ANMC GUIDELINES FOR MANAGEMENT OF HYPERTENSIVE DISORDERS IN PREGNANCY

INTRODUCTION

Hypertensive disorders of pregnancy include chronic hypertension, gestational hypertension, preeclampsia without severe features, preeclampsia with severe features, eclampsia, and HELLP.

It is important to understand that hypertensive disorders of pregnancy are progressive and any diagnosis requires close follow up.

Patients with chronic hypertension are 4-5x more likely to develop preeclampsia (superimposed preeclampsia) than patients without hypertension. Thus, of patients with chronic hypertension 15-40% will develop superimposed preeclampsia. Patients who develop superimposed preeclampsia have higher rates of adverse maternal and fetal outcomes including a 3x higher risk of placental abruption, increased risk of fetal growth restriction, and increased risk of perinatal death.

Patients with chronic hypertension also have an increased risk of gestational diabetes, cesarean delivery, and postpartum hemorrhage.

When managed expectantly, 10-20% of patients with gestational hypertension will develop severe hypertension – this risk is greatest with gestational hypertension is diagnosed before 30wga. Of patients with gestational hypertension, 0.5% will ultimately progress to eclampsia, and 1-2% will develop HELLP syndrome.

I. DEFINITIONS

Elevated blood pressure

- Systolic BP (SBP) \geq 140mmHg or diastolic BP (DBP) \geq 90mmHg

Severe range blood pressure

- SBP \geq 160 mmHg and/or DBP \geq 110 mmHg

Proteinuria: Abnormal amount of protein in urine

- The diagnosis of proteinuria is made with a Total Protein / Creat > 0.3, or a 24 hour urine specimen > 300 mg, or 2+ dipstick

If Total P/CR	< 0.15	negative for significant proteinuria
If	> 0.3	positive for significant proteinuria
If	0.16-0.29	get 24-hour urine for total protein

- Proteinuria can be misrepresented on contaminated urine specimens. Consider a reflex CCUA on all P:C \geq 0.15. If necessary, repeat the test on a clean specimen, e.g. 0-5 squamous cells, or on a catheterized specimen.

Thrombocytopenia

- Platelet count < 100,000/microliter

Renal insufficiency

- Creatinine (Cr) > 1.1mg/dL or a doubling of serum Cr concentration from baseline in the absence of other kidney disease

Impaired liver function

- Elevated liver transaminases (AST and ALT) to twice normal concentration
- Persistent severe right upper quadrant (RUQ) pain and/or severe epigastric pain not accounted by alternative diagnoses

Pulmonary edema

- Signs and symptoms of pulmonary edema include shortness of breath, crackles on lung exam, chest x-ray with diffuse infiltrates, and hypoxemia

Cerebral or visual symptoms

- Headache not improved with Tylenol
- Scotoma seeing spots in vision

II. DIAGNOSIS

Preeclampsia

Newly elevated blood pressures after 20 weeks gestational age or within the first 6wks of the post-partum period

- Two readings of SBP \ge 140 mmHg and/or DBP \ge 90 at least 4 hours apart
- SBP \geq 160 and/or DBP \geq 110 twice can be within a short interval (15 minutes)

AND

Proteinuria

OR

In the absence of proteinuria, new onset of hypertension with the new onset any the following:

- Thrombocytopenia
- Renal insufficiency
- Impaired liver function
- Pulmonary edema
- New onset headache unresponsive to acetaminophen and not accounted for by alternative diagnoses
- Visual disturbances

Preeclampsia with severe features (any of these)

Diagnosis of preeclampsia (as above) with ANY of the following:

- Systolic blood pressure of 160 mm Hg or higher, or diastolic blood pressure of 110 mm Hg or higher on two occasions at least 4 hours apart while the patient is on bed rest (unless antihypertensive therapy is initiated before this time)
- Thrombocytopenia
- Impaired liver function
- Renal insufficiency
- Pulmonary edema

- New-onset headache unresponsive to acetaminophen and not accounted for by alternative diagnoses
- Visual disturbances

HELLP syndrome

[<u>H</u>emolysis (abnormal peripheral smear, elevated bilirubin, elevated LDH), <u>E</u>levated <u>Liver enzymes</u>, <u>Low Platelets</u>]

LDH> 600 IU/L AST >2x normal ALT >2x normal Platelets $<100,000 \times 10^{9}$ /L (Not all lab abnormalities are required for diagnosis)

-Common symptoms: RUQ pain, malaise, N/V

<u>Eclampsia</u>

New onset generalized seizures in pregnancy. Eclampsia should be suspected in all cases of generalized tonic-clonic seizures in a pregnant patient without prior history of seizure disorder and no other clear cause of seizure.

