SEVERE PRE-ECLAMPSIA

DEFINITIONS
- **Pre-eclampsia**: pregnancy induced hypertension with significant proteinuria +/- oedema affecting virtually any organ system in the body
- **Severe pre-eclampsia**: Diastolic blood pressure >110 mmHg or systolic blood pressure >160 mmHg on more than two occasions, with significant proteinuria

Maternal and fetal complications associated with severe pre-eclampsia

<table>
<thead>
<tr>
<th>Maternal</th>
<th>Fetal</th>
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<tbody>
<tr>
<td>Eclampsia</td>
<td>Prematurity</td>
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<tr>
<td>Placental abruption</td>
<td>Intrauterine growth restriction</td>
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<tr>
<td>Severe hypertension</td>
<td>Respiratory distress syndrome</td>
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<tr>
<td>Risk of cerebral haemorrhage</td>
<td>Acute fetal distress</td>
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<tr>
<td>Pulmonary oedema</td>
<td>Placental abruption</td>
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<tr>
<td>Renal failure</td>
<td>Intrauterine death</td>
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<tr>
<td>Liver failure or ruptured liver</td>
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<tr>
<td>Disseminated intravascular coagulation (DIC)</td>
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<td>and/or HELLP syndrome</td>
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<tr>
<td>Pulmonary haemorrhage</td>
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<tr>
<td>Aspiration pneumonia</td>
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<td>Retinal detachment</td>
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<td>Circulatory collapse</td>
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<td>Maternal death</td>
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RECOGNITION AND ASSESSMENT

**Symptoms**
- Headache
- Visual disturbance
- Epigastric pain
- Vomiting

**Signs**
- Hyperreflexia with clonus
- Abdominal tenderness – right upper quadrant
- Proteinuria of at least 1+ or >0.3 g in 24 hr with or without symptoms
- Papilloedema
- Liver tenderness

**Investigations**

**Urine**
- Dipstick measurement; proteinuria of at least 1+
- Confirm using a 24 hr collection
- >300 mg protein or urinary protein/creatinine ratio >30 mg/mmol with or without symptoms

**Blood**
- FBC
- If platelet count <100 x 10^9/L perform clotting studies
- LFT
- ALT or AST rising or >70 IU/L
- U&E and uric acid
- Group & save
- Rapidly changing biochemical and haematological picture
IMMEDIATE MANAGEMENT
- Admit all women with severe pre-eclampsia or eclampsia
- Give high dependency care – see High dependency care guideline
- Carefully explain problem and management to woman and birth partner

Multi-disciplinary team planning
- Ensure early involvement and liaison between senior obstetrician, intensive care specialists, delivery suite (DS) midwife co-ordinator and neonatologist in assessment and management of women with suspected or proven severe pre-eclampsia and eclampsia

Monitoring
- Start high dependency care chart

Minimum requirement
- Maternal pulse and BP – with woman rested and sitting at a 45° angle every 15 min until stabilised, then every 30 min
- Ensure appropriate cuff size used and placed at level of heart
- Use multiple readings to confirm diagnosis
- Use an automated machine that has been validated for use in pregnancy
- Oxygen saturations continually and recorded hourly – obstetric review if <96%
- Respiratory rate hourly
- Temperature 4-hrly
- Fetal heart rate – continually by electronic fetal monitoring (EFM) – see Electronic fetal monitoring guideline

Examine
- Optic fundii for signs of haemorrhage and papilloedema
- Assess for hyperreflexia and clonus

TREATMENT
- Give antacid prophylaxis e.g. ranitidine 150 mg oral 6-hrly (if oral inappropriate, 50 mg IM 6-hrly)
- If fetus <34 weeks’ gestation, give betamethasone two 12 mg doses IM 12 or 24 hr apart (depending on clinical situation) to promote fetal lung maturity

Blood pressure control

| The aim of anti-hypertensive therapy is to maintain systolic BP <160 mmHg and prevent cerebral haemorrhage and hypertensive encephalopathy |

When
- In women with a systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg, begin antihypertensive treatment

How
- Oral and IV labetalol, oral nifedipine (unlicensed) and IV hydralazine, are commonly used agents of choice for severe hypertension – see Drug treatment regimen below

