University Hospitals Sussex
NHS Foundation Trust

Medical Disorders

Maternity Protocol: MP028

Date agreed: March 2022

Guideline Reviewer:	Abirami Kalaparan
Version:	2
Approval Committee:	Women's Services Safety and Quality Committee
Date agreed:	March 2022
Review date:	March 2025

Contents

Cardiac Disease in Pregnancy

1.0 Background

Cardiac disease remains the largest single cause of indirect maternal deaths in the UK (MBRRACE report 2020 showed that 23% of maternal deaths were due to cardiac disease). Most cardiac morbidity and mortality are due to acquired heart disease (e.g. ischaemic heart disease, cardiomyopathy) and sudden adult death syndrome rather than congenital heart disease. The main focus of this guideline is the care of women with pre-existing heart disease.

There are several physiological changes in pregnancy that place additional pressure on the hearts of woman / pregnant person with cardiac disease. These include:

Antepartum

- Systemic vasodilation: occurs early in pregnancy, starting by week 5 and reaching its maximum by the middle of the second trimester.
- Cardiac output: increases throughout pregnancy. By 24 weeks gestation the increase in cardiac output is around 40% above the non-pregnant state. This increase is 15% higher in a twin pregnancy.[vi]
- Heart rate: increases by 10-20 bpm by term, representing a 20-25% increase.
- Pulmonary vascular resistance: decreases.
- Left ventricular contractility: despite these haemodynamic changes, contractility and left ventricular ejection fraction do not appear to alter in pregnancy.

Intrapartum

- Cardiac output: maximum increase occurs during labour and immediately after delivery. This increased cardiac output reflects increased pre-load from uterine contractions due to an auto-transfusion of 300-500mls of blood from the uterus, increased catecholamine levels and increases in heart rate. [v] Pain and anxiety will also increase the maternal heart rate.

- With these changes in mind it is clear to see that woman with cardiovascular compromise are at highest risk of pulmonary oedema during the second stage of labour and immediately postpartum. The haemodynamic changes of pregnancy largely return to non-pregnant values by 2 weeks post-delivery.[vi]

2.0 Pre-pregnancy Assessment

2.1 Women/pregnant people with known congenital or acquired heart disease should be referred for pre-pregnancy review and counselling.

2.2 The European Society of Cardiology has recommended that maternal risk assessment be undertaken according to the modified World Health Organisation (WHO) classification (appendix 1. Other risk scoring tools exist, which incorporate clinical factors known to be predictive e.g. previous arrhythmia, heart failure and functional class (ref CARPEG & ZAHARA). However, it should be remembered that these risk scores are obtained from cohorts of women with structural and congenital heart disease and do not include other cardiac disease e.g. ischaemic heart disease or other co-morbidity.

2.3 Regardless of the cause of cardiac insufficiency, the ability of the heart to tolerate pregnancy will be related to

1. Presence of pulmonary hypertension
2. Haemodynamic significance of any lesion
3. Functional class (NYHA class – see appendix 2)
4. Presence of cyanosis

2.4 Other predicators of cardiac events in pregnant women with heart disease include:

1. History of transient ischaemic attack (TIA) or arrhythmia
2. History of heart failure
3. Left heart obstruction (mitral valve area <2 cm^2, aortic valve area <1.5cm^2, aortic valve gradient >30mmHg)
4. Myocardial dysfunction (left ejection fraction <40%)

2.5 If patients have a poor functional status pre-pregnancy (NYHA III –IV), then the outcome of pregnancy is likely to be poor regardless of the underlying pathology. However special consideration should be taken in women with:

1. Mitral stenosis (increased risk of pulmonary oedema)
2. Marfan syndrome and other aortopathies (risk of aortic dissection or rupture)
3. Pulmonary hypertension) risk of maternal death)

3.0 Antenatal Management

3.1 All women/ pregnant people with acquired or congenital cardiac disease listed in Table 1 (but not exhaustive) should be referred early in pregnancy to the Combined Cardiac Obstetric clinic [CCO). This is generally held on the first Thursday of each month in the antenatal clinic.

3.2 Referrals should be made by letter to Dr Rachael James (if urgent this can be done by email using Dr James' BSUH email account) and copied to the assistant admin manager Sharon Norris via her BSUH email account. Appointments are booked by Sharon Norris who also women written information about the clinic prior to the appointment.

3.3 A woman / pregnant person without documented heart disease who develops cardiac symptoms in pregnancy should be discussed with a consultant obstetrician. If further investigation is required, referral should be to Dr James and the woman will be seen in her general clinic.

Table 1: Conditions to be referred early to CCO

Conditions where early referral is indicated
• Ischaemic heart disease (previous MI, PCI)
• Native valve disease
• Heart valve replacement
• Cardiomyopathy (dilated cardiomyopathy, hypertrophic cardiomyopathy, previous peri-partum cardiomyopathy)
• Marfan syndrome, bicuspid valve aortopathy, type IV Ehlers Danlos (vascular)
• Treated cardiac arrhythmia (SVT, AF, VT)
• Congenital heart disease
• Pulmonary hypertension

3.4 In the Combined Cardiac Obstetric clinic women will be seen by a Consultant Cardiologist (Dr Rachael James), a Consultant Obstetrician, a Consultant Anaesthetist (Dr Vanessa Fludder) and a Senior Midwife.

3.5 All patients should have a named midwife.

3.6 If possible patients on Warfarin should be converted to LMWH as early as possible. If this is not possible (e.g. patients with metallic heart valves who are not felt to be suitable for treatment with LMWH) Warfarin should be changed to LMWH by 36 weeks at the latest or at least 5 days prior to planned delivery if earlier than 36weeks, due to risk of fetal intracranial haemorrhage.

3.7 The expectation for those women in WHO Class I and majority of Class II and II/III is for their antenatal care to be delivered at their local maternity unit.

3.8 Some women will require on-going surveillance in the CCO clinic at BSUH.

3.9 Women /pregnant people in class III and IV should receive their antenatal care at BSUH.

3.10 A minority of woman / pregnant people in class III and IV will require delivery in a specialist congenital cardiac centre or one with expertise in managing pulmonary hypertension.

3.11 Some women /pregnant people will be advised to deliver at RSCH where there is specialist cardiology provision 24 hours a day 7 days a week due to the nature of their cardiac lesion or condition.

4.0 Antenatal In-patient Care

4.1 All women / pregnant people with congenital heart disease (or if their partner has congenital heart disease) should be referred for a fetal echocardiogram at the Evelina Children's Hospital (St Thomas' hospital) in London.

4.2 If a woman is decompensating she should be admitted for close observation.

- Admission will usually be to the cardiology ward 6A.
- Admission should be in discussion with Dr James who will typically be the named consultant.
- Anaesthetic, obstetric and midwifery teams should review the woman daily.

4.3 Antenatal steroids should be discussed with Dr James (smaller divided doses maybe advised if the woman is at risk of fluid overload).

4.4 A Consultant Neonatologist should counsel the woman if delivery is planned prior to 34 weeks gestation.

4.5 VTE prophylaxis should be reviewed regularly.

4.6 Dose and timing of VTE prophylaxis in relation to planned IOL/operative delivery date should be considered (LMWH prophylaxis should not be given 12 hours prior to delivery and treatment dose not for at least 24 hours).

5.0 Labour and Delivery

5.1 A delivery plan should be made in the CCO clinic by 36 weeks. A copy of this should be kept in the patient's maternity notes and in the high-risk folder on labour ward.

5.2 Most women / pregnant people with cardiac disease are able to deliver vaginally.

5.3 Spontaneous labour is preferable. If induction of labour is necessary consideration as to the method of induction should be made in conjunction

with the CCO clinic, particularly if a drop in systemic vascular resistance may be detrimental which is a potential side effect of prostaglandins.

5.4 If a woman / pregnant person with cardiac disease have been advised by the CCO clinic to attend as soon as possible if she feels that she is in labour for an early epidural, then she MUST NOT is turned away.

5.5 As soon as a woman with cardiac disease is admitted to labour ward she should be brought to the attention of the obstetric registrar/consultant as well as the anaesthetic registrar/consultant.

5.6 Midwifery team, obstetric and anaesthetic teams should read the labour plan.

5.7 Specific consideration to use of fluids with regards to the risk of fluid overload, safety of bolused Oxytocin and use of Ergometrine and other uterotonics should be documented in the management plan made in the CCO clinic.

5.8 Where possible women / pregnant people on treatment dose LMWH should stop 24 hours prior to labour. Where this is not practical due to VTE risk, the woman should be commenced on an unfractionated heparin infusion 24 hours prior to a planned delivery. This should be stopped 4-6 hours prior to delivery and re-commenced 4 hours following delivery provided there are no concerns regarding haemostasis.

6.0 Delivery in Cardiac Theatres

6.1 Occasionally the mother's condition will necessitate delivery in cardiac theatres.

6.2 The decision will be made by the multidisciplinary maternal cardiology team and a written plan will be made and circulated. A Consultant Cardiac Surgeon will liaise with the cardiac theatre team. Where appropriate the neonatology team will be contacted to arrange delivery at a mutually convenient time.

