

## Management of Hypertension

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## Overview

- Why JNC 7?
- New features and key messages of JNC 7
- Patient evaluation
- Why prehypertension?
- The goal is to get to goal
- Approach to rational therapy
  - What to choose first?
  - Where to go next?
- Cases

## Why the need for JNC 7?

- Need for clear, concise guideline with greater clinical utility
- Significant number of patients still without adequate BP control
  - 1991-1994: 27% of patients with HTN were controlled
  - 1999-2000: 34% of patients with HTN were controlled
  - Clinical trials achieve control rates between 60-70%
  - Healthy People 2010 goal is 50%

JNC 7 Express. JAMA. 2003 Sep 10; 290(10):1314

## Why the need for JNC 7?

- Greater clinical utility
  - Simplify BP classification
  - Limit risk stratification
- Incorporate new trial data

JNC 7 Express. JAMA. 2003 Sep 10; 290(10):1314

## New Features and Key Messages

- Above 115/75 mmHg, CVD risk doubles with each BP increase of 20/10 mmHg
- Prehypertension
  - SBP 120–139 mmHg
  - DBP 80–89 mmHg
  - Require health-promoting lifestyle modifications to prevent CVD
  - Patient involvement is key

[http://hin.nhlbi.nih.gov/nhbpep\\_slides/menu.htm](http://hin.nhlbi.nih.gov/nhbpep_slides/menu.htm); Accessed October 20, 2003; 8:15AM

## New Features and Key Messages

- Thiazide-type diuretics should be included in initial drug therapy for most
- Compelling indications for other drug classes remain in the guideline
- Most patients require two or more drugs to achieve goal BP
- If BP is >20/10 mmHg above goal, initiate therapy with two agents

[http://hin.nhlbi.nih.gov/nhbpep\\_slides/menu.htm](http://hin.nhlbi.nih.gov/nhbpep_slides/menu.htm); Accessed October 20, 2003; 8:15AM

## Patient Evaluation

1. Two consecutive blood pressure measurements
2. Assess lifestyle and identify other CV risk factors or concomitant disorders that affects prognosis and guides treatment
3. Reveal identifiable causes of high BP
4. Assess the presence or absence of target organ damage and CVD

[http://hin.nhlbi.nih.gov/nhbpep\\_slides/menu.htm](http://hin.nhlbi.nih.gov/nhbpep_slides/menu.htm); Accessed October 20, 2003; 8:15AM

## BP Measurement Techniques

| Method           | Brief Description   |
|------------------|---|
| In-office        | <ul style="list-style-type: none"> <li>• Two readings, 5 minutes apart</li> <li>• Sitting in chair, not on exam table</li> <li>• Confirm elevated reading in contralateral arm</li> </ul> |
| Self-measurement | <ul style="list-style-type: none"> <li>• Provides information on response to therapy</li> <li>• May help improve adherence to therapy</li> <li>• Evaluate "white-coat" HTN</li> </ul>     |

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| Self-measurement         | Provides information on response to therapy. May help improve adherence to therapy and evaluate "white-coat" HTN.                                 |
| Ambulatory BP monitoring | Indicated for evaluation of "white-coat" HTN. Can be used to confirm self-measurement when inconsistent with in-office measurement. Reimbursable. |

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## Self-Measurement of BP

- Improves awareness and adherence
- Instruction on proper use and technique should be provided
- Home measurement devices should:
  - Have an arm cuff
  - Be checked in office regularly
- Validated meters:
  - BMJ 2001;322:531-536.
  - [omronhealthcare.com](http://omronhealthcare.com)
- Daily Logs



## Self-Measurement of BP

- Home measurements of >135/85 mmHg (or 125/75 in diabetes or renal disease) are considered hypertensive
- At least 50% of measurements should be at or below goal



## Prevention

## Blood Pressure Classification

| BP Classification    | SBP mmHg* | DBP mmHg | Lifestyle Modification | Drug Therapy** |
|----------------------|-----------|----------|------------------------|----------------|
| Normal               | <120      | and <80  | Encourage              | No             |
| Prehypertension      | 120-139   | or 80-89 | Yes                    | No             |
| Stage 1 Hypertension | 140-159   | or 90-99 | Yes                    | Single Agent   |
| Stage 2 Hypertension | ≥ 160     | or ≥ 100 | Yes                    | Combo          |

\*Treatment determined by highest BP category; \*\*Consider treatment for compelling indications regardless of BP

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## Why Prehypertension?

