Hypertension in pregnancy including pre-eclampsia

Chapter contents

Hypertension is the most common medical disorder of pregnancy. The types of hypertension seen are chronic hypertension, gestational hypertension and pre-eclampsia.

Hypertensive disorders usually arise for the first time in the second half of pregnancy but can occur in women with pre-existing hypertension. They are among the leading causes of maternal death and carry risks for the fetus including preterm birth, intrauterine growth restriction and

death. The death rate has reduced enormously but there remains a significant morbidity burden.

Anaesthetists are rarely called on to be involved in the management of chronic hypertension or the mild end of the spectrum of pre-eclampsia. Recent confidential enquiries into maternal deaths emphasise that inadequate treatment of systolic hypertension is a serious failing. Systolic hypertension can result in fatal intracranial haemorrhage and has contributed to deaths from aortic dissection. The long-term consequences include chronic hypertension and an increase in lifetime cardiovascular risk.

The remainder of this section is concerned with pre-eclampsia. Oedema may be seen as an associated feature; the incidence is 85% but it is not diagnostic. Proteinuria is almost always seen as well but is not required to be present for the diagnosis.

This section draws from UHCW CG 1015 [279]. NICE guidance was published in June 2019 [280]; UHCW guidance is being updated.

Pathophysiology of pre-eclampsia

Pre-eclampsia is the extreme end of the continuum of a maternal systemic inflammatory response causing endothelial dysfunction [281,282]. Placental factors are secreted in response to a deficient placentation process (poor decidual invasion, in which fetal syncytiotrophoblasts fail to invade beyond the superficial uterine decidua to establish an efficient placental blood supply) combining restriction of uteroplacental blood flow through lack of structural remodelling with spiral artery atherosis, both of which lead to placental ischaemia.

Overt maternal disease develops when uteroplacental hypoxia stimulates release of antiangiogenic factors that injure the placental and maternal vasculature [283]. Placental soluble factor reduces bioavailability of Vascular Endothelial Growth Factor impairing endogenous nitric oxide production and increases sensitivity to pro-inflammatory cytokines. Renal changes are concentrated in the glomerulus with profound endothelial swelling and basement membrane disruption.

Diagnosis and definitions

Definitions are syndromic, based on non-specific or arbitrary features. The traditional diagnosis was based on hypertension, oedema and proteinuria. Oedema was removed as it is not a useful indicator. In 2018 proteinuria itself was removed as a required part of the diagnosis, so that pre-eclampsia can be diagnosed on hypertension and placental insufficiency alone [284].

Hypertension is blood pressure of 140 mmHg systolic or higher, or 90mmHg diastolic or higher.

Chronic hypertension is hypertension that is present at the booking visit or before 20 weeks or if the woman is already taking antihypertensive medication when referred to maternity services. It can be primary or secondary in aetiology.

Gestational hypertension is new hypertension presenting after 20 weeks without significant proteinuria.

Severe hypertension is defined as systolic blood pressure 160 mmHg or greater ± diastolic blood pressure 110 mmHg or greater.

Pre-eclampsia is new onset of hypertension (over 140 mmHg systolic or over 90 mmHg diastolic) presenting after 20 weeks **and** the coexistence of one or more of the following new-onset conditions: proteinuria, maternal organ dysfunction or uteroplacental dysfunction, as below.

Eclampsia is a convulsive condition associated with pre-eclampsia.

HELLP syndrome is haemolysis, elevated liver enzymes and low platelet count.

Severe pre-eclampsia is pre-eclampsia with severe hypertension that does not respond to treatment **or** is associated with ongoing or recurring severe headaches, visual scotomata, nausea or vomiting, epigastric pain, oliguria and severe hypertension, **as well as** progressive deterioration in laboratory blood tests such as rising creatinine or liver transaminases or falling platelet count, **or** failure of fetal growth or abnormal doppler findings.

Pre-eclampsia in detail

New onset of hypertension (over 140 mmHg systolic or over 90 mmHg diastolic) after 20 weeks of pregnancy and the coexistence of one or more of the following new-onset conditions:

1. proteinuria (urine protein:creatinine ratio of 30 mg $mmol^{-1}$ or more or albumin:creatinine ratio of 8 mg $mmol^{-1}$ or more, or at least 1 g L^{-1} [2+] on dipstick testing) or
2. other maternal organ dysfunction:
   - renal insufficiency (creatinine 90 micromol L^{-1} or more)
   - liver involvement (elevated transaminases [alanine aminotransferase or aspartate aminotransferase over 40 IU L^{-1}] with or without right upper quadrant or epigastric abdominal pain)
   - neurological complications such as eclampsia, altered mental status, blindness, stroke, clonus, severe headaches or persistent visual scotomata
   - haematological complications such as thrombocytopenia (platelet count below 150×10^9 L^{-1}), disseminated intravascular coagulation or haemolysis
3. uteroplacental dysfunction such as fetal growth restriction, abnormal umbilical artery doppler waveform analysis, or stillbirth

Significant proteinuria will need to be evaluated if a reagent-strip device shows proteinuria. It is diagnosed if the urinary protein:creatinine ratio is greater than 30 mg $mmol^{-1}$. Once diagnosed the quantification does not need to be repeated.