6.3 In the event of delivery in cardiac theatres some drugs and equipment will need to be taken:

- LSCS tray
- Uterotonic drugs: Oxytocin (5 vials), Syntometrine (1 Vial), Ergometrine (2 vials), heamobate (8 vials), Misoprostol (5 tablets), TXA (2 vials)
- Regional anaesthesia set (epidural set, spinal set, appropriate drapes)
- Resuscitaire (fully checked by midwife attending delivery)

7.0 Post -Partum Care

7.1 Specific post-partum considerations will be documented in the CCO clinic delivery plan.

7.2 Women / pregnant people who deliver in cardiac theatres will often need postnatal care on the cardiac ICU or CCU. These women should receive daily cardiology, midwifery and obstetric reviews.

Appendix 1: Modified WHO classification of maternal cardiovascular risk: principles

Risk Class	Risk of pregnancy by medical condition
I	No detectable increased risk of maternal mortality and no/mild increase in morbidity
II	Small increased risk of maternal mortality and moderate increase maternal morbidity
III	Significantly increased risk of maternal mortality or severe morbidity. Expert counseling is required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring is needed throughout pregnancy, childbirth and the puerperium
IV	Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated. If pregnancy occurs termination should be discussed. If pregnancy continues care should be as for class III.

Modified World Health Organization (WHO) Classification of Maternal Cardiovascular Risk: application[1]

WHO Class I	Uncomplicated small or mild • Pulmonary stenosis • Patent ductus arteriosus (PDA) • Mitral valve prolapse Successfully repaired simple lesions • Ventricular septal defect (VSD) • Atrial septal defect (ASD) • Anomalous pulmonary venous drainage • PDA
WHO Class II (restricted to patients previously well and uncomplicated)	• Unoperated ASD or VSD • Repaired Tetralogy of Fallot (without sequalae) • Most arrhythmias

WHO Class II-III (depending on the individual)	• Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native valve disease or tissue heart valve replacement not considered in class I or IV • Marfan syndrome without aortic dilation • Aorta <45mm associated with bicuspid aortic valve disease • Repaired aortic coarctation
WHO Class III	• Mechanical valve replacement • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Marfan syndrome with aortic dilation 40-45mm • Aortic dilation 45-50mm associated with bicuspid aortic valve disease
WHO Class IV (Pregnancy contraindicated)	• Pulmonary hypertension • Severe systemic ventricular dysfunction (LV EF <30%, NYHA class III-IV) • Previous peripartum cardiomyopathy with residual impairment of left ventricular function • Severe mitral/severe symptomatic aortic stenosis • Marfan syndrome with aortic dilation >45mm • Aortic dilation >50mm associated with bicuspid aortic valve disease • Native severe aortic coarctation

Appendix 2: New York Heart Association classification of heart failure

Class	Patient symptoms
Class I (mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, rapid/irregular heartbeat (palpitation) or shortness of breath (dyspnea).
Class II (mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary activity causes fatigue, rapid/irregular heartbeat (palpitation) or shortness of breath (dyspnea).
Class III (moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, rapid/irregular heartbeat (palpitation) or shortness of breath (dyspnea).
Class IV (severe)	Unable to carry out physical activity without discomfort. Symptoms of fatigue, rapid/irregular heart beat (palpitation) or shortness of breath (dyspnea) are present at rest. If any physical activity is undertaken discomfort increases.

Epilepsy

1.0 Epilepsy in Pregnancy

1.1. Epilepsy is a chronic neurological disorder of various aetiologies characterised by recurrent unprovoked seizures and is the commonest neurological disorder (NICE 2012). Epilepsy complicates approximately 0.5% to 1 of pregnancies.

1.2. Maternal mortality rate is 2-3 times higher in people with epilepsy, this increases 10 fold in pregnancy,

1.3. MMBRACE UK report -2016-18 showed that twice as many women with epilepsy (22) died during or up to one year from causes related to epilepsy.

1.4. SUDEP was the main cause of death of these women (15), majority had uncontrolled epilepsy pre-pregnancy.

2.0 Causes of Epilepsy

2.1 30% Idiopathic

2.2 Diagnosis should be made by a specialist medical practitioner – usually a neurologist with experience in epilepsy

2.3 Different types of Epilepsy based on varying clinical characteristics and seizure activity e.g. Tonic-clonic seizures, absent seizures.

2.4 Epilepsy is the tendency to have spontaneously reoccurring seizures but do not assume a habitual seizure until the following have been ruled out

2.5 **Other causes of seizures in pregnancy**

2.6 **Eclampsia.** It is important to remember that epileptic women can also have Eclampsia and this diagnosis should be excluded first.

2.7 Substance misuse, drug or alcohol withdrawal.

2.8 Medical : diabetes, liver failure, hypopituitarism, hypoadrenalism.

2.9 Electrolyte imbalance: hyponatraemia, hypocalcaemia

2.10 Neurological: intracranial bleed / mass or cerebral infarction/ intracranial VTE.

2.11 Sepsis and other infections including meningitis

3.0 Risks of Epilepsy in Pregnancy

3.1 While 2/3 women /pregnant people with epilepsy will have no significant change in their seizure frequency during pregnancy, there is a group of such patients 33% who will have increased seizures.

3.2 The experience in a previous pregnancy is not a reliable indicator of what will happen in subsequent pregnancies.

3.3 Adjustment to medication is likely to be required as anticonvulsant concentrations decline as pregnancy progresses due to the physiological changes in fluid volume that occur in pregnancy

3.4 Effect of epilepsy (Lancet 2015 – Epilepsy in pregnancy and reproductive outcomes – systematic review)

- Miscarriage
- Hypertensive disorders
- Fetal bradycardia
- Still birth
- Maternal and fetal hypoxia and acidosis
- Abruption and PPH

3.5 Increase risk of Pre Term Delivery (OR 1.16)

3.6 Risk IUGR and SGA 7-10% in both treated and untreated women with epilepsy.

3.7 Stillbirth and neonatal death significantly higher in infants. Children had a threefold increased risk for developing seizures themselves.

3.8 Increased rate of congenital malformation in offspring of mothers with epilepsy appears to be related to anti-epileptic drug exposure in utero. Risk is dependent on the type number and dose of Anti Epileptic drugs.

3.9 Most common malformations are neural tube defect, cardiac malformations, facial clefts and skeletal malformations.

AED	Congenital malformation	Risk
None		2-2.3%
Carbamazepine	Cardiac and facial cleft	2 -5%
Lamotrigine	Cardiac and facial cleft	2 -5%
Levetriacetam	Cardiac ad neural tube defect	1-2%
Sodium valproate	Neural tube, facial left, hypospadias, poor cognitive development	6 -10%
Phenytoin	Facial clefts, poor cognitive development	1-2 %

Monotherapy		3 -5%
Polytherapy		56-8%
Polytherapy with valproate		10%

3.10 Lamotrigine and Carbamazepine monotherapy in lower doses are considered the safest.

3.11 The concerns regarding congenital malformations may cause compliance issues with patients. It is important to counsel these women about the risks and benefits of the medications and written information should also be given.

4.0 Management of Women with Epilepsy

4.1 Pre-conception

4.1.1 Information and counselling about contraception – conception, pregnancy, caring for children and breastfeeding should be given to childbearing age women with epilepsy to enable them to make informed decisions and choices (NICE guidelines 2004).

4.1.2 Women /pregnant people with epilepsy should be referred to maternal medicine clinic/MEDIOBS or their neurologist for pre-conceptual advice via their GP

4.1.3 Women/ pregnant people with epilepsy should have their medication (including AEDs) reviewed pre-pregnancy. Lamotrigine and carbamazepine are considered the safest agent.

4.1.4 The risk of congenital malformation is increased with polytherapy. This should be minimised by changing medication prior to pregnancy and the lowest effective dose of AEDs should always be used. If taking sodium valproate consider weaning off to an alternative AED on the advice of a neurologist. Avoid any abrupt withdrawal of AEDs.

4.1.5 All women / pregnant people with Epilepsy should take 5 mgs of Folic acid before pregnancy (RCOG 2016) and continue until at least 12 weeks gestation

4.2 Antenatal care

4.2.1 Women / pregnant people with epilepsy should be attending the Medical Obstetric Clinic/ Maternal Medicine clinic as early as

possible. There after they should be seen as appropriate (usually 20, 28, 32, 36 weeks).

4.2.2 Inform their Neurologist if on AEDs or the Epilepsy nurses that they are pregnanct.

4.2.3 All pregnant people should be encouraged to notify their pregnancy or allow their clinician to notify the pregnancy to UK Epilepsy and Pregnancy Register. (www.epilepsyandpregnancy.co.uk) Tel 0800 389 1298.

4.2.4 Aim for seizure free pregnancy. Women / pregnant people who plan to stop AED therapy during pregnancy should be informed of the possibility of Status Epilepticus and sudden and sudden unexplained death in epilepsy (SUDEP)

4.2.5 Morning sickness may require an alteration in drug times – woman who has hyperemesis gravidarum consider giving drugs via an alternative route.

4.2.6 Routine monitoring of AED plasma levels is not recommended, unless seizure frequency increases in pregnancy or if they are on lamotrigine. Change the dose of lamotrigine accordingly, aiming for a therapeutic level.

4.2.7 Usual 12-13 week scan for dating and to check for anencephaly and other neural tube defects and at 20-22 weeks for anatomical anomalies.

4.2.8 Referral to Evelina Hospital for a fetal cardiac scan between 18 – 22 weeks should be made for be all women / pregnant people with epilepsy taking AEDs.

