk of infection. They retain 40% of tensile strength at 14 days and take months to absorb (half-life is 10 weeks)

Staples are associated with lower incidence of infection compared to sutures when used to close contaminated wounds

**However,** they may cause track formation and allow bacterial migration into the wound

### Adhesives and glues

**Types:**

- **Biological agents:** e.g. fibrin-based glues, gelatin-based hydrogels, and composite glues
- **Synthetic agents:** cyanoacrylates and polymeric sealants
  - **Non-resorbable:** limited to surface applications
  - **Resorbable (biodegradable):** for external and internal use
- **Genetically engineered protein glues**

### Adhesive strips

- Adhesive strips are used after wound is closed with sutures (subcuticular sutures)
- It is used to approximate wound edges and reduce wound tension. This tends to improve wound cosmesis
- Adhesive strips are not used as a primary method of wound closure

Adhesives and glues are fast to use, cyanoacrylates show antimicrobial features

Tapes are easy to apply but are not suitable for moist and mobile areas (detach). They are not an alternative to sutures

## Suture materials

| Suture Material | Absorption Time in Days | Structure |
|---|---|---|
| **Polyglycolic acid (Dexon)** | 90-120 | Monofilament |
| **Polyglactin (Vicryl)** | 60-90 | Multifilament |
| **Polyglactic 910 (Vicryl Rapid)** | 7-14 | Multifilament |
| **Polydioxanone (PDS)** | 180-210 | Monofilament |
| **Polyglecaprone (Monocryl)** | 90-120 | Monofilament |
| **Polytrimethylene carbonate (Maxon)** | 180-210 | Monofilament |

# Hysterectomy

## Abdominal hysterectomy

Steps of abdominal hysterectomy are:

- Laparotomy with good exposure of surgical field
- Cut and ligate the round ligament
- Clamp, cut, and ligate the ovarian ligament (if the ovaries will be preserved), or the infundibulopelvic ligament (if oophorectomy is indicated)
- Dissect the broad ligament down to the side wall of the uterus toward uterine vessels
- Mobilize the bladder
- Clamp, cut, and ligate uterine vessels
- Clamp, cut, and ligate the uterosacral ligaments
- Incise the vagina and remove the uterus
- Close the vaginal cuff

## Vaginal hysterectomy

Steps of vaginal hysterectomy are:

- A circumferential incision is made in the cervix
- The bladder is dissected upwards
- The anterior peritoneum is opened (through the utero-vesical peritoneal fold)
- The posterior peritoneum is opened (through the pouch of Douglas)
- The uterosacral ligaments are cut and ligated
- The uterine arteries are cut and ligated
- The round ligaments are cut and ligated

- The tubes and ovaries may be removed at this stage
- The uterus and cervix are removed
- McCall culdoplasty is performed to prevent enterocele
- The cardinal and uterosacral ligaments are incorporated in closure of vaginal vault

## Complications

| Serious risks | Incidence |
|---|---|
| Overall risk of serious complications | 4:100 (common) |
| Bladder and/or ureter injury – Disturbance of bladder function | 7:1000 (uncommon) |
| Bowel injury | 4:10000 (rare) |
| Haemorrhage requiring blood transfusion | 23:1000 (common) |
| Return to the theatre | 7:1000 (uncommon) |
| Pelvic abscess/infection | 2:1000 (uncommon) |
| Venous thrombosis or pulmonary embolism | 4:1000 (uncommon) |
| Death within 6 weeks | 32:100000 (rare) |

Frequent risks include wound infection, incisional pain, delayed wound healing or keloid formation, paresthesias, and urinary tract infection

# Enhanced Recovery in Gynaecology

## Preoperative phase

- Preoperative risk assessment to improve surgical outcomes
- Determination of location of immediate postoperative recovery based on surgery and individual risks e.g. elective admission to high dependency care or intensive care unit
- Preoperative education, verbal and written information, which covers surgery, postoperative care, hospital stay, and pain control
- Discharge plan, with availability of appropriate support

## Perioperative phase

- Clear fluids should be stopped 2 hours prior to anaesthesia
- Preoperative carbohydrate drinks, in non-diabetics, reduced postoperative thirst, hunger, anxiety, and insulin resistance
- Mechanical bowel preparation is not recommended
- Long-acting sedative premedication are not recommended to facilitate early mobilization
- Intraoperative hypothermia should be prevented
- Prophylactic antibiotics should be used according to the procedure
- Mechanical and pharmacological thromboprophylaxis (as indicated)
- Nasogastric tube should be avoided
- Vaginal and abdominal drains should be avoided
- Vaginal packs should be avoided whenever possible (interfere with early immobilisation)
- Postoperative pain strategies (e.g. spinal, epidural, and regional approaches) are highly recommended to reduce the need for postoperative narcotics

## Postoperative phase

- Early feeding and reduction of IV fluid infusion is recommended to avoid nausea and to shorten hospital stay
- Early immobilisation should be encouraged through effective analgesia
- Anti-emetics with laxatives should be used proactively
- Early catheter removal and monitoring of voiding and post-voiding residuals to ensure good bladder function

## Discharge

- Discharge criteria:
  - Immobilisation
  - Pain is well controlled with no or oral analgesics
  - Patient is passing flatus
  - Patient can drink and eat regular eat
- Laxatives are prescribed and should be used till the patient has her first bowel movement
- Patients can be discharged with the urinary catheter in place. Education on urinary catheter care should be delivered to the patient

# Prevention of Surgical Site Infection

Strategies to prevent surgical site infection are classified into pre-operative, intra-operative and post-operative phases as follow:

## Pre-operative phase

For patient

For staff

1. showering

Showering or having a bath with soap the day before or on the day of surgery

2. Nasal decolonization

If the risk of staph aureus surgical site infection is high, nasal mupirocin with chlorhexidine body wash are recommended based on:

- The type of procedure.
- Individual patient risk factors.
- The increased risk of side effects in preterm infants.
- Potential impact of infection
- Maintain surveillance on resistance to mupirocin.

