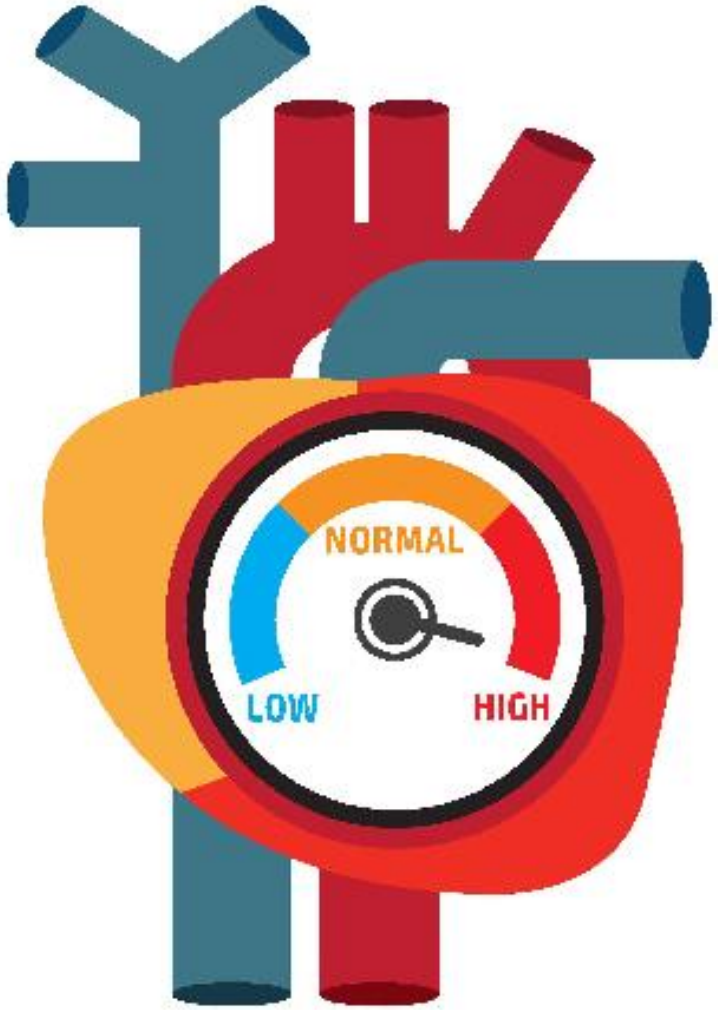

Hypertensive disorders in pregnancy

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Agenda

- Blood pressure in pregnancy and proper measurement
- Chronic hypertension in pregnancy
- Gestational hypertension
- Pre-eclampsia
- Eclampsia
- HELLP syndrome
- Postpartum management