Chronic Hypertension (CHTN)

Hypertension that pre-dates pregnancy OR onset of hypertension before 20th week of gestation OR use of antihypertensive medications before pregnancy OR failure to normalize blood pressure after 12wks postpartum

CHTN with Superimposed Preeclampsia

Preeclampsia in a woman with a history of hypertension before pregnancy or before 20 wks of gestation

CHTN with Superimposed Preeclampsia w/severe features.

Preeclampsia in a woman with a history of hypertension before pregnancy or before 20 wks of gestation with the presence of severe symptoms

Gestational hypertension

Blood pressure elevation after 20 weeks GA without proteinuria

- Two readings of SBP \ge 140 mmHg and/or DBP \ge 90 at least 4 hours apart
- SBP \geq 160 and/or DBP \geq 110 twice can be within a short interval (15 minutes)

If blood pressure elevation persists ≥ 12 weeks postpartum the diagnosis is changed to chronic hypertension.

SCREENING AND INITIAL EVALUATION

ALL women should have Blood pressure (BP) evaluation at initial and all prenatal visits

There is no role for universal urine dipstick testing to screen for preeclampsia in routine prenatal care in the asymptomatic non-hypertensive patient. On the other hand, do obtain a clean catch urine sample if the patient has:

- BP > 140/90
- Symptoms of preeclampsia
- Signs / symptoms of a urinary tract infection
- Multiple gestation
- Chronic hypertension or currently on anti-hypertension medication.

Pregnancy and health history

- Determine if patient has a history of chronic hypertension, gestational hypertension, preeclampsia, or eclampsia
 - This may require a review of past medical records with attention to vital signs at clinic and hospital visits.
 - Note pre-term or early term deliveries and perinatal outcomes.
- Women with chronic hypertension (CHTN), pre-gestational diabetes, chronic kidney disease, a multiple gestation pregnancy; a history of gestational hypertension, preeclampsia, eclampsia, or HELLP should also have:
 - Comprehensive metabolic panel (CMP) to evaluate creatinine (Cr), potassium (K), and liver function (AST, ALT)
 - Baseline evaluation for proteinuria

When to refer for additional evaluation

- Abnormal kidney function consider renal ultrasound, referral to OB/GYN
 - Cr > 1.1
 - Proteinuria
 - K < 3.0
- History of chronic hypertension >4 years
 - Most women have essential hypertension, but 10% of women with CHTN will have underlying renal or endocrine disorders.

EARLY INTERVENTION TO PREVENT PREECLAMPSIA

Low dose aspirin

- Evidence supports daily low dose aspirin (81mg) when started between 12-28wk of pregnancy (ideally before 16wk) reduces the occurrence of preeclampsia, preterm birth, and IUGR in women at increased risk.
- The harms of low-dose aspirin in pregnancy are considered to be small
- Aspirin is RECOMMENDED for the following women:
 - History of pre-eclampsia
 - Multifetal gestation
 - Chronic hypertension
 - Preexisting Type 1 or Type 2 DM
 - Renal disease
 - Autoimmune disease (such as systemic lupus erythematosus or antiphospholipid antibody syndrome)
- Daily aspirin should be continued until delivery

<u>Calcium supplementation</u> (1.5-2g) in women with low baseline calcium intake (<600mg/day)

- Most multivitamins and prenatal vitamins only have 200-300mg of calcium
- Recommend 1.5-2g supplemental calcium in divided doses for Alaskan Native patients with low dietary calcium intake especially if patient is lactose intolerance, or have a known low dietary calcium intake.

<u>Vitamin D supplementation</u> – Recommended for all pregnant Alaskan women to be supplemented with 1,000 IU/day in addition to a daily prenatal vitamin containing 400 IU/day (not to exceed 4,000 IU/day)

The following interventions are NOT recommended for prevention of pre-eclampsia

- Supplementation with vitamin C or vitamin E
- Restriction of dietary salt intake
- Bedrest or restriction of physical activity

EVALUATION

Screening for hypertensive disorders in pregnancy is recommended for all pregnant women at the first prenatal visit and throughout the remainder of pregnancy.

Initiate an evaluation for hypertensive disorders of pregnancy when:

- Elevated BP with systolic BP (SBP) 140 to < 160 mmHg or diastolic BP (DBP) 90 to < 110 on <u>TWO</u> occasions at least 4hr apart
 - If one abnormal reading, consider having patient present to triage/hospital or stay in clinic for repeat BP
 - Elevated BP should be confirmed before initiating laboratory work up.
- New onset severe range blood pressure SBP ≥ 160 or DBP ≥ 110 should have work up initiated immediately and patient sent to triage for evaluation
- New onset symptoms
 - Headache not improved with acetaminophen
 - Visual changes (seeing spots in vision)
 - Persistent right upper quadrant or epigastric pain
 - New onset proteinuria or renal impairment
- Fetal growth restriction

Evaluation should include:

- Clean catch urinalysis (CCUA) and urine total protein : creatinine ratio
 - If >5 squamous cells or evidence of UTI, then invalid for protein assessment
- Ultrasound for fetal growth
- NST
- CMP (assessment of Cr, AST, ALT)
- CBC

