



**CLINICAL PRACTICE GUIDELINE**

**Hypertension in pregnancy: Medical management**

This document should be read in conjunction with the [Disclaimer](#)

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## Medical management

### Aim

The aim of this guideline is to standardise the approach to the management of severe pre-eclampsia and eclampsia in the immediate pre- and post- delivery interval in order to improve the outcome for the mother and child<sup>1</sup>.

### Background

Hypertensive disorders during pregnancy occur in women with pre-existing primary or secondary chronic hypertension, and in women who develop new-onset hypertension in the second half of pregnancy. Hypertensive disorders during pregnancy carry risks for the woman and the baby. Although the rate of eclampsia in the United Kingdom (UK) appears to have fallen, hypertension in pregnancy remains one of the leading causes of maternal death in the UK<sup>2</sup>.

In Western Australia alone, Hypertension occurs in 4.0% of all pregnancies, 2.7 % due to Pre-Eclampsia and 13.6% due to Essential Hypertension. 2.4 % of Perinatal Deaths are due to Hypertension in pregnancy<sup>3,4</sup>.

### Key Point

#### Transfer to a tertiary setting is indicated for:

- All pre term pregnancies with severe pre eclampsia, eclampsia or HELLP syndrome
- All term pregnancies complicated by eclampsia or HELLP syndrome
- Any pregnancy in which the health care provider believes his/her health care facility would be unable to manage the complications of hypertension in pregnancy.

Note: [MgSO4 therapy](#) should be considered prior to transfer in women with severe pre eclampsia, eclampsia or HELLP syndrome<sup>5</sup>, **provided that the women will be accompanied in transfer by a Medical Practitioner (in case of respiratory arrest)**.

For women who are having antenatal care in a community setting, i.e. CMP if systolic blood pressure is 140-160 or diastolic 90-100, recheck in 15minutes. If the blood pressure remains high then consult and refer to support hospital for assessment and plan. If the woman's blood pressure is above 160 systolic or 100 diastolic then consult and recommend transfer to support hospital via ambulance.

### Definitions

#### Hypertension in pregnancy<sup>6</sup>

1. **Systolic** blood pressure greater than or equal to **140** mmHg and/or
  2. **Diastolic** blood pressure greater than or equal to **90** mmHg (Korotkoff 5)
- These measurements should be confirmed by **repeated readings over several hours**<sup>6</sup>.

Normal pregnancy is characterized by a fall in blood pressure, detectable in the first trimester and usually reaching a nadir in the second trimester. Blood pressure rises towards pre-conception levels towards the end of the third trimester.

Detecting a rise in blood pressure from 'booking' or preconception blood pressure (> 30/15 mmHg), rather than relying on an absolute value, has in the past been considered useful in diagnosing pre-eclampsia in women who do not reach systolic blood pressures of 140 mmHg or diastolic blood pressures of 90 mmHg<sup>6</sup>. Available evidence however, does not support the notion that these women have an increased risk of adverse outcomes.<sup>7, 8</sup> Nevertheless such a rise may be significant in some women, particularly in the presence of hyperuricemia and proteinuria. Further data are required and in the meantime, closer monitoring of pregnant women with an increment in blood pressure of  $\geq 30$  mmHg systolic and/or 15 mmHg diastolic is appropriate.

### Severe hypertension in pregnancy

**Systolic** blood pressure greater than or equal to **170** mmHg and/or **diastolic** blood pressure greater than or equal to **110** mmHg.

This represents a level of blood pressure above which the risk of maternal morbidity and mortality is increased. It is generally acknowledged that severe hypertension should be lowered promptly, albeit carefully, to prevent cerebral haemorrhage and hypertensive encephalopathy<sup>6, 9</sup>. This degree of hypertension requires urgent assessment and management. It is important to acknowledge that systolic as well as diastolic hypertension increases the risk of cerebral haemorrhage.

### White Coat Hypertension

Defined as hypertension in a clinical setting with normal blood pressure away from this setting when assessed by 24 hour ambulatory blood pressure monitoring or home blood pressure monitoring using an appropriately validated device. Women with this condition present early in pregnancy with apparent chronic hypertension, but their outcomes are better than those of women with true chronic hypertension. They may generally be managed without medication by using repeated ambulatory or home blood pressure monitoring. A small proportion will go on to develop preeclampsia<sup>10</sup>.

### Proteinuria

Defined as the urinary excretion of  $\geq 0.3$  g protein in a 24-hour specimen. This will usually correlate with  $\geq 30$  mg/dL ( $\geq 1+$  reading on dipstick) in a random urine determination with no evidence of urinary tract infection<sup>9, 11</sup>.

### Oedema

Oedema is no longer included in the definition of pre-eclampsia as it occurs equally in women with and without this condition. Nevertheless rapid development of generalised oedema should alert the clinician to screen for preeclampsia<sup>6</sup>.

## Recording Blood pressure in pregnancy

The woman should be seated comfortably with her legs resting on a flat surface. In labour, the blood pressure may be measured in the left arm in lateral recumbency. The supine posture should be avoided because of the supine hypotension syndrome. Measurement of blood pressure should be undertaken in both arms at the initial visit to exclude rare vascular abnormalities such as aortic coarctation, subclavian stenosis and aortic dissection. Generally the variation in blood pressure between the upper limbs should be less than 10 mmHg.

The systolic blood pressure is accepted as the first sound heard (K1) and the diastolic blood pressure the disappearance of sounds completely (K5)(8-10). Where K5 is absent, K4 (muffling) should be accepted. Correct cuff size is important for accurate blood pressure recording. A large cuff with an inflatable bladder covering 80% of the arm circumference should be used if the upper arm circumference is greater than 33 cm. This helps to minimise over-diagnosis of hypertension during pregnancy<sup>6, 12, 13</sup>.