Physiological cardiovascular changes in pregnancy

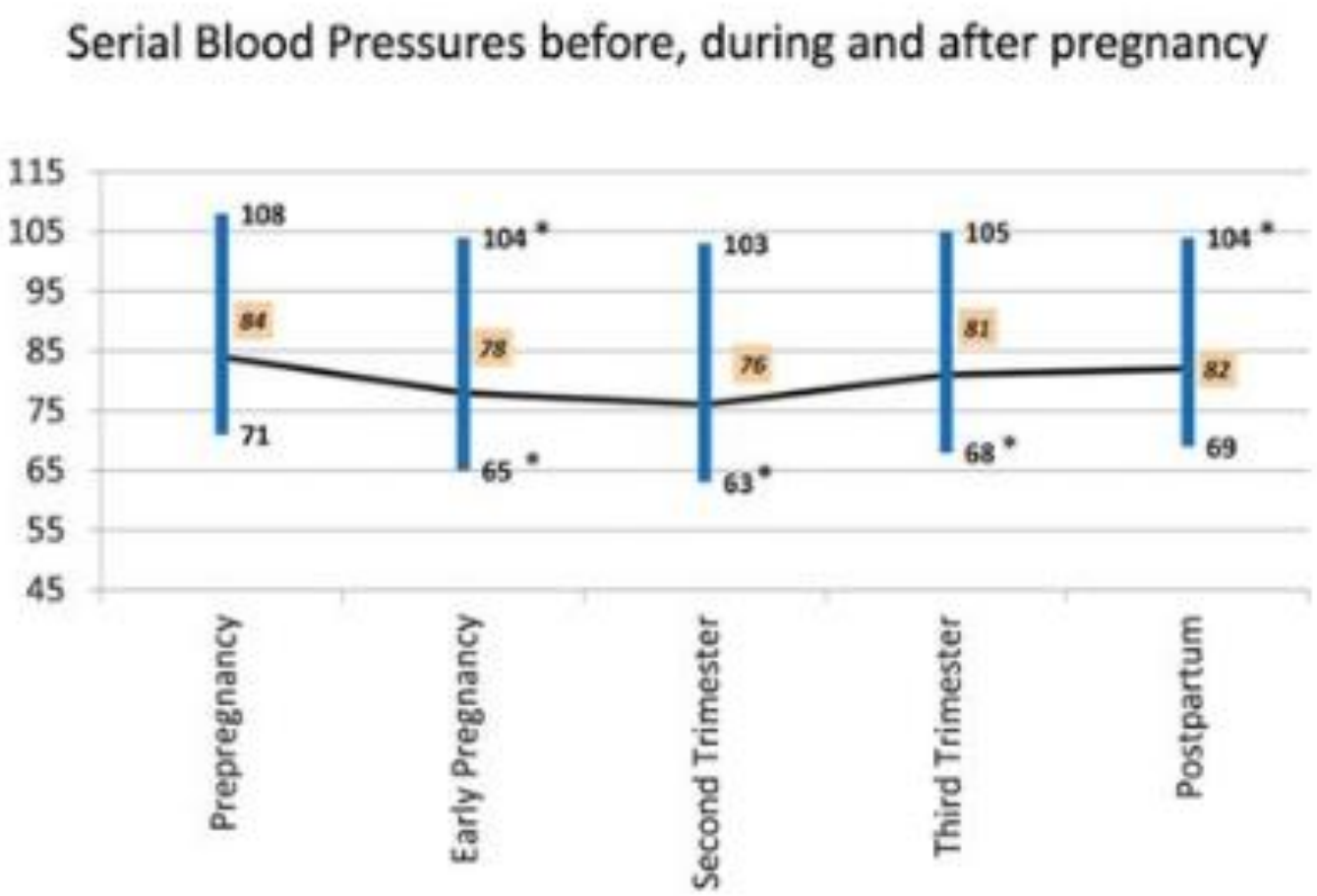
↑ Blood volume

↑ Cardiac output

↑ Heart rate

↓ Systemic vascular resistance

↓ Blood pressure



Blood pressure falls gradually at first trimester, reaching a nadir around 22–24 weeks, rising again from 28 weeks, and reaching preconception levels by 36 weeks of gestation

- How to measure blood pressure accurately?
  - Five-minute rest before measurement, seated at 45-degree angle, arm at the level of the heart
  - Avoid using automated devices (under-estimate BP)
  - Use suitable cuff size (if circumference >=33 cm use large cuff)
  - Keep the rate of deflation 2-3 mm/s
  - Use Korotkoff 5
  - Avoid digit preference

- Diagnosis of hypertension:

Systolic BP > 140 mmHg

OR

Diastolic BP > 90 mmHg

- Women who are pregnant and hypertensive have either:
  - Chronic hypertension (with/ without superimposed pre-eclampsia)

  OR

  - Pregnancy Induced Hypertension (PIH); which is further subdivided into:
    - Non-proteinuric PIH (Gestational hypertension)
    - Pre-eclapmsia

Chronic Hypertension

- The presence of hypertension before 20 weeks' gestation

OR

- Persistent hypertension beyond 6 weeks postpartum

- Affects **1 - 5%** of pregnant women
- Can be either:

Essential (primary) hypertension

- Multifactorial with genetic and environmental contributions

Secondary hypertension

- Renal disease is the most common cause in pregnant women

- **Pre-pregnancy counselling:**

1. Counsel about potential complications in pregnancy
2. Address exacerbating factors and suggest lifestyle modifications (smoking cessation, weight loss, exercise, reduced alcohol intake, and low-salt diet)
3. Optimize blood pressure control
4. Screen for end-organ damage (e.g., creatinine levels)
5. Medication review