4.2.9 Serial growth serial scans from 28 weeks are required for women /pregnant people with epilepsy treated with AEDs with review in Maternal medicine (RSCH)/ MEDIOBS (PRH)

4.2.10 Women/ pregnant people with generalised Tonic-Clonic seizures should be informed that the fetus may be at relatively higher risk of harm during a seizure although the absolute risk remains very low and may depend on seizure frequency.

4.2.11 There is insufficient evidence to recommend routine use of oral Vitamin K for mothers taking AEDs to prevent haemorrhagic disease of the new born.

4.3 Labour

4.3.1 Women should be reassured that most will have normal labour and delivery

4.3.2 Women with epilepsy should have their care in the obstetric units with facilities for maternal and neonatal resuscitation.

4.3.3 Home birth is not recommended. Any woman with epilepsy planning a home birth should have a documented discussion about place of birth with her obstetrician and a supervisor of midwives.

4.3.4 Decision regarding suitability of water birth should individualise and based on the seizure status of the women; advice from the epilepsy specialist and the availability of safety precaution or equipment like a net should be sought. Women must be made aware of their risk of drowning whilst having a seizure in water

4.3.5 Continuous fetal monitoring is recommended only in women at high risk of seizures or following an intrapartum seizure.

4.3.6 A diagnosis of epilepsy is not an indication for induction of labour.

4.3.7 Caesarean section is only indicated for obstetric indications unless epilepsy is poorly controlled and there is a significant risk of seizures in labour.

4.3.8 Lack of sleep, pain and dehydration increase the risk of a seizure during labour, it is therefore important to avoid these triggers in labour.

4.3.9 Women should continue with the medication during labour orally or parentally.

4.3.10 Risk of seizure is approximately 3.5% for women in labour with known epilepsy.

4.3.11 Risk of seizure in the first 24 hours is 1-2%. Those at high risk seizures consider prophylactic use of Benzodiazepines e.g. Clobazam (10mg)

4.3.12 IV access should be obtained at the onset of labour in women in whom IV access is likely to be difficult (e.g. raised BMI) or in women who are having repeated seizures.

4.3.13 TENS machine may be used in labour (Epilepsy action 2005)

4.3.14 Entonox can be used. Avoid hyperventilation as this can trigger a seizure (Epilepsy Action 2005)

4.3.15 Pethidine should only be used with caution as it can induce seizure. Diamorphine should be used in preference (Epilepsy Action (2005)

4.3.16 Epidural and spinal can be used

4.4 Acute Management of Seizures

4.4.1 **ABC Airway:** Place woman in left lateral or displace gravid uterus to maternal right.

4.4.2 **Breathing:** Give oxygen by face mask

4.4.3 **Circulation:** Observation, check pulse, blood pressure and urine output.

4.4.4 Call for help – fast bleep 2222 (maternal collapse)

4.4.5 Intravenous access 14g take blood, uric acid, platelet count, clotting, liver function test, blood glucose, serum calcium, serum sodium

4.4.6 Exclude Eclampsia, if there is clinical uncertainty then start MgSO4 as per Eclampsia protocol

4.4.7 Seizure should be treated as soon as possible to reduce the risk of maternal and fetal hypoxia

4.4.8 If seizure requires terminating (on-going > 2minutes) give IV Lorazepam (4 mg over 2 minutes) repeated every 10-20 minutes or Diazepam 10mg IV or PR

4.4.9 In refractory cases, iv Phenytoin can be used. Loading dose 18mg/kg to a maximum rate of 50mg/

4.4.10 CTG should be started immediately after a seizure

4.5 Status Epilepticus

4.5.1 Status Epilepticus is a **life threatening medical emergency** defined as a seizure lasting ≥ 5 minutes, or ≥ 2 seizures without return to consciousness, or ≥3 Tonic-Clonic seizures within 1 hour

Stage 1: 0-10 minutes

Start Benzodiazepine treatment ASAP

- Resuscitate, secure airway, give oxygen, left lateral tilt or displace gravid uterus to maternal right.
- Establish IV access in largest vein possible
- IV benzodiazepine
  - Lorazepam 4mg IV bolus
    Alternate: Diazepam 10mg IV bolus or Diazepam 10mg PR (if no Lorazepam)
- Give second dose of Lorazepam 4mg IV bolus (or diazepam 10mg IV/PR) after 10 minutes if seizures continue unless cyanosed or hypoxic.

Stage 2: 10 - 30 minutes

Call MET team on 2222: Start emergency antiepileptic drug therapy ASAP

- Regular monitoring: neurology Obs + HR, BP, Temp, Sats, RR, BM
- Consider non-convulsive status.
- Start IV anti-epileptic drug ASAP
  - Phenytoin 20mg/kg IV infusion
    Alternatives: Sodium Valproate 30mg/kg IV infusion or Leveiracetam IV infusion 30mg/kg
- Investigations: ECG, ABG, bloods (FBC, U&Es, LFTs, Ca^{2+}, Mg^{2+}, clotting, antiepileptic drug levels
- If history of alcohol excess, consider 50% glucose IV and/or Pabrinex IV

Stage 3: 30-60 minutes

Alert Anaesthetist/ITU

- Establish aetiology, identify and treat medical complications.
- Further investigations: CXR, brain imaging, LP
- All post-ictal patients must have a written management plan to include planned and active monitoring (including those that have regained consciousness)

Stage 4: 30-90 minutes

Primary end point – suppression of epileptic activity on EEG

- Transfer to ITU; establish intensive care, EEG monitoring & ICP monitoring where appropriate.
- Initiate long-term maintenance anti-epileptic therapy (restart patients usual antiepileptic drugs).

4.6 Postnatal

Risk of seizure is higher compared to in pregnancy, this is due to increased stress, sleep deprivation and reduced AED compliance.

4.6.1 All babies born to mothers taking enzyme -inducing AED should be offered Vitamin K IM at delivery to prevent haemorrhagic disease of the new born

4.6.2 Women /pregnant people who have had their AED increased in pregnancy should have their medication reviewed after discussion with neurology within one month of delivery. They may need to be reduced to pre-pregnancy level to avoid toxicity

4.6.3 Women / pregnant people should be encouraged to breastfeed as evidence suggests that the risk of adverse cognitive outcomes is not increased in children exposed to AEDs in breast milk.

4.6.4 Any woman/ pregnant person who has had a seizure during labour should be observed closely for the next 72 hours.

4.6.5 Parents should be informed about which safety measures May reduce the risk of accidents. Leaflets are available from the British Epilepsy Association – but they should be reassured that the risk to the infant caused by maternal seizure is low.

4.6.6 Ensure that referral to the contraception service is made in the postnatal period.

4.6.7 Barrier contraception should be discussed for use prior to review by the contraception service.

Hypothyroidism and Hyperthyroidism in pregnancy

1.0 Hypothyroidism in pregnancy - Introduction

Hypothyroidism is a common condition that affects about 1% of the pregnant population. Prior to the development of the fetal thyroid axis, the fetus is dependent on maternal levothyroxine and this is essential for fetal neurodevelopment.

Pregnant people who are diagnosed with untreated hypothyroidism in the first trimester require rapid treatment with levothyroxine to achieve euthyroidism. This also applies to women/ pregnant people who have under treated pre-existing primary hypothyroidism.

Patient information leaflet (Pregnancy and Hypothyroidism) available at - **http://www.bsuh.nhs.uk/departments/diabetes-and-endocrinology/patient-information-leaflets/**

1.1 Known Primary Hypothyroidism

1.1.1. Confirm (from the woman's / pregnant person's past medical history) the cause of her primary hypothyroidism. Most women will have autoimmune primary hypothyroidism, some may be hypothyroid after treatment for hyperthyroidism with surgery or radioiodine (see additional information in section 2.3).

1.1.2. Thyroid function should be optimised pre-conception, aiming for a TSH ≤2.5mIU/l, without causing TSH suppression**.**

1.1.3. Thyroid function tests should be checked once in each trimester (first one at booking). Following any adjustments in thyroxine dose, thyroid function should be checked in 4-6 weeks.

1.1.4. Women should be advised to take levothyroxine on an empty stomach. The levothyroxine should be taken at a different time to their vitamins or mineral supplements.

1.1.5. Women with morning sickness or hyperemesis gravidarum should be advised to take their levothyroxine last thing at night.

1.1.6. Obstetric reviews should be carried out at 24 and 32 weeks, with thyroid function tests if due.

1.1.7. Assuming optimised control pre-pregnancy, levothyroxine should be reduced to pre-pregnancy doses immediately following delivery.

1.1.8. Thyroid function tests should be performed 6-8 weeks post-partum. The patient should be informed of this and it should be documented on the discharge summary. The GP can then titrate the dose of levothyroxine if necessary.

1.1.9. 'T3' (tri-iodothyronine) does not cross the placenta: women on T4/T3 combination therapy should be converted to levothyroxine alone with appropriate dose titration. Women taking T3 therapy should be referred to their endocrinologist preferably in the pre-conception period, or discussed urgently as soon as a pregnancy is confirmed.

1.2 Screening for thyroid dysfunction in pregnancy

1.2.1 Thyroid function tests should be checked pre-conception and/or as early in pregnancy as possible in all women with Type 1 diabetes or other autoimmune endocrine conditions, or a personal or family history of thyroid disease.