- Patients normotensive at age 55 have a 90% lifetime risk to develop HTN
- Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
- Prehypertensive: 120–139 / 80–89 mmHg
  - Require health-promoting lifestyle modifications to prevent CVD
- **Public health goal: Prevent hypertension and cardiovascular disease before it happens**

## Causal Factors for Hypertension

- Excess body weight
  - 122 million Americans are overweight or obese
- Excess dietary sodium
  - Mean intake: Men 4100 mg; Women 2750 mg
  - 75% from processed foods
- Reduced physical activity
- Inadequate fruit, vegetable and potassium intake
- Excess alcohol consumption

Hypertension 2003;289:2560-2572.

## Lifestyle Modification

| Modification                      | Approximate SBP Reduction (range) |
|-----------------------------------|-----------------------------------|
| Weight reduction                  | 5-20 mmHg/ 10 kg weight loss      |
| Adopt DASH eating plan            | 8-14 mmHg                         |
| Dietary sodium reduction          | 2-8 mmHg                          |
| Physical activity                 | 4-9 mmHg                          |
| Moderation of alcohol consumption | 2-4 mmHg                          |

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## Impact of a 5 mmHg Reduction

|                        | Overall Reduction |
|------------------------|-------------------|
| Stroke                 | 14%               |
| Coronary Heart Disease | 9%                |
| All Cause Mortality    | 7%                |

Hypertension 2003;289:2560-2572.

## Public Health Strategy: Lower Sodium

- Healthy eating options are less available
- Foods with lower sodium and calories are higher in cost
- American Public Health Association and National High Blood Pressure Education Program
  - Food industry including manufacturers and restaurants should reduce sodium in the food supply by 50% over the next 10 years



**Dietary Approaches to Stop Hypertension**

- Lowers systolic BP
  - in normotensive patients by an average of 3.5 mm Hg
  - In hypertensive patients by 11.4 mm Hg
- Copies available from NHLBI website

<http://www.nhlbi.nih.gov/health/public/heart/hbp/dash/>

## DASH Eating Plan

- Low in saturated fat, cholesterol, and total fat
- Emphasizes fruits, vegetables, and low fat dairy products
- Reduced red meat, sweets, and sugar containing beverages
- Rich in magnesium, potassium, calcium, protein, and fiber
- 3 -1.5 g sodium per day
- Can reduce BP in 2 weeks

Sacks FM. NEJM. 2001; 344:3-10.

## Sample Menu

- **Breakfast**
  - 1 whole-wheat bagel
  - 2 tablespoons peanut butter
  - 1 medium orange
  - 1 cup fat-free milk
  - Decaffeinated coffee
- **Lunch**
  - Spinach salad made with 4 cups of fresh spinach leaves, 1 sliced pear, 1/2 cup mandarin orange sections, 1/3 cup unsalted peanuts and 2 tablespoons reduced-fat red wine vinaigrette
  - 12 reduced-sodium wheat crackers
  - 1 cup fat-free milk
- **Dinner**
  - Herb crusted baked cod
  - 1 cup bulgur
  - 1/2 cup fresh green beans, steamed
  - 1 sourdough roll with 1 teaspoon trans-free margarine
  - 1 cup fresh berries with chopped mint
  - Herbal iced tea

## Classification of Blood Pressure

## Changes in BP Classification

| JNC 6 Category | SBP/DBP         | JNC 7 Category  |
|----------------|-----------------|-----------------|
| Optimal        | < 120/80        | Normal          |
| Normal         | 120-129/80-84   | Prehypertension |
| Borderline     | 130-139/85-89   |                 |
| Hypertension   | ≥ 140/90        | Hypertension    |
| Stage 1        | 140-159/90-99   | Stage 1         |
| Stage 2        | 160-179/100-109 | Stage 2         |
| Stage 3        | ≥ 180/110       |                 |

Hypertension 2003;289:2560-2572.