- All staff should wear specific non-sterile theatre wear in all areas.
- Movements in and out of the operating area should be kept to a minimum

❸ **Hair removal**

- Don't remove hair routinely. but if it is necessary, use electronic clippers with disposable heads.
- Don't use Razors as they increase the risk of surgical site infection

❹ **Patient theatre wear**

There should be specific theatre wear that allows easy access and maintains comfort and dignity

❺ **Mechanical bowel preparation**

It's not needed routinely to prevent surgical site infection

❻ **Accessories**

Jewelry, nail polish, and artificial nails should be removed before surgery

❼ **Antibiotic prophylaxis**

- A Single dose of antibiotics is given when anaesthesia is induced (or earlier if a tourniquet will be used)
- A second dose is given if surgery is longer than the half-life of the antibiotic
- Antibiotic treatment in addition to prophylaxis is needed for infected/dirty wounds.
- Inform patients about the use of antibiotics.

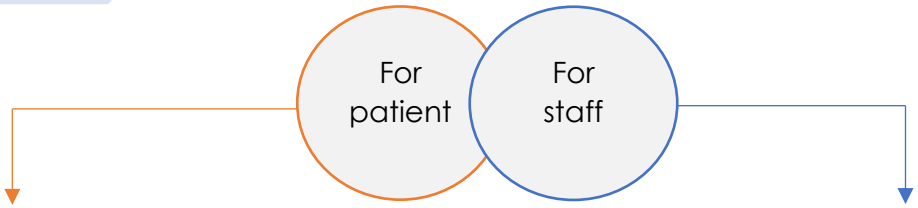
**Indications of prophylactic antibiotics**

① clean surgery only if involves the placement of implant/prosthesis and not used for clean uncomplicated surgery without implants

② Clean-contaminated surgery

③ contaminated surgery

## Intra-operative phase




1. **Incise drapes**

Use iodophor impregnated drapes unless the patient has an iodine allergy

2. **Antiseptic skin preparation**

- Use antiseptic preparation to clean the incision immediately before surgery
- Be aware of the risk of skin antiseptics on babies due to the risk of chemical injury of chlorhexidine with both alcohol and aqueous solution.

**Hand decontamination**

- Before the 1st operation on the list, wash hands with an aqueous antiseptic solution with a single-use brush or pick for nails.
- next time, use alcoholic hand rub or antiseptic solution but if soiled, wash again with an antiseptic solution.

**Sterile gowns and gloves:**

The operating team should Wear sterile gowns and 2 pairs of gloves if the risk of glove perforation and sequences of contamination is high.

| Types of antiseptic skin Preparation | Usage |
|---|---|
| An alcohol-based solution of chlorhexidine | First choice |
| An aqueous solution of chlorhexidine | In Surgical site is next to mucous membranes |
| An alcohol-based solution of povidone-iodine | If chlorhexidine is contraindicated |
| An aqueous solution of povidone-iodine | If both an alcohol-based solution and chlorhexidine are contraindicated |

**3 Diathermy**

- Do not use it for a surgical incision to decrease the risk of surgical infection.
- If diathermy is used, use vaporization to dry antiseptics and avoid pooling alcohol-based preparations.

**4 Homeostasis**

- Maintain patient temperature during surgery
- Maintain adequate perfusion during surgery and O2 saturation >95% during surgery and recovery

**5 Closure methods**

- Consider using sutures rather than staples to close skin to decrease surgical site infection in the caesarean section
- Antimicrobial triclosan-coated sutures especially for paediatric surgery reducing surgical site infection

**6 Wound dressings**

Cover surgical incisions with appropriate interactive dressing at the end of surgery

Wound irrigation and intracavity lavage are not recommended.

Antiseptics and antibiotics applied before wound closure should not be used outside clinical trials

## post-operative phase

1. **Changing dressings**
   - Use the anti-septic anti-touch technique to change or remove the dressing
2. **Postoperative cleansing**
   - Use sterile saline for wound cleansing up to 48 hours after surgery.
   - patients can shower safely 48 hours after surgery.
   - Tap water is used to cleanse wounds after 48 hours if separated or for draining pus.
3. **Dressings for wound healing by secondary intention**
   - Do not use Eusol, gauze, or moist cotton gauze or mercuric antiseptic solutions. Do not use dextranomer, enzymatic treatment for debridement
   - Use appropriate interactive dressing.
   - Ask tissue viability nurse for appropriate dressing

Topical antibiotics for wound healing by primary intention It's not recommended.

Do not give insulin routinely to non-diabetics to adjust postoperative glucose level.

# Laparscopic Vascular Injuries

## Risk of vascular injuries

Vessels at risk in laparoscopic gynaecological surgery include:

| | |
|---|---|
| **Inferior epigastric artery** | There is a 'safe zone' where ports can be inserted with a low likelihood of injuring the inferior epigastric artery. This could be from <1 cm from the midline or >8 cm from the midline. Insertion of ports more than two-thirds along the line between the midline and the anterior superior iliac spine will also fall in this 'safe zone' |
| **Aorta** | The insertion of the Veress needle and first trocar should be in the supine position before raising the legs into the Trendelenburg position |
| **Common iliac arteries** | Right common iliac artery is at higher risk of injury during instrumentation of the umbilicus |
| **Venous system** | An injury to the vena cava is more likely when a trocar is inserted next to the midline instead of in the midline. The left iliac vein crosses the midline caudal to the umbilicus and can be injured even by a midline trocar. Sharp and blunt dissection can cause bleeding as well |
| **Corona mortis** | It is an anastomosis between the obturator and the external iliac or inferior epigastric arteries or veins situated behind the superior pubic ramus, which may be injured during pelvic lymphadenectomy |

## Prevention

Key considerations for reducing vascular injury in laparoscopic gynaecological surgery:

- **Preoperative assessment:**
  - In the elective setting, appropriate preoperative assessment, including identification and treatment of anaemia.
  - In the emergency setting, availability of transfusable blood and cell salvage consideration.

- **Laparoscopic abdominal entry techniques:**
  - Seventy-five percent of vascular injuries occur at the time of entry using either a Veress needle or primary trocar.
  - The RCOG Green-top Guideline recommends open entry or use of Palmer's point in women with a low body mass index to reduce the risk of posterior abdominal wall vascular injury
  - Abdominal pressure:
    - The RCOG recommends an alternative method of entry, either open Hasson or Palmer's point, after 2 unsuccessful attempts to insert the Veress needle via the umbilicus.
    - High abdominal pressures should only be used during initial entry before reducing the pressure to 10–15 mmHg.
  - Previous surgery:

    Previous surgery is a risk factor for complications in further laparoscopy. Periumbilical adhesions are present in 52% with previous midline laparotomy.