   Stop teratogenic agents (ACEIs, ARBs, Statins, Thiazide diuretics) and switch to alternative

- **Antenatal management –Medications:**

  - Stop teratogenic antihypertensive agents (ACEIs, ARBs, Thiazide diuretics) and switch to one of the following:

    1. Labetalol –Non-selective adrenergic receptor blocker

       Avoid if asthmatic patient

    1. Nifedipine –Calcium channel blocker
    2. Methyldopa –Centrally acting α2-adrenergic agonist

       May cause tiredness, headache, depression, and occasionally hepatitis

- Offer pregnant women with chronic hypertension **Aspirin** 75–150 mg once daily from 12 weeks (or before 16 weeks) <u>to reduce the risk of pre-eclampsia</u>

- **Antenatal management –Follow-up:**

  - Hypertension may improve in early pregnancy due to physiological changes and some women may stop their medication for several weeks.

  - Continue antihypertensive treatment unless:

    sustained systolic blood pressure less than 110mmHg

    OR

    sustained diastolic blood pressure less than 70mmHg

- Aim for a target blood pressure of **135/85 mmHg**

  There's an association between low diastolic BP in pregnancy and low birth weight therefore treatment should be reduced if diastolic BP is persistently < 80 mmHg

- In women with chronic hypertension, schedule additional antenatal appointments based on the individual needs of the woman and her baby. This may include:
    - Weekly appointments if hypertension is poorly controlled
    - Appointments every 2 to 4 weeks if hypertension is well-controlled
- Appointments should include measurement of BP and urine dipstick to check for proteinuria (superimposed pre-eclampsia)

- **Maternal complications:**

1. Superimposed pre-eclampsia : 20-30%

Superimposed preeclampsia is defined as preeclampsia in the setting of maternal chronic hypertension

2. Deterioration of renal function if already affected prior to pregnancy, if renal function was normal before; pregnancy does NOT affect the course of the disease

3. Placental abruption: risk increased 3 folds

- **Fetal complications:**

1. Intrauterine Growth Restriction (IUGR): 10-15% (risk is further increased if superimposed pre-eclampsia occurred)

2. Prematurity: 20-30%. This is frequently iatrogenic due to maternal or fetal indications

3. Stillbirth

- **Timing of birth:**

Timing of delivery should be guided by the severity of hypertension, the presence of proteinuria, and maternal and fetal wellbeing

- Women with chronic hypertension whom BP is stable < 160/110 should be delivered **after 37 weeks** unless there's maternal or fetal indications

- If BP is sustained > 160/110 or there's maternal or fetal compromise, a senior obstetrician can take the decision of a planned preterm birth (after a course of antenatal corticosteroids if time permits)

- **Postpartum management:**
  - **Peak** postpartum BP usually occurs at **3-5 days**
  - After delivery, aim for a target BP of **< 140/90 mmHg**
  - In women with chronic hypertension who have given birth, measure blood pressure:
    - Daily for the first 2 days after birth
    - At least once between day 3 and day 5 after birth
    - As clinically indicated after that

- If a woman has taken **methyldopa** to treat chronic hypertension during pregnancy, **stop within 2 days after birth** and change to an alternative antihypertensive treatment (to avoid exacerbation of postnatal depression)

- Offer review at 6-8 weeks postpartum for appropriate contraception and future pre-pregnancy counselling
  - Avoid estrogen containing contraception (combined) in women with hypertension due to their potential to exacerbate sodium retention and hypertension

Pregnancy induced hypertension

- Blood pressure >= 140 mmHg systolic **OR** >= 90 mmHg diastolic on two separate occasions at least four hours apart after 20 weeks gestation in a previously normotensive woman

- If systolic BP > 160 mmHg **OR** diastolic BP > 110 mmHg, can be diagnosed in a single occasion

- Final diagnosis only made postpartum (blood pressure normalizing within 6 weeks of delivery)

1. Non-proteinuric PIH (Gestational hypertension)

- **No proteinuria!**
- In women with gestational hypertension, a full assessment should be carried out
- Antenatal monitoring is needed to ensure that proteinuria does not develop, and pre-eclampsia becomes apparent (SCREENING)
- Risk of progression to pre-eclampsia is 20-30%