## Classification of Hypertension in pregnancy

This classification of the hypertensive disorders in pregnancy reflects the pathophysiology of the constituent conditions as well as the risks and potential outcomes for both mother and baby. The following clinical classification has been adopted by numerous International and National bodies, differing predominantly in whether they require proteinuria or not for the diagnosis of pre eclampsia. The International Society for the Study of Hypertension in Pregnancy (ISSHP) guideline no longer requires proteinuria for the diagnosis of pre eclampsia, leaving on the British NICE guideline with this requirement<sup>17</sup>.

The classification is as follows:

- Preeclampsia – eclampsia
- Gestational hypertension
- Chronic hypertension
  - essential
  - secondary
  - white coat
- Preeclampsia superimposed on chronic hypertension<sup>6, 14</sup>

### Pre eclampsia

This is a multi-system disorder characterised by hypertension and involvement of one or more other organ systems and/or the fetus. Raised BP is commonly but not always the first manifestation. Proteinuria is also common but should not be considered mandatory to make the clinical diagnosis<sup>6</sup>

Diagnosis can be made when:

1. hypertension arises after 20 weeks gestation

2. accompanied by one or more of the following signs of organ involvement:

- **Renal involvement**
  - Significant proteinuria – a spot urine protein / creatinine ration  $\geq 30\text{mg} / \text{mmol}$
  - Serum or plasma creatinine greater than or equal to  $90 \text{ micromol/L}$  or
  - Oliguria  $< 80\text{mL} / 4 \text{ hours}$
- **Haematological involvement**
  - Thrombocytopenia  $< 100,000 / \mu\text{L}$
  - Haemolysis :schistocytes or red cell fragments on blood film, raised bilirubin, raised lactate dehydrogenase  $> 600\text{mIU/L}$ , decreased haptoglobin
  - DIC
- **Liver involvement**
  - Raised transaminases
  - Severe epigastric or right upper quadrant pain
- **Neurological involvement**
  - Convulsions (Eclampsia)
  - Persistent visual disturbances (photopsia, scotomata, cortical blindness, posterior reversible encephalopathy syndrome, retinal vasospasm)
  - Persistent, new headache
  - Stroke
- **Pulmonary oedema**
- **Fetal growth restriction (FGR)**

### **Gestational hypertension**

- New onset of hypertension arising after 20 weeks gestation
- No additional maternal or fetal features of preeclampsia
- Resolves within 3 months postpartum

The earlier the gestation at presentation and the more severe the hypertension, the higher the likelihood of developing preeclampsia or an adverse pregnancy outcome<sup>6, 14</sup>.

### **Chronic hypertension**

Pre-existing hypertension is a strong risk factor for the development of preeclampsia and requires close clinical surveillance.

#### **1- Essential**

BP greater than  $140/90 \text{ mmHg}$  preconception or prior to 20 weeks without an underlying cause<sup>15</sup>

or

BP less than  $140/90$  entering pregnancy on antihypertensives

## 2- Secondary

Hypertension due to:

- chronic kidney disease (e.g. glomerulonephritis, reflux nephropathy and adult polycystic kidney disease)
- renal artery stenosis
- systemic disease with renal involvement (e.g. diabetes mellitus, systemic lupus erythematosus)
- endocrine disorders (e.g. pheochromocytoma, Cushing's syndrome and primary hyperaldosteronism)
- coarctation of the aorta

### **Preeclampsia superimposed on chronic hypertension**

This is diagnosed when a woman with pre-existing hypertension develops systemic features of preeclampsia, after 20 weeks gestation. Worsening or accelerated hypertension should increase surveillance for preeclampsia but is not diagnostic.

### **Risk Factors for Pre Eclampsia<sup>1, 16</sup>**

#### **Moderate risk**

- Age 40 years or more
- First pregnancy
- Multiple pregnancy
- Interval since last pregnancy of more than 10 years
- Body mass index of 35 or more at presentation
- Family history of pre-eclampsia

#### **High risk**

- Chronic hypertension
- Chronic kidney disease
- Hypertensive disease during a previous pregnancy
- Diabetes
- Autoimmune disease

### **Investigation Of New Onset Hypertension after 20 Weeks Gestation**

Any woman presenting with new hypertension after 20 weeks gestation should be assessed for signs and symptoms of preeclampsia. Initially assessment and management in a day assessment unit may be appropriate. If features of preeclampsia are detected, admission to hospital is indicated. The presence of severe hypertension, headache, epigastric pain, oliguria or nausea and vomiting are ominous signs which should lead to urgent admission and management, as should any concerns about fetal wellbeing.

**Maternal**

- The following investigations should be performed in all women with new onset hypertension after 20 weeks gestation.
- Spot urine PCR
- FBP
- Urea, creatinine, electrolytes
- Liver function tests
- Ultrasound assessment of fetal growth, amniotic fluid volume and umbilical artery Doppler assessment

If features of preeclampsia are present, additional investigations should include:

- Urinalysis for protein and urine microscopy on a carefully collected mid-stream urine sample.
- If there is thrombocytopenia or a falling haemoglobin, investigations for disseminated intravascular coagulation and / or haemolysis are indicated

**Table 1**

| Test      | Age Group | Levels deemed to be elevated (KEMH Lab) |
|-----------|-----------|---|
| LDH       | >16 years | > 618u/L                                |
| ALT       | >15 years | > 35 u/L                                |
| AST       | >15 years | > 32 u/L                                |
| Uric Acid | >15 years | > 0.36 mmol/L                           |