MANAGEMENT

CHRONIC HYPERTENSION

- Initial prenatal evaluation as above
- If severe hypertension and/or cardiac, renal, or connective tissue disorders early OB consultation or referral

- For pregnant women w/CHTN and poorly controlled BP, the use of home BP monitoring is suggested
- For women with well controlled CHTN who are accustomed to exercising, it is recommended that moderate exercise be continued during pregnancy

Antihypertensive Therapy

- ACE inhibitors are contraindicated and should be stopped as soon as pregnancy is diagnosed
- All BP medications can be discontinued initially with BP recheck in 1 wk
 - If initial blood pressure is well controlled, consider discontinuing BP medications in first trimester and re-start for:
 - persistent chronic hypertension when systolic pressure is 160 mm Hg or more, diastolic pressure is 110 mm Hg or more, or both. (See Appendix III)
 - In the setting of comorbidities or underlying impaired renal function, treating at lower blood pressure thresholds may be appropriate.

Monitoring

- Prenatal care visits Q 4wks until 32wks then Q2wks if BP remains well controlled
- Initial ultrasonography (US) at 8-10 wks
- Anatomy US at 20-22wk
- Growth US repeated at 28-32wga and then Q3-4 weeks
- Antenatal testing

	0	
•	Well controlled:	
	No meds	No antenatal testing
	On meds	NST + AFI Q week starting at 36wk
•	Not well controlled	
	On meds	NST 2x /wk + AFI Q week starting at 32wk
•	If FGR develops:	
	At Dx	NST 2x /wk + AFI Q week + Doppler 1x /wk
	If oligohydramnios	- •••
	At Dx	NST / wk plus repeat AFI / MVP 24 hrs initially

- Labs: Baseline and if BP is difficult to control or exam changes
 - CBC, CMP (Cr, AST/ALT), and urine P:C ratio or urine dip for proteinuria
- Obtain baseline EKG:
 - If poorly controlled hypertension for more than 4 years or those suspected of having long-standing hypertension based on age (older than 30 years) are more likely to have cardiac hypertrophic changes, cardiomegaly, and ischemic heart disease

Delivery

Well controlled:	
No meds	39 -39 6/7 wks
On meds	39 -39 6/7 wks

 Not well controlled On meds > 37wks

GESTATIONAL HYPERTENSION

- Diagnosis \geq 37wga -> DELIVER
- Diagnosis < 37wga
 - Daily kick counts
 - BP check twice weekly
 - One check can be at home if patient has BP cuff and is reliable
 - Antenatal testing w/ NST + AFI weekly at diagnosis
 - If FGR develops: At Dx
 If oligohydramnios At Dx
 NST 2x /wk + AFI Q week + Doppler 1x /wk
 NST / wk plus repeat AFI / MVP 24 hrs initially
 - Labs w/each prenatal visit
 - CBC, CMP (Cr, AST/ALT), and urine P:C ratio or urine dip for proteinuria
 - Growth US every 3-4 weeks

*If develops laboratory values or signs/symptoms consistent with pre-eclampsia, adjust management to new diagnosis.

Delivery

37-38 wks

PREECLAMPSIA WITHOUT SEVERE FEATURES

- Transfer if higher level of care as needed for further evaluation and management
- DELIVER if:
 - Diagnosis ≥ 37wga
 - Diagnosis \geq 34wga < 37 wga and if any of the following
 - Reversed end-diastolic flow on umbilical artery Doppler studies
 - Oligohydramnios (AFI <5cm, MVP < 2cm)
 - Persistent BPP $\leq 6/10$
 - Fetal death
 - Lethal anomaly or extreme prematurity

Consider course of late-preterm corticosteroids, if not previously given during this pregnancy, with initiation of induction of labor – not to delay delivery process.

- Expectant Management if diagnosis < 37wga without any findings noted above
 - Transfer to ANMC at diagnosis or 37wks if undelivered
 - Inpatient vs outpatient management
 - Outpatient management of preeclampsia without severe features can be considered if medical adherence with home care and follow-up guidelines is assured and followed.
 - Inpatient management:
 - Regular diet
 - Bed rest NOT recommended
 - Vital signs Q6hrs while awake (BP, HR, urine output)
 - Daily weight, best in AM

- Daily evaluation for CNS and GI symptoms, fetal movement, vaginal bleeding, contractions
- At least daily NST
- Fluid restriction NOT recommended
- Outpatient management:
 - Daily patient self-assessment of fetal movement and maternal symptoms
 - Weekly provider visits
 - BP check twice weekly these can been done at time of antenatal testing and/or provider visit
 - Antenatal testing w/ NST twice weekly + AFI Q week at diagnosis
 - If FGR develops: At Dx NST 2x /wk + AFI Q week + Doppler 1x /wk If oligohydramnios At Dx NST / wk plus repeat AFI / MVP 24 hrs initially
 - Labs w/each weekly prenatal visit
 - CBC, CMP (Cr, AST/ALT), and urine P:C ratio or urine dip for proteinuria
 - Growth US every 3-4 weeks
- Antihypertensive Medications
 - Persistent hypertension when systolic pressure is 160 mm Hg or more, diastolic pressure is 110 mm Hg or more, or both. (See Appendix III)

* If patient develops signs or symptoms of severe features or evidence of worsening disease, adjust management to management of preeclampsia with severe features.