- Management:
  - Admit to hospital for management **if BP >= 160/110 mmHg**
  - Start Antihypertensive treatment for all women diagnosed with PIH
  - Aim for a BP of 135/85 or less (but avoid hypotension)
    - Antihypertensive agents:

    1. Labetalol
    2. Nifedipine
    3. Methyldopa

- Monitoring:
  - Measure BP at least once or twice weekly (unless admitted then measure every 15-30 minutes until it falls below 160/110 mmHg)
  - Do urine dipstick to check for proteinuria once or twice weekly –with BP measurement (daily if admitted to hospital)
  - Measure full blood count, liver function and renal function at diagnosis and then weekly

- Fetal assessment:
  - Offer fetal heart auscultation at every antenatal appointment
  - Carry out ultrasound assessment at diagnosis and, if normal, repeat every 2 to 4 weeks
  - Carry out a CTG only if clinically indicated (if BP >= 160/110 mmHg)

- **Delivery and postpartum**:
  - If BP remains under 160/110 mmHg delivery between 37-39 weeks is appropriate (while monitoring closely for progression to severe hypertension, preeclampsia, and fetal growth restriction)
  - If delivery becomes indicated < 37 weeks gestation, consider a course of antenatal corticosteroids prior to planned preterm birth (without delaying delivery)
  - Gestational hypertension may be predictive of chronic hypertension later in life and is important in regard to patient counselling and preventative medical decisions

2. Pre-eclampsia

- Preeclampsia is diagnosed by elevated blood pressure and significant proteinuria after 20 weeks' gestation in a patient known to be previously normotensive.

- Trophoblastic disease or multiple gestation can present with preeclampsia before 20 weeks' gestation

- Significant proteinuria:
  - Use an automated reagent-strip reading device for dipstick screening for proteinuria
  - If dipstick screening is positive (1+ or more), use spot (protein : creatinine) ratio or spot (albumin : creatinine) ratio to quantify proteinuria in pregnant women
  - Gold standard test to quantify proteinuria: 24-hour urine collection
    - Inconvenient so not routinely recommended


Urilyzer 500 Pro

- Thresholds for diagnosis of significant proteinuria:
  - Spot Protein : Creatinine ratio >= 30 mg/mmol
  - Spot Albumin : Creatinine ratio >= 8 mg/mmol
  - 24-hour urine collection >= 300 mg

- **Risk factors:**
- Nulliparity
- Multiple gestation
- Obesity (BMI >= 35)
- Medical disorders: chronic hypertension, pregestational diabetes, chronic kidney disease
- Autoimmune disease: SLE or APLS
- Personal or family History of preeclampsia
- Molar pregnancy
- Conception via assissted reproductive technologies
- Advanced maternal age (40 years)

- **Risk reduction:**

Low-dose Aspirin 75-150 mg starting before 16 weeks gestation until delivery for patients with one or more high risk factors **OR** two or more moderate risk factors

High risk	Moderate risk
Chronic hypertension	Advanced maternal age > 40 years old
Pregestational diabetes	BMI >= 35 kg/ m2
Chronic kidney disease	Nulliparity (primigravida)
Systemic lupus erythematosus	Interpregnancy interval > 10 years
Antiphospholipid syndrome	Multiple gestation
Pre-eclampsia/Eclampsia in a previous pregnancy	Family history of pre-eclampsia

- **Pathophysiology:**
- It is clear that preeclampsia is a **systemic** disease, and the placenta is the root cause of preeclampsia.

- The proposed insult to the placenta is an immunologic alteration in trophoblastic function and reduction in trophoblast invasion. This in turn reduces vascular remodelling and physiological vasodilation of spiral arteries, reducing perfusion, and increasing velocity of blood in the intervillous space.

- This leads to both inflammation and endothelial damage and dysfunction.