## Blood Pressure Classification

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## "The Goal is to Get to Goal!"

|               |                                     |
|---------------|-------------------------------------|
| Hypertension  | -PLUS-<br>Diabetes or Renal Disease |
| < 140/90 mmHg | < 130/80 mmHg                       |



## "The Goal is to Get to Goal!"

|               |                                     |
|---------------|-------------------------------------|
| Hypertension  | -PLUS-<br>Diabetes or Renal Disease |
| < 140/90 mmHg | < 130/80 mmHg                       |

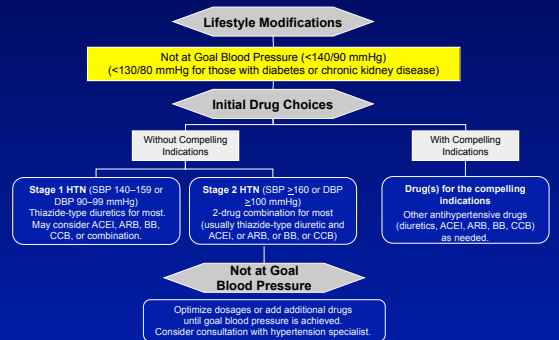
- ✓ Measurements and goals should be provided to the patient verbally and in writing at each office visit



## Treatment Overview

- Lifestyle modification
  - Same as for prevention
- Pharmacologic treatment
  - Initial therapy
  - Combination therapy
- What to do when a patient is still not at goal?
- Follow-up and monitoring
- Cases

## Algorithm for Treatment of Hypertension



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## What to choose first?

- Initial antihypertensive therapy without compelling indications
  - JNC 6: Diuretic or a beta-blocker
  - JNC 7: Thiazide-type diuretics
- Most outcome trials base antihypertensive therapy on thiazides

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## Antihypertensive and Lipid-Lowering to Prevent Heart Attack Trail (ALLHAT)

- Randomized, double blind, multi-center, study
- Conducted between 1994-2002, average follow-up 4.9 years
- N=33,357
- Evaluate whether CCB, ACEI or Doxazosin would decrease fatal coronary heart disease, or non-fatal MI when compared to a diuretic

ALLHAT. JAMA. 2002 288(23):2981-97



## ALLHAT: Endpoints

- Primary Endpoint
  - Fatal coronary heart disease or non-fatal MI
- Secondary Endpoints:
  - All cause mortality
  - Fatal and non-fatal stroke
  - Combined coronary heart disease
  - Combined cardiovascular disease
- Goal Blood Pressure: <140/90

ALLHAT. JAMA. 2002 288(23):2981-97

## ALLHAT: Drug Titration

| Step 1 Agents  | Initial Dose | Dose 1     | Dose 2     | Dose 3   |
|----------------|--------------|------------|------------|----------|
| Chlorthalidone | 12.5 mg qd   | 12.5 mg qd | 12.5 mg qd | 25 mg qd |
| Amlodipine     | 2.5 mg qd    | 2.5 mg qd  | 5 mg qd    | 10 mg qd |
| Lisinopril     | 10 mg qd     | 10 mg qd   | 20 mg qd   | 40 mg qd |
| Doxazosin      | 1 mg qd      | 2 mg qd    | 4 mg qd    | 8 mg qd  |

Step 2 Agents: Reserpine, Clonidine, or Atenolol

Step 3 Agent: Hydralazine

## ALLHAT: Drug Titration

| Step 2 Agents | Dose 1                      | Dose 2     | Dose 3     |
|---------------|-----------------------------|------------|------------|
| Reserpine     | 0.05 mg qd or<br>0.1 mg qod | 0.1 qd mg  | 0.2 mg qd  |
| Clonidine     | 0.1 mg bid                  | 0.2 mg bid | 0.3 mg bid |
| Atenolol      | 25 mg qd                    | 50 mg qd   | 100 mg qd  |

| Step 3 Agent | Dose 1    | Dose 2    | Dose 3     |
|--------------|-----------|-----------|------------|
| Hydralazine  | 25 mg bid | 50 mg bid | 100 mg bid |