**Safe abdominal entry techniques**

- Use the entry technique with which you are most familiar
- Avoid previous scars when choosing the entry point
- Make an adequate skin incision to avoid the need for the use of excessive pressure to pass the trocar through the skin
- If using the Veress needle, insert it vertically and stop insertion as soon as the peritoneum is penetrated
- Consider insertion of Veress and primary trocar with the woman in a supine rather than Trendelenburg position
- Increase the pneumoperitoneum pressure to at least 20 mmHg before inserting trocars
- Consider open technique or Palmer's point entry in women with a low body mass index or previous surgery

- **Instruments:**
  Unintended electrosurgical arcs can occur from monopolar instruments or thermal injury from excessive use of energy devices.

- **Camera angle:**
  Surgeons and their assistants should be encouraged to keep the camera tilt as close to zero.

## Management

**Signs of vascular injury during laparoscopy**

- Retroperitoneal haematoma (stable or enlarging in size) may be seen superior to the sacral promontory area
- Active bleeding coming directly from the major vessels
- Free blood in the abdominal cavity
- Haemodynamic instability

- **Anterior abdominal wall vascular injury:**
  - The most common vascular injury overall is laceration of the inferior epigastric artery during placement of lateral trocars in the lower abdomen.
  - Bleeding may present immediately or delayed after 2-3 days in the form of abdominal wall hematomas causing pain, abdominal wall or flank ecchymosis.
  - Techniques to control immediate bleeding:
    ① Electrosurgery to coagulate the bleeding point.
    ② A Foley catheter may be inserted through the port site, and the balloon inflated in the peritoneal cavity. The balloon can then be pulled up against the bleeding point with a resultant tamponade effect.
    ③ The lacerated inferior epigastric vessels can be sutured using an Endo CloseTM suture, a straight needle or intracorporeal suturing.
    ④ Conservative management should be done if the woman has an abdominal wall haematoma but is hemodynamically stable.

⑤ Percutaneous embolisation of the bleeding vessel can be undertaken if interventional radiology is readily available.

⑥ Conversion to open surgery may be considered for rapidly expanding haematomas or haemodynamically unstable patients.

- **Posterior abdominal wall vessel injury:**

Injuries to the posterior abdominal wall vessels are potentially life-threatening vascular injuries. When the patient is haemodynamically compromised and a major vascular injury is suspected or diagnosed, then immediate conversion to midline laparotomy is advised.

- **Immediate action following a major vascular injury:**

① Declare a major vascular emergency:

All team members must realise this is a potentially life-threatening emergency.

② Arrest the bleeding with direct pressure:

- Major vascular injury usually requires a midline laparotomy; and laparoscopy depends on the operator experience.
- A multidisciplinary team approach is advocated, seeking senior surgical help (vascular or general surgery input).
- Leaving the trocar that caused the injury in place rather than removing it will limit blood loss while preparations can be made.
- If vascular injury below the bifurcation of the aorta is suspected but not visible clearly and laparotomy is considered, direct pressure on the vessel using laparoscopic instruments.
- External pressure on the aorta just underneath the xiphisternum may decrease further blood loss.

③ Communicate effectively with the team:

Anaesthetist colleagues may delegate a member of the team to communicate with the switchboard and blood bank to announce the major haemorrhage protocol to obtain high priority blood products.

④ Resuscitate and continue fluid resuscitation:

The anaesthetic team secures sufficient peripheral access to give fluids/emergency medication. An indwelling catheter inserted to assist with fluid balance management.

⑤ Monitor and investigate:

- More invasive monitoring in the form of arterial/central lines.

- Blood can be taken for urgent full blood count, urea and electrolytes, liver function tests, coagulation screen and crossmatch samples.

⑥ Other considerations:

- Closing theatre doors helps to keep the environment relatively relaxing.
- keep on top of swab counts and empty clinical bins.
- Theatre staff can obtain more appropriate equipment such as laparotomy/vascular sets.
- Inform and update the woman's partner or family members

⑦ Risk management:

- A team member needs to scribe all that is occurring in time sequence.
- An incident form will need to be completed once the medical emergency ended.
- Retrospective documentation from all staff members is extremely useful

## Postoperative care

- **Immediate postoperative period:**
  - Fluid balance and haemodynamic stability must be closely monitored in an intensive care unit/high dependency unit.
  - Antibiotics may be required if there is evidence of infection or as prophylaxis.
  - The risk of venous thromboembolism should be assessed and consideration given for the need for thromboprophylaxis mechanical initially.

- **Later postoperative care:**
  - A thorough debrief with the woman and her family to explain the complications.
  - In the case of major vessel injury in women of reproductive age, advice to avoid pregnancy for several months to allow successful healing before the haemodynamic challenge of pregnancy.

# Nerve Injuries in Gynaecologic Surgery

## Mechanism of injury

| Type of injury | Example |
|---|---|
| **Compression and stretch injuries** | • Improper placement of self-retaining retractors e.g. Balfour retractors, prolonged positioning in stirrups |
| **Transection injuries** | Incorrectly sited surgical incisions:<br>• Pfannenstiel and low transverse incisions extending beyond the lateral margin of the inferior rectus abdominus muscle can cause injury to lateral cutaneous branches of iliohypogastric and ilioinguinal nerves. The risk is highest if the incision is below anterior superior iliac spine (ASIS) and 5 cm superior to pubic symphysis |
| **Entrapment nerve injuries** | • This most commonly occurs with pelvic floor reconstruction surgery<br>• Risk of chronic nerve-related pain with Pfannenstiel incisions (7%) due to entrapment of ilioinguinal and iliohypogastric nerves |