Severe headache

Headaches are common in pregnancy. Severe headache can occur as a symptom or complication of severe-pre-eclampsia or be coincidental. **Red flags** for immediate action are [285]:

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- Sudden-onset headache / thunderclap or worst headache ever.
- Headache that takes longer than usual to resolve or persists for more than 48 hours.
- Has associated symptoms – fever, seizures, focal neurology, photophobia, diplopia, neck stiffness. Consider subarachnoid haemorrhage or meningitis.
- Vomiting – consider cerebral venous sinus thrombosis or other causes of raised intracranial pressure.
- Excessive use of opioids.

Posterior reversible encephalopathy syndrome (PRES) can present with headache in the third trimester. PRES is associated with headaches, seizures and cortical blindness, caused by vasogenic brain oedema. Treat hypertension and administer magnesium sulfate.

Reversible cerebral vasoconstriction syndrome (RCVS) only occurs postpartum and is associated with severe hypertension and recurrent thunderclap headaches. The hallmark of RCVS is multifocal segmental cerebral artery vasoconstriction on cerebral angiography. This is treated with nimodipine and will eventually resolve.

Blood tests

You should review the patient's blood test results: she will be having repeated blood tests if she has moderate or severe hypertension, monitoring hepatic and renal function, electrolytes, full blood count, and hepatic function with transaminases and bilirubin (alkaline phosphatase will be elevated due to pregnancy and is not helpful here). Coagulation screens are indicated in severe pre-eclampsia.

Urate levels

Urate levels (uric acid levels) are raised in pre-eclampsia. This is because of renal dysfunction and the oxidative stress associated with pre-eclampsia. Higher urate levels are associated with a worse prognosis. Repeating the estimation of urate levels does not provide information

that should influence the management of pre-eclampsia. **Urate levels are not diagnostic.**

The normal level rises during pregnancy and is approximately:

28 weeks	300 µmol L^{-1}
32 weeks	350 µmol L^{-1}
36 weeks	400 µmol L^{-1}
40 weeks	450 µmol L^{-1}

Management aims

The disease-modifying treatment is delivery of the placenta. All other treatments are palliative, supportive or aimed at preventing complications.

The primary aims in the management of pre-eclampsia are:

- To deliver the fetus in optimum condition.
- To control maternal hypertension.
- To prevent eclampsia and the other complications.

Anaesthetists may become involved for:

- Epidural analgesia in labour.
- Urgent control and reduction of arterial blood pressure.
- Invasive monitoring of arterial blood pressure.
- Anaesthesia for caesarean section.
- Enhanced maternal care.
- General advice and support.

Severe pre-eclampsia must be managed in the EMC environment.

Target blood pressure

As the risks of subarachnoid haemorrhage and aortic dissection have become better understood, the target blood pressures have fallen. NICE

recommends that pharmacological treatment is offered at a blood pressure above 140/90, and that the treatment target on antihypertensive medication should be 135/85 or less [286].

Case responsibility

Management of severe pre-eclampsia is a team effort involving senior obstetricians, anaesthetists and midwives.

All cases of severe pre-eclampsia are under the care of a consultant obstetrician. All significant events, decisions and actions should be notified to or made by the consultant – usually by the duty obstetrician.

You must also ensure that you have appropriate senior anaesthetic input as required. Any conflicts of opinion in management should be resolved through joint senior review of the patient. Failure to have sufficiently senior review of patients with severe pre-eclampsia is associated with maternal death [287].

Enhanced maternal care in pre-eclampsia

See page 378 for general points about critical care.

Indications

Severe pre-eclampsia – the treatment recommendations in this section are not appropriate for mild pre-eclampsia, which is usually managed more conservatively in level 0 care.

Immediate actions

- Apply monitoring of blood pressure with an arterial line, pulse and oxygen saturation.
- Administer supplemental oxygen if SpO_2 < 96%, usually through nasal cannulas.
- Check that the laboratory samples have been sent (FBC, coagulation screen, crossmatch, biochemistry including liver function tests – all repeated at least every 12 hours; group and screen).

- Start the enhanced maternal care observations chart.
- Auscultate the patient's chest for pulmonary oedema and repeat this examination regularly every four hours. Ensure that the respiratory rate is being recorded.
- Patient on monitored sips of water only with oral ranitidine 150 mg BD or omeprazole 20 mg BD .
- Neurological assessment using AVPU (alert, responding to voice, responding to pain, unresponsive).
- Thromboprophylaxis with antiembolism stockings, encouragement of leg movement and (if delivery is not indicated) enoxaparin.