## ALLHAT: Inclusion

- Inclusion:
  - > 55 years old
  - Stage 1 or 2 HTN
  - With one risk factor:
    - Prior MI or stroke > 6 mo in past
    - LVH
    - Type 2 Diabetes
    - Smoker
    - HDL <35
    - Atherosclerotic cardiovascular disease

ALLHAT. JAMA. 2002 288(23):2981-97

## ALLHAT: Exclusion

- Exclusion:
  - Symptomatic or hospitalized for heart failure
  - Known EF <35%
- Prior medications were stopped with the first dose of study medication

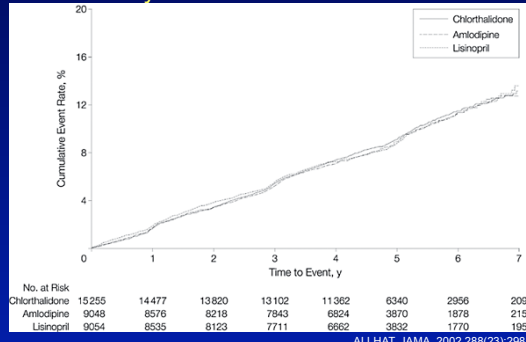
ALLHAT. JAMA. 2002 288(23):2981-97

## ALLHAT: Patients

- Average age = 67
- Black 32%
- Women 47%
- Baseline BP: 146/84
- Receiving antihypertensive treatment 90%
- Prior MI or Stroke: 23%
- Type 2 Diabetes: 36%

ALLHAT. JAMA. 2002 288(23):2981-97

## ALLHAT: Cumulative Event Rates for Fatal Coronary Heart Disease or Nonfatal MI



## ALLHAT: BP Outcomes

- Number (%) of patients achieving SBP control
- Better BP control achieved on chlorthalidone
- More than 2 drugs were required for BP control by more than 60% of patients

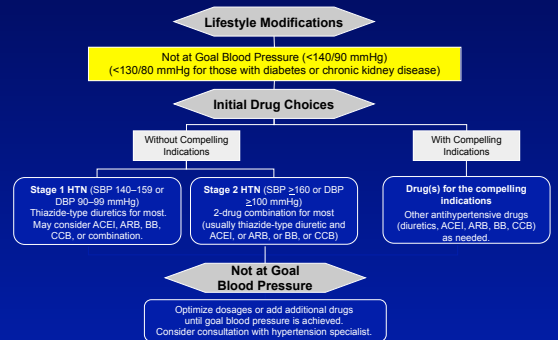
|          | Chlorthalidone, n (%) | Amlodipine, n (%) | Lisinopril, n (%) | p value A v C | p value L v C |
|----------|-----------------------|-------------------|-------------------|---------------|---------------|
| Baseline | 4149 (27.2)           | 2497 (27.6)       | 2381 (26.3)       | 0.56          | 0.12          |
| 1 year   | 7434 (57.8)           | 4200 (55.2)       | 3806 (50.6)       | <0.001        | <0.001        |
| 2 years  | 7161 (61.0)           | 3951 (57.4)       | 3625 (54.1)       | <0.001        | <0.001        |
| 3 years  | 6836 (63.9)           | 4046 (63.4)       | 3597 (59.2)       | 0.54          | <0.001        |
| 4 years  | 6293 (67.1)           | 3709 (65.8)       | 3360 (63.1)       | 0.15          | <0.001        |
| 5 years  | 3615 (68.2)           | 2118 (66.3)       | 1813 (61.2)       | 0.09          | <0.001        |

ALLHAT. JAMA. 2002;288(23):2981-97

## ALLHAT: Conclusions

- ACEI and Dihydropyridine CCB's are no better than thiazide type diuretics at reducing cardiovascular risk
- Antihypertensive therapy based on thiazide type diuretics yields better BP control
- Thiazide type diuretics are significantly less expensive
- Thiazide type diuretics are an effective economical first choice antihypertensive

## Algorithm for Treatment of Hypertension



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## Is it appropriate to start 2 agents?