## Lumbosacral injury

| Nerve | Anatomy | Cause of injury | Presentation |
|---|---|---|---|
| **Femoral nerve** | • L2-L4 (It passes infero-laterally through psoas muscle and emerges from its lateral border. It exits the pelvis beneath | • The most common cause is abdominal hysterectomy (compression of nerve against the pelvic sidewall as it emerges | • It is the most common gynaecological associated neuropathy (11%) |

| | | | |
|---|---|---|---|
| | the inguinal ligament, lateral to femoral vessels) | from lateral border of psoas by excessively deep retractor blades:<br>▪ Incidence of nerve injury with self-retaining retractor is 8% (versus < 1% if not used)<br>• Inappropriate positioning: hyperflexion, abduction, and external rotation of hip result in kinking of the femoral nerve under the inguinal ligament | • It results in loss of sensation over the anterior and medial thigh and medial calf<br>• Hip flexion, adduction, and knee extension are affected<br>• Inability to climb stairs is a characteristic feature |
| **Ilioinguinal and iliohypogastric nerves** | • They originate from T12-L1; both are sensory<br>▪ Iliohypogastric nerve pierces external oblique aponeurosis above superficial inguinal ring, ilioinguinal nerve emerges through it | ▪ Injury is caused by suture entrapment at lateral borders of low transverse or Pfannenstiel incisions.<br>▪ Incidence of nerve injury following Pfannenstiel incision is 3.7% | • Ilioinguinal nerve: loss of sensation over mons, lateral labia, and upper inner thigh<br>• Iliohypogastric nerve: loss of sensation |
| **Genitofemoral nerve** | • It originates from L1–L2<br>▪ It traverses the anterior surface of psoas and lies immediately lateral to external iliac vessels | The most common cause of injury is pelvic side wall surgery and during removal of the external iliac lymph nodes | Loss of sensation over the labia and femoral triangle |

| | | | |
|---|---|---|---|
| | ▪ It divides into a genital branch, which enters deep inguinal ring, and a femoral branch, which passes deep to the inguinal ligament within femoral sheath | | |
| **Lateral cutaneous nerve of the thigh** | ▪ It originates from L2–L3<br>▪ It emerges from lateral border of psoas → crosses iliac fossa anterior to iliacus → enters thigh posterior to lateral end of inguinal ligament | During pelvic surgery (similar to causes of femoral nerve injury) | Loss of sensation over anterior and posterolateral thigh |
| **Obturator nerve** | ▪ It originates from the anterior branches of L2-L4<br>▪ Nerve converges behind the psoas muscle then passes over pelvic brim anterior to sacroiliac joint and posterior to common iliac vessels to enter the thigh via obturator foramen | ▪ Retroperitoneal surgery<br>▪ Excision of endometriosis<br>▪ Passage of a trocar through obturator foramen<br>▪ Insertion of trans-obturator tapes<br>▪ During paravaginal defect repairs | ▪ Loss of sensation over upper medial thigh<br>▪ Loss of thigh adduction (minor ambulatory issues) |
| **Sciatic and common** | ▪ It originates from L4 to S3 | ▪ The most common site of injury for sciatic | ▪ Loss of sensation below the knee |

| | | | |
|---|---|---|---|
| **peroneal nerves** | ▪ It emerges from the pelvis below piriformis muscle, curving laterally and downward through the gluteal region<br>▪ Common peroneal nerve and tibial nerve emerge at mid-thigh<br>▪ Common peroneal nerve curves anteriorly around neck of the fibula | nerve is the sciatic notch<br>▪ The most common site of injury for peroneal nerves is the lateral aspect of fibular neck<br>▪ The most common cause of injury is improper lithotomy positioning with hyperflexion of thighs<br>▪ Common peroneal nerve may be compressed at the fibular neck in lithotomy position | except the medial foot<br>▪ Loss of hip extension and knee flexion |
| **Pudendal nerve** | ▪ It originates from S2 to S4<br>▪ It exits the pelvis through the greater sciatic foramen below the piriformis<br>▪ It runs behind lateral third of sacrospinous ligament and ischial spine alongside internal pudendal artery and immediately re-enters the pelvis through lesser sciatic foramen to pudendal canal (Alcock's canal) | The most common cause is entrapment injuries during sacrospinous ligament fixation (the nerve runs behind lateral aspect of sacrospinous ligament) | ▪ Loss of sensation over the perineum<br>▪ Nerve entrapment causes postoperative gluteal, perineal and vulval pain, it worsens in the seated position if the nerve is damaged |

## Brachial plexus injury

- **Anatomy:**
  - The brachial plexus originates from nerve roots C5–T1
  - It supplies the upper limb and lies within the posterior triangle of the neck

- **Causes of brachial plexus injuries:**

  Stretch injury is the most common cause of brachial plexus injury

| Nerve or root | Cause of injury | Clinical features |
|---|---|---|
| **Upper root of brachial plexus (C5-6)** | Hyperabduction of the arm e.g.<br>▪ When arm boards are extended beyond 90 degrees from the long axis of operating table<br>▪ When an arm unintentionally falls from the arm board | ▪ Erb's palsy or 'waiter's tip' deformity<br>▪ It consists of loss of shoulder abduction, loss of flexion of the elbow and supination |
| **Lower root of brachial plexus (C8–T1)** | Lower roots may be stretched if shoulder braces are used during laparoscopic surgery (to support in steep Trendelenburg position) | ▪ Klumpke's palsy (claw hand)<br>▪ Loss of sensation over medial arm, forearm and medial 2 fingers |
| **Radial nerve (C5-T1)** | Pressure on the humerus during arm positioning may cause radial nerve compression (radial nerve winds around a spiral groove on the back of the humerus) | ▪ Loss of wrist and finger extension<br>▪ Loss of sensation over the dorsal tips and lateral 3 and half fingers |
| **Ulnar nerve (C8-T1)** | ▪ Undue pressure over the medial aspect of elbow during arm board positioning causes ulnar nerve compression around the medial epicondyle (ulnar nerve enters the forearm posterior to medial epicondyle of humerus) | ▪ Claw hand<br>▪ Loss of sensation over the medial 1 and half fingers |

## Diagnosis of nerve injuries

- Diagnosis is made by neurological examination and electromyography (EMG)
  If neuropathy is diagnosed, refer to a neurologist
- EMG should be performed 3–4 weeks after suspicion of nerve damage (denervation of afflicted muscle)

## Treatment of nerve injuries

- **Conservative management:**
  Most neuropathies will resolve spontaneously with minimal intervention
  - Sensory neuropathies resolve within 5 days
  - Motor deficits may take up to 10 weeks
  - Occasionally neuropathies may persist beyond 1 year
- **Painful neuropathy:**
  - It often responds to medications e.g. tricyclic anti-depressants and GABA antagonists
  - Failure to resolve is rare after 6 months. In persistent cases, local nerve blockade or even surgical nerve excision or decompression can be considered
- **Motor impairment:**
  Physiotherapy should be considered to manage motor impairment, secondary to retraction or stretching
- **Nerve repair:**
  Failure to resolve e.g. complete nerve transection may require specialist repair e.g. microsurgical techniques (e.g. repair of transected obturator nerve has an excellent prognosis)