Further actions

Discuss with the obstetricians and midwives. Formulate a plan for delivery of the fetus and placenta with the obstetrician. This plan should include consideration of all elements in this section on pre-eclampsia.

Timing of delivery

Before 34 weeks, pre-eclampsia is managed conservatively without same-day delivery, unless refractory severe hypertension develops or other maternal or fetal indications as in the consultant plan.

After 34^{+0} weeks, birth is normally recommended for women who have pre-eclampsia with severe hypertension when their blood pressure has been controlled (and the corticosteroid course completed).

Delivery between 34^{+0} weeks and 36^{+6} depends on maternal and fetal condition and risk factors. After 37^{+0} weeks birth is recommended within 24-48 hours unless the woman has severe hypertension.

Magnesium sulfate treatment

Consider magnesium sulfate treatment, using the Collaborative Eclampsia Trial regimen, if the features of severe pre-eclampsia are present as above, and birth is planned within 24 hours.

Indications for referral to general adult critical care unit

The following indications should prompt a discussion between you and the obstetrician and midwife coordinator as to whether referral to the critical care unit is appropriate. While enhanced maternal care rooms are an appropriate location for patients with a restricted range of single disorders, you should consider whether the patient's needs have become more complex when one or more of the following complications arise.

- The patient needs level 3 care including ventilation.
- Step-down from level 3, or severe pre-eclampsia with any of the following complications:
    - Eclampsia.
    - HELLP syndrome.
    - Haemorrhage.
    - Hyperkalaemia.
    - Severe oliguria.
    - Coagulation support.
    - Intravenous antihypertensive treatment.
    - Initial stabilisation of severe hypertension.
    - Evidence of cardiac failure.
    - Abnormal neurology.

Antihypertensive stabilisation and treatment is usually managed on labour ward in Coventry.

Antihypertensive treatment

Extreme pre-eclamptic hypertension causes direct arterial injury that predisposes the patient to intracranial haemorrhage, one of the main causes of death in the hypertensive diseases of pregnancy. Anti-hypertensive treatment will prevent haemorrhage but not disease progression or eclampsia.

Women with severe hypertension who are in critical care during pregnancy or after birth are treated immediately with one of the following:

- Labetalol (oral or intravenous).
- Hydralazine (intravenous).
- Nifedipine (oral alternative).

Oral treatment is with labetalol; nifedipine in those for whom labetalol is not suitable, and methyldopa as the third choice. Methyldopa must be stopped within 2 days after the birth.

The treatment aim is to keep systolic blood pressure reliably below 150 mmHg, ideally below 135 mmHg, and diastolic blood pressure between 80 and 100 mmHg. This is to reduce complications and prevent the rare events of death from intracranial haemorrhage and aortic dissection.

Epidural analgesia is indicated in pre-eclampsia. It is useful to reduce fetomaternal stress and to prevent pain-induced hypertension, and it decreases the chance that general anaesthesia will be needed for caesarean section. It is not effective as an antihypertensive agent in itself.

You should use an arterial line for invasive blood pressure monitoring in any woman who fits this definition, or who is receiving intravenous vasoactive medications.

Do not cause the systemic blood pressure to fall precipitately and keep both mother and fetus under continuous monitoring, including blood samples every twelve hours at least.

In the acute situation, mean arterial blood pressure should be maintained below 140 mmHg. Give urgent and effective treatment if this level is repeatedly attained, as cerebral autoregulation may be lost. Do not allow the mean blood pressure to fall below 100 mmHg as this may compromise placental perfusion.

Severe hypertension refractory to treatment is an indication for expedited or operative delivery.

Monitor the response to antihypertensive treatment to ensure that the blood pressure falls, identify adverse effects and modify treatment according to response.

Monitoring blood pressure non-invasively

Automated oscillotonometers may significantly underestimate the diastolic blood pressure, particularly in severe pre-eclampsia. Non-invasive blood pressure readings should be taken with the arm at the level of the heart, using or a validated automated oscillotonometer with a cuff of adequate size: 1½ times the arm circumference. Use Korotkoff phase V (disappearance) if checking blood pressure manually.

Choice of drug for acute hypertension

Oral labetalol is the preferred drug. Use hydralazine in women with asthma or add hydralazine in those who do not respond to labetalol alone. Women of African or Caribbean origin may be less responsive to labetalol alone.

The treatment aim is a systolic blood pressure reliably under 150 mmHg, ideally under 135 mmHg, with maternal and fetal stabilisation.

Avoid ACE inhibitors, as they are associated with fetal hypotension and irreversible renal failure. Avoid esmolol because it is associated with fetal bradycardia.

When emergency intravenous treatment is needed, for a systolic blood pressure above 150-160 mmHg and with an arterial line in place, we recommend intravenous labetalol given by an anaesthetist.

Labetalol is started orally in the dose of 100 mg twice daily; doses of 200 mg four times daily may be required. The obstetricians will give a stat dose of 200 mg orally in severe pre-eclampsia.