PREECLAMPSIA WITH SEVERE FEATURES

Initial Steps

- Prompt OB consultation
- Consider initial infusion of 500 ml of lactated ringers (LR) IV as a bolus, as many patients will have vasoconstriction, within overall daily fluid restriction.
 - Do not bolus fluid if: SOB or SpO2 < 95%, or renal impairment
 - Consider continued IV fluids if evidence of hemoconcentration or oliguria
- Treat severe range BP as soon as possible (30- 60 minutes) with antihypertensive medications see Appendix IV
- Start Magnesium sulfate for seizure prophylaxis see Appendix V
- Transfer to tertiary care center once stable (stretcher, medical escort)

Maternal stabilization and DELIVER immediately if:

- \geq 34wga (can initiate course of late pre-term corticosteroids with induction)
- < 34wga and any of the following:
- Maternal
 - Uncontrolled severe hypertension

- Persistent headache
- Persistent epigastric pain
- Persistent CNS Sx
- Stroke, MI
- HELLP
- Worsening renal function
- Eclampsia
- Pulmonary edema
- Placental abruption

Fetal

- Non-reassuring fetal heart status
- Intrauterine fetal demise
- Lethal anomaly or extreme prematurity
- Persistent reversed end diastolic umbilical artery flow

Consider course of corticosteroids, or rescue corticosteroids as per guideline, with initiation of induction of labor – not to delay delivery process.

- During this time, patient should be treated with:
 - Mg for seizure prophylaxis
 - Antihypertensive medication
 - Labor induction
- EXPECTANT MANAGEMENT if <34wk and stable (without any of the signs or symptoms listed above), manage as an inpatient until 34 0/7wga with the following:
 - Administer corticosteroids or rescue corticosteroids as per guideline
 - Mg for seizure prophylaxis for initial 48hours
 - Antihypertensive medication
 - Vital signs, intake and output, symptoms of severe pre-eclampsia Q6 hrs while awake
 - Daily weight, best in AM
 - CBC, CMP daily; can do every other day if values are stable
 - NST daily
 - Growth US Q 2-3wks
 - Umbilical artery Doppler studies Qwk if intrauterine growth restriction present
 - DELIVER if worsening disease or non-reassuring fetal status
 - Fluid restriction NOT recommended if stable

ECLAMPSIA

Initial Steps – maternal stabilization

- Place patient in 'position of safety' until more alert
- Give magnesium STAT IM/IV (See Appendix V)
- If eclampsia occurs while on Mg, bolus with 6 gm and increase drip to 3gm/hr IV
- Treat severe hypertension (See Appendix IV)
- Oxygen by mask at 8 L/minute when seizures resolved
- Continuous fetal monitoring,

- Anticipate non-reassuring fetal heart rate in the immediate postictal period.
- Allow for in utero resuscitation (with standard measures)
- If non-reassuring FHR persists after 30 minutes, stat OB consultation
- Transport to tertiary care center <u>after</u> stabilization (stretcher, medical escort, magnesium sulfate, oxygen, IV Fluids)

Deliver AFTER maternal stabilization

- SEIZURE IS NOT AN INDICATION FOR CESAREAN DELIVERY
 - Urgent cesarean delivery as a result of responding to the non-reassuring fetal tracing immediately after a seizure is cautioned, as the risk of maternal cerebrovascular hemorrhage is extremely high at this time.
 - Continue MagS04 during the cesarean delivery
- Please stabilize with adequate magnesium sulfate first if a cesarean delivery must be done despite the risk, e. g., status epilepticus
- Remember 'Primum non nocere' a.k.a. 'do no harm', most eclamptic seizures resolve spontaneously

SPECIAL CIRCUMSTANCES

Cesarean delivery while on Mg

- DO NOT DISCOTINUE Mg
 - The ½ life of Mg is 5 hours. Discontinuing at the time of cesarean delivery only minimally decreases the concentration and potentially increases the risk of a seizure.

Fluid Management

- Maternal death in hypertensive disease of pregnancy is much more the result of pulmonary edema than renal failure, so judicious fluid administration seems prudent.
- In uncomplicated preeclampsia, total fluids should be restricted to 100 -120 mL/h (3000 cc/24 hr total: IVF, boluses, PO, piggybacks), and the urine output monitored hourly.
- If one feels the patient remains vasoconstricted (urine output < 20 cc/ hr) and may benefit from additional fluid boluses, please consult an OB/GYN.