**Notes:**

- Patients with severe early onset preeclampsia warrant investigation for associated conditions e.g. systemic lupus erythematosus, underlying renal disease, antiphospholipid syndrome or thrombophilias. The timing of these investigations will be guided by the clinical features.
- Acute Fatty Liver can also present itself as HELLP syndrome.
- Although a very rare disorder, undiagnosed pheochromocytoma in pregnancy is potentially fatal and may present as preeclampsia<sup>17, 18</sup>. Measurement of fasting plasma free metanephrines/normetanephrines or 24 hour urinary catecholamines should be undertaken in the presence of very labile or severe hypertension.
- Subsequent management will be based on the results of ongoing blood pressure measurement and these investigations – see table 2 below<sup>6</sup>
- Amongst women referred for assessment of new onset hypertension, a number will have normal blood pressure and investigations. These women are considered to have transient or labile hypertension. Repeat assessment should be arranged within 3-7 days as many will subsequently develop pre-eclampsia



**Table 2 Ongoing Investigation of women with hypertension in pregnancy**

| Classification           | Modality  | Frequency  |
|--------------------------|---|--|
| Chronic Hypertension     | Urinalysis for protein*<br>Pre Eclampsia bloods | Each visit<br>If sudden increase in BP or<br>new proteinuria   |
| Gestational Hypertension | Urinalysis for protein<br>Pre Eclampsia bloods  | 1-2 x per week<br>Weekly   |
| Pre Eclampsia            | Urinalysis for protein<br>Pre Eclampsia bloods  | At time of diagnosis: if non-<br>proteinuric, repeat daily<br>Twice weekly or more<br>frequent if unstable |

### Assessment of Severity in Pre Eclampsia

All patients with pre eclampsia must be regarded as being at risk of major maternal and fetal complications. However, there are certain indicators of particular concern when they occur in a woman with definite pre eclampsia:

- HELLP syndrome – any component (see section on HELLP Syndrome Page 14)
- Severe hypertension refractory to usual treatment
- Renal impairment – creatinine greater than 106µmol/L
- Pulmonary oedema
- Persistent neurological symptoms – headache / altered mental state / clonus
- “Pre eclamptic angina” – severe epigastric pain and/or vomiting with abnormal liver enzymes
- Fetal growth restriction

Pre eclampsia usually pursues a course of deterioration, sometimes slowly and sometimes quickly. It may evolve from mild to moderate to severe over a period of hours or days, and requires frequent reassessment by medical staff.

### Management of pre-eclampsia and gestational hypertension

Preeclampsia is a progressive disorder that will inevitably worsen if pregnancy continues. Current therapy does not ameliorate the placental pathology nor alter the pathophysiology or natural history of preeclampsia. Delivery is the definitive management and is followed by resolution, generally over a few days but sometimes much longer. Obstetric consultation is mandatory in all women with severe pre eclampsia. In those women with preeclampsia presenting at extreme preterm



gestations consultation with KEMH should be arranged. At mature gestational age, delivery should not be delayed. Even so, it is important to control severe hypertension and other maternal derangements before subjecting the woman to the stresses of delivery<sup>6</sup>.

Prolongation of pregnancy in the presence of preeclampsia carries no benefit for the mother but is desirable at early gestations to improve the fetal prognosis as in general, fetal outcome is proportional to gestational age at delivery<sup>18</sup>. In cases of preterm preeclampsia before 34 weeks, delivery should be delayed for at least 24-48 hours if maternal and fetal status permit, to allow fetal benefit from antenatal corticosteroids administered for lung maturation<sup>19</sup>. Continuation of pregnancy carries fetal risk and some stillbirths will occur despite careful monitoring.

The management of women with preeclampsia between gestational ages of 24-32 weeks should be restricted to those centres with appropriate experience and expertise. Clear “endpoints” for delivery should be defined for each patient (Table 3), such that the decision to terminate the pregnancy is based on agreed criteria. In many cases, the timing of delivery will be based upon a number of factors, maternal and/or fetal rather than a single absolute indication for delivery.

In the presence of HELLP syndrome, expectant management is harmful with a 6.3% incidence of maternal death and an increased risk of placental abruption. In such cases delivery should be planned as soon as feasible.

**Table 3 Indications for delivery in women with preeclampsia or gestational hypertension<sup>6</sup>**

| <b>Maternal</b>   | <b>Fetal</b>                    |
|---|---------------------------------|
| Gestational Age >37weeks  | Severe fetal growth restriction |
| Inability to control hypertension   | Non-reassuring fetal status     |
| Deteriorating platelet count  |                                 |
| Deteriorating liver function  |                                 |
| Deteriorating renal function  |                                 |
| Placental abruption   |                                 |
| Persistent neurological symptoms<br>Eclampsia                                     |                                 |
| Persistent epigastric pain, nausea or vomiting with abnormal liver function tests |                                 |
| Acute pulmonary oedema  |                                 |

**Table 4 Timing of Delivery and gestation of presentation of preeclampsia**

| <b>Gestation at onset</b> | <b>Pre-viable &lt;23 weeks</b>  | <b>23 – 31<sup>+6</sup></b>   | <b>32 – 36<sup>+6</sup></b>  | <b>37<sup>+0</sup> onwards</b>        |
|---------------------------|---|---|--|---------------------------------------|
| <b>Delivery Plan</b>      | Consult with KEMH: likely to need termination of pregnancy or extreme preterm delivery. High risk patient | Consult and transfer to KEMH: likely to need preterm delivery. Aim to prolong pregnancy where possible. | Aim to prolong pregnancy where possible, deliver in an institution with appropriate paediatric care. | Plan delivery on best day in best way |

Except in the situation of acute fetal compromise, urgent delivery is not helpful in pre eclampsia and the mother must be resuscitated before being subjected to the delivery process. Therefore, in severe pre eclampsia, delivery must always be preceded by:

- control of severe hypertension
- attention to fluid status
- correction of coagulopathy (usually thrombocytopenia)
- control of eclampsia, or prophylaxis against eclampsia if indicated (see below)

A team approach, involving obstetrician, midwife, neonatologist, anaesthetist and physician provides the best chance of achieving a successful outcome for mother and baby. Regular and ongoing reassessment of both the maternal and fetal condition is required. Careful daily assessment for clinical symptoms and signs should be complemented by regular blood and urine tests as indicated (Table 1 and 3).