## Prevention of nerve injuries

- **Identification of women at higher risk:**
  - Thin body habitus
  - Ill-developed abdominal wall muscles
  - Narrow pelvis
  - Surgery > 4 hours
  - Surgery > 2 hours in lithotomy position

- **Avoidance of nerve compression by self-retractor blades:**

  The following interventions may reduce risk:

  - After positioning the retractors, ensure visually and by direct palpation that psoas muscle is not entrapped between the blade and the pelvic side wall
  - Use the shallowest retractor blade sufficient to provide adequate exposure (degree of nerve injury is proportional to blade length)
  - Use rolled up laparotomy pads to cushion retractor blades against pelvic side wall
  - Retractor blade position should be monitored intermittently and re-adjusted accordingly
  - Hand-held retractors should be selected over self-retaining wherever possible
- **Correct preoperative positioning:**
  - Correct preoperative positioning in lithotomy stirrups, so hip and knee are moderately flexed, hip minimally abducted and externally rotated. Stirrups or boots should be at equal height
  - Excessive movement around the hip joint should be avoided since they may result in stretch and/or compression of the sciatic and femoral nerves.
  - Common peroneal nerve injury can be avoided by placing paddings between the lateral fibular heads and the stirrup
  - Shoulder braces, if used, should be positioned over the acromio-clavicular joint to prevent brachial plexus injury
  - Upper arm should be pronated, and padding should be adequately draped over the postero-medial elbow. This prevents ulnar nerve compression against the operating table
  - Arm boards should be placed at an angle not more than 90 degrees from the long axis of the table
- **Proper abdominal incision:**
  - Extending abdominal incision beyond the lateral margins of the rectus muscles should be avoided (to avoid ilioinguinal and iliohypogastric nerve injury)
  - If a wide incision is necessary, it should be curved upward to avoid nerve course
  - During fascial closure of low abdominal incisions, care must be taken not to incorporate tissue more than 1.5 cm away from the fascial edge

# Uterine Perforation

## Incidence

| | |
|---|---|
| **General incidence** | • 0.002% - 1.7% |
| **Hysteroscopy** | • 1.6% (general incidence)<br>• Division of intrauterine adhesions: 0.8-1.8%.<br>• Hysteroscopy for postmenopausal bleeding: 0.2-2%. |
| **Intrauterine device placement** | • 0.1%<br>• 15% of cases are associated with abdominal/pelvic viscera injury<br>• 3-7.5% are associated with bowel injury |
| **Termination of pregnancy** | • 0.5% (elective termination of pregnancy)<br>• 9% of cases end in hysterectomy |

**Most common location**

- Anterior wall (40%)
- Cervical canal (36%)
- Fundus - the least common (13%)

**Most common instrument**

- Suction cannula (50%)
- Hegar dilator (25%)

**Most serious location**

Perforation of the internal os and lower uterus (vs. uterine body) because it is often lateral, and therefore, it may involve uterine vessels

## Risk factors

- **High risk surgery:**
  - Most common procedures are surgical termination of pregnancy (TOP) and evacuation of retained products of conception (ERPC)
  - Risk is doubled in 2nd trimester compared to 1st trimester
  - Postpartum evacuation of ERPC in women with postpartum haemorrhage is associated with 5% risk of perforation
- **Uterine characteristics:**
  - Tight cervix
  - Postmenopausal uterus
  - Acute anteversion, retroversion or retroflexion
  - Parous uterus
- **Uterine abnormalities:**
  - Infection & pyometra.
  - Intrauterine adhesions.
  - Uterine anomalies.
- **High risk surgeons:**

  There is 5-fold increase in risk of perforation when the procedure is conducted by junior staff

## Diagnosis

- Passage of an instrument beyond anticipated length of the uterus
- Loss of resistance to instrumentation passage
- Sudden loss of vision due to sudden loss of fluid during hysteroscopy
- Noticeable bleeding
- Collapse

## Prevention

### Preoperative measures

- Medical rather than surgical termination of pregnancy in 2nd trimester, whenever possible
- Bimanual examination prior to surgery
- Experienced surgeon
- Cervical preparation with prostaglandins or misoprostol (not beneficial in postmenopausal): consider oral or vaginal cervical preparation prior to procedure

### Intraoperative measures

- Adequate and gradual cervical dilation, use half sized dilators, avoid excessive force.
- Use of Hawkins-Ambler dilators (less force than Hager dilators)
- Ultrasound or laparoscopic guidance

## Management

If perforation is caused by a dilator up to 5 mm, a curette, coil insertion or polyp forceps

- Conservative management
  - Admission
  - Administration of IV antibiotics
  - Close observation for 24 hours. This includes observation of vital signs and bowel sounds
  - Patients can be dismissed home if they remain asymptomatic after 24 hours

* Bowel sounds may be initially present as peritonitis may take days to develop

If perforation is caused by larger instruments, tissues grasped, avulsion attempted, or bleeding is present **OR** If perforation occurs while using laser or activated resection loop or during TOP or ERPC

- Laparoscopy
  - Small perforation with slight bleeding
    - No further action is needed. Cauterization may be used to control small bleeders
    - The procedure can be completed under laparoscopic visualization
  - Large perforation
    - A large perforation may be sutured via laparoscopy, an experienced surgeon may be called to perform the procedure. Laparotomy may be done if an experienced colleague is not available
  - Active bleeding or large hematoma
    - Perform laparotomy
    - Assistance from a urologist or a general surgeon may be needed
    - Hysterectomy: may be performed in a few cases. However, most hysterectomy cases are associated with delayed diagnosis

## Gynecologic surgery

### Abstract

Surgery is a major part of obstetrics and gynaecology practice, and surgical skills are mandatory in all subspecialties including oncology, urogynecology, infertility, obstetrics, and fetal medicine. In addition to practical training, principles of surgery, surgical complications, and postoperative care should be clearly understood. In this chapter, we will discuss general principles of surgery, postoperative care and will cover common surgical complications, their diagnosis, and how to manage these complications.