Acute control of severe hypertension is achieved with 50 mg intravenously over at least five minutes, repeated at ten-minute intervals is the systolic blood pressure does not reduce below 160 mmHg, to a maximum dose of 200 mg. Maintenance therapy is with intravenous labetalol (neat solution via syringe driver only – 100 mg in 20 mL, or

5 mg mL^{-1}) at a dose of 20 mg h^{-1} doubled every thirty minutes to a usual maximum of 160 mg h^{-1}. 10% of patients may be resistant to its effects and in these cases, intravenous hydralazine should be used instead.

The most important contraindication to labetalol in the labour ward is maternal asthma (use hydralazine instead), but you should remember that it is a potent β-blocker, contraindicated in known cardiac disease. Hyperglycaemia or hypoglycaemia can occur, and it should be used with care in diabetes.

Hydralazine is given as a first treatment of intravenous hydralazine 5 mg (10 mg may be given), administered slowly. Observe the effect over 20 minutes. Do not give further doses in this time, as hydralazine does not act immediately. Then set up an infusion of 40 mg made up to 40 mL with sodium chloride 0.9% solution, given via syringe pump. Infusion rates are typically around 1-5 mL h^{-1}.

Hydralazine may cause tachycardia; nifedipine may be used to reduce the hydralazine dose and any complicating tachycardia. Hydralazine can cause headaches, anxiety and hyperreflexia, mimicking deteriorating pre-eclampsia [288]. Intravenous hydralazine should not normally be used for more than six hours before switching to oral or intravenous labetalol. Intravenous treatment can cause a sudden drop in arterial blood pressures due to the revealed hypovolaemia. 500 mL of Hartmann's solution will help prevent damaging hypotension and fetal distress (do not use unless hydralazine is used; this is not a fluid challenge for oliguria). Use continuous cardiotocographic monitoring.

Nifedipine is useful with hydralazine, instead of labetalol or occasionally as sole treatment while awaiting intravenous treatment. Sublingual nifedipine causes too rapid a fall in blood pressure and uteroplacental perfusion and the oral form should be used. The dose is 10-20 mg. Nifedipine may cause profound hypotension with magnesium therapy.

Fluids in severe pre-eclampsia

See [289] for a discussion. Fluid overload is a contributing factor in up to one in two deaths from pre-eclampsia. Iatrogenic pulmonary oedema is

much more common than renal failure: run these patients on the dry side.

That being said, the recent reductions in mortality rate have been particularly marked in relation to pulmonary oedema and renal failure; the changes in fluid regimes have been successful [290].

General principles

- Careful control of fluid balance is of paramount importance.
- Limit maintenance fluids to 80 mL h^{-1} unless there are other ongoing fluid losses (for example, haemorrhage).
- Intravenous fluids should always be infused using a volumetric pump.
- Antepartum oliguria indicates early delivery.
- Immediate postpartum oliguria must not be treated with aggressive fluid therapy.
- Do not preload with intravenous fluids before establishing low-dose epidural analgesia.
- Do not use volume expansion unless hydralazine is used as an antenatal antihypertensive agent.
- Perform frequent clinical assessment.
- Transient oliguria occurs regularly in pre-eclampsia and is only rarely complicated by acute renal failure. Fluid management of oliguria need not be as aggressive as in general surgical patients. Indeed, it may be useless, as oliguria arises from glomerular structural problems not adverse haemodynamic factors.
- Avoid fluid challenges. Diuretics are only indicated in overt fluid overload or pulmonary oedema.
- The reduced colloid osmotic pressure found in association with severe pre-eclampsia increases the risk of pulmonary oedema at 'normal' filling pressures. Pulmonary oedema is usually associated with fluid therapy. The peak incidence is at 48-72 hours postpartum.

- Hypovolaemia due to obstetric haemorrhage must be corrected, carefully so as not to cause pulmonary oedema.
- For management of pulmonary oedema see page 440.

Fluid balance

You should maintain strict fluid balance control with hourly urine measurement. The usual fluid regime for maintenance is Hartmann's solution to 80 mL h^{-1}, adjusted for other fluid inputs, to a maximum of 1 mL kg^{-1} h^{-1} when adjusted for low body mass.

Observe for the onset of pulmonary oedema. Auscultate the chest regularly (every four hours) for signs. Mild hypoxia is a useful early marker, although other causes such as infection must be excluded. Continuous pulse oximetry must be used.

Central venous pressure monitoring in severe pre-eclampsia

CVP monitoring is only rarely used today and usually only when intravenous access is not possible by another route. It is no longer needed for close management of oliguria, and the vasoactive medications used in severe pre-eclampsia do not require central venous administration. Insertion of a CVP line is now an indication for transfer to level 2 critical care owing to midwife unfamiliarity with the technique.

Management of postpartum oliguria

Antepartum oliguria should not precipitate any specific intervention other than to encourage early delivery.