The only controlled studies of bed rest for preeclampsia have shown no significant maternal or fetal benefit<sup>20</sup>. However, admission to hospital allows close supervision of both mother and fetus as progress of the disorder is unpredictable. Outpatient monitoring may be appropriate in milder cases after a period of initial observation.

### **Outpatient management**

Women with mild gestational hypertension can be cared for at home, in as long as:

- there are no obstetric contraindications
- there are no geographic contraindications
- there is no evidence of fetal compromise
- the patient has her blood pressure monitored regularly either at home by a visiting midwife with obstetrician back up or in MFAU <sup>21</sup>
- the patient visits the clinic 1-2 times per week

**Note:** Any evidence of maternal and or fetal compromise or failure to respond to outpatient treatment requires hospitalisation.

## Inpatient management

### Maternal

- Evaluate patient to determine if the admission should be to Labour and Birth Suite or to the ward.
- Perform baseline laboratory evaluations (FBP, Serum creatinine, LDH, ALT, AST, Uric Acid and PCR)
- Review by obstetric registrar/ Consultant, at least daily (including weekends and public holidays) to evaluate the patient for evidence of maternal deterioration (headaches, visual changes, or epigastric distress)

### Fetal

- Fetal surveillance by biophysical Profile, Doppler studies and cardiotocography as appropriate.
- Administer betamethasone 11.4 mg IM x 2 doses, 24 hours apart, if appropriate. Corticosteroid therapy in pregnancies between 23 and 36+6 weeks accelerates fetal lung maturity, decreases Respiratory Distress Syndrome (RDS), intraventricular haemorrhage (IVH) and the risk of fetal death in these pregnancies.

## Special management issues for hypertensive crises (BP of $\geq$ 170/110).

- Admit to the Adult Special Care Unit/Labour and Birth Suite for close observation and antepartum care. Manage in the Adult Special Care Unit postpartum until the crisis has resolved.
- Evaluate and stabilize with frequent maternal and continuous fetal surveillance.
- Consider [MgSO<sub>4</sub> therapy](#) for seizure prophylaxis.

Magnesium sulphate should be considered for women with pre-eclampsia for whom there is concern about the risk of eclampsia. This is usually in the context of severe pre-eclampsia **once a delivery decision has been made** and in the immediate postpartum period. In women with less severe disease the decision is less clear and will depend on individual case assessment<sup>1</sup>.

- Anaesthesia: May consider epidural/spinal anaesthesia if maternal platelet count is  $> 100,000$  and platelet function is normal.

## Drug Therapy

### Antihypertensive Therapy

Evidence suggests that antihypertensive drug therapy confers no clear benefit to women with mild pre eclampsia<sup>22-24</sup>. Randomized control trials of women with mild pre eclampsia remote from term, which compared antihypertensive drug therapy with no medication or a placebo, have been reported. In some of these trials, the frequency of proteinuria, progression to severe disease, and neonatal respiratory distress syndrome were higher in the women not treated.<sup>25-28</sup> These observations however have not been confirmed in other trials.<sup>29-31</sup>

In the absence of compelling evidence, treatment of mild to moderate hypertension in the range 140-160/90-100 mm Hg should be considered an option and will reflect local practice. Above these levels, treatment should be considered mandatory<sup>6</sup>.

In women with severe pre eclampsia, or those who have received treatment for hypertensive crisis, maintenance control of BP is essential to reduce the risk of cerebral events and to prolong the pregnancy for fetal benefit where possible. However, the maternal blood pressure must not be lowered too drastically because inadequate placental perfusion may occur where placental circulation has adapted to a higher blood pressure.

### Acute Treatment of Severe Hypertension

Antihypertensive treatment should be commenced in all women with a systolic blood pressure  $\geq 170$  mm Hg or a diastolic blood pressure  $\geq 110$  mm Hg because of the risk of intracerebral haemorrhage and eclampsia<sup>22</sup>. Whilst there is no controlled trial to determine how long severe hypertension may be left untreated, it is recommended that treatment be administered promptly aiming for a gradual and sustained lowering of blood pressure.

A recent systemic review of the literature regarding antihypertensive agents used for the management of severe hypertension acknowledged that each medication had benefits and risks.<sup>56</sup> Both intravenous and oral agents may be used depending on the clinical situation.

The agent of choice for the acute treatment of hypertension is oral [nifedipine](#). This is administered as a 10mg oral dose initially, with a repeat dose of 10mg if there is inadequate response after 30 minutes. Headache is frequently a side effect.

[Intravenous labetalol](#) is the agent of choice for intravenous administration. This is administered as a 20-80mg bolus dose over 2 minutes. Associated side effects may be bradycardia, bronchospasm and headache.

The third agent of choice is [hydralazine](#). This is administered as an intravenous or intramuscular dose of 5-10mg every 20-30 minutes to control hypertension of  $\geq 170$  systolic and / or 110 diastolic.

