Objectives

- 1. Understand the clinical impact of hypertension.
- 2. Understand the classification system of hypertension.
- 3. Appreciate treatment strategies for hypertension.

I. Rationale for Treating Hypertension

- A. Reduce cardiac risk
 - 1. Coronary artery disease
 - 2. Heart failure and LVH
- B. Reduce cerebrovascular risk
 - 1. Stroke and TIA
 - 2. Intra-cranial hemorrhage
 - 3. Dementia
- C. Reduce vascular risk
 - 1. Peripheral vascular disease
 - 2. Aneurysms and dissections
- D. Reduce the incidence and slow the progression of kidney disease

II. Hypertensive Classifications

- A. 7th Report of the Joint National Commission identified level of blood pressure, major risk factors, and target organ damage as critical in managing hypertension
- B. Blood Pressure Levels

	Blood Pressure, mmHg					
	Systolic		Diastolic			
Normal	<120	and	<80			
Pre-Hypertension	120-139	or	80-89			
Hypertension						
Stage 1	140-159	or	90-99			
Stage 2	>160	or	>100			
Stage 2	>160	or	>100			

Table 1

- C. Major Risk Factors
 - 1. Hypertension
 - 2. Cigarette smoking
 - 3. Obesity (BMI > 30)
 - 4. Physical inactivity
 - 5. Dyslipidemia
 - 6. Diabetes mellitus
 - 7. Microalbuminuria or GFR < 60 cc/min
 - 8. Age (men > 55, women > 65)
 - 9. Family history of CVD (men < 55, women < 65)
- D. Target Organ Damage
 - 1. Heart
 - a. Left ventricular hypertrophy
 - b. Angina or prior myocardial infarction
 - c. Prior coronary revascularization
 - d. Heart Failure
 - 2. Brain (stroke or TIA)
 - 3. Chronic Kidney Disease
 - 4. Peripheral Arterial Disease
 - 5. Retinopathy

III. Hypertensive Treatments

- A. Behavioral Modification
 - 1. Diet
 - a. Sodium Restriction
 - b. DASH diet high fruit and vegetable content
 - 2. Weight Loss
 - 3. Exercise
 - 4. Alcohol Moderation
- A. Pharmacologic Treatments
 - 1. Diuretics
 - a. Rationale
 - i. Sodium is a well known mediator of volume status
 - ii. Optimal cardiac function is dependent upon appropriate filling pressures
 - iii. Correction of a hypervolemic state will improve cardiac function and blood pressure
 - b. Distal Tubule Diuretics (thiazide type)
 - i. Impair maximal urinary dilution, possibly leading to hyponatremia
 - ii. Enhance tubular calcium reabsorption role in treating kidney stones
 - c. Loop Diuretics
 - i. More effective than other diuretics at lower GFR
 - ii. Block tubular calcium reabsorption role in treating hypercalcemia

- d. Collecting Tubule Diuretics (potassium-sparing)
 - i. Limited utility as single diuretic therapy only 2-3% of filtered sodium is reabsorbed at this site
 - ii. Best used in conjunction with thiazide or loop diuretics in patients who develop hypokalemia
- e. Proximal Tubule Diuretics (acetazolamide)
 - i. Result in non-anion gap metabolic acidosis (acquired proximal RTA)
 - ii. Due to magnitude of natriuresis (50-60% filtered sodium reabsorbed in proximal tubule), leads to loss of potassium in urine
- 2. Renin-Angiotensin Blockade
 - a. Rationale
 - i. Angiotensin II has effects on the cardiovascular system apart from influencing blood pressure.
 - ii. Blockade of the renin-angiotensin system has been shown to prevent LVH and improve ventricular modeling.
 - iii. Angiotensin II has maladaptive effects on glomerular hemodynamics in nephropathy and proteinuria.
 - iv. A small drop in GFR and a small rise in potassium concentration are related to the mechanism of action of renin-angiotensin-aldosterone blockade.
 - b. Angiotensin Converting Enzyme Inhibitors (ACE-i)
 - i. Leads to high levels of bradykinin production. Predisposed patients (10% of general population, 20% of Asian population) can develop a non-productive cough.
 - ii. Teratogenic in pregnancy. Oligohydramnios lead to pulmonary dysplasia and limb malformation.
 - iii. Can cause ARF in unsuspected bilateral renal artery stenosis.
 - c. Angiotensin Receptor Blockers (ARB) No associated cough.

- 3. Beta-Blockers
 - a. Rationale
 - i. Beta blockers impart significant survival advantage over placebo following myocardial infarction.
 - ii. Beta blockers are protective after coronary revascularization and in patients with heart failure.
 - iii. Primary cardiovascular prophylaxis with beta blockers has not been demonstrated.
 - c. Consideration
 - i. Non-selective beta-blockade can lead to bronchospasm in patients with reactive airways.
 - ii. Chronotropic effect
- 1. Calcium Channel Blockers
 - a. Non-Dihydropyridine (verapamil, diltiazem) onotropic effects
 - b. Dihydropyridine associated with sodium retention and edema formation
- 2. Vasodilators (hydralazine, prazosin, clonidine, minoxidil)
 - a. Limited benefit apart from blood pressure lowering
 - b. Should be used as 4th or 5th line agent

IV. Drug Selection

- 1. Uncomplicated Hypertension
 - a. Thiazide diuretics are effective and well-tolerated first line anti-hypertensive agents.
 - b. Many patients require multiple agents to achieve adequate blood pressure control.
 - c. If BP is inadequately controlled on one agent, switching to another single agent is unlikely to achieve control.

- 2. Complicated Hypertension
 - a. For many patients with specific risk factors or target organ damage, particular classes of anti-hypertensive agents provides benefit above and beyond that of blood pressure lowering.

		Recommended Drugs**					
Compelling Indication*	Diuretic	BB	ACEI	ARB	CCB	Aldo ANT	Clinical Trial Basis*
Heart failure	*	*	*	*		*	ACC/AHA Heart Failure Guideline ³⁹ , MERIT-HF ⁴⁰ , COPERNICUS ⁴¹ , CIBIS ⁴² , SOLVD ⁴³ , AIRE ⁴⁴ , TRACE ⁴⁵ , ValHEFT ⁴⁸ , RALES ⁴⁷
Post myocardial infarction		*	*			*	ACC/AHA Post-MI Guideline ³⁴ , BHAT ³⁵ , SAVE ⁷⁰ , Capricorn ³⁷ , EPHESUS ³⁸
High coronary disease risk	*	*	*		*		ALLHAT ²⁷ , HOPE ²⁸ , ANBP2 ³⁰ , LIFE ²⁶
Diabetes	*	*	*	*	*		NKF-ADA Guideline ^{18,17} , UKPDS ⁴⁸
Chronic kidney disease			*	*			NKF Guideline ¹⁷ , Captopril Trial ⁴⁹ , RENAAL ⁵⁰ , IDNT ⁵¹ , IRMA2 ⁵⁴ , REIN ⁵⁵ , AASK ⁵²
Recurrent stroke prevention	*		*				PROGRESS ²⁹

Table 2

V. Conclusion

Hypertension is classified according to it severity. Treatment is based upon major risk factors and target organ damage. Selection of first line therapy is based upon secondary benefits of certain drugs in certain conditions.