- **Pre-eclampsia with severe features:**

  - Blood pressure of 160 mmHg systolic or 110 mmHg diastolic which is persistent
  - Signs, symptoms, or lab values of severe preeclampsia with any elevated blood pressure

- Signs and symptoms of severe preeclampsia include:
    1. Cerebral or visual disturbances (e.g.; persistent headache, blurred vision, scotomata)
    2. Persistent epigastric or right upper quadrant pain
    3. Pulmonary edema

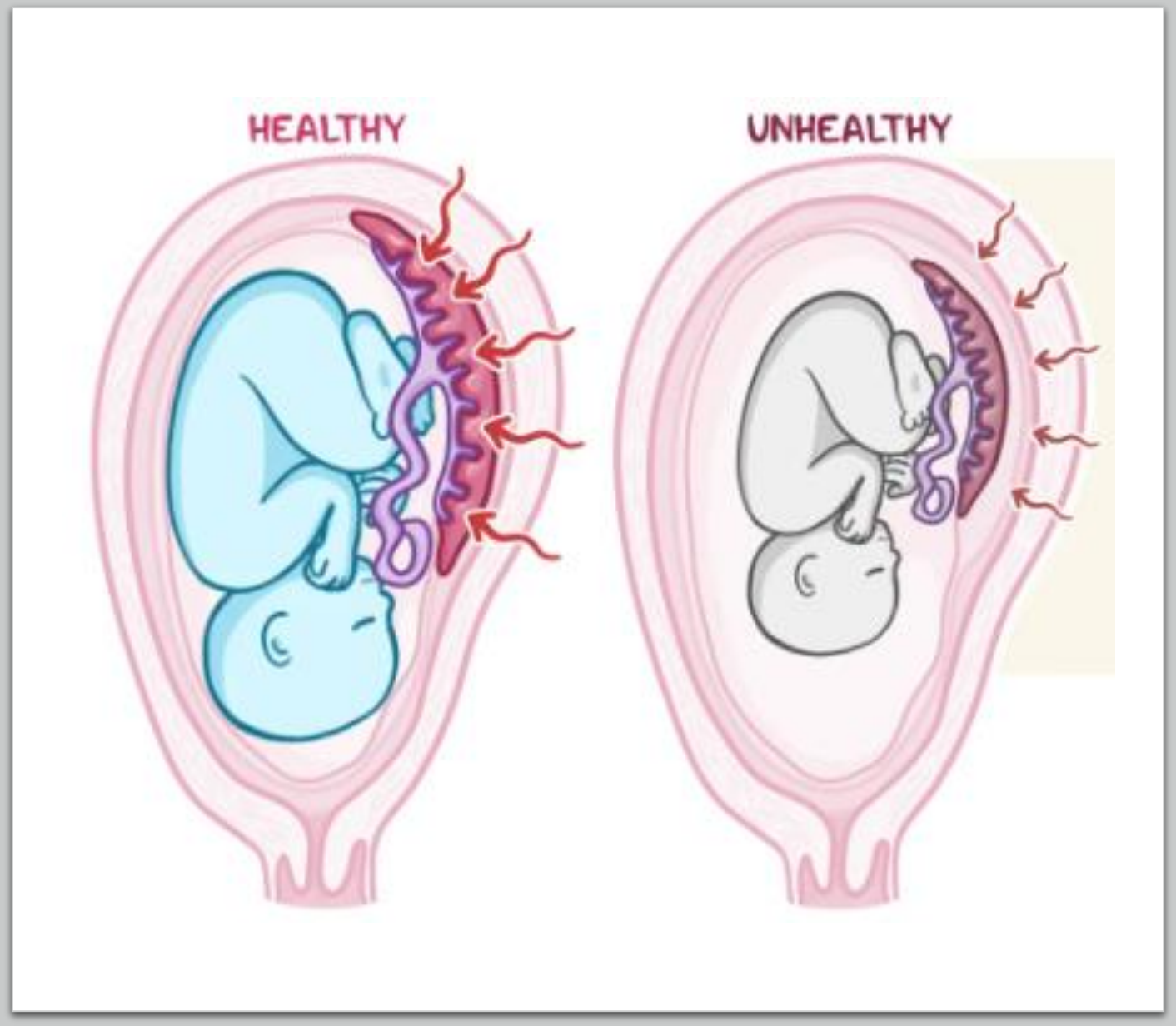
- Symptoms that can be seen with severe preeclampsia but are **not diagnostic** include nausea and vomiting, decreased urine output, hematuria, or rapid weight gain (5 lb or more in 1 week)