### Keywords

Hysterectomy, laparoscopy, hysteroscopy, postoperative complications

### Further readings

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# Audit

## Audit prospective

- Audit is an inspection approach, held by the medical organization, to assess and improve outcomes
- What can be audited:
  - A structure or service provision (e.g. multi-disciplinary team vs. individual care)
  - A Process (clinical practice that has been evaluated in research):
    Compared to outcome measure, it is achieved by smaller audit, with less cost, it is easier to interpret, and can directly measure quality of care
  - An outcome: e.g. adverse effects, patient conditions

### Limitations of outcome audit

- Not direct measurement of provided outcomes
- Not all patients receiving substandard care will have poor outcomes
- many factors contribute to eventual outcome
- outcomes may be delayed
- Larger sample size may be needed

## Audit cycle

- **Selection of the topic:**
  It should be common issue, associated with high rate of morbidity and mortality or disability




S. A. Shazly, N. Eltaweel (eds.), *MRCOG Part 2*, https://doi.org/10.1007/978-3-030-78048-7_26

- **Identification of appropriate standard:**
  - Review criteria: They are statements to assess specific healthcare decisions.

    Review criteria should:
    - Be measurable
    - Related to important aspects of care
    - Lead to valid judgment (based on research evidence)
  - Standard and target level of performance:

    It refers to the percentage of events that fulfill the criterion
  - Benchmarking:

    It means setting a level of care as a goal to be attended (insufficient evidence this step is necessary)

- **Data collection to assess performance:**
  - Data should be collected so it can answer an audit question
  - Data collectors should follow Data protection act
  - Caldicott nationally agreed principles include:
    - Justify the purpose
    - Do not use patient-identifiable information (unless extremely necessary)
    - If patient-identifiable information needed, use the minimal necessary amount
    - patient-identifiable information collection should be limited to personnel who are required to access these data
    - Both clinical and non-clinical staff should be aware of their responsibilities
    - Someone in each organization should ensure it complies with legal requirements
  - Data collection may be through routinely collected data, clinical records, or from direct observation or questionnaire
  - Data collector may be the PI (if it is small) or care providers (e.g. midwives, obstetricians) if large
  - Data management: using excel, access or Epi info
  - Data analysis

- **Implementation of changes to improve care if necessary:**

  Change does not necessary takes place and causes of failure may be just considered

## Failure of audit

Common causes include:

- Failure to participate
- Attitudes to audit
- Failure to continue or complete audit cycle
- Failure to provide supportive environment
- Lack of resources (e.g. time, lack of training, and cost)

# Consents and Ethics

## Terms

When counselling a patient about surgery and complications, it is important to discuss not only what complications may occur, but also how common these complications are. Terms used to describe incidence are:

- Very common (1:1-1:10): Like a person in a family
- Common (1:10 – 1:100): like a person in a street
- Uncommon (1:100 – 1:1000): like a person in a village
- Rare: (1:1000 – 1:10000): like a person in a small town
- Very rare (< 1:10000): Like a person in a large town

## Consent items

A consent form should cover the following items:

- **Name of the procedure:**
  The name of procedure should be detailed e.g. subtotal abdominal hysterectomy with preservation of the ovaries
- **The nature of the procedure:**
  The nature of the procedure should be discussed with the patient. For example, hysterectomy involves removal of the uterus which will turn her infertile. The cervix will be left for technical causes which means that she should continue to undergo cervical screening. Similarly, removing or leaving the ovaries in situ should be discussed including reasons and sequences of surgical management of the ovaries

- **Benefits:**
  Anticipated positive outcomes of surgery and their likelihood should be discussed with the patient. For example, abdominal hysterectomy should treat heavy menstrual bleeding. However, pain, particularly non-cyclic pelvic pain, may not improve

- **Risks:**
  Patients should be counselled about risks associated with surgery and their likelihood. This includes less common, but serious risks and more common risks. Some factors e.g. obesity may increase incidence of these risks

- **Additional procedures:**
  If there is a considerable probability of an additional intraoperative procedure, it should be discussed in priori and a consent should be obtained. Examples include blood transfusion and repair of unintentional injuries. If an ovarian pathology is unexpectedly found intraoperatively, oophorectomy should not be performed without consent. Therefore, this probability should be discussed and documented

- **Alternatives:**
  Other alternatives to surgery, including no treatment, should be discussed and their advantages and disadvantages should be explained

- **Anaesthesia:**
  Women should discuss type of anaesthesia with the anaesthetist before surgery

## Surgical risks

It is important to discuss the risks of each surgery and their incidence with the patient

- **Abdominal hysterectomy:**

| Serious risks | Incidence |
|---|---|
| Overall risk of serious complications | 4:100 (common) |
| Bladder and/or ureter injury – Disturbance of bladder function | 7:1000 (uncommon) |
| Bowel injury | 4:10000 (rare) |
| Haemorrhage requiring blood transfusion | 23:1000 (common) |

| | |
|---|---|
| Return to the theatre | 7:1000 (uncommon) |
| Pelvic abscess/infection | 2:1000 (uncommon) |
| Venous thrombosis or pulmonary embolism | 4:1000 (uncommon) |
| Death within 6 weeks | 32:100000 (rare) |

Frequent risks include wound infection, incisional pain, delayed wound healing or keloid formation, paresthesias, and urinary tract infection

- **Amniocentesis:**

| Serious risks | Incidence |
|---|---|
| Failure to obtain a sample of amniotic fluid | 6% in the first attempt |
| blood stained samples | 0.8% |
| Miscarriage | 1% |
| Foetal injury | Rare (case reports) |
| Maternal bowel injury | Rare |
| Amniotic fluid leakage (temporary or prolonged) and preterm labour | < 1% |
| Chorioamnionitis, severe sepsis | 1:1000 |
| Failure of cell culture | 0.5% - 10% |

Frequent risks include mild discomfort at needle insertion site

- **Caesarean section:**

| Serious risks | Incidence |
|---|---|
| Emergency hysterectomy | 8:1000 (uncommon) |
| Need for delayed surgery e.g. curettage | 5:1000 (uncommon) |
| Admission to intensive care unit | 9:1000 (uncommon) |
| Thromboembolic disease | 4-16:10000 (rare) |
| Bladder injury | 1:1000 (rare) |
| Ureteric injury | 3:10000 (rare) |
| Death | 1:12000 (very rare) |
| Future rupture uterus (in subsequent pregnancies) | 2-7:1000 (uncommon) |

| | |
|---|---|
| Antepartum stillbirth (in subsequent pregnancies) | 1-4:1000 (uncommon) |
| Placenta praevia and accreta (in subsequent pregnancies) | 4-8:1000 (uncommon) |

| Frequent risks | Incidence |
|---|---|
| Persistent abdominal/incision discomfort | 9% |
| Repeat caesarean section (in subsequent pregnancies) | 25% |
| Readmission to hospital | 5% |
| Haemorrhage | 0.5% (uncommon) |
| Infection | 6% |
| Foetal laceration | 1-2% |