Ideally, the patient's urine output will be at or above 0.4 mL kg^{-1} h^{-1}. You should usually wait to see if the urine output is low over a four-hour period – as a guide, expect 100 mL urine in 4 hours. If you are in any doubt, seek advice from the obstetricians and from senior anaesthetists. Remember oliguria is common for six hours postpartum in a normal pregnancy, especially when oxytocin has been used. Management is expectant.

If the patient is oliguric (urine output < 0.4 mL kg^{-1} h^{-1}), determine the fluid balance over the last 24 hours and correct any fluid deficits due to long labour or operative delivery etc. Do not however give fluid challenges – this may precipitate pulmonary oedema. The albumin level should be measured urgently. Consider stopping any magnesium infusion if there is concern over renal side-effects.

Check the arterial blood gases to determine whether metabolic acidosis is present.

If the plasma creatinine level is less than 100 µmol L^{-1}, and there is no HELLP and no bleeding, oliguria will be transient and self-limiting.

Oliguria is dangerous when creatinine rises above 125 µmol L^{-1}. Complete anuria for more than one hour is very rare and may herald total renal failure.

Furosemide is usually reserved for treatment of heart failure or pulmonary oedema.

The management of oliguria in pre-eclampsia with an adequate fluid status involves consultant-level discussion and cannot be safely determined in a fixed protocol. You should ensure that appropriate advice is available to the team. A renal physician should usually be involved in the multidisciplinary team.

Magnesium treatment

The proven anticonvulsant therapy required in pre-eclampsia is to control systemic blood pressures. Signs of cerebral irritability should be repeatedly sought: presence of headaches or flashing lights, ankle clonus of more than three beats or an aura of convulsion.

Magnesium sulfate may be considered for primary prevention of convulsions in severe pre-eclampsia, but only after consultation with the consultant obstetrician. The MAGPIE trial showed some benefit [291] but the results are believed to be equivocal due to the very high number needed to treat (63 for severe pre-eclampsia at best) in order to prevent one seizure [292]. The primary action of magnesium is to relieve cerebral vasospasm. It is useful especially when signs of cerebral ischaemia are

present. If the infusion is commenced, it should be continued for twenty-four hours. Magnesium infusions halve the risk of eclampsia in these circumstances.

The occurrence of tonic-clonic convulsions makes the diagnosis of **eclampsia**. Ensure that the patient has been placed into the left lateral position and that oxygen therapy and intravenous access have been established. Check the patient's history and medication for the prior existence of epilepsy or other epileptogenic condition. Check for hypoglycaemia.

Administer a bolus of intravenous magnesium sulfate if it has not already been given. Magnesium should be given for at least twenty-four hours after the convulsion. Evidence from the Collaborative Eclampsia Trial clearly shows that magnesium sulfate is the treatment of choice for the primary treatment and secondary prevention of eclamptic convulsions [293]. 10% of women will convulse again on magnesium therapy. The consultant anaesthetist on call must be informed.

Eclamptic convulsions are usually self-limiting and will terminate after about ninety seconds. They may eventually be lethal if left untreated.

There is robust evidence indicating that magnesium sulfate is the treatment of choice [294]; the focus of treatment priorities is to start magnesium promptly.

NICE recommends the consideration of magnesium sulfate if one or more features of severe pre-eclampsia is present [295]:

- Ongoing or recurring severe headaches.
- Visual scotomata.
- Nausea or vomiting.
- Epigastric pain.
- Oliguria and severe hypertension.
- Progressive deterioration in laboratory blood tests (such as rising creatinine or liver transaminases, or falling platelet count).

Magnesium administration

Magnesium infusions are used for prophylaxis in severe pre-eclampsia, the treatment of eclampsia and also fetal neuroprotection.

Magnesium infusions are used in preterm labour (from 23^{+0} to 29^{+6} weeks) to reduce the risk of neonatal cerebral palsy [296], at the same dose as for severe pre-eclampsia.

Remember that magnesium sulfate is synergistic with non-depolarising neuromuscular blocking drugs and their action will be potentiated. Use them only in reduced doses with careful neuromuscular monitoring – it is better to give more suxamethonium if muscle relaxants are needed, together with atropine to counteract potential bradycardia. Fasciculations with administration of suxamethonium may not occur after magnesium treatment.

Magnesium administration is associated with an increased incidence and severity of obstetric haemorrhage.

Flushing and a feeling of surface heat are common with magnesium treatment. Nausea, vomiting and flushing are early signs of magnesium toxicity. ECG signs can occur: PR and QRS prolongation. Deep tendon reflexes disappear, and apnoea and cardiac arrest may follow.

Rapid administration of magnesium can cause asystole.

The antidote for magnesium overdose is 10 mL of 10% calcium gluconate given by slow intravenous bolus.

There is a box on the resuscitation trolley on labour ward containing everything you need to commence magnesium treatment.