POSTPARTUM MANAGEMENT

- If on MgS04, continue for 12-24 hours from delivery or last seizure, whichever occurred last
- Depending on clinical condition, consider continued Pitocin IV drip
- Avoid methergine (could cause vasospasm and increase BP)
- Monitor intake and output every 4-8 hours until discharge
- Continue or initiate antihypertensive therapy when $SBP \ge 150mmHg$ or $DBP \ge 100mmHg$ on two occasions at least 4 hours apart
- If SBP \geq 160mmHg or DBP \geq 110mmHg on two checks 15 minutes apart, treat with IV antihypertensive medications within 30 minutes and initiate Mg.
- -If using NSAIDs in those patients without renal dysfunction, then one may need to adjust anti-HTN meds accordingly

- Women should be discharged with information about signs and symptoms of preeclampsia
- Treat w/Mg for at least 24hrs if patient develops severe hypertension or preeclampsia associated with:
 - Headache not improved with acetaminophen
 - Visual changes (spots in vision)
 - Altered mental status
 - Persistent right upper quadrant or epigastric pain
 - Shortness of breath
 - Thrombocytopenia
 - Abnormal liver enzymes
- Consider straight catheter urine collection for accurate assessment of proteinuria in postpartum period

Women with a history of a pregnancy affected by a diagnosis of least preeclampsia are at increased risk of cardiovascular disease later in life. This risk is twice as high as the baseline risk in all women with preeclampsia, and 4-8x higher in women who had recurrent preeclampsia or a delivery before 34 0/7wga due to preeclampsia.

Thus, additional recommendations include:

- Referral to primary care for evaluation and management of arteriosclerotic cardiovascular disease risk factors
- At least yearly assessment of blood pressure, fasting blood glucose, and BMI
- Pre-conception counseling and assessment prior to next pregnancy

POST-DISCHARGE

In women with preeclampsia and superimposed preeclampsia, BP usually decreases within the first 48hrs after delivery, but will increase again around 3-6 days postpartum and should be monitored closely.

- Monitor for 72hr postpartum, if discharged before this time, she should return for blood pressure check at 72h postpartum
- Blood pressure check again at 7-10days postpartum
- If PP BP is > 150 / 100, then:
 - Change anti-HTN regimen
 - Change lifestyle
 - Consult OB/GYN
 - If changes made, then re-appt one week
 - Smooth transition to primary care provider

Additionally, pre-eclampsia and eclampsia can develop up to 6wks postpartum and should be considered when a patient presents with elevated blood pressures, headache, visual changes, and/or right upper quadrant or epigastric pain in the postpartum period.

If new onset PEC or GHTN, then obtain CMP, CBC, and pre-eclampsia screen If prior PEC or GTHN, then it is not necessary to repeat pre-eclampsia screen

If both severe HTN and severe features develop:

-Admit -Initiate MagS04 as above

SUMMARY OF DELIVERY TIMES AND MONITORING

	Start	NST	AFI	Delivery
Chr HTN – no meds	-	-	-	39-39 6/7 wks
Chr HTN – controlled on meds	36	1x/wk	1x/wk	39-39 6/7 wks
Chr HTN – difficult to control	32	2x/wk	1x/wk	<u>></u> 37
Gestational HTN	36	1x/wk	1x/wk	37-38 wks
Preeclampsia	at Dx	2x/wk	1x/wk	<u>> 37</u>
Preeclampsia, severe < 34 wks	at Dx	Hosp	Hosp	Steroids
Preeclampsia, severe > 34 wks	at Dx	Hosp	Hosp	at Dx

APPENDICES

- I. Measuring Blood Pressure
- II. Diagnosing proteinuria
- III. Treating antepartum hypertension
- IV. Treating severe hypertension
- V. Magnesium administration
 - a. Administrating Magnesium with an IV
 - b. Administering Magnesium without an IV
- VI. Alternatives to Magnesium
- VII. Antenatal corticosteroids
- VIII. Delivery and Monitoring Summary

I. MEASURING BLOOD PRESSURE

The systolic blood pressure is the pressure at which a heartbeat is first heard, the diastolic blood pressure is the pressure at which the sound disappears (Korotkoff phase V). To reduce inaccurate readings:

- An appropriate size cuff should be used (length 1.5 times upper arm circumference or a cuff with a bladder that encircles 80% or more of the arm).
- BP cuff should be placed in middle of upper arm in line with her sternum
- The blood pressure level should be taken with the patient sitting comfortably in an upright position with legs uncrossed after a 10-minute or longer rest period.
- For patients in the hospital, the blood pressure can be taken with either the patient sitting up or in the left lateral recumbent position with the patient's arm at the level of the heart.
- BP should be taken while she is not talking or moving
- The patient should not use tobacco or caffeine for 30 minutes preceding the measurement.
- Although validated electronic devices can be used, a mercury sphygmomanometer is preferred because it is the most accurate device

II. DIAGNOSING PROTEINURIA

Urine must be clean catch specimen and not collected in the setting of urinary tract infection – a dirty catch or UTI can falsely elevated the amount of protein in urine. If there are >5 squamous cells on urinalysis, suspect dirty catch.