Notes
- Consider insertion of arterial line in woman who will be receiving continuous IV antihypertensive; close liaison with anaesthetist is essential
- Avoid rapid fall in blood pressure as this can potentiate fetal distress
- Aim to keep blood pressure <150/80–100 mmHg

Prevention of seizures
- Administer magnesium sulphate prophylaxis – See Magnesium sulphate below
Severe eclampsia 2013–15

Fluid management

Amount of fluid
- Avoid fluid overload – limit total IV input to 1 mL/kg/hr; max 80 mL/hr
- include all drugs administered in the hourly volume input of fluid
- if oxytocin required, use a reduced fluid oxytocin regimen
- Always use syringe driver or IVAC to control delivery of fluids

Type of fluid
- If marked hypovolaemia due to haemorrhage (>500 mL), haemolysis or DIC, give blood +/- blood products – discuss with haematologist

Monitoring
- Measure fluid input and output hourly
- insert Foley indwelling catheter to measure urine output
- When pre-eclampsia is complicated by pulmonary oedema, persistent oliguria or significant blood loss, consider CVP monitoring after discussion with anaesthetist

Oliguria
- During labour and after delivery, oliguria is not uncommon
- renal failure is unusual in pre-eclampsia and is usually associated with additional problems e.g. haemorrhage and sepsis
- give woman with severe pre-eclampsia controlled fluid and wait for natural diuresis to occur approximately 36–48 hr after delivery
- If oliguria <100 mL over 2 consecutive 4 hr periods, check U&E and auscultate chest
- if no signs of fluid overload, give 250 mL colloid fluid challenge and assess response
- if oliguria persists, senior review and consider furosemide and central venous pressure (CVP) monitoring
- if prolonged antenatal oliguria or anuria, prepare for delivery

Thromboembolism
- Give thromboprophylaxis (See VTE – Thromboprophylaxis guideline)

DELIVERY

Timing of delivery
- Once woman stable, consultant obstetrician and anaesthetist make decision to deliver.
- Liaise with neonatology team
- If fetus premature and delivery can be delayed, give betamethasone – two 12 mg doses IM 12 or 24 hr apart (depending on clinical situation) to promote fetal lung maturity.
- Reassess benefits of continuing the pregnancy after 24 hr

Mode of delivery
- Consider fetal presentation and condition, together with likelihood of success of induction of labour
- after 34 weeks’ gestation with a cephalic presentation, consider vaginal delivery
- in <32 weeks’ gestation, prefer caesarean section
- If vaginal delivery planned, plan short second stage with consideration of elective operative vaginal delivery

Notes
- An epidural is a useful method of controlling blood pressure and providing analgesia but may be contraindicated in low platelet count
- If oxytocin indicated for induction of labour or augmentation, give IV via a syringe driver and administer a reduced fluid regime

Managing third stage of labour
- Manage third stage with 5 units oxytocin IM

*Do not give ergometrine or syntometrine in any form for prevention of haemorrhage as this can further increase blood pressure*
Severe eclampsia 2013–15

**ECLAMPSIA**
- One or more convulsions superimposed on pre-eclampsia
- See Eclampsia guideline

**HELLP SYNDROME**
- Haemolysis, elevated liver enzymes and low platelets (HELLP) occurs in approximately 4–12% of women with severe pre-eclampsia. It is associated with a high perinatal mortality

**Symptoms**
- Can present with vague symptoms which often delay diagnosis
- nausea
- vomiting
- epigastric pain and right upper-quadrant pain
- A unique feature of HELLP syndrome is ‘coca-cola’ appearance of urine; small amounts of dark black urine are produced

**Diagnosis**
- Confirmed by:
  - fragmented red cells on blood film
  - platelet count <100 x 10^9/L
  - Elevated AST >75 IU/L significant and >150 IU/L is associated with maternal morbidity
  - Severe hypertension is not always a feature of HELLP syndrome and degree of severity rarely reflects overall severity of the disease