1.3 New diagnosis of Hypothyroidism or Subclinical hypothyroidism in pregnancy

1.3.1 Women with newly diagnosed hypothyroidism in pregnancy should be started on levothyroxine as soon as possible. The starting dose can be discussed with the Endocrinology team (Endocrinology SpR on Bleep 8809 or Endocrine Secretaries on x 64311).

1.3.2 Treatment of subclinical hypothyroidism (a normal fT4 and an elevated TSH) in pregnancy is the same as treatment of known or newly diagnosed hypothyroidism, though the starting dose of levothyroxine may be different.

1.3.3 Thyroid function tests should be repeated every 4-6 weeks until euthyroidism is achieved

1.3.4 The dose of levothyroxine should be up-titrated rapidly aiming for a TSH >0.1 but <2.5mUI/l.

1.3.5 Once euthyroidism is achieved follow the "known hypothyroidism" guidelines.

1.3.6 The levothyroxine dose is likely to need reducing in the post natal period but again this depends on the pre-pregnancy thyroid function tests. It may be reasonable to opt for a trial off the levothyroxine, and for the GP to reassess symptoms and biochemistry 6-8 weeks post-partum. The Endocrine Team are happy to discuss individual cases.

2.0 Hyperthyroidism in pregnancy - Introduction

Hyperthyroidism affects about 2 per 1000 pregnancies. The vast majority (about 95%) of pregnant people with hyperthyroidism will have autoimmune hyperthyroidism (Graves' disease). In general the diagnosis will have been made prior to pregnancy and the majority of woman will already be on treatment.

People who become pregnant with untreated hyperthyroidism have increased risks of miscarriage, intrauterine growth restriction, premature labour and perinatal mortality. On very rare occasions there can be an extension of a retrosternal goitre causing tracheal obstruction. This complication is of particular relevance if intubation is required.

The importance of Graves' disease for the fetus is that thyroid-stimulating antibodies (TSH receptor stimulating antibodies) can cross the placenta causing fetal or neonatal thyrotoxicosis. Women who have been treated for Graves' disease in the past (with surgery or radioiodine therapy) and are now hypothyroid (on levothyroxine) or euthyroid, may still have circulating antibodies.

Like many other autoimmune diseases Graves' disease will have a tendency to improve during pregnancy with the titre of TSH receptor stimulating antibodies falling. This means that often the requirement for anti-thyroid treatment will fall. Exacerbations may occur in the first trimester mostly related to the thyroid stimulating effect of beta-HCG. Auto-immune hyperthyroidism may also flare in the puerperium as the pregnancy induced reduction of the TSH receptor stimulating antibodies is lost.

Hyperemesis gravidarum can be associated with a transient hyperthyroid state. Beta-HCG and TSH have a common subunit and hence beta-HCG can stimulate the thyroid to release T4. The hyperthyroidism will normally resolve when the hyperemesis resolves.
The patient will have high levels of T4 and low TSH as in hyperthyroidism. The differentiating features will be that the TSH receptor stimulating antibodies will be negative and the clinical features associated with hyperthyroidism such as exophthalmos will be absent.
The main stay of treatment is to control the symptoms from the high levels of T4 (such as tremors, sweats, palpitations and anxiety). This can be achieved using beta-blockers such as propranolol. However, if the patient is not very symptomatic and the thyrotoxicosis is transient, they can be managed expectantly without the need

for treatment. Treatment with anti-thyroid drugs should be avoided as when the hyperthyroidism resolves there is a risk of hypothyroidism affecting the fetus.

2.1 Known Hyperthyroidism

2.1.1 Women / pregnant people with hyperthyroidism due to Graves' disease or a toxic thyroid nodule will in general be under an endocrinologist.

2.1.2 The endocrinologist should be informed as soon as pregnancy is confirmed.

2.1.3 If a patient is on block and replace treatment (with carbimazole or propylthiouracil [PTU] in combination with levothyroxine) and considering pregnancy this should ideally be changed to a dose titration regime prior to conception.

2.1.4 Urgent discussion should be made for those women that become pregnant whilst on block and replace therapy (high dose carbimazole or PTU in combination with levothyroxine). This should be done by telephone discussion with their Endocrinologist, and subsequent referral for follow-up in pregnancy.

2.1.5 Current recommendations are to treat hyperthyroidism in pregnancy with PTU in the first trimester then switch to carbimazole for the second and third trimesters[i], swapping back to PTU whilst breast feeding. Medication changes should be undertaken by the woman's Endocrinologist.

2.1.6 The target fT4 should be in the upper third of the non-pregnant reference range to avoid fetal hypothyroidism.

	TSH (mU/L)	Thyroxine (pmol/L)	Tri-iodothyronine(pmol/L)
Non- pregnant	0.27 - 4.2	12 - 22	3.1 – 6.8
First trimester	0 - 5.5	10 - 16	3 – 7
Second trimester	0.5 -3.5	9 – 15.5	3 – 5.5
Third trimester	0.5 - 4	8 – 14.5	2.5 – 5.5

2.1.7 For women / pregnant people with symptoms of hyperthyroidism (tachycardia, tremor or anxiety) they can continue with beta-blockers (propranolol) as the risks of IUGR are outweighed by the maternal and fetal benefits.[ii]

2.1.8 The woman / pregnant person should be reviewed following the 20 week anomalies scan in an ANC. TSH receptor antibody titre (request as TRAb on blood form and send in yellow top bottle) should be sent at this time as well as thyroid function.

2.1.9 All women / pregnant people with positive antibodies should be highlighted to the neonatal team, as there is the possibility of neonatal thyrotoxicosis.

2.1.10 For TRAB positive women, a growth scan, antenatal clinic review and thyroid function testing should be arranged for 28 weeks gestation, with additional scans if there is any concern regarding fetal growth.

2.1.11 For TRAB negative women, a growth scan and antenatal clinic review with thyroid function testing should be arranged for 28 weeks gestation, with additional scans if there is any concern regarding fetal growth.

2.1.12 Blood for thyroid function tests should be taken by the community midwife 1 week prior to the ANC appointments at 28 and 34 weeks so that results are available to inform obstetric reviews.

2.1.13 If surgery for thyroidectomy becomes necessary it is best performed in the second trimester. Indications for surgery could include dysphagia, stridor (related to goitre), suspected/confirmed malignancy or allergy to antithyroid medication, in discussion with the endocrinologists and thyroid surgeon.

2.1.14 Treatment with radioactive iodine is absolutely contraindicated in pregnancy.

2.1.15 Women / pregnant people with Graves' disease should be made aware of the increased risk of relapse in the post-partum period.

2.1.16 Post-partum, anti-thyroid medication should be taken immediately after breast feeding. PTU is the antithyroid drug of choice in breast feeding women.

2.1.17 A patient information leaflet (Pregnancy and Hyperthyroidism) is available on the BSUH intranet and should be made available to the patient. **http://www.bsuh.nhs.uk/departments/diabetes-and-endocrinology/patient-information-leaflets/**

2.1.18 The reported fetal risks associated with propylthiouracil and Carbimazole

Major:
Choanal atresia, Cardiovascular abnormalities, Oesophageal atresia, Anal and intestinal abnormalities, Omphalocele and omphalomesenteric duct abnormalities, Cardiovascular abnormalities, Renal/urinary tract abnormalities.

Minor:
Aplasia cutis. Facial abnormalities, skeletal and limb abnormalities, renal/urinary tract abnormalities.

The reported risks associated with untreated hyperthyroidism in pregnancy include: increased risk of miscarriage, intrauterine growth restriction, low birth weight, premature labour, preeclampsia, congestive heart failure and fetal death.

2.2 Woman / pregnant people who have been previously treated for hyperthyroidism

2.2.1 Woman / pregnant people who have been previously treated for hyperthyroidism due to Graves' and are now euthyroid or hypothyroid may still have circulating antibodies. These patients should also have their TSH receptor-stimulating antibody levels checked with follow-up as indicated (see section 2.2.8 – 2.2.11).

2.3 New Diagnosis of Hyperthyroidism in pregnancy

2.3.1 It is important to differentiate between new onset hyperthyroidism and gestational hyperthyroidism (associated with hyperemesis).

2.3.2 An endocrine assessment may be useful.

2.3.3 Careful history as to the timing of when the symptoms of hyperthyroidism (e.g. heat intolerance, anxiety, palpitations) occurred. If they began concurrently with the symptoms of excessive vomiting then the hyperthyroidism is more likely to be associated with hyperemesis gravidarum.

2.3.4 A personal or strong family history of thyroid disease or other autoimmune disorders may support a diagnosis of Graves' disease

2.3.5 Clinical assessment of the patient for stigmata of hyperthyroidism should be carried out. If exophthalmos and a goitre with a bruit on auscultation are present this supports the diagnosis of Graves' disease.

2.3.6 Thyroid auto-antibodies (antiTPO AB and TRAB, sent in a 5ml yellow top bottle) should be sent. If positive this again supports the diagnosis of Graves'.

2.3.7 Initial treatment should be for symptomatic benefit if associated with hyperemesis gravidarum, using propranolol. The hyperthyroid biochemical picture will resolve following resolution of the hyperemesis.