- In ALLHAT, 60% of patients achieved SBP control
- The mean number of drugs to achieve BP control was 1.6
- Inadequate titration of drug regimens is a primary reason patients do not reach BP goal
- Patients and providers should be educated that more than one antihypertensive is the norm not the exception

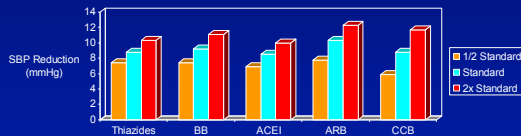
## Low Dose Combinations

- Meta-analysis of 354 randomized trials of antihypertensives: BB, ACEI, ARB, & CCB
- n=56,000 patients
- Placebo adjusted reductions in SBP and DBP
- Dose of each agent expressed as a multiple of a standard dose
- Prevalence in adverse effects based on dose

Law MR et al. BMJ. 2003; 326:1427

## Low Dose Combinations

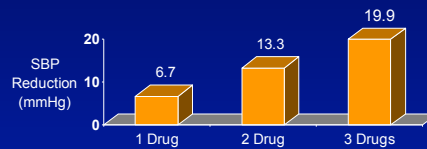
- All five drug categories produced similar BP reductions
- Blood pressure reduction achieved with half standard dose was only 20% lower than standard dose



Law MR et al. BMJ. 2003; 326:1427

## Low Dose Combinations

- BP lowering effects from different drug categories were additive



Law MR et al. BMJ. 2003; 326:1427

## Low Dose Combinations

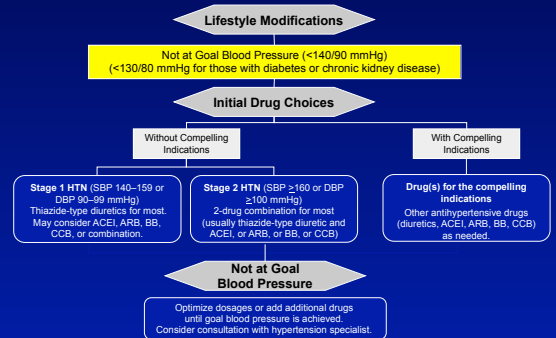
- Adverse effects in all drug categories, except ACEI, were dose related
- Prevalence of adverse effects in combination was less than additive

### Conclusion:

Utilization of low dose combination therapy can effectively reduce blood pressure while limiting the incidence of side effects

Law MR et al. BMJ. 2003; 326:1427

## Algorithm for Treatment of Hypertension



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## Risk Reduction

- Risk stratification is deemphasized in JNC 7
- Risk reduction is still an important consideration when selecting antihypertensives
- Compelling indications remain in the guidelines

## Compelling Indications for Individual Drug Classes

| Compelling Indication     | Initial Therapy Options   | Clinical Trial Basis   |
|---------------------------|---------------------------|--|
| Heart failure             | THIAZ, BB, ACEI, ARB, ARA | ACC/AHA Heart Failure Guideline, MERIT-HF, COPERNICUS, CIBIS, SOLVD, AIRE, TRACE, ValHEFT, RALES |
| Postmyocardial infarction | BB, ACEI                  | ACC/AHA Post-MI Guideline, BHAT, SAVE, Capricorn, EPHEBUS  |
| High CAD risk             | THIAZ, BB, ACEI, CCB      | ALLHAT, HOPE, ANBP2, LIFE, CONVINCe  |



## Compelling Indications for Individual Drug Classes

| Compelling Indication       | Initial Therapy Options    | Clinical Trial Basis                                     |
|-----------------------------|----------------------------|--|
| Diabetes                    | ACEI, ARB, CCB, THIAZ, BB, | NKF-ADA Guideline, UKPDS, ALLHAT                         |
| Chronic kidney disease      | ACEI, ARB                  | NKF Guideline, Captopril Trial, RENAAL, IDNT, REIN, AASK |
| Recurrent stroke prevention | THIAZ, ACEI                | PROGRESS   |

## "The Goal is to Get to Goal!"

|                         |                                     |
|-------------------------|-------------------------------------|
| Hypertension            | -PLUS-<br>Diabetes or Renal Disease |
| <b>&lt; 140/90 mmHg</b> | <b>&lt; 130/80 mmHg</b>             |

- ✓ Patients should return for follow-up and adjustment of medications every 1-2 months until the BP goal is reached