**Management**
As for severe pre-eclampsia plus:
- Evaluate severity
- Hourly BM
- Monitor conscious level and look for signs of confusion
- Stabilise
- Early blood transfusion – these women are often profoundly anaemic
- Contact haematologist early for advice about replacement of clotting factors
- Corticosteroids recommended as they lead to a more rapid resolution of the biochemical abnormalities but it is unclear if they reduce morbidity
- Deliver
- Postnatal recovery often more complicated, with oliguria and a slow recovery of biochemical parameters

**POSTNATAL MANAGEMENT AND FOLLOW-UP**
- Up to 44% of convulsions occur postpartum especially at term. Assess carefully and continue high dependency care for a minimum of 24 hr
- Continue antihypertensive medication after delivery
- If BP falls to <130/80 mmHg, reduce antihypertensive treatment
- **While in-patient** – measure BP at least 4 times per day
- **If transferred to community** – measure BP every 1–2 days for up to 2 weeks, until antihypertensive treatment stopped and no hypertension. Include medical care plan for monitoring on discharge documentation
- Persisting hypertension and proteinuria at 6 weeks can indicate renal disease, investigate further
- Be aware of risk of late seizures and review carefully before discharge
- Offer follow-up to discuss events, treatment and future pregnancy care
- **Follow-up at 6 weeks**
- Discuss events, treatment and future pregnancy care
- Check BP and urine. Investigate persisting hypertension and proteinuria at 6 weeks as may indicate renal disease, investigate further
DRUG TREATMENT REGIMENS

LABETALOL

- Beta-blocker with additional arteriolar vasodilating action

Contraindications

- Asthma
- Cardiogenic shock
- AV Block

Cautions

- Heart failure
- Diabetes

Side effects

- Postural hypotension
- Tiredness
- Headache
- Weakness
- Rashes
- Tingling scalp
- Difficult micturation
- Epigastric pain
- Nausea, vomiting

Labetalol regime on delivery suite

<table>
<thead>
<tr>
<th>Oral therapy</th>
<th>Acute treatment (IV)</th>
<th>Maintenance treatment (IV)</th>
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</thead>
<tbody>
<tr>
<td>If tolerated, 200 mg stat with further 200 mg after 1 hr</td>
<td>50 mg IV bolus over 1 min (10 mL labetalol 5 mg/mL) Can be repeated every 5 min to a maximum of 200 mg Can cause excessive bradycardia reversed by giving atropine sulphate 600 microgram IV</td>
<td>Where continuous IV doses required, consider insertion of arterial line in discussion with anaesthetist Neat labetalol 5 mg/mL at a rate of 4 mL/hr via syringe driver Set target BP and record Start infusion at 4 mL/hr and double every 30 min to maximum 32 mL/hr (160 mg) until BP lowered and stabilised at acceptable level usual max dose 200 mg total Start at: 4 mL/hr (double every 30 min if necessary) 8 mL/hr 16 mL/hr 32 mL/hr (maximum) Convert to oral therapy – dose dependent on IV dose that was required</td>
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NIFEDIPINE

- Calcium-channel blocker, relaxes vascular smooth muscle and dilates coronary and peripheral arteries
Severe eclampsia 2013–15

**Contraindications**
- Known hypersensitivity
- Gastrointestinal obstruction
- Hepatic impairment
- Inflammatory bowel disease
- Crohn's disease
- Cardiogenic shock

**Treatment**
- Pre-load with 300 mL of IV colloid before administration
- 10 mg capsule orally, repeat every 30 min, up to 3 doses – Consider SR tablets for longer-term regulation of BP

<table>
<thead>
<tr>
<th>Do not give sublingually must swallow whole</th>
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</table>
- Monitor fetal heart rate by continuous electronic fetal monitoring (EFM) – see Electronic fetal monitoring guideline
- Measure maternal BP every 5 min in first 30 min after initial administration as may reduce quickly

**Side effects**
- Headache
- Flushing
- Dizziness
- Tachycardia
- Palpitation
- May induce exaggerated fall in blood pressure

**HYDRALAZINE**
- Direct acting vasodilator

**Contraindications**
- Known hypersensitivity
- Idiopathic systemic lupus erythematosus
- Severe tachycardia
- High output heart failure
- Myocardial insufficiency due to mechanical obstruction
- Cor pulmonale
- Dissecting aortic aneurysm
- Acute porphyria