- An additional sign that does not establish a diagnosis but does need increased attention for preeclampsia is the rapid elevation of the patient's blood pressure from baseline

- Laboratory findings diagnostic of **severe preeclampsia** include:

1. Platelet count below 150 000 platelets per µL
2. Serum creatinine 90 micromol/litre or more, or a doubling of the patient's baseline creatinine level
3. Liver enzyme (aspartate aminotransferase/alanine aminotransferase) elevation of more than double the upper limit of normal

- Fetal findings associated with preeclampsia may include intrauterine growth restriction (IUGR), oligohydramnios, and other signs of uteroplacental insufficiency. However, none of these findings is diagnostic of preeclampsia or preeclampsia with severe features.



Definitive management for gestational hypertension, preeclampsia, and eclampsia is delivery because the placenta is the insulting agent and removal of the placenta will lead to resolution of the disease process

- **Management of pre-eclampsia without severe features (mild pre-eclampsia):**
  - At term: delivery, typically at 37 weeks or at time of diagnosis if after 37 weeks
  - Preterm: optimal treatment prior to 37 weeks is usually expectant management

- Expectant management of preterm patient with mild pre-eclampsia:
  - Antihypertensive treatment with aim to keep BP < 135/85
  - Monitoring of BP (at least every 48 hours), more frequently if admitted to hospital
  - Repeat laboratory tests 2-3 times per week
  - Fetal monitoring: ultrasound assessment at diagnosis, if normal then every 2 weeks. CTG at diagnosis and repeat when indicated

- **Management of pre-eclampsia with severe features:**

  urgent delivery *after* maternal stabilization is indicated

  - Admission
  - IV line, foley catheter insertion, strict intake/output recordings, fluid management
  - IV antihypertensive agent (+/- MgSO4)
  - Course of antenatal corticosteroids (should NOT delay urgent delivery)
  - Laboratory assessments (repeat every 6 hours if still not delivered)
  - Delivery when the mother is stable (usually by CS)

- IV antihypertensive treatment:

    1. Labetalol: 20 mg IV bolus, if persistently elevated: 40, 80, and 80 boluses up to a maximum dose of 220 mg, at 10-minute intervals

    2. Hydralazine: 5 mg IV bolus, if persistently elevated: further 5 mg boluses up to a maximum dose of 15 mg, at 30-minute intervals

       (Colloid should be infused prior to treatment if the baby is undelivered to protect the uteroplacental circulation and prevent hypotension and fetal distress)

       - If no IV access, use immediate release oral nifedipine

- Magnesium Sulphate:
  - Benefits:
    1. Seizure prophylaxis (decrease the risk of eclampsia by more than 50%)
    2. Neuroprotection (evidence of benefit from 24 weeks till 32 weeks)
  - Dose:
    - 4 gram bolus over 5-15 minutes, then
    - 1 g/h infusion for 24 hours

- ATTENTION!!
  - MgSO4 has *narrow therapeutic window* –therapeutic range is 4 to 6 mEq/L
  - Check serum magnesium level 4 hours after the loading dose and then every 6 hours as needed or if symptoms suggest magnesium toxicity

- Patients are monitored **hourly** for signs and symptoms of magnesium toxicity:
  - Loss of patellar reflexes (at 8 to 10 mEq/L)
  - Respiratory depression or arrest (at 12 mEq/L)
  - Mental status changes (at 12 mEq/L) followed by ECG changes and arrhythmias

- If magnesium toxicity develops:
  - Stop magnesium sulphate
  - Check the patient's vital signs
  - Check plasma levels
  - Administer 1-g calcium gluconate IV over 3 minutes, and consider diuretics

- Urine output and fluid management:
  - Patients with preeclampsia are frequently hypovolemic due to third spacing and increased capillary permeability, these same abnormalities also increase their risk of pulmonary edema
  - Limit maintenance fluids to 80 ml/hour unless there are other ongoing fluid losses (for example, haemorrhage)
  - Urine output usually returns to normal about 12 to 24 hours after delivery