## When a Patient is Still Not at Goal?

- Optimize dosages or add additional drugs until goal blood pressure is achieved
- What do you do when you are using several effective medications?
  - Consider causes of resistant hypertension
  - Assure drug therapy is rational
  - “Tricks of the trade”

## Identifiable Causes of Hypertension

- Sleep apnea
- Drug-induced or related causes
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing's syndrome
- Pheochromocytoma
- Coarctation of the aorta
- Thyroid or parathyroid disease

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## Causes of Resistant Hypertension

- Improper BP measurement
- Excess sodium intake
- Inadequate diuretic therapy
- Medication
  - Inadequate doses
  - Drug actions and interactions:
    - Nonsteroidal antiinflammatory drugs (NSAIDs), illicit drugs, sympathomimetics, oral contraceptives
  - Over-the-counter (OTC) drugs and herbal supplements
- Excess alcohol intake
- Identifiable causes of HTN

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## Drug-Induced Hypertension: Prescription Medications

- Steroids
- Estrogens
- NSAIDS
- Phenylpropanolamines
- Cyclosporine/tacrolimus
- Erythropoietin
- Sibutramine
- Methylphenidate
- Ergotamine
- Ketamine
- Desflurane
- Carbamazepine
- Bromocryptine
- Metoclopramide
- Antidepressants
  - Venlafaxine
- Buspirone
- Clonidine

## COX-2 Inhibitors and NSAIDs

- Inhibition of cyclooxygenase, inhibits prostaglandin synthesis that normally maintains afferent arteriole vasodilatation
- Afferent vasoconstriction decreases renal perfusion → increased BP
  - Increasing salt and water retention
  - Increasing rennin release
- COX-1 is thought to be primary enzyme responsible for renal vasodilatory prostaglandins

## COX-2 Inhibitors and NSAIDs

- However, COX-2 inhibitors are no less likely to increase BP than other NSAIDs
- Case reports of severe increases in BP exists in patients after one dose or more typically after 4 weeks for regular usage
- Consider scheduled acetaminophen as an alternative to NSAIDs in patients with difficult to manage hypertension

Drugs Aging. 2004; 21:479-84; JAMA. 2001; 286:954-59

## Drug-Induced Hypertension: Street Drugs and Herbal Products

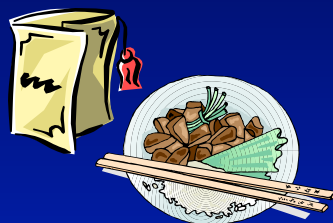
- Cocaine
- Ma huang “herbal ecstasy”
- Nicotine
- Anabolic steroids
- Narcotic withdrawal
- Methylphenidate
- Phencyclidine
- Ketamine
- Ergot-containing herbal products
- St John’s wort

## Substances Associated with HTN

- Food Substances
  - Sodium Chloride
  - Ethanol
  - Licorice
  - Tyramine-containing foods (with MAOI)
- Chemicals
  - Lead
  - Mercury
  - Thallium and other heavy metals
  - Lithium salts

## Rational Combination Therapy:

### Chinese Menu Approach



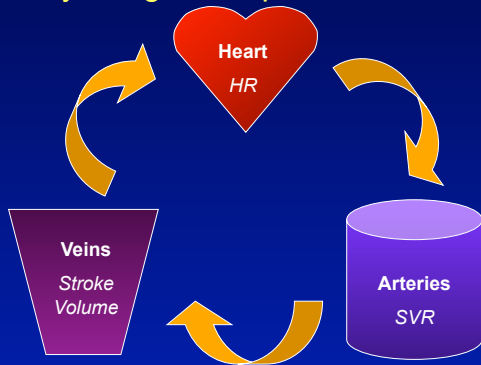
## Algebra of Blood Pressure

$$BP = \text{Cardiac Output} \times \text{SVR}$$

$$CO = \text{HR} \times \text{Stroke Volume}$$

$$BP = \text{HR} \times \text{Stroke Volume} \times \text{SVR}$$
A diagram illustrating the algebra of blood pressure. The equation BP = HR x Stroke Volume x SVR is shown. The 'HR' is represented by a red heart icon, 'Stroke Volume' is represented by a purple funnel icon, and 'SVR' is represented by a purple cylinder icon. A downward arrow points from the 'Stroke Volume' term in the equation above to the funnel icon in the diagram below.