1. Magnesium sulfate ($MgSO_4$) is presented as 10 mL ampoules of 50% concentration (0.5 g mL^{-1}) that contain approximately 2 mmol mL^{-1} of Mg^{2+}.
2. Make up 50 mL of a 20% $MgSO_4$ solution (contains 10 g $MgSO_4$):
   - 2 x 10 mL $MgSO_4$ (5 g per ampoule).
   - 3 x 10 mL sodium chloride 0.9% solution.

   5 mL solution now contains 1 g $MgSO_4$ (equating to 200 mg mL^{-1}). The syringe should be mounted into an infusion pump.

3. Give 4 g (20 mL) of the 20% $MgSO_4$ solution, over 10 minutes. Set the pump with a volume to be infused of 20 mL at a rate of 120 mL h^{-1}. Be sure to limit this infusion so that the entire syringe is not given.
4. Observe for cardiac or respiratory arrest while loading – this can occur with rapid bolus infusion.
5. Maintain an intravenous infusion at 1 g h^{-1} $MgSO_4$ (5 mL h^{-1}).
6. Clinical monitoring is sufficient when this dose regimen is used.
    - The respiratory rate should be checked before treatment and every 15 minutes during treatment and should be 10 per minute or more.
    - Patellar reflexes should be checked before treatment, 30 minutes after the loading dose and hourly thereafter (use biceps tendon if epidural block established), and should be present.
7. **If convulsions persist**, give a further bolus of 2 g (10 mL) over 5 minutes (i.e. set the pump with a volume to be infused of 10 mL at a rate of 120 mL h^{-1}).
    - Then increase the rate of infusion to 1.5 g h^{-1} $MgSO_4$ (7.5 mL h^{-1}).
    - If possible, take blood for magnesium levels prior to giving the bolus dose.
    - Consider alternative diagnoses for seizures.
    - The woman may need CT scan or ventilation.
8. If the woman is still antenatal, stabilise her condition before making plans for birth.

Magnesium therapy and oliguria

The kidney excretes magnesium and toxicity is more likely if the renal output is poor. If the urine output is less than 20 mL h^{-1} review the

patient and consider using plasma creatinine to guide the magnesium therapy.

Creatinine < 100 µmol L^{-1}	Continue as above.
	Check Mg^{2+} every 2 hours.
Creatinine 100-150 µmol L^{-1}	Reduce $MgSO_4$ infusion to 1 g h^{-1} (5 mL h^{-1}).
	Check Mg^{2+} every 2 hours.
Creatinine > 150 µmol L^{-1}	Stop the $MgSO_4$ infusion.
	Check Mg^{2+} immediately and every two hours.
	If Mg^{2+} concentration is under 3.5 mmol L^{-1}, infuse $MgSO_4$ at 0.5 g h^{-1} (2.5 mL h^{-1}). Seek advice from the consultant obstetrician.

If the urine output is less than 10 mL h^{-1} do not use $MgSO_4$. Call the consultant obstetrician.

Although magnesium toxicity is very rare with this dosing regime, the use of magnesium in severe renal impairment is associated with irreversible cardiac arrest.

Magnesium toxicity

1. If signs of toxicity (respiratory rate below 10 or absent deep reflexes) are found the infusion should be halted, supplemental oxygen administered if not already given and a blood sample for magnesium level taken. If there is no rapid clinical improvement, consider administering intravenous 10 mL of 10% calcium gluconate (1 g) slowly, especially if tendon reflexes are absent.
2. Check the blood magnesium concentration if you are concerned that it lies outside the therapeutic range, (symptoms or signs of toxicity or recurrent seizures); if using a different regimen than the one above; or if renal function is impaired (urine output less than

100 mL in four hours or urea level above 10 mmol L^{-1}). Check levels at one hour, four hours, and then six-hourly.

3. The therapeutic range is 2.0-3.5 mmol L^{-1}.
4. Serum Mg^{2+} levels:

> 5.0 mmol L^{-1}	Stop $MgSO_4$ infusion. Ask for consultant advice. Give 1 g calcium gluconate over 10 minutes (10 mL of 10% solution, or 2.2 mmol Ca^{2+}).
3.5-5.0 mmol L^{-1}	Stop the $MgSO_4$ infusion for 15 minutes. Restart at half previous rate if urine output > 20 mL h^{-1}. If urine output < 20 mL h^{-1} ask for consultant advice before restarting magnesium.
2-3.5 mmol L^{-1}	Therapeutic range.
< 2 mmol L^{-1}	Increase the infusion rate to 3 g h^{-1} (15 mL h^{-1}) for 2 hours. Re-check serum concentration and clinical state.

HELLP syndrome

This is characterised by:

- **H**aemolysis.
- **E**levated **L**iver enzymes.
- **L**ow **P**latelets.

It is an ominous form of severe pre-eclampsia – the extreme end of the continuum of liver complications, with an incidence of less than 0.5%. Clinical features are:

- Epigastric pain.
- Right upper quadrant tenderness.
- Nausea and vomiting.