- **Caesarean section for placenta praevia:**

| Serious risks | Incidence |
|---|---|
| Emergency hysterectomy | 11% (very common) in all women with praevia, 27% in women with praevia and previous caesarean section |
| Need for laparotomy following caesarean section | 7.5% (common) |
| Thromboembolic disease | 3% (common) |
| Bladder or ureteric injury | 6% (common) |
| Future placenta praevia | 2.3% (common) |
| Massive obstetric haemorrhage | 21% very common) |

Frequent risks include maternal admission to intensive care, infection, blood transfusion, admission to neonatal intensive care

- **Diagnostic hysteroscopy:**

| Serious risks | Incidence |
|---|---|
| Overall risk | 2:1000 (uncommon) |
| Uterine injury | Uncommon |
| Bowel, bladder, or vascular injury | Rare |
| Failure of initiation or completion of the procedure | Uncommon |

| | |
|---|---|
| Infertility | Rare |
| Death | 3-8:100000 (very rare) |

Frequent risks include infection and bleeding

- **Diagnostic laparoscopy:**

| Serious risks | Incidence |
|---|---|
| Overall risk (15% of bowel injuries are missed intraoperatively) | 2:1000 (uncommon) |
| Laparotomy | Uncommon |
| Portal site hernia | < 1:100 (uncommon) |
| Death | 3-8:100000 (very rare) |

Frequent risks are infection, bruising, shoulder pain, and wound gaps

- **Female sterilisation:**

| Serious risks | Incidence |
|---|---|
| Failure and unplanned conception | 2-5:1000 with clips (uncommon)<br>2:1000 with hysteroscopic sterilisation (uncommon)<br>This incidence may be higher than effective long acting reversible contraception |
| Visceral or vascular injury | 2:1000 (uncommon) |
| Death | 1:12000 (very rare) |
| Regret | Common (more common in women younger than 30, has no children, or if it is performed at the time of abortion) |

Frequent risks include changes in menstruation secondary to cessation of hormonal contraception but not female sterilisation itself

- **Morcellation at myomectomy or hysterectomy:**

| Serious risks | Incidence |
|---|---|
| Unintended morcellation of undiagnosed uterine sarcoma | • In premenopausal women (<50 years):<br>▪ General risk associated with hysterectomy or myomectomy is 1:1250<br>▪ Risk associated with uterine fibroids is approximately 1: 800 (women with uterine fibroids)<br>• In menopausal women:<br>▪ The risk is 6:1000<br>▪ Risk is 7.5-15.5:1000 above the age of 60<br>▪ The peak age of uterine sarcoma is 50 to 55 years |
| Worsening the prognosis of an existing sarcoma | Age-adjusted 10-year survival rate of women with uterine sarcoma is 32% with morcellation compared to 57% without morcellation |
| Disseminated fibroids (presence of benign fibroids within the abdominal and pelvic cavity) | The risk ranges from 1:120 (uncommon) to 1:1200 (rare) |

- **Operative vaginal delivery:**

| Serious risks | Incidence |
|---|---|
| Third- and fourth-degree perineal tear | 1-4:1000 with vacuum (common), 8-12:1000 with forceps (very common) |
| Significant vaginal or vulval tears (vaginal tear/abrasions are very common) | 10% with vacuum, 20% with forceps |
| Subgaleal haematoma | 3–6:1000 (uncommon) |
| Intracranial haemorrhage | 5–15:10000 (uncommon) |
| Facial nerve palsy | Rare |

| Frequent risks | Incidence |
|---|---|
| Postpartum haemorrhage | 10-40% (very common) |
| Forceps marks on baby's face or chignon | Very common |

| | |
|---|---|
| (vacuum cup marking) on the scalp | |
| Cephalhaematoma | 1–12:100 (common) |
| Facial or scalp lacerations | 10% (common) |
| Neonatal jaundice/hyperbilirubinaemia | 5-15% (common) |
| Retinal haemorrhage | 17-38% (very common) |
| Episiotomy | 50-60% with vacuum, 90% with forceps |

- **Repair of third and fourth-degree perineal tears:**

| Serious risks | Incidence |
|---|---|
| Stool and/or flatus incontinence | Common |
| Persistence of incontinence symptoms or abnormal sphincter structure requiring caesarean section in future pregnancies | Uncommon |
| Haematoma | Rare |
| Failure of repair with subsequent interventions e.g. secondary repair | Rare |
| Rectovaginal fistula | Very rare |

| Frequent risks | Incidence |
|---|---|
| Faecal urgency | 26% (very common) |
| Perineal pain and dyspareunia | 9% (common) |
| Wound infection | 8% (common) |

Other frequent risks include postpartum difficulty and discomfort in passing stools, suture migration and urinary infection

- **Vaginal prolapse surgery:**

| Serious risks | Incidence |
|---|---|
| Bladder/urinary tract injury | 2:1000 (uncommon) |
| Bowel injury | 5:1000 (uncommon) |
| Haemorrhage that indicates transfusion or reoperation | 2% (common) |
| Pelvic abscess | 3:1000 (uncommon) |
| Bladder dysfunction (new or persistent) | Variable |

| | |
|---|---|
| Venous thrombosis | Common |
| Pulmonary embolism | Uncommon |
| Death | 37:100000 (rare) |

Frequent risks include urinary tract infection or urinary symptoms, vaginal bleeding, pain, or wound infection

- **Surgical removal of products of conception:**

| Serious risks | Incidence |
|---|---|
| Uterine perforation | 1:1000 (uncommon) |
| Cervical trauma | < 1:1000 (uncommon) |
| Preterm labour in future pregnancies | Odds ratio 1.29 |

| Frequent risks | Incidence |
|---|---|
| Bleeding for up to 2 weeks (longer bleeding requires investigations) | Common |
| Heavy bleeding requiring blood transfusion | Up to 3:1000 (uncommon) |
| Localised pelvic infection | 4% (common) |
| Retained products of conception | 4% (common) |
| Repeat surgery for retained products of conception | 3:1000 (uncommon) to18:1000 (common) |
| Intrauterine adhesions after early pregnancy loss | 19% with any management, 17.5% after surgical evacuation |