## Physiologic Components of BP



## Thiazide Diuretics

Veins

- Mechanism: inhibit Na/K pumps in the distal tubule
- Examples:
  - Hydrochlorothiazide 12.5-25 mg daily
  - Chlorthalidone 12.5-50 mg daily
- Effective first line agent and provides synergistic benefit
- As single agent more effective if CrCl >30 ml/min
- Compelling indications: HF, High CAD risk, Diabetes, Stroke, ISH

Thiazides

## Loop Diuretics

Veins

- Mechanism: Inhibit Na/K/Cl ATPase in ascending loop of henle
- Examples:
  - Furosemide 20 mg BID
- Typically only beneficial in patients with resistant HTN and evidence of fluid; effective if CrCl <30 ml/min
- MUST be dosed at least twice daily (Lasix = Lasts six hours)
- Administer AM and lunch time to avoid nocturia

Thiazides  
Loops

## Aldosterone Receptor Antagonists

Veins

- Mechanism: inhibit aldosterone's effect at the receptor, reducing Na and water retention
- Examples:
  - Spironolactone 25 mg daily
- Can provide as much as 25 mmHg BP reduction on top of 4 drug regimen in resistant hypertension
- Monitor SCr and K
- Compelling indications: HF

Thiazides  
Loops  
Aldosterone Ant.

Am J Hypertension. 2003; 16:925-930.

## Nitrates

Veins

- Mechanism: Direct venodilation by release of nitric oxide
- Examples:
  - Isosorbide dinitrate 10 mg TID
  - IMDUR 30 mg daily
- In renal patients with resistant hypertension addition to 3-4 drug regimen may help get patient to goal
- Provide 8h nitrate free interval daily
- Compelling indications: Angina

Thiazides  
Loops  
Aldosterone Ant.  
Nitrates


## ACEI & ARB's

Veins

- Mechanism: Inhibit vasoconstriction by inhibiting synthesis or blocking action of angiotensin II; provides balanced vasodilation
- Examples:
  - Enalapril 2.5-40 mg daily -BID
  - Lisinopril 5 - 40 mg daily
  - Irbesartan 150-300 mg daily
  - Losartan 25-100 mg Daily - BID
- Monitor: SCr, K
- Compelling indications: HF, post-MI, High CAD risk, Diabetes, CKD, Stroke

Thiazides  
Loops  
Aldosterone Ant.  
Nitrates  
ACEI  
ARB

## Beta Blockers




Heart

Beta Blockers

- Mechanism: Competitively inhibit the binding of catecholamines to beta-adrenergic receptors
- Examples:
  - Atenolol 25-100 mg PO daily
  - Metoprolol 25 -100 mg PO daily or BID
  - Carvedilol 6.25-25 mg PO BID
- Monitor: HR, Blood Glucose in DM
- Not contraindicated in asthma or COPD but use caution
- Compelling indications: HF, post-MI, High CAD risk, Diabetes

## Diltiazem and Verapamil




Heart

Beta Blockers  
Diltiazem  
Verapamil

- Mechanism: Decrease calcium influx into cells of vascular smooth muscle and myocardium
- Examples:
  - Diltiazem 60-480mg q6h to daily
  - Verapamil 60-480 q8h to daily
- Monitor: HR
- Verapamil causes constipation
- Relatively contraindicated in heart failure
- Compelling indications: Diabetes, High CAD risk

## Alpha<sub>2</sub> Agonists: Central Acting Agents




Heart

Beta Blockers  
Diltiazem  
Verapamil

Via Central Mechanism:  
Clonidine

- Mechanism: false neurotransmitters reduce sympathetic outflow reducing sympathetic tone
- Examples:
  - Clonidine 0.1-0.6 mg PO BID-TID; patch
  - Methyl dopa, Guanabenz, Guanfacine
- Monitor: HR
- Side effects often limiting: Dry mouth, orthostasis, sedation
- Clonidine patch can be useful in elderly patients with labile blood pressure
- Withdrawal: real at doses  $\geq$  0.3 mg

## Dihydropyridine Calcium Channel Blockers




Arteries