**Table 4 - Acute blood pressure lowering for severe hypertension**<sup>32-35</sup>

| Medication                  | Dose   | Route   | Onset of action  |
|-----------------------------|--|---|--|
| <a href="#">Nifedipine</a>  | 10mg IR tablet<br>Maximum 40mg                 | Oral  | 30-45 minutes. Repeat after 45 minutes if response is inadequate |
| <a href="#">Labetalol</a>   | 20-80mg<br>Max 80mg/dose <sup>36</sup>         | IV bolus over 2 minutes.<br>Repeat every 10 minutes prn | Maximal effect usually occurs within 5 minutes of each dose.     |
| <a href="#">Hydralazine</a> | 5-10mg<br>(First dose 5mg if fetal compromise) | IV bolus over 2 minutes<br>IM injection                 | 20 minutes. May be repeated after 20 minutes.                    |

**Note:** Blood pressure should not be allowed to fall below a level of 140/80.

### Ongoing treatment for hypertension

In terms of lowering blood pressure in preeclampsia, a number of drugs have demonstrated safety and efficacy (Table 4). First line drugs include [methyldopa](#), and [labetalol](#)<sup>37-39</sup>. Second line agents are [hydralazine](#), [nifedipine](#) and prazosin<sup>40-43</sup>. Angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers are contraindicated in pregnancy. Their use in the third trimester has been associated with fetal death and neonatal renal failure. All of the drugs in Table 4 along with enalapril, captopril and quinapril are considered compatible with breastfeeding<sup>44</sup>.

Antihypertensive therapy should be considered:

- When the SBP  $\geq 150$  mm Hg at least twice in a 24 hour period separated by four hours.
- When DBP  $\geq 95$  mm Hg at least twice in a 24 hour period separated by four hours
- Following the acute treatment of severe hypertension (170/110)<sup>22</sup>

**Table 5. Guidelines for selecting antihypertensive drug treatment in pregnancy<sup>6</sup>**

| Drug                        | Dose   | Action                                       | Contraindications                  | Practice points  |
|-----------------------------|--|--|------------------------------------|--|
| <a href="#">Methyldopa</a>  | 250-750 mg tds   | Central                                      | Depression                         | Slow onset of action over 24 hrs. Dry mouth, sedation, depression, blurred vision.<br>Withdrawal effects: rebound hypertension |
| <a href="#">Labetalol</a>   | 100-400 mg tds   | B blocker with mild alpha vasodilator effect | Asthma, Chronic airways limitation | Bradycardia, bronchospasm, headache, nausea, scalp tingling which usually resolves within 24-48 hrs (labetalol only)           |
| <a href="#">Nifedipine</a>  | 20 mg SR once a day to a maximum of 60mg SR once a day | Calcium channel antagonist                   | Aortic Stenosis                    | Severe Headache associated with flushing and tachycardia.<br>Peripheral oedema, constipation                                   |
| <a href="#">Prazosin</a>    | 0.5- 5mg tds   | Alpha blocker                                |                                    | First dose effect-orthostatic hypotension  |
| <a href="#">Hydralazine</a> | 25-50 mg tds   | Vasodilator                                  |                                    | Flushing, headache, nausea, lupus-like syndrome  |

It is important to control severe hypertension at any gestation and post-partum. Induction of labour or Caesarean section does not control hypertension even though delivery begins the process of resolution of preeclampsia. Thus, antihypertensive medication will usually be required even when delivery has been arranged<sup>6</sup>. When either of these has been unsuccessful, consider consultation with Obstetric Physician. In some cases of severe hypertension, it is necessary to add a second or even third agent.

## Fetal surveillance in pregnant women with hypertension

| Hypertension  | Modality  | Frequency   |
|---|---|---|
| <b>Chronic hypertension</b>                           | <ul style="list-style-type: none"> <li>• Early dating ultrasound</li> <li>• U/s for fetal growth /AFV/ doppler</li> </ul> | <ul style="list-style-type: none"> <li>• First trimester</li> <li>• 3<sup>rd</sup> trimester: repeat as indicated</li> </ul>                            |
| <b>Gestational hypertension</b>                       | <ul style="list-style-type: none"> <li>• U/s for fetal growth / AFV/ doppler</li> </ul>                                   | <ul style="list-style-type: none"> <li>• At time of diagnosis and 3 – 4 weekly</li> </ul>   |
| <b>Preeclampsia</b><br>+ / - fetal growth restriction | <ul style="list-style-type: none"> <li>• U/s for fetal growth/ AFV/ doppler</li> <li>• Cardiotocography</li> </ul>        | <ul style="list-style-type: none"> <li>• At time of diagnosis. Subsequent frequency is dependent on the clinical progression of the disease.</li> </ul> |

AFV = Assessment of amniotic fluid volume

## Eclampsia

Eclampsia remains rare in Australia. There are no reliable clinical markers to predict eclampsia and conversely, the presence of neurological symptoms and/or signs is rarely associated with seizures<sup>6, 45</sup>. Seizures may occur antenatally, intra-partum or postnatally, usually within 24 hours of delivery but occasionally later. Hypertension and proteinuria may be absent prior to the seizure and not all women will have warning symptoms such as headache, visual disturbances or epigastric pain<sup>46</sup>. The further from delivery that the seizure occurs, the more carefully should other diagnoses be considered. Cerebral venous thrombosis in particular may occur in the first few days of the puerperium. It should be remembered that eclampsia is not the commonest cause of seizures in pregnancy and the differential diagnosis includes epilepsy and other medical problems that must be considered carefully, particularly when typical features of severe preeclampsia are lacking.

### Management of eclampsia

There are four main aspects to care of the woman who sustains eclampsia<sup>6</sup>.

#### 1. Resuscitation

Resuscitation requires institution of intravenous access, oxygen by mask, assuring a patent airway and institution of intravenous access<sup>6</sup>. Intravenous Midazolam (0.1 – 0.2mg /kg IV or IM) may be given if the seizure is long.

Intravenous [Magnesium Sulphate](#) is the agent of choice.

See Loading dose- 4gm over 20 mins (rate 150 mL/hr for 20 mins only = 50mL).



## 2. Prevention of further seizures

Following appropriate resuscitation, treatment should be continued with Magnesium Sulphate.

Ref. Administration of [Magnesium sulphate](#)

## 3. Control of hypertension

Control of severe hypertension to levels below 160/100 mmHg by parenteral therapy is essential as the threshold for further seizures is lowered after eclampsia, likely in association with vasogenic brain oedema. In addition, the danger of cerebral haemorrhage is real.