2.3.8 If there is a strong suspicion of Graves' disease, discuss with an Endocrinologist. Generally, treat with high doses of carbimazole (45-

60mg) or PTU (450-600mg) daily, repeat TFTs in 4 weeks and gradually reduce the dose.

2.3.9 **Neonatal/feta thyrotoxicosis**

This results from transplacental passage of thyroid-stimulating antibodies. It occurs in 1% of babies born to mothers with a past or current history of Grave's disease.

TSH receptor-stimulating antibodies should be checked in the first trimester, if titre is high or in subsequent measurements the titre has not fallen, fetal thyrotoxicosis should be anticipated and ultrasound should be organised to check for fetal growth, heart rate and fetal neck (goitre).

Treatment is with anti-thyroid drugs; these are given to the mother and if she is euthyroid to combine it with levothyroxine.

3.0 Post-partum thyroiditis

3.0.1 Post-partum thyroiditis may occur up to 1 year after the baby has been born.

3.0.2 Women with Type 1 diabetes or a personal or family history of thyroid disease are more at risk.

3.0.3 There should be a low threshold for checking thyroid function tests.

3.0.4 An endocrine assessment may be helpful if results are abnormal.

3.0.5 The Endocrine Society Clinical Guidelines recommend post-partum screening thyroid function tests at 3 and 6 months for high risk women / pregnant people.

Inflammatory Bowel Disease

1.0 Introduction

Inflammatory bowel disease (IBD) is a group of chronic bowel disease, including Crohn's disease (CD) and ulcerative colitis (UC). 50% of patients are diagnosed before 35 years of age.

UC is characterised by relapsing and remitting episodes of inflammation limited to the mucosal layer of the colon. CD can affect any part of the gastrointestinal system from the mouth to perianal area and is characterised by transmural inflammation and skip lesions.

Clinical features of UC are:

- Liquid diarrhoea
- Lower abdominal pain
- Urgency of defaecation
- Passage of blood and mucus per rectum

Compilations include colonic dilation (toxic megacolon) and malignancy

Clinical features of CD are:

-Crampy abdominal pain
- Diarrhoea
- Weight loss

Complications include bowel perforation, stricture formation, peri-anal disease, fistular, malabsorption and abscess formation.

Effects of pregnancy on IBD

Women with IBD have similar fertility rates to the general population. The exceptions are women / pregnant people with active disease or those who have undergone extensive abdominal surgery.

Women in remission at the time of conception are more likely (80-90%) to have a normal pregnancy. The risk of relapse is similar to a non-pregnant state which is 30%.

2/3 of patients with active disease at conception will have persistent flare-ups during pregnancy. Higher rates of miscarriage, preterm birth and IUGR have been found in those with active disease.

Pre-pregnancy counselling

Patients planning on getting pregnant should have an education session with their IBD nurse specialist. It is useful to summarise their illness, treatment to date and possible treatment plans in the events of relapse during pregnancy.
It is important to advise them to conceive during remission and that good control during pregnancy reduces the risk of adverse pregnancy outcomes.

Women / pregnant people should be reassured about the safety profiles of their medications and encouraged to take them. The smallest dose to treat and maintain remission should be used.

Mycophenolate and methotrexate should be stopped and replaced by suitable alternatives at least 3 months prior to conception.

Medications used to treat IBD

Drug	**Use in pregnancy**	**Safe in breastfeeding**	**Comments**
Aminosalicyates	Yes	Yes	High dose folic supplementation (5mg/day)
Metronidazole	Yes	Yes	Use short course for flare of CD and perianal CD
Steriods (prednisolone and hydrocortisone)	Yes	Yes	Can achieve rapid disease remission 40mg OD weaning by 5mg/week
Thiopurines (azathipoprine and mercaptopurine)	Yes	Yes	
Calcineurin Inhibitors	Yes	Yes	Use for fulminant colitis and rescue therapy in steroid-refractory UC
Biologics (infliximab and adalimumab)	Yes	Yes	Discontinue by early third trimester Avoid live vaccines in newborns
Mycophenolate	No	No	Associated with multiple congenital abnormalities
Methotrexate	No	No	Tetratogenic

Antenatal management:

Patients with IBD identified at booking should be referred to a Maternal Medicine clinic following their dating scan (Monday pm at PRH or Monday pm at RSCH Sussex House).

The Obstetrician should notify the IBD nurse at RSCH or the patient's gastroenterologist that the patient is pregnant and organise MDT follow up.

Take a detailed history of their diagnosis, current medication and last flare up. Identify any previous surgeries and if there are any complications of IBD (such as perianal disease / fistulae).

Counsel the patient that the risk of exacerbation is around 30% and more likely to have a postpartum flare up.

Organise growth scans at 28, 32 and 36 weeks and review after each scan to check for IUGR.

Women with prior surgery, including ileostomy and proctocolectomy and pouch surgery tolerate pregnancy well. Vaginal deliveries are possible following ileoanal anastomosis.

Caesarean section is usually only required for obstetric indications. In cases of severe peri-anal disease resulting in scarred rectum and perineum, vaginal delivery should be avoided. Pelvic MRI can be used in pregnancy to assess fistulae and help inform decisions regarding mode of delivery.

Induction of labour should be reserved for obstetric reasons unless the disease remains active near or at term when optimal treatment cannot be provided because of the pregnancy.

Women / pregnant people on regular steroids will require hydrocortisone in labour (100mg every 6-8 hours) to avoid an adrenal crisis.

Anyone with complex decisions to be made, or who have refractory disease should be referred into the joint Medical Obstetric clinic at RSCH on a Wednesday morning run by Dr Carol Postlethwaite .

Diagnosis of IBD disease activity in pregnancy

The criteria for diagnosis of active disease is similar to those in the non pregnant state.

Symptoms including abdominal pain, stool frequency and rectal bleeding. Tests to look at include FBC,U&E, CRP, Albumin and Faecal calprotectin (non invasive marker for intestinal inflammation).

Ultrasound examination of the abdomen is the imaging of choice however MRI without contrast in the second and third trimester should be reserved for more complex cases or where ultrasound is inconclusive.

Treatment should be discussed with the Gastroenterology Ref team and if they require inpatient admission a review by the medical team should be organised.

Renal Disease in Pregnancy

Introduction: Renal physiological changes in pregnancy

Pregnancy is associated with substantial alterations to renal structure and function:

- Renal blood flow and glomerular filtration rate (GFR) mirrors cardiac output. GFR increases by approximately 80% above non-pregnant levels by the 2nd trimester. It then falls to about 45% above non pregnant levels by term.
- The increase in blood flow results in an increase in kidney length by about 1 cm.
- Progestogenic effects and later in pregnancy compression from the gravid uterus causes dilation of the renal calyces, ureters and bladder. This is more marked on the right due to the physiological uterine dextrotation (due to the sigmoid colon).
- Renal hydronephrosis is considered normal up to a pelvi-calyceal diameter of 5 mm on the left and 15 mm on the right. The ureters can be dilated up to 2 cm in the third trimester.
- Ureteric dilation is rarely seen below the pelvic brim.

Renal Function tests in pregnancy

Physiological variable	Direction of change	% Increase OR normal levels for Pregnancy
Renal Plasma Flow	↑	**60% - 80%**
Glomerular filtration rate	↑	**55%**
Creatinine Clearance	↑	**120 – 160 mL/min**
Protein excretion	↑	**≤ 300mg/24hr**
Urea	↓	**2.0 – 4.5 mmol/L**
Creatinine	↓	**25 – 75 mmol/L**
Bicarbonate	↓	**18 – 22 mmol/L**
Uric acid	↑	**1st tri- 0.14-0.23** **2nd tri.- 0.14 – 0.29** **3rd tri.- 0.21 -0.38**

1.0 Referral criteria to MEDIOBS (PRH)/Maternal medicine clinic (RSCH)

1.1. Pregnant women with chronic renal disease (see list in appendix 1)

1.2. Pregnant women on dialysis or post renal transplant

2.0 Woman who require Consultant led antenatal care

2.1 Pregnant people with a history of recurrent urinary tract infections (UTI). This is defined as three or more culture proven UTIs in one year outside of pregnancy or 2 UTIs in pregnancy.

2.2 Pregnant people aged > or = 40 years old with hypertension > or = 140/90 with a urine protein creatinine ratio >30 mg/mmol (significant proteinuria). These woman should be referred as early as possible

2.3 Pregnant people on treatment for essential hypertension with or without significant proteinuria.

3.0 Urinary tract infection

3.0.1 This is a common and important diagnosis in pregnancy. Asymptomtic bacteriuria will affect 2-7% of pregnant woman/people, acute cystitis will complicate about 1% of pregnancies and 1-2% of pregnancies will be complicated by acute pyelonephritis.

3.0.2 **Asymptomatic bacteriuria (ASB)**

3.0.3 ASB is defined as the colonization of the urinary tract system in the absence of clinical symptoms of urinary tract infection.

3.0.4 Screening for ASB can be carried out using urine reagent strips. These strips will detect 50% of woman with ASB if the strip tests positive for >trace protein, >trace of blood, positive for nitrites or leucocytes.

3.0.5 Midstream urine (MSU) culture is the gold standard for diagnosing ASB and also allows for antibiotic sensitivity to be determined.