Proteinuria is diagnosed when:

- Spot urine w/protein:creatinine (P:C) ratio $\geq 0.3 \text{ mg/dL}$
 - If urine $0.15 \le P:C < 0.3$ consider 24hr urine protein
- 24hr urine collection w/ \ge 300mg
- Urine dipstick with $\geq 2+$ protein on two separate occasions (only when no other method of evaluation is available)

III. TREATING ANTEPARTUM HYPERTENSION

- Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB) should be discontinued in pregnancy and avoided during pregnancy as they are associated with fetal anomalies
- No difference in outcome or safety between labetalol, methyldopa, and nifedipine.
- Labetalol should be avoided in women with history of asthma, heart disease, and congestive heart failure
- Goal BP is:
 - 120 < SBP < 160
 - 80 < DBP < 110

Drug	Dosage	Comments		
Labetalol	200–2,400 mg/d orally in two to three divided doses. Commonly initiated at 100–200 mg twice daily	Potential bronchoconstrictive effects. Avoid in women with asthma, preexisti myocardial disease, decompensated ca function, and heart block and bradycar		
Nifedipine	30-120 mg/d orally of an extended-release	Do not use sublingual form.		
6	preparation. Commonly initiated at 30–60 mg once daily (extended-release)	Immediate-release formulation should generally be reserved for control of sev acutely elevated blood pressures in hospitalized patients. Should be avoide tachycardia.		
Methyldopa	500–3,000 mg/d orally in two to four divided doses. Commonly initiated at 250 mg twice or three times daily	Safety data up to 7 years of age in offs May not be as effective as other medications, especially in control of se hypertension. Use limited by side effec profile (sedation, depression, dizziness)		
Hydrochlorothiazide	12.5-50 mg daily	Second-line or third-line agent		

Table 2. Common Oral Antihypertensive Agents in Pregnancy

Source: ACOG Practice Bulletin #203 page 35

IV. TREATING SEVERE HYPERTENSION

- GOAL IS TREATMENT WITHIN 30-60 MINUTES
- No significant difference between the efficacy or safety between hydralazine, labetalol, or nifedipine.
- If no IV, start with immediate release Nifedipine 10mg PO, if not available give Labetalol 200mg PO, repeat in 30min if needed
- Switch to IV medications when available
- Choice of medication should depend on clinician comfort with the medication and patient factors.
- Max out one agent before moving to a different one see algorithms below
- Avoid labetalol in setting of bradycardia, history of asthma, heart disease, congestive heart failure
- Goal BP 140-150 systolic, 90-100 diastolic
- Once BP threshold achieved, repeat BP measurement Q 10 minutes x 1 hour, then Q 15 minutes x 1 hour, then Q 30 minutes x 1 hour, and then Q1hr x 4 hours.

Drug	Dosage	Comments	Onset of A
Labetalol	10–20 mg IV, then 20–80 mg every 10–30 minutes to a maximum cumu- lative dosage of 300 mg; or constant	Tachycardia is less common and fewer adverse effects than other agents.	1–2 minutes
	infusion 1–2 mg/min IV	Avoid in women with asthma, preexisting myocardial disease, decompensated cardiac function, and heart block and bradycardia.	
Hydralazine	5 mg IV or IM, then 5–10 mg IV every 20–40 minutes to a maximum cumulative dosage of 20 mg; or constant infusion of 0.5–10 mg/hr	Higher or frequent dosage associated with maternal hypotension, headaches, and abnormal fetal heart rate tracings; may be more common than other agents.	10-20 minu
Nifedipine (immediate release)	10–20 mg orally, repeat in 20 minutes if needed; then 10–20 mg every 2–6 hours; maximum daily dose is 180 mg	May observe reflex tachycardia and headaches.	5–10 minute

Table 3. Antihypertensive Agents Used for Urgent Blood Pressure Control in Pregnancy

Abbreviations: IM, intramuscularly; IV, intravenously.