## 4. Delivery

Arrangements for delivery should be decided once the woman's condition is stable. In the meantime, close fetal monitoring (continuous CTG) should be maintained. There is no role, with currently available treatment, for continuation of pregnancy once eclampsia has occurred, even though many women may appear to be stable after control of the situation has been achieved.

## Prevention of eclampsia in the woman with preeclampsia

The drug of choice for the prevention of eclampsia is magnesium sulphate<sup>47</sup>. Although there is good evidence for the efficacy of this therapy, the case for its routine administration in women with preeclampsia in countries with low maternal and perinatal mortality rates is less than compelling<sup>48</sup>.

Evidence indicates that magnesium sulphate is the superior drug to use in the prevention and the treatment of eclamptic seizures.<sup>18,19</sup>

In the patient with known renal disease or myasthenia gravis however, phenytoin sodium is the anti-seizure medication of choice. Phenytoin sodium is administered in a total dose of 15mg/kg at an infusion rate of 40mg/min with continuous cardiac and blood pressure monitoring.

## Administration of Magnesium Sulphate

See Clinical Guideline [HTN in Pregnancy: Magnesium Anticonvulsant Therapy](#)

**Magnesium Sulphate should not be prescribed for the prevention of eclampsia without discussion with the Consultant Obstetrician on call.**

Magnesium sulphate therapy is recommended for use antepartum, intrapartum and within the first 24 hours postpartum for severe pre-eclampsia (as defined on page 2) when the following factors are present:

- persistently elevated blood pressure despite adequate hypotensive therapy and appropriate fluid management,
- evidence of CNS dysfunction, thrombocytopenia or liver disease<sup>2, 5, 15</sup>.

**Before discontinuation of MgSO<sub>4</sub> therapy:**

- the blood pressure should be stable (consistently below 150/100)
- the patient should have adequate diuresis
- the patient should be clinically improved (absence of headache, epigastric pain).

**Postpartum Management**

- Monitor the patient in the Adult Special Care Unit<sup>49</sup> or Labour and Birth Suite until she begins to recover.
- Continue magnesium sulphate until stabilisation and adequate diuresis is achieved.
- Antihypertensive therapy should be commenced if the BP is >150 mmHg systolic or >100 mmHg diastolic in the first four postpartum days. Options for antihypertensive therapy include:
  - [Labetalol](#) 100mg TDS to start
  - [Atenolol](#) 50mg daily. On rare occasions, may need increasing to 100mg/day.
  - [Nifedipine](#) SR 20mg BD to start.
  - [Enalapril](#) 5-10mg daily.

**Resolution of preeclampsia**

After delivery, all clinical and laboratory derangements of preeclampsia recover, but there is often a delay of several days, and sometimes longer, in return to normality. On the first day or two after delivery, liver enzyme elevations and thrombocytopenia will often worsen before they reverse. Hypertension may persist for days, weeks or even up to three months and will require monitoring and slow withdrawal of antihypertensive therapy. Resolution is still assured if the diagnosis was pre-eclampsia and there is no other underlying medical disorder. The woman and her family are often overwhelmed and distressed from their experience and appropriate counselling post partum should include psychological and family support.

All women who develop preeclampsia and gestational hypertension are at risk of these disorders in future pregnancies and should receive appropriate counselling before embarking upon another pregnancy<sup>6</sup>.

**NOTE: Magnesium Sulphate may also be used antenatally prior to preterm birth for Neuro Protection of the fetus post birth- to reduce the incidence of cerebral palsy.**

See Preterm Birth guideline

**HELLP syndrome**

HELLP Syndrome is a variant of severe preeclampsia (**H**aemolysis, **E**levated **L**iver enzymes and **L**ow **P**latelet) count. Maternal mortality is reported to be as high as 1-2%

The elements of this variety of severe pre eclampsia are:

- thrombocytopenia (common)

- haemolysis (rare) and
- elevated liver enzymes (ALT, LDH - common).

Epigastric or right upper quadrant pain in a woman with preeclampsia often represents hepatic involvement. This is called 'Pre eclamptic Angina' <sup>43</sup>. The pain responds poorly to analgesia but both the pain and associated increases in liver enzymes (AST, ALT) may subside (albeit temporarily) after blood pressure lowering, particularly with vasodilators. If the cause of epigastric or right upper quadrant pain is not clear, close ongoing assessment is required, with careful review of all indicators of maternal and fetal wellbeing and appropriate imaging of the liver and gallbladder<sup>6</sup>.

Thrombocytopenia is the commonest hematologic abnormality seen in preeclampsia; the lower limit of the normal platelet count in pregnancy is approximately  $140 \times 10^9/L$  but the risk of spontaneous bleeding is not significantly increased until the count falls below  $50 \times 10^9/L$ . Even so, there are concerns with central neuraxial anaesthesia and analgesic techniques at higher levels ( $50-75 \times 10^9/L$ ), and surgical bleeding may be increased even with moderate thrombocytopenia<sup>6</sup>.

**In a woman with pre eclampsia, the presence of any one of the following is an indicator of severe disease, even if not suggested on other criteria such as severity of hypertension:**

- a maternal platelet count of  $<100,000 \times 10^9/L$
- a transaminase level or LDH more than double the normal upper limit
- haemolysis of any quantity

## Management of HELLP Syndrome

### Antenatal management

If the platelet count is sufficiently low to present a hazard for operative delivery, a platelet transfusion should be considered<sup>6</sup> (consult with Consultant Haematologist or Obstetric Physician).

### Postpartum management

If there is significant bleeding attributed to pre-eclamptic thrombocytopenia at any time in the puerperium a platelet transfusion should be given<sup>6</sup> (consult with Consultant Haematologist or Obstetric Physician).