- Signs and symptoms of pre-eclampsia.

The commonest associated complications (more than 5%) of HELLP syndrome are disseminated intravascular coagulation (consumption coagulopathy), placental abruption, acute renal failure, pulmonary oedema and pleural effusion. Mortality is more than 1%.

Diagnosis can be made when:

- Serum bilirubin and transaminases are elevated (ALT or AST rising to above 70 iu L^{-1}).
- Haemolysis is seen on abnormal peripheral blood smear.
- The platelet count is below 100×10^9 L^{-1}.

The transaminase rise indicates hepatic ischaemia. The haematology department may be able to run a haemolysis screen. Ask for a screen with manual differential and biochemical estimation of haptoglobin.

All cases must be managed at consultant level.

Specific points

- Management is supportive. Consider discussing the case with the Liver Unit at Queen Elizabeth Hospital in Birmingham, particularly if liver function does not steadily improve over a few days, or if transaminases are rising rapidly.
- Ultrasound or MRI scanning can show haemorrhage or ischaemia.
- Platelet transfusion should be arranged if the count is below 20×10^9 L^{-1} for vaginal delivery and 50×10^9 L^{-1} for caesarean section. Extra blood should be ordered. (HELLP is not an indication for immediate operative delivery.)
- Coagulopathy will normally need treatment with fresh frozen plasma. Discuss with a consultant haematologist.
- Regional techniques are contraindicated due to the risk of bleeding. If there is a labour epidural in place, remove it as soon as possible after delivery. The platelet count nadir is likely to be at 24-72 hours postpartum.

- Fluid balance must be strictly controlled. Guidelines may be varied depending on the extent of hepatic impairment. For example, sodium chloride 0.9% solution may be indicated rather than Hartmann's solution.
- The risk of thromboembolic disease is increased and heparin should be administered regularly.
- All drugs administered should have minimal hepatic and renal metabolism.
- Severe hypoglycaemia may occur and should be sought vigilantly. This may more commonly indicate severe sepsis.
- HELLP syndrome may occur in the postpartum period and this is particularly associated with pulmonary oedema and acute renal failure.

The continuum of hepatic disease associated with pre-eclampsia includes acute fatty liver of pregnancy. This is rare and dangerous. Differentiation from HELLP syndrome is through profound hypoglycaemia and marked hyperuricaemia. Hepatic failure may follow. Treatment is supportive with consideration of transfer to the regional liver unit.

Epidural analgesia in pre-eclampsia

Epidural analgesia is indicated for patients with pre-eclampsia:

- Good analgesia reduces the swings in blood pressure that are otherwise seen during contractions due to catecholamine release.
- Uteroplacental perfusion is improved so long as hypotension does not occur.

Epidurals used in this situation are managed much as any other. However, there are some caveats.

- There is a higher risk of coagulation problems, including vertebral canal haematoma, due to pre-eclampsia and its treatment. In general, with a normal coagulation screen, and platelet count $> 75 \times 10^9\ L^{-1}$ and not falling, CNB may be safely undertaken in these

patients; see 'Indications for haematological investigations' on page 156 for details. Many patients with mild pre-eclampsia will not need further investigations before an epidural.

- Do not preload with intravenous fluids before establishing low-dose epidural analgesia [297]. Beware fluid overload in these patients: their albumin concentration and thus colloid osmotic pressure is reduced and they are more at risk of developing pulmonary oedema.
- Pre-eclamptic patients are more sensitive to the effect of vasopressor drugs such as ephedrine and metaraminol. However, vasopressors should be used as indicated to prevent and treat hypotension.
- The use of hypotensive drugs in labour may exacerbate the vasodilator effects of an epidural and the dose may need to be reduced. Epidural analgesia by infusion may be preferable, especially in severe pre-eclampsia.

Anaesthesia for caesarean section in pre-eclampsia

Assessment and choice of technique

The obstetric team should discuss with you any planned birth in a woman with pre-eclampsia [298].

You should assess as for any operative procedure, paying particular attention to:

- Laboratory results, including platelets and coagulation studies as indicated (see page 156).
- Facial oedema, dysphonia, stridor or respiratory distress – these signs are associated with glottic oedema and difficult intubation.
- Cerebral irritability (visual disturbances, hyperreflexia and clonus).
- Urine output.
- The extent to which the patient has been resuscitated and hypertension controlled.

The patient should give informed consent but since choice of technique is more likely to be modified by medical advice, you must be prepared to make a firm recommendation to the patient.

The quick onset of vasodilation in a patient who is relatively hypovolaemic may give rise to marked hypotension – a disaster for a compromised fetus. Traditionally this has contraindicated the use of spinal anaesthesia. We believe however that carefully managed, the benefits of spinal anaesthesia outweigh the risks where it is otherwise indicated, for both mild and severe pre-eclampsia except as below.