# Medical Education

## Types of assessment

| | |
|---|---|
| **Formative assessment** | • Formal and informal assessment procedures<br>• It is conducted by the educator during the learning process<br>• The aim of this tool is to provide feedback that modifies teaching and learning activities in the future<br>• The feedback is qualitative (not quantitative) |
| **Summative assessment** | • This typically assess outcomes of a learning process<br>• An example is final exams and royal college membership exams<br>• Commonly described as high stakes |
| **Norm Referenced test** | • It is conducted to compare and rank examinees (relative to each other)<br>• Results of this test determine how the examinees performed compared to a hypothetical average student based on sample data |
| **Criterion-referenced tests** | • Performance of the examinees is compared to an expected criterion regardless of performance of other examinees<br>• This includes exams that have an assigned pass mark before the exam is taken |
| **Equating** | • This procedure includes adjustment of test scores. Thereby, examinees of 2 or more forms of a test become comparable<br>• For example, comparing results of MRCOG part 2 exams at 2 different dates, so that the pass score corresponds to the same percentile in both exams e.g. 61% corresponds to the 50$^{th}$ percentile in one exam, and 67% corresponds to the 50$^{th}$ percentile in the second exam |

## Methods of learning

| | |
|---|---|
| **Reflection** | • This learning approach uses the actions and outcomes of a particular event as a method of learning<br>• Thereby, reasons of the events, and positive and negative aspects driven from analysis of the event are the method of learning. Knowledge can be applied in future situations |
| **Vicarious Learning** | • A method of learning that is derived from hearing or observation<br>• This is an indirect method of learning that does not involve direct teaching |
| **Transformative learning** | • This method includes learning from critical reflection to improve attitude and perspective |
| **Experiential learning** | • It is an active learning process that refers to learning from personal experience<br>• Unlike didactic learning where the role of the learner is passive, experiential learning is associated with active participation by the learner |
| **Appraisal** | • This process involves several tools to provide evaluation on past achievement<br>• It should involve assignment of future goals and plans to achieve these goals |

# Medical Statistics

## Diagnostic tests

Diagnostic test characteristics are important to determine diagnostic test performance

| Group | Disease Present | Disease Absent |
|---|---|---|
| Test positive | a | b |
| Test negative | b | d |

- **Sensitivity:**
  - It refers to the ability of the test to correctly identify diseased patients
  - Sensitivity = a / (a + c)

- **Specificity:**
  - It refers to the ability of the test to correctly diagnose those without the disease
  - Specificity = d/ (b + d)

- **Positive predictive value (PPV):**
  - It refers to how likely is it that this patient has the disease if the test result is positive
  - PPV = a / (a + b)

- **Negative predictive value (NPV):**
  - It refers to how likely is it that this patient does not have the disease if the test result is negative
  - NPV = d / (c + d)

- **Likelihood ratio (LR):**
  - It refers to how much more likely is it that a patient who tests positive is diseased compared with those who test negative
  - Positive LR = sensitivity / (100 – specificity)
  - Negative LR = (100 – sensitivity) / specificity

## Risks

- **Relative Risk or risk ratio (RR):**
  - Relative risk (RR) is the ratio of risk in an exposed group to a non-exposed group

| Group | Disease Present | Disease Absent |
|---|---|---|
| Exposed | a | b |
| Control | b | d |

  - It can be calculated by RR = [a / (a + b)] / [c / (c + d)]
  - A relative risk of 1 means there is no difference in risk between control and exposed groups.

- **Absolute risk (incidence or prevalence rate):**
  - Absolute risk is the probability of developing a disease over time
  - Absolute risk reduction or risk difference is the difference between an exposed group disease rate and a control/unexposed groups event rate.

- **Odds Ratio (OR):**
  - It is the relative risk among the exposure group of a study relative to the control group
  - It is calculated by (OR) = [a / b] / [c / d]

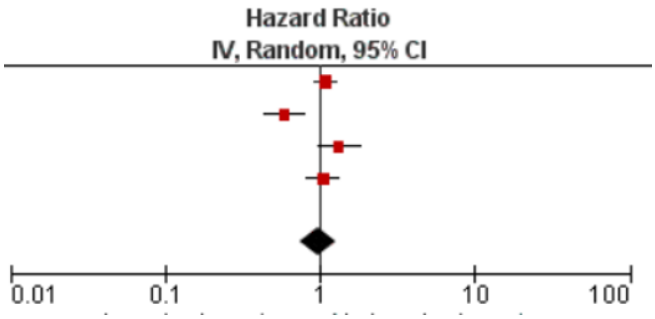
- **Attributable risk (AR):**
  - AR is the difference in rate of a disease between an exposed and an unexposed population
  - It is calculated in the same was as absolute risk reduction (ARR)

## Numbers Needed to Treat (NNT)

- NNT measures the number of patients who need to be treated to prevent one case with adverse outcomes
- NNT = 1 / (EER - CER)
  EER = experimental event rate (incidence in group receiving treatment)
  CER = control event rate (incidence measured outcome in control)

## Meta-analysis assessment

- Interpretation of meta-analysis is achieved by reading the 'forest plot'. The forest plot consists of a range of effect for each study and a 'diamond' that pools effect size of all these studies. It is important to be able to read this diamond to interpret results
- If assessment involves odds or hazard ratios, a diamond that crosses the value 1 means that there is no difference in outcome between cases and controls. If it assessment involves mean difference, a diamond that crosses the value '0' means that there is no difference between cases and controls




- The width of the diamond indicates the range of confidence interval

## Abstract

Medical knowledge and surgical skills are the cornerstones of clinical excellence. Nevertheless, proficiency of clinical practice cannot be achieved without obtaining a satisfactory background on research, medical education, quality improvement, and ethics. In this chapter, we will cover the

essence of medical audit, consent and ethics, medical education, and basic statistical knowledge as recommended by the royal college of obstetricians and gynaecologists

## Keywords

Medical education, statistics, research, audit, quality improvement

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