In the absence of bleeding, consider a platelet transfusion in the first 72 hours only if the count falls below 40,000 and there is concern of possible bleeding (e.g. after Caesarean Section).

If the count remains below 40,000 after 72 hours from delivery without significant bleeding and without sign of impending recovery, consultation with the Consultant Haematologist or Obstetric Physician is indicated.

## Chronic hypertension

Hypertension affects up to 13.6% of the West Australian adult population<sup>4</sup>, the prevalence increasing with age. The diagnosis can be difficult in women whose blood pressure before pregnancy or early in the first trimester is unknown. Very rarely preeclampsia can present before 20 weeks' gestation and the physiological fall in blood pressure in the second trimester can obscure pre-existing chronic hypertension<sup>6</sup>.

Women with chronic hypertension have an increased risk of accelerated hypertension in the third trimester, superimposed preeclampsia, fetal growth restriction, placental abruption, premature delivery and stillbirth. These events are seen more often in women who develop preeclampsia and are not correlated with actual blood pressure levels<sup>37, 45</sup>. The exception to this appears to be uncontrolled hypertension in the first trimester when later fetal and maternal morbidity and mortality are markedly increased<sup>9</sup>. Other indicators of poor prognosis include a failure of blood pressure to normalize in the second trimester, the presence of secondary hypertension, a history of longstanding severe hypertension, and concurrent cardiovascular and/or renal disease.

The woman with chronic hypertension, whether essential or secondary, should be observed frequently during pregnancy by an obstetrician and by a physician familiar with the management of hypertension in pregnancy<sup>6</sup>.

Benefits of therapy for the treatment of mild chronic hypertension in pregnancy have not been proven. In general, treatment is considered when systolic blood pressure exceeds 150 mm Hg and/or diastolic pressure exceeds 95 mm Hg on several occasions. Possible benefits include reduction in hospital admission (when the hypertension is not due to pre-eclampsia) and prolongation of gestation when uncontrolled hypertension would result in delivery. For agents used, see below.

### Baseline assessments

#### Maternal

- Ophthalmic examination.
- **Spot urine protein: creatinine ratio** where there is doubt about proteinuria on dipstick, i.e., +1 or +2 proteinuria.
- Serum electrolytes.
- ECG (if not done recently).
- 24 hour urine catecholamines if there is severe hypertension.

#### Fetal

- Baseline ultrasound for the assessment of fetal anatomy.
- Follow-up ultrasound at 26-28 weeks.
- From 28 weeks, ultrasound every 2-3 weeks to evaluate fetal growth.
- Weekly non-stress tests from 30 weeks.

## Oral Drug Therapy

**Methyldopa**: a centrally acting adrenergic agonist is the most commonly prescribed medication for the treatment of hypertension in pregnancy. Start at a dose of 250mg TDS, increasing to a maximum of 750mg TDS as required.

**Labetalol**: is an alpha and beta-blocking agent. Commence at a dose of 100mg TDS, increasing up to 400 mg TDS as required

**Nifedipine**: a calcium channel blocker that can be used in acute hypertensive situations. Nifedipine may be added as a second line agent to either labetalol or methyldopa. Commence at 20mg SR once a day increasing to a maximum dose of 60mg SR once a day as required.

Atenolol and other highly selective beta blocker drugs are not recommended for prolonged use in pregnancy as they have been associated with fetal growth restriction<sup>39, 50, 51</sup>. The use of ACE-inhibitors and angiotensin receptor blockers is contraindicated in pregnancy. They have been associated with an increased risk of fetal, particularly cardiovascular, malformations in early pregnancy in one study and are known to cause adverse sequelae for the fetus in late pregnancy<sup>52</sup>. Diuretics, although not teratogenic, may restrict the natural plasma volume expansion of pregnancy and are not recommended for the treatment of hypertension.

Consider low dose aspirin on or before 16 weeks gestation.<sup>53</sup> [**RCA recommendation**]

## Post-partum management of women with chronic hypertension

In many women with chronic hypertension or superimposed pre-eclampsia, blood pressure is unstable for 1-2 weeks after delivery and may be difficult to control. It may be particularly high on the third to the sixth day after delivery and it is often necessary to increase or commence antihypertensive medication at that time. All of the agents mentioned earlier are compatible with breast feeding, as are the ACE inhibitors enalapril, captopril and quinapril<sup>6</sup>.

## Chronic hypertension with superimposed preeclampsia

As already mentioned, the main risk of chronic hypertension in pregnancy is the development of superimposed preeclampsia in the second half of pregnancy which occurs in about 20% of women. This is of considerable concern as the risks to both mother and fetus are greater than those of chronic hypertension alone. Management of superimposed preeclampsia should be as outlined above for pre-eclampsia unless specific diagnostic issues, such as some secondary causes of hypertension, are present<sup>6</sup>. It is recommended that all women with a hypertensive complication of pregnancy have a postpartum hypertension follow-up. Depending on the severity of the hypertension this follow-up should be 2-6 weeks after discharge from hospital.

## Preconception counselling

For women with a history of, or significant risk factors for pre-eclampsia

### Background

The risk of recurrence of pre-eclampsia depends on the presence of absence of risk factors, gestational age at the time of onset, and the severity of pre-eclampsia in the previous pregnancy<sup>13</sup>.

Pre-eclampsia complicates 2–3% of all pregnancies<sup>54</sup> and the risk of recurrent pre-eclampsia in a second pregnancy was found to vary according to the gestational age at delivery in the first pregnancy. The risk is progressive, with the greatest risk attributed to those women who were delivered earliest in the previous pregnancy<sup>55</sup>.