Choice of technique: mild and moderate pre-eclampsia

You should proceed with anaesthesia for caesarean section as otherwise indicated. The preferred technique is spinal anaesthesia.

Choice of technique: severe pre-eclampsia

You should inform the consultant anaesthetist on call about any patient with severe pre-eclampsia who needs a caesarean section.

The preferred technique is spinal anaesthesia but there a number of specific indications for general anaesthesia:

- Coagulopathy and risk of vertebral canal haematoma (see page 156).
- Ongoing seizures, decreased conscious level or cerebral oedema.
- Other indications e.g. acute fetal compromise.

You should make every effort to control hypertension prior to anaesthetising the patient. This may mean placing the fetus' needs after those of the mother. If it is imperative to proceed prior to stabilisation on an antihypertensive regimen, then general anaesthesia is the preferred technique.

You must call for senior help in these circumstances and notify the consultant anaesthetist on call.

Sensitivity to intravenous vasoactive drugs

Pre-eclamptic patients are more sensitive to the effect of vasopressor drugs such as ephedrine and metaraminol. Women with pre-eclampsia may well develop less hypotension after spinal anaesthesia than do healthy women. Vasopressors should be used as indicated to prevent and treat hypotension, but use them with care, with arterial lines if severe pre-eclampsia, and be prepared to use lower doses or terminate use early. Occasionally a patient with have a paradoxically greater need for vasoconstrictor drugs after spinal anaesthesia.

You should use arterial line monitoring for induction in all cases of severe pre-eclampsia whether using general or regional anaesthesia. Use ergometrine with care, arterial line monitoring and dose reduction.

Oxytocin has a less predictable pharmacodynamic profile in severe pre-eclampsia [299]. While it should always be used with care when given as an intravenous bolus, use additional caution in severe pre-eclampsia.

Ergometrine is safe and effective when given in small, monitored, intravenous doses. Use 500 mcg diluted to 10 mL with sodium chloride 0.9% solution and give 25-50 mcg.

General anaesthesia and pre-eclampsia

It is important that the blood pressure is controlled prior to induction as described above.

In patients with severe pre-eclampsia, once the blood pressure is controlled, you should anticipate the hypertensive response to laryngoscopy by giving 20-30 mcg kg^{-1} of alfentanil one minute prior to induction. (20 mcg kg^{-1} if magnesium is being used, 30 mcg kg^{-1} if not.) You must inform the paediatrician if alfentanil is used and be wary of neuromuscular blocker potentiation.

An otherwise standard technique should then be used. Ensure that small endotracheal tubes are available prior to induction and start with a size 7.0 mm.

Postoperative enhanced maternal care

You should consider certain patients for postpartum enhanced maternal care.

- Eclamptic patients – these patients may require a period of ventilation on the critical care unit after caesarean section.
- Patients with severe pre-eclampsia.
- Patients who are oliguric before delivery, even if they have only mild pre-eclampsia.
- Patients with mild pre-eclampsia who, after a period of two hours observation in recovery post-delivery are seen to be oliguric or require parenteral hypotensive or anticonvulsant treatment.
- Patients with coagulopathy.
- Other patients about whom you are concerned.

Consult with the obstetrician to determine a plan for the patient.

The postpartum period in pre-eclampsia

Although delivery of the placenta results in resolution of pre-eclampsia, and mothers are usually better within 48 hours of delivery, they may still deteriorate.

The peak incidence of complications such as pulmonary oedema and eclamptic convulsions is after delivery.

General principles of management

Work as a team with the obstetricians and midwives.

- Ask the woman about severe headache and epigastric pain at each contact.
- Fluid balance and the management of oliguria are as important in the postnatal period as in the antenatal period.
- Antepartum magnesium sulfate is usually continued for 24 hours after delivery, longer if indicated.

- Monitor the blood pressure and use continuous pulse oximetry. Treat hypertension.
- Observe for the onset of cerebral irritability and treat accordingly. Magnesium sulfate is the treatment of choice.
- Give analgesia as indicated; give epidural diamorphine if the caesarean section was under epidural or use an intravenous morphine infusion if no diamorphine has been given. Diclofenac should not be given for 24 hours after delivery in severe pre-eclampsia due to the potential effects on renal and platelet function. Give dihydrocodeine 30 mg QDS until NSAIDs can be used.
- The patient should be 'nil by mouth' for 24 hours after a caesarean section in severe pre-eclampsia. Continue acid reflux suppression intravenously or orally until the mother is eating and drinking normally. This may be delayed further owing to the development of paralytic ileus. Check for bowel sounds when assessing for pulmonary oedema.
- Thromboprophylaxis: ensure that subcutaneous heparin has been prescribed. Do not delay giving thromboprophylaxis unless the coagulation times are proven to be significantly prolonged.
- Continue observations and investigations from the antenatal period until it is agreed by the responsible consultant that the high-risk period has passed.
- Oral antihypertensives are usually started 24 hours after delivery.

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