3.0.6 Bacteriuria is only considered significant if the colony count exceeds 100,000/ml on a urine MSU specimen.

3.0.7 Urine culture resulting in a non-significant or mixed growth should be repeated on a fresh MSU specimen.

3.1 Acute cystitis

3.1.1 Clinical features include urinary frequency, urgency, dysuria, haematuria, proteinuria, pyrexia and suprapubic pain.

3.1.2 Dipstick urine and send mid-stream urine (MSU) for culture and sensitivity. The presence of nitrites and leucocytes on a urine dip is suggestive of a UTI but not diagnostic.

3.1.3 UTI is confirmed by significant bacteriuria following culture of an MSU sample in the presence of symptoms of cystitis.

3.1.4 If cystitis is considered to be the most likely clinical diagnosis even with a dipstick negative for leucocytes and nitrites treat the woman for UTI. Provided other possible diagnoses for the symptoms have been ruled out.

3.2 Management of asymptomatic bacteriuria and acute cystitis

3.2.1 As a result of increased urinary stasis and upper urinary tract dilation associated with pregnancy there is an increased risk of pyelonephritis. It is therefore important that asymptomatic bacteriuria and acute cystitis is treated.

3.2.2 Choice of antibiotic treatment of asymptomatic bacteriuria depends upon the sensitivity of the causative organism.

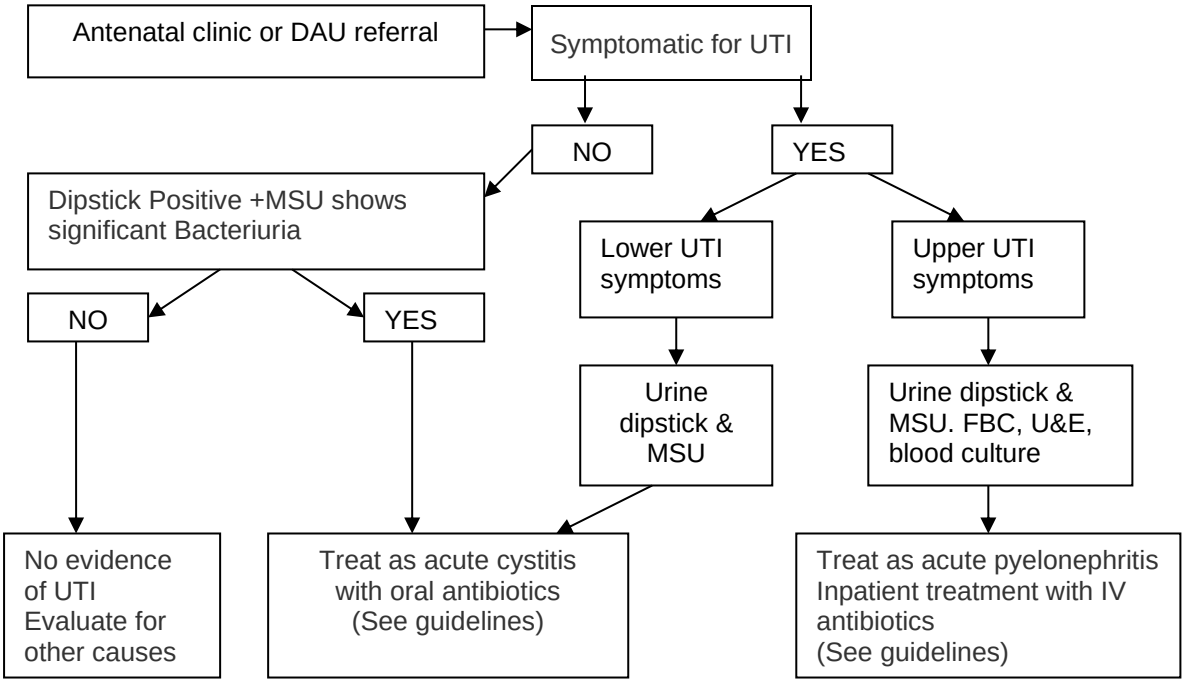
3.2.3 In the presence of symptoms of acute cystitis 7-day course of treatment with broad-spectrum antibiotic such as Cefalexin, Nitrofurantoin or amoxicillin based on recent culture and susceptibility results

3.2.4 Cefalexin 500 mg BD given for 7 days is effective against the majority urinary pathogens.

3.2.5 Nitrofurantoin 50mg QDS IR or 100mg BD MR is an alternative if the patient is allergic to penicillin and less than 26 weeks. It should be avoided in the third trimester due the risk of precipitating neonatal haemolytic anaemia.

3.2.6 Trimethoprim 200mg BD can be used in the 2nd and 3rd trimester. It should be avoided in the 1st trimester due to its antifolate action or Amoxicillin 500mg TDS

3.2.7 Complicated cases and cases of multiple resistances should be discussed with a microbiologist.



3.3 Prophylaxis for recurrent UTI

3.3.1 Once a woman/ pregnant person has had three or more microbiology confirmed UTIs in pregnancy antibiotic prophylaxis should be commenced.

3.3.1 An ultrasound scan of the renal tract should be arranged.

Check sensitivity results from MSU samples before commencing prophylactic antibiotic.

3.3.2 Low dose cephalosporins (cephalexin 125 mg ON) is commonly used. If allergic then discuss with microbiology about appropriate prophylaxis.

3.3.3 Woman/ pregnant people who usually take prophylaxis outside of pregnancy should continue with antibiotic prophylaxis appropriate for pregnancy.

3.4 Acute Pyelonephritis

3.4.1 Acute pyelonephritis complicates about 1-2% of pregnancies. Bacteraemia complicates about 15-20% of cases. Rarely it will be a cause of septic shock. E.coli is the most common causative organism.

3.4.2 Clinical features include fever, loin and/or abdominal pain, nausea and vomiting, rigors and haematuria. These are normally associated with concurrent symptoms of cystitis.

3.4.3 The diagnosis is confirmed by the finding of significant bacteriuria following the culture of a MSU (midstream urine) specimen.

3.4.4 The diagnosis is associated with pre-term labour and low birth weight babies.

3.5 Management of acute pyelonephritis

3.5.1 Women / pregnant people with symptoms of acute pyelonephritis should be admitted to the antenatal ward for treatment.

3.5.2 All patients admitted with pyelonephritis should be discussed with the on-call consultant or registrar.

3.5.3 Initial investigation should include a MSU, blood tests for FBC, U&Es, CRP and blood cultures. If patient is clinically septic a lactate level should also be obtained using a venous blood gas.

3.5.4 Treatment with broad-spectrum IV antibiotics should be commenced immediately without waiting for culture results. The woman should be kept well hydrated with a low threshold for IV fluids.

3.5.5 IV cefuroxime 1.5 g TDS

3.5.6 If the woman / pregnant person is penicillin allergic then commence Gentamycin with Microbiology advice

3.5.7 Following discussion with microbiology gentamycin maybe used as adjunctive treatment in severe cases. If used levels must be monitored according to hospital guidelines.

3.5.8 The antibiotics should be rationalised and changed as appropriate according to culture results.

3.5.9 IV antibiotics should be continued until the woman has been apyrexial for 24 hours then converted to appropriate oral antibiotics for 7 days.

3.5.10 Women who do not respond to treatment after 48-72 hours of treatment should have imaging of the renal tract by ultrasound to detect anomalies, obstruction and stones.

3.5.11 Women / pregnant people who grow Klebsiella or Proteus or those organisms associated with renal stones should also have imaging of the renal tract by USS.

4. Chronic Kidney disease

Chronic kidney disease (CKD) is rare in pregnancy (affecting 0.15% of all pregnancies). This is in part due to the associated reduced fertility. Diabetes and hypertension are the commonest causes of CKD. Other common causes of CKD are chronic pyelonephritis and primary glomerulonephritis.

Pregnant people can present with a variety of pre-existing renal conditions. Examples of these and their effects on pregnancy can be found in Appendix 2. Please note that this is not an exhaustive list.

Special consideration should be given to those patients who require dialysis and who have had transplants. Please refer to sections 5 and 6 for specific guidance for these patients.

4.1 Pre-pregnancy advice and counselling

4.1.1 The GP should refer all women with CKD to a preconception clinic for review as fertility and pregnancy outcome will be affected by the degree of renal insufficiency.

4.1.2 The outcome of pregnancy will depend upon the degree of renal impairment, the presence and degree of hypertension, the presence and degree of proteinuria and underlying renal disease.

4.1.3 The possible risks to the mother include accelerated loss of renal function, escalating hypertension during pregnancy and increasing proteinuria. Those at highest risk of accelerated loss are those with stage 3 and 4 chronic kidney disease (see table below).

Stage	Description	e-GFR (ml/min/1.73sq.m)
1	Kidney damage and normal /raised GFR	>90
2	Kidney damage and mildly reduced GFR	60 - 90
3	Moderately reduced GFR	30 - 59
4	Severely reduced GFR	15 - 29
5	Kidney failure	< 15 (or dialysis)

4.1.4 Women / pregnant people with stage 1 and 2 disease can be advised that pregnancy outcome is normally good without adverse outcome on the long term course of their disease although they are still at risk of antenatal complications.

4.1.5 Woman / pregnant person should be advised against pregnancy if suffering from severe renal insufficiency or those requiring dialysis, severe or uncontrolled hypertension, nephrotic syndrome, scleroderma, polyarteritis nodosa, active lupus nephritis or diabetic nephropathy (if serum creatinine >124µmol/l as there is a 40% risk of accelerated renal deterioration).