Source: ACOG Practice Bulletin #203 page 35

V. MAGNESIUM ADMINISTRATION See Contraindications and Alternatives below.

- a. Administering Magnesium with an IV
 - Loading dose or seizure:

- Administer Magnesium sulfate [40g/liter] with a 4-6g IV bolus over 20min, use with infusion pump
- Maintenance: 1-2g/hr
- Monitor:
 - Intake and output, consider placement of foley catheter
 - Reflexes, if depressed -> concern for magnesium toxicity, no established therapeutic level, concern if respiratory or cardiovascular depression
 - BP Q15-30 min and continuous fetal monitoring
- Concern for Mg toxicity: treat with calcium gluconate 10%, give 10cc IV over 2 minutes
- Repeat seizure: Re-bolus w/6g bolus and increase drip to 3g/hr
- Duration: Mg should be continued until 12- 24hr postpartum depending on clinical scenario or 24hr after last seizure – whichever has the longest duration

b. Administrating Magnesium w/o an IV

- Loading dose or if seizing:
 - 1. Magnesium sulfate 50% give 5g IM (10mL) in each buttock (10g total)*
- Maintenance: Magnesium sulfate 50% give 5g IM (10mL) every 4-6 hours*
- * Add Lidocaine 1% 1mL to each injection to minimize discomfort
- Monitor:
 - Intake and output, consider placement of foley catheter
 - Reflexes, if depressed -> concern for magnesium toxicity
 - No established therapeutic level, concern if respiratory or cardiovascular depression
 - BP Q15-30 min and continuous fetal monitoring
- Concern for Mg toxicity: Treat with calcium gluconate 10%, give 10cc IV over 2 minutes
- Repeat seizure: repeat loading dose
- Duration: Mg should be continued until 12- 24hr postpartum depending on clinical scenario or 24hr after last seizure – whichever has the longest duration

VI. ALTERNATIVES TO MAGNESIUM

Contraindications to MagS04:

Myasthenia gravis, hypocalcemia, moderate to severe renal failure, cardiac ischemia, heart block, or myocarditis.

Use with caution in pulmonary edema

Consult with OB/GYN.

In setting of contraindication to Mg or no Mg available:

- Lorazepam 2-4mg IV x 1, repeat once in 10-15 min if persistent seizure
- Diazepam 5-10mg IV Q 5-10min; max dose 30mg

- Phenytoin 15-20mg/kg IV x 1, repeat 10mg/kg x 1 in 20min if not hypotensive
- Keppra 500mg IV or PO Q12h

VII. ADMINISTERING CORTICOSTEROIDS

- Dosing options
 - Betamethasone 12mg IM Q 12 hours x 2 doses
 - Dexamethasone 6mg IM Q 6 hours x 4 doses
- When to administer in setting of preeclampsia
 - Consider administration of corticosteroids, and initiation of induction of labor with diagnosis of severe preeclampsia and a viable fetus at ≥ 34 weeks and < 37 weeks – if the patient has not previously had corticosteroids during this pregnancy.
 - It is suggested that corticosteroids, or rescue corticosteroids as per guideline, be administered and <u>delivery deferred for 48 hours</u> if:
 - Maternal and fetal conditions remain stable for women with severe preeclampsia and a viable fetus at 33 6/7 weeks or less of gestation and the patient has <u>none</u> of the following.

Maternal

- Uncontrolled severe hypertension
- Persistent headache
- Persistent epigastric pain
- Persistent CNS Sx
- Stroke, MI
- HELLP
- Worsening renal function
- Eclampsia
- Pulmonary edema
- Placental abruption

Fetal

- Non-reassuring fetal heart status
- Intrauterine fetal demise
- Lethal anomaly or extreme prematurity
- Persistent reversed end diastolic umbilical artery flow

It is recommended that corticosteroids, or rescue corticosteroids as per guideline, be given if the fetus is viable and at 33 6/7 weeks or less of gestation, but that <u>delivery not</u> <u>be delayed</u> after initial maternal stabilization regardless of gestational age for women with severe preeclampsia which is complicated by any of the above.

VIII. SUMMARY OF DELIVERY TIMES AND MONITORING

	Start	NST	AFI	Delivery
Chr HTN – no meds	-	-	-	39-39 6/7 wks
Chr HTN – controlled on meds	36	1x/wk	1x/wk	39-39 6/7 wks
Chr HTN – difficult to control	32	2x/wk	1x/wk	<u>></u> 37
Gestational HTN	36	1x/wk	1x/wk	37-38 wks

Preeclampsia	at Dx	2x/wk	1x/wk	<u>> 37</u>
Preeclampsia, severe < 34 wks	at Dx	Hosp	Hosp	Steroids
Preeclampsia, severe > 34 wks	at Dx	Hosp	Hosp	at Dx

References

ACOG and major benchmarks

Chronic hypertension in pregnancy. ACOG Practice Bulletin No. 203. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133:e26–50.

Gestational hypertension and preeclampsia. ACOG Practice Bulletin No. 202. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133:e1-25.

Emergent therapy for acute-onset, severe hypertension during pregnancy and the postpartum period. ACOG Committee Opinion No. 767. American College of Obstetricians and Gynecologists. Obstet Gynecol 2019;133:e174–80.

Low-dose aspirin use during pregnancy. ACOG Committee Opinion No. 743. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;132:e44–52.