**Cautions**
- Renal impairment
- Hepatic impairment
- Ischaemic heart disease
- Cerebrovascular disease

**Side effects**
- Tachycardia
- Palpitations
- Flushing
- Hypotension
- Fluid retention
- Gastrointestinal disturbances
- Headache
- Dizziness
- Rarely: rashes, fever, peripheral neuritis, polyneuritis, paraesthesia, abnormal liver function, agitation, anxiety, dyspnoea
Hydralazine regimen

<table>
<thead>
<tr>
<th>Acute treatment</th>
<th>Maintenance treatment</th>
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<tr>
<td>• Consider pre-loading with 300 mL colloid before administration</td>
<td>• Where continuous IV doses required, consider insertion of arterial line in discussion with anaesthetist</td>
</tr>
<tr>
<td>• 5 mg by slow IV bolus diluted with 10 mL sodium chloride 0.9% – can be repeated after 20–30 min – Some Trusts prefer to mix 20 mg in 20 mL</td>
<td>• 40 mg in 40 mL sodium chloride 0.9% via syringe driver e.g. 1000 microgram/mL solution</td>
</tr>
<tr>
<td>• Check BP every 5 min for 30 min or until stable at acceptable limit, then every 15 min for further 60 min</td>
<td>• Start infusion at 2 mL/hr</td>
</tr>
<tr>
<td>• Continually monitor fetal heart rate by EFM</td>
<td>• Increase rate in 2 mL/hr increments to a maximum of 20 mL/hr</td>
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MAGNESIUM SULPHATE 50%

Cautions
• Renal impairment
• Hepatic impairment

Side effects (generally associated with hypermagnesaemia)
• Nausea
• Vomiting
• Thirst
• Flushing of skin
• Hypotension
• Arrhythmias
• Coma
• Respiratory depression
• Drowsiness
• Confusion
• Loss of tendon reflexes
• Muscle weakness
• Colic and diarrhoea (following oral administration)

Seizure prophylaxis
• Administer 2 concentrations:
  • one as loading dose
  • one as continuous infusion for 24 hr or until 24 hr after delivery (or after last seizure or until diuresis, whichever is later)
  • can just be stopped without tapering dose

Magnesium sulphate 50%

<table>
<thead>
<tr>
<th>Loading dose</th>
<th>Maintenance dose</th>
<th>Dose for recurrent seizures</th>
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<tbody>
<tr>
<td>• 4 g IV</td>
<td>• 1 g/hr IV</td>
<td>• Give 2 g bolus for weight &lt;70 kg</td>
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<tr>
<td>• Add 8 mL (4 g) magnesium sulphate 50% to 12 mL sodium chloride 0.9% – total volume 20 mL</td>
<td>• Add 10 mL (5 g) magnesium sulphate 50% to 40 mL sodium chloride 0.9% – total volume 50 mL</td>
<td>• Add 4 mL (2 g) magnesium sulphate 50% to 12 mL sodium chloride 0.9% and administer by slow bolus injection over 5–10 min</td>
</tr>
<tr>
<td>• Administer via syringe driver over 10–20 min (infusion rate of 60–120 mL/hr)</td>
<td>• 10 mL = 1 g magnesium sulphate</td>
<td>• Give 4 g bolus for weight &gt;70 kg</td>
</tr>
<tr>
<td></td>
<td>• Start IV infusion via syringe driver at 10 mL/hr</td>
<td>• Add 8 mL (4 g) magnesium sulphate 50% to 12 mL sodium chloride 0.9% and administer by slow bolus injection over 5–10 min</td>
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<td>• Increase maintenance dose to 2 g/hr IV</td>
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Observations

- Continuous pulse oximetry
- Urine output hourly
- Respiratory rate hourly
- Deep tendon reflexes

Check serum magnesium levels

*Stop magnesium sulphate if:*

- Urine output <100 mL in 4 hr
- Respiratory rate ≤12 breaths/min
- Oxygen saturation <90%
- Patellar reflexes absent (not due to regional anaesthesia)

| 97% of magnesium is excreted in urine. Oliguria can lead to toxicity. Antidote – 10 mL calcium gluconate 10% IV over 10 min |