4.1.6 The effects that renal disease has on pregnancy include increased rates of miscarriage, increased risk of IUGR, increased risk of pre-eclmapsia, pre-mature birth and intrauterine death.

4.1.7 Renal function should be assessed pre-pregnancy and the woman appropriate counseled as to the risk pregnancy will have to her renal function.

4.1.8 Hypertension should be controlled pre-pregnancy. Ideally this should be <140/90. In women with longstanding hypertension consider echocardiography.

4.1.9 Where hypertension is controlled using ACE inhibitors these should be changed pre-conception or shortly after pregnancy is confirmed. Safe alternatives would include labetalol, methyldopa or nifedipine.

4.1.10 Statins should be stopped pre-conception.

4.2 Midwifery care of a patient with CKD

4.2.1 At booking the midwife should identify the history of chronic kidney disease, document current medication, measure baseline blood pressure, perform urinalysis, send a urine sample for PCR (Protein Creatinine Ratio), send blood for FBC, U&Es and arrange a baseline renal ultrasound scan.

4.2.2 The renal patient proforma should be printed and placed in the patients handheld notes (Appendix 2). The results of the investigations in section 4.2.1 should be documented on the renal disease proforma.

4.2.1 If the patient is taking ACE inhibitors these should be stopped and discussion with either a Consultant obstetrician or their Renal physician immediately.

4.2.2 Recommend high dose folic acid (5 mg OD) if not already taking this.

4.2.3 At booking low dose aspirin (150mg OD) should be commenced from 12 weeks to reduce the risk of pre-eclampsia.

4.2.4 The patient should be referred to the maternal medicine clinic (RSCH) or MEDIOBS (PRH) and should be seen prior to 12 weeks.

4.2.5 Blood pressure and urine dip should be performed at least every 2 weeks from 22 weeks gestation. Blood pressure should be controlled at a level <135/85 where possible. Increasing hypertension and/or increasing proteinuria should prompt referral to the Day Assessment Unit for assessment by a registrar.

4.2.6 A low threshold for treatment of asymptomatic bateriuria and acute cystitis will help prevent preterm labour. (see section 3.3)

4.2.7 VTE risk should be assessed using the VTE algorithm in the obstetric notes. If a woman has a PCR >300 (or proteinuria >3 g/ 24 hours) she should be commenced on prophylactic LMWH throughout pregnancy and post partum for 6 weeks unless contraindicated by the severity of renal failure. Lesser degrees of proteinuria constitute a risk for VTE and may influence decision to start LMWH prophylaxis.

4.3 Obstetric antenatal management of patients with CKD

4.3.1 All patients with CKD should be referred to the maternal medicine clinic (RSCH) or MEDIOBS (PRH) clinic and should be seen before 12 weeks.

4.3.1 All patients should have a dating scan, combined screen and fetal anomaly scan as per normal.

4.3.2 Growth scans should be arranged for 28, 32 and 36 weeks. Arrange a 24-week growth scan if the clinical picture is moderate to severe.

4.3.3 Woman / pregnant person with CKD should be reviewed in maternal medicine clinic or MEDIOBS at least every 4 weeks

<u>Investigations to perform before each appointment include:</u>

4.3.4 U&Es to assess for any deterioration in renal function. This should be done more frequently (every fortnight) if felt to be clinically necessary.

4.3.5 A FBC to assess for anaemia and thrombocytopenia. Woman with chronic renal failure are more likely to become anaemic due to poor production of erythropoietin and shortened red cell life span. If found to be anaemic request bloods for ferratin, B12 and folate levels. Treat the anaemina with ferrous sulphate if iron deficiency is the cause (most likely)

4.3.6 Liver function tests (more frequently in heavy proteinuria) to monitor albumin levels.

4.3.7 PCR or 24-hour urine collection should be performed every 4 weeks.

4.3.8 An MSU should be sent every 4 weeks (regardless of dipstick result) to assess for asymptomatic bacteriuria. Management of asymptomatic bacteriuria is the same as for patients without CKD (see section 3.3).

4.3.9 If haematuria is present on a dipstick then microscopy should be requested to check for red cell casts. If red cell cast are present this suggests active renal parenchymal pathology and urgent advice should be sought from a renal physician. Normal red cell morphology should be discussed with the Urology team as this suggests lower renal tract pathology.

4.3.10 Renal biopsy may be indicated in the presence of florid nephrotic syndrome before 16-20 weeks or suspected rapidly progressing glomerulonephritis. This decision should be made in conjunction with a Consultant Renal physician.

4.3.11 Admission to the antenatal ward should occur if there is uncontrolled hypertension, deteriorating renal function or proteinuria, superimposed pre-eclampsia or polyhydramnios.

4.3.12 Whilst admitted to the antenatal ward women with CKD should be discussed with their renal physician as depending upon the clinical situation dialysis may become necessary.

4.3.13 Delivery should be considered if there is deterioration of the renal function, superimposed pre-eclampsia or evidence of IUGR with abnormal dopplers (absent/reversed end-diastolic flow or evidence of redistribution).

4.3.14 Mode of delivery will be determined by normal obstetric considerations.

4.3.15 If there is no deterioration in the clinical picture IOL should be recommended no later than 40 weeks gestation.

4.4 Post-partum management of Patients with Kidney disease

4.4.1 Patients with known or newly diagnosed kidney disease in pregnancy should resume their established care with an early planned postpartum review in the renal clinic.

4.4.2 Patients with known or newly diagnosed renal disease in pregnancy should be offered contraceptive advice.

4.4.3 Breast-feeding should be encouraged in woman with chronic kidney disease.

5.0 Pregnancy in woman / pregnant person on dialysis

5.1 Incidence

5.1.1 Frequency of pregnancy in women /pregnant person on chronic dialysis appears to be increasing, ranging 1–7%.

5.1.2 Conception is more likely in women with residual renal function and those just beginning dialysis.

5.1.3 The incidence of pregnancy is lower in women on peritoneal dialysis than on haemodialysis.

5.2 Pregnancy outcome

5.2.1 Spontaneous miscarriage is common and occurs in 21% of pregnancies reaching the second trimester.

5.2.2 Preterm delivery is common.

5.2.3 The mean gestational age at delivery is 32 weeks.

5.2.4 Premature deaths contribute to the low infant survival rate of 30–50%. Perinatal outcome is better for women who conceive prior to starting dialysis than those who conceive after starting dialysis (73.6% versus 40.2%).

5.2.5 There is no significant difference in overall infant survival between women who receive peritoneal dialysis and those who receive haemodialysis.

5.2.6 Maternal complications include hypertension (40–80%), hypertensive crisis, pre-eclampsia, anaemia and placental abruption.

5.2.7 Approximately half of these women / pregnant people will be delivered by caesarean section

Recommendations for management

5.3.1 All women / pregnant people will need folate supplementation in the dosage of 5mg/day.

5.2.8 Nephrologist and dietician should be consulted regarding managing patients Nutrition.

5.2.9 Protein intake, calcium requirement and weight gain should be planned and monitored in conjunction with dietician and nephrologist .

5.2.10 Fluid intake should be determined individually, taking into account urine output and the type/frequency of renal replacement therapy the woman is receiving.

5.2.11 They also need measurement of 25-hydroxy vitamin D levels in each trimester and supplementation if these are found to be low.

5.2.12 Most people on dialysis tend to have high phosphate levels but if the levels are low, oral phosphate supplements can be used.

5.2.13 In addition, vitamin C, thiamine, riboflavin, niacin and vitamin B6 need to be supplemented

5.2.14 Management of haemodialysis and peritoneal dialysis should be Planned and managed in conjunction with the renal physician and according to local renal unit protocol

5.2.15 The aim is to maintain a predialysis blood urea of <15–20 mmol/l.

5.2.16 The maternal diastolic blood pressure should be maintained at between 80–90 mmHg.

5.2.17 Peritoneal dialysis can be continued safely during pregnancy. As pregnancy progresses, due to the size of the enlarging uterus it may become impossible to continue with peritoneal dialysis and there should be a switch to haemodialysis. Although the possibility of peritonitis exists, increased incidence has not been reported during pregnancy.

5.2.18 If caesarean section is necessary those on peritoneal dialysis will need to be changed temporarily to haemodialysis.

Management of anaemia

5.2.19 The erythropoietin dose may need to be increased by 50–100% to maintain the haemoglobin between 10–11 g/dL

5.2.20 In addition, intravenous iron supplementation may be required to maintain iron saturation of at least 30%.

6.0 Pregnancy in renal transplant recipients

6.0.1 Incidence

Pregnancy is estimated to occur in 12% of transplanted women of childbearing age and the number of kidney transplant recipients who conceive seems to be increasing.

6.1 Pregnancy outcome

6.1.1 The miscarriage rate is similar to the general population

6.1.2 Ninety-five percent of gestations end successfully.

6.1.3 The incidence of congenital anomalies is similar to the general population.

6.1.4 The ectopic pregnancy rate is higher and this is related to adhesions from previous surgery and peritoneal dialysis.