RCOG

Severe Pre-Eclampsia/Eclampsia, Management (Green-top 10A). Royal College of Obstetricians and Gynaecologists 1/3/2006 <u>http://www.nice.org.uk/cg107</u> (Accessed 2/1/19)

USPSTF

Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force recommendation statement. LeFevre ML; U.S. Preventive Services Task Force. Ann Intern Med. 2014 Dec 2;161(11):819-26

Cochrane Library

Duley L, Henderson-Smart DJ, Meher S, King JF Antiplatelet agents for preventing preeclampsia and its complications. Cochrane Database Syst Rev. 2007 Apr 18;(2):CD004659. (Accessed 2/1/19)

Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensivedisorders and rela ted problems. Cochrane Database Syst Rev. 2018 Oct 1;10:CD001059. doi: 10.1002/14651858.CD001059.pub5. Review. (Accessed 2/1/19)

Duley L, Henderson-Smart DJ, Chou D. Magnesium sulphate versus phenytoin for eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 10. Art. No.: CD000128. DOI: 10.1002/14651858.CD000128.pub2. (Accessed 2/1/19)

Duley L, Gülmezoglu AM, Chou D. Magnesium sulphate versus lytic cocktail for eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 9. Art. No.: CD002960. DOI: 10.1002/14651858.CD002960.pub2. (Accessed 2/1/19)

Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2. (Accessed 2/1/19)

Duley L, Henderson-Smart DJ. Magnesium sulphate versus diazepam for eclampsia. Cochrane Database of Systematic Reviews 2003, Issue 4. Art. No.: CD000127. DOI: 10.1002/14651858.CD000127. (Accessed 2/1/19)

Other (alphabetical)

Altman D; Carroli G; Duley L; Farrell B; Moodley J; Neilson J; Smith D Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. Lancet 2002 Jun 1;359(9321):1877-90.

Chang EY; Menard MK; Vermillion ST; Hulsey T; Ebeling M The association between hyaline membrane disease and preeclampsia. Am J Obstet Gynecol 2004 Oct;191(4):1414-7

Chobanian AV, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure *JAMA*. 2003;289:2560-2571. (Level III) <u>http://jama.ama-assn.org/cgi/content/full/289/19/2560</u>

Clark SL, et al. Severe preeclampsia with persistent oliguria: management of hemodynamic subsets. Am J Obstet Gynecol 1986; 154: 490-4

Côté AM, Brown MA, Lam E, von Dadelszen P, Firoz T, Liston RM, Magee LA. Diagnostic accuracy of urinary spot protein:creatinine ratio for proteinuria in hypertensive pregnant women: systematic review. BMJ. 2008;336(7651):1003.

Duckitt K, Harrington D.Risk factors for pre-eclampsia at antenatal booking: a systematic review of controlled studies.BMJ 2005; 330:565–7.

Hutcheon JA, Lisonkova S, Magee LA, Von Dadelszen P, Woo HL, Liu S, Joseph KS. Optimal timing of delivery in pregnancies with pre-existing hypertension. BJOG. 2011 Jan;118(1):49-54. doi: 10.1111/j.1471-0528.2010.02754.x. Epub 2010 Nov 4.

Kirshon B, et al. Role of volume expansion in severe preeclampsia. Surg Gynecol Obstet 1988; 167: 367-71

Koopmans CM et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. Lancet. 2009 Sep 19;374(9694):979-88. Epub 2009 Aug 3.

Milne, F, Redman, C, Walker, J, et al. The pre-eclampsia community guideline (PRECOG): how to screen for and detect onset of pre-eclampsia in the community. BMJ 2005; 330:576.

Papanna R, Mann LK, Kouides RW, Glantz JC. Protein/creatinine ratio in preeclampsia: a systematic review. Obstet Gynecol. 2008;112(1):135.

Ruano R, Fontes R S, Zugaib M. Prevention of preeclampsia with low-dose aspirin: a systematic review and meta-analysis of the main randomized controlled trials. Clinics.2005;60(5):407-414.

Spong CY, Mercer BM, D'alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. Obstet Gynecol. 2011 Aug;118(2 Pt 1):323-33.

Tomlinson MW, et al. Fluid management in the complicated obstetric patient. The Global Library of Women's Medicine 2008; DOI 10.3843/GLOWM.10192.

Visintin C, Mugglestone MA, Almerie MQ, Nherera LM, James D, Walkinshaw S, Guideline Development Group. Management of hypertensive disorders during pregnancy: summary of NICE guidance. BMJ. 2010;341:c2207.

Special thanks to Betsy Nobmann, PhD, Nutrition, former IHS Area Nutrition Director for information on calcium intake in Alaska Native women.

Revised 6/24/19 njm Revised 2/23/19 njm Revised 3/23/18 njm Revised 4/22/16 njm Revised 2/5/16 njm Revised 6/30/15njm Revised 5/5/14njm Revised 3/17/14 nim Revised 10/1/12 njm Revised 6/7/11 njm Revised 11/29/10 njm Revised 3/1/06 njm Revised 1/20/04 njm Revised 1/24/95 Reviewed 1/23/94 Written 1/19/94