- Fetal assessment and delivery:
  - CTG should be done at diagnosis and continuous fetal heart monitoring is required if in labour
  - Usually delivery by CS, unless mother and fetus are stable and cervix favourable then could try IOL by vaginal prostaglandins
  - If the patient is being delivered by CS, keep in mind:
    - Anaesthesia: GA can be dangerous as endotracheal intubation can exacerbate hypertension; regional anesthesia is preferred if time permits
    - Platelet count: > 80 000 per µL needed for regional anaesthesia, also if GA is being used a minimum of 50 000 per µL is needed for CS

- Maternal complications of pre-eclampsia:
    - Renal failure
    - Acute cardiac failure
    - Pulmonary edema
    - Thrombocytopenia
    - Disseminated intravascular coagulopathy
    - Cerebrovascular accidents

- Fetal complications:
    - Prematurity
    - IUGR
    - RDS
    - IUFD

Eclampsia

- Eclampsia should be the presumed diagnosis in obstetric patients with seizures and/or coma without a known history of epilepsy or other causes of seizures

- Occurs in about 1% of patients with pre-eclampsia

- Eclampsia is an **obstetric emergency** that can occur antepartum, intrapartum, or postpartum

- The pathophysiology of eclamptic seizures is unknown but is related to arterial vasospasm and may occur when mean arterial pressure exceeds the capacity of cerebral autoregulation, leading to cerebral edema and increased intracranial pressure

- Management:
  - Appropriate management of ABCs (airway, breathing, and circulation) with measures taken to avoid aspiration
  - Seizure control with 6-g $MgSO_4$ IV bolus. If the patient has a seizure during or after the loading dose, an additional 2-g IV bolus of $MgSO_4$ can be given.
  - Treat seizures refractory to $MgSO_4$ with IV phenytoin or a benzodiazepine (e.g., lorazepam).
  - Treat status epilepticus with lorazepam. Patients with status epilepticus may require intubation to correct hypoxia and acidosis and to maintain a secure airway.
  - Prevent maternal injury with padded bedrails and appropriate positioning.
  - Control of severe hypertension

- Delivery is indicated after maternal stabilization, and emergency cesarean delivery should always be anticipated in case of rapid maternal or fetal deterioration

    - During acute eclamptic episodes, fetal bradycardia is common. It usually resolves in 3 to 5 minutes

HELLP Syndrome

- **H**emolysis
- **E**levated **L**iver enzymes
- **L**ow **P**latelets

- Often presents with nonspecifi c complaints such as malaise, abdominal pain, vomiting, shortness of breath, or bleeding

- Hypertension is not always a clinical feature

- Management is the same as for severe pre-eclampsia

- Transfusion of red cells, platelets, or factors may be required immediately prior to delivery depending on severity of anemia and thrombocytopenia

Postpartum management of PlH

1. BP monitoring and management of complications –shall any occur
2. Medication review
3. Follow-up at 6-8 weeks postpartum

- BP monitoring:
  - At least 4 times a day while the woman is an inpatient
  - At least once between day 3 and day 5 after birth (more frequent if she’s taking antihypertensive treatment, until she’s able to stop it)

- Medication review:
  - If a woman has taken methyldopa to treat pre-eclampsia, stop within 2 days after the birth and change to an alternative treatment if necessary (postnatal depression risk)
  - If she’s breastfeeding, use safe antihypertensive agent:
    - Enalapril (appropriate monitoring of maternal renal function and maternal serum potassium)
    - Nifedipine/ Amlodipine

- Follow-up:

1. Make sure BP stabilized and any laboratory abnormalities resolved
2. Counselling about risk of recurrence: about 20%, if needed preterm delivery risk is higher
3. Counselling about long term risks: chronic hypertension, ischemic heart disease, and stroke
4. Risk reduction in future pregnancies (low-dose aspirin)

Thank you!

- References:

1. NICE guideline –Hypertension in pregnancy: diagnosis and management
2. Obstetrics and Gynaecology an evidence-based text for the MRCOG
3. THE JOHNS HOPKINS MANUAL OF GYNECOLOGY AND OBSTETRICS