6.1.5 Hypertension pre-dates pregnancy in about 70% of kidney transplant recipients.

6.1.6 Superimposed pre-eclampsia and urinary tract infection occur in up to 40% of these women.

6.1.7 Acute bacterial pyelonephritis is relatively common.

6.1.8 There is also a higher risk of developing gestational diabetes.

6.1.9 The incidence of preterm delivery, preterm premature rupture of membranes and fetal growth restriction is as high as 60%.

6.1.10 Opportunistic infections are more common in immunosuppressed, pregnant kidney transplant patients. Of these, rubella, cytomegalovirus, toxoplasmosis, herpes simplex and hepatitis B and C can affect the fetus.

6.2 Timing of pregnancy

6.2.1 The following guidelines have been recommended for women who have had renal transplants who are contemplating pregnancy.

6.2.2 There should have been no rejection in the previous year.

6.2.3 Graft function should be adequate and stable

6.2.4 There should be no or minimal proteinuria (<500 mg/24 hours)

6.2.5 The woman / pregnant people should be on maintenance immunosuppression and stable dosage (for example, prednisolone ≤15 mg/day, azathioprine ≤2 mg/kg/day, ciclosporin ≤5 mg/kg/day).

6.2.6 There should be no acute infections that can affect the fetus (for example, cytomegalovirus).

6.2.7 Co-morbid conditions (for example, hypertension, diabetes) should be optimally assessed and managed.

6.3 Pre-Pregnancy counselling

6.3.1 This must include a discussion on the impact of pregnancy on acute rejection and graft loss.

6.3.2 The risk of acute rejection correlates with the pre-pregnancy serum creatinine levels as well as the interval between transplant and pregnancy.

6.3.3 Long-term survival of the graft appears similar in those undertaking pregnancy to those who do not become pregnant. Acute rejection in pregnancy occurs in 9–14% of women but the incidence of serious episodes of rejection is 5%, which is similar to the rates observed in non-pregnant transplant patients.

6.3.4 Little is known about the impact of pregnancy on chronic rejection.

6.4 Management of immunosuppressive regimens

6.4.1 Immunosuppressive agents should be continued at pre-pregnancy dosages.

6.4.1 Prednisolone, azathioprine, ciclosporin and tacrolimus are all safe to use in pregnancy.

6.4.2 Mycophenolate mofetil ('MMF') is best avoided in pregnancy due to risk of it causing facial malformation: rituximab, sirolimus or everolimus should also be avoided.

6.4.3 Breastfeeding while on immunosuppressive drugs is controversial because of concerns for the effects on the baby. However, these recommendations are not absolute. New evidence is emerging regarding low levels of drug excretion into breast milk (for example, on azathioprine).

6.5 Antenatal management

6.5.1 Multidisciplinary care needed with involvement of senior obstetrician, renal physician and specialist midwife. This can be done in the Joint Obstetric Medicine clinic at RSCH under Dr Carol Postlethwaite.

6.5.2 Women / pregnant people should be tested for cytomegalovirus, HIV, herpes simplex virus and hepatitis B and C.

6.5.3 Those found to be cytomegalovirus negative should have their titres rechecked in each trimester.

6.5.4 Oral glucose tolerance tests or, in cases where there is strong suspicion, blood sugar monitoring, should be arranged to diagnose gestational diabetes.

6.6 Management of hypertension

6.6.1 Methyldopa, Labetalol and Nifedipine are safe to use in these women.

6.6.1 Blood pressure should be maintained at a level of <135/85 ideally.

6.6.2 Magnesium sulphate prophylaxis can also be used safely in severe pre-eclampsia. The loading dose of magnesium remains the same.

6.6.3 The infusion of magnesium must be decreased according to the level of elevated creatinine over the normal pregnancy level and should be discussed with renal physician.

6.6.4 Uric acid is a less helpful marker since it can be raised in transplant patients without pre-eclampsia.

6.7 Labour management

6.7.1 In the absence of any obstetric complications, delivery is timed for 38–40 weeks of gestation.

6.7.2 Vaginal birth is the preferred route of delivery.

6.7.3 Prostaglandins and Oxytocin are both safe to use for cervical ripening or induction.

6.7.4 The allograft, located in the false pelvis, does not obstruct delivery of the fetus.

6.7.5 Caesarean section may be necessary for obstetric indications or if there are concerns related to severe pelvic osteodystrophy.

6.7.6 Early liaison with and involvement of the urology surgical team or renal transplant surgeons is advisable when elective caesarean section is planned.

6.7.7 Labour should be covered with hydrocortisone (100mg 6-8hourly) in women who are on immunosuppressive dosages of steroids.

6.8 Neonatal problems

6.8.1 Paediatrician should be informed.

6.8.2 Neonates can have thymic atrophy, transient leucopenia or thrombocytopenia, adrenocortical insufficiency, septicaemia and cytomegalovirus/hepatitis infection

<u>Appendix 1</u> - Conditions to be referred directly to Maternal Medicine/MEDIOBS and pregnancy effect

Renal Disease	Effect
Chronic Glomerulonephritis & Focal Glomeruonephritis	Usually no adverse effect in the absence of hypertension. Urinary Tract infection is more common
IgA nephropathy	Risk of uncontrolled/sudden escalating hypertension and worsening renal function.
Pylonephritis	Bacteriuria in pregnancy can lead to exacerbation Multi organ failure, including acute respiratory distress syndrome may ensue
Reflux nephropathy	Thought to be risk of sudden escalating hypertension; however, consensus now is that results are satisfactory when preconception function is only mildly affected & hypertension is absent. Vigilant screening for urinary tract infection is necessary.
Urolithiasis	Infection may be more frequent Stents can be successfully placed and ureterostomy performed during pregnancy. There is limited data on lithotripsy in pregnancy.
Polycystic Kidney Disease	Functional impairment and hypertension are minimal during childbearing years
Diabetic nephropathy	Usually there is no adverse effect on the renal lesion but there is increases risk of infection and pre-eclampsia.
Systemic lupus erythematosus	The prognosis is most favourable if disease is in remission for > 6 months preconception Higher doses of steroids may be needed postpartum Flare of lupus nephritis in pregnancy should be discussed with consultant obstetrician as severe lupus nephritis can be potentially life threatening, needing immediate treatment and termination may be needed.
Polyarteritis nodosa	Fetal prognosis is poor and maternal death often occurs. Therapeutic termination should be considered
Scleroderma	If the onset occurs during pregnancy there can be rapid overall deterioration. Reactivation of quiescent disease can occur postpartum
Previous urinary tract surgery	May be associated with other malformations of the urogenital tract. Urinary tract infection is common Renal function may undergo reversible decrease Caesarean section may be necessary to maintain continence mechanism if an artificial sphincter is in situ There are no other significant obstructive problems
After nephrectomy, solitary/ pelvic kidney	May be associated with other malformation. Pregnancy well tolerated Dystocia rarely occurs with pelvic kidney

Appendix 2 – Renal patient proforma

Attach patient label here

EDD by LMP: _____/_____/_____

EDD by USS : _____/_____/_____

Underlying renal condition

_____

Booking BP _____/ _____ mmHg

Baseline Bloods (Send FBC, U&Es & LFTs at booking)

Hb: _____ g/dL Plt: _____ Albumin _____

Baseline urine PCR: _____

MSU Sent at booking?

YES / NO

Recommended 5mg Folic acid? YES / NO (if NO why? _____)

Recommended 150mg Aspirin OD? YES / NO (if NO Why? _____)

ACE Inhibitors Stopped? YES / NO (if NO Why? _____)

Baseline renal scan requested? ☐

Growth scans arranged for 28 / 32 / 36 weeks? ☐

Gestation (Weeks)	Haemaglobin	Creatinine	Urea	Albumin	PCR	MSU sent? YES/NO	BP (mmHg)
12							
14							
16							
18							
20							
22							
24							
26							
28							
30							
32							
34							
36							

Reference List:

1. Modified Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. *Heart* 2006;**92**:1520-1525.

2. Saving lives, improving mother's care. MBRRACE 2020

3. Cardiovascular physiology of pregnancy. Sanghavi M, Rutherford JD. Circulation 2014; 130: 1003-1008

4. RCOG Green-top Guideline No. 68. Epilepsy in pregnancy

5. Management of pregnant women with epilepsy: a multidisciplinary collaborative approach to care. *The Obstetrician & Gynaecologist / volume 19, Issue 4 August 2017*

6. Girling J. Thyroid disease in pregnancy. **The Obstetrician & Gynaecologist** 2008;10:237–243

7. Management of thyroid dysfunction during pregnancy and post-partum: an Endocrine Society Clinical Practice Guideline. ***J Clin Endocrinol Metab, 97: 2543–2565, 2012.***

8. Inflammatory bowel disease in pregnancy. *Dipawita Kapoor. The Obstetrician & Gynaecologist / Volume 18, Issue 3*

9. NICE Fertility, pregnancy, and breastfeeding with Crohn's disease. August 2020

10. Handbook of Obstetric Medicine. *Catherine Nelson-Piercy*

Appendix 3 - Anti-hypertensive medications in CKD and Pregnancy

Commonly used	**rarely used**	**Contraindicated**
Nifedipine	Beta-blockers	ACE inhibitors
Labetalol	Alpha-blockers	Angiotensin receptor blockers
Methyldopa	Amlodipine	Aliskiren
Hydralazine	Verapamil	Spironolactone
		Moxonidine
		Minoxidil (3rd trimester)
		Thiazide diuretics
		Diltiazem