### Key points

1. All women with significant risk factors for developing pre-eclampsia planning a future pregnancy should be counselled appropriately about risk factors, symptoms and management<sup>54</sup>.
2. Women at significant risk of developing pre-eclampsia should be offered calcium<sup>56</sup> and low dose Aspirin<sup>54, 57</sup> supplements.
3. Women planning a pregnancy who are at significant risk for developing pre-eclampsia should receive preconception counselling by appropriate obstetrician or obstetric physician.

### Significant risk factors for developing pre-eclampsia<sup>58</sup>

It is likely that development of preeclampsia requires a combination of underlying susceptibility and a triggering event. Many susceptibility factors for preeclampsia have been identified (see Table below) but to date no accurate predictive tool, using either clinical or laboratory markers, has been developed<sup>59</sup>. Such a tool applied early in pregnancy would allow intervention that might modify outcomes<sup>6</sup>.

### Risk factors associated with preeclampsia<sup>6</sup>

| Risk Factor                       | Relative Risk [95% CI] |
|-----------------------------------|------------------------|
| Previous history of pre-eclampsia | 7.19 [5.85, 8.83]      |
| Antiphospholipid antibodies       | 9.72 [4.34, 21.75]     |
| Pre-existing diabetes             | 3.56 [2.54, 4.99]      |
| Multiple pregnancy                | 2.91 [2.04, 4.21]      |
| Nulliparity                       | 2.91 [1.28, 6.61]      |
| Family history of pre-eclampsia   | 2.90 [1.70, 4.93]      |
| Elevated BMI >25                  | 2.47 [1.66, 3.67]      |
| Maternal age ≥ 40                 | 1.96 [1.34, 2.87]      |
| Diastolic BP ≥ 80mmHg at booking  | 1.38 [1.01, 1.87]      |

A number of other factors are also associated with an increased risk of preeclampsia including chronic hypertension, pre-existing renal disease, autoimmune disease, >10 years since previous pregnancy, short sexual relationship prior to conception, other thrombophilias e.g. Factor V Leiden and possibly periodontal disease<sup>12</sup>, maternal age < 20 yrs or ≥ 35 yrs<sup>4, 13</sup>.

### **Women recommended to attend preconception counselling (or as early as possible if pregnant)**

Preconception counselling and early pregnancy referral<sup>6</sup> to KEMH is recommended for women with:

- a history of pre-eclampsia prior to 34 weeks gestation or severe early onset pre-eclampsia < 28 weeks gestation.
- thrombophilias<sup>12</sup> (acquired or congenital)
- severe pre-gestational diabetes (Type 1 or Type 2)
- connective tissue disease e.g. systemic lupus erythematosus<sup>12</sup> (SLE), rheumatoid arthritis
- chronic renal disease<sup>12</sup>

### **Management Strategies for prevention of pre-eclampsia**

#### **Calcium Supplementation**

Calcium supplement supplementation appears to almost halve the risk of pre-eclampsia and reduces the rare occurrence of the composite outcome 'death or serious morbidity'<sup>56</sup>. There were no other clear benefits, or harms.

Offer all women at increased risk of pre-eclampsia (particularly women with a low dietary calcium intake) calcium supplements of 1200mg – 2000mg daily.

#### **Low Dose Aspirin**

Commence low dose Aspirin on or before 16 weeks gestation.<sup>53</sup> **[RCA recommendation]** Low dose aspirin (100mg) has moderate benefits when used for prevention of pre-eclampsia and its consequences, and is safe to use in pregnancy<sup>57</sup>. In view of this potential benefit, and the relative absence of maternal or neonatal complications, low dose aspirin is indicated for the secondary prevention of pre-eclampsia in women at increased risk. In most cases, aspirin may be ceased at 37 weeks gestation although continuation beyond this period is not unsafe.

#### **Use of Clexane with Aspirin**

Clexane is used with aspirin<sup>2</sup> for patients with Antiphospholipid syndrome in consultation with the Maternal Fetal Medicine specialist or the Obstetric Physician.

#### **Antioxidants<sup>60</sup>**

Vitamin C, vitamin E<sup>48, 54, 61</sup>, Fish Oil, Selenium and Lycoprene provide no benefit<sup>60</sup>.



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## Related WNHS policies, procedures and guidelines

Obstetrics & Gynaecology guidelines: [Hypertension in Pregnancy: Midwifery Care](#) ; [HTN: Magnesium Anticonvulsant Therapy](#)

Pharmacy Medication Monographs: Atenolol; Enalapril; Hydralazine ; Labetalol; Magnesium ; Methyldopa ; Nifedipine

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|--|--|-------------------|------------|
| Keywords:  | Hypertension, pre-eclampsia, PE, eclampsia, convulsions, HELLP, thrombocytopenia, platelets, magnesium sulphate, hydralazine, labetalol, nifedipine, methyldopa, gestational, fetal, chronic hypertension, hypertension in pregnancy, preconception counselling  |                   |            |
| Document owner:                                  | Obstetrics & Gynaecology Directorate   |                   |            |
| Author / Reviewer:                               | Head of Department Obstetrics; Consultant Physician  |                   |            |
| Date first issued:                               | November 2003 (Medical Management) & April 2012 (Preconception Counselling)  |                   |            |
| Reviewed dates:<br>(since Jan 2015 amalgamation) | January 2015 (amend Aug 2016, Nov 2017)<br>Feb 2018- removed diazoxide & added CMP statement);<br><b>Dec 2020 (RCA amendment- statements added regarding aspirin use before 16 weeks)</b>  | Next review date: | Feb 2021   |
| Endorsed by:                                     | Obstetrics & Gynaecology Directorate Management Committee [OOS approved with Medical and Midwifery Co directors]   | Date:             | 15/01/2021 |
| NSQHS Standards (v2) applicable:                 | 1  Governance, 4  Medication Safety, 8  Recognising & Responding to Acute Deterioration |                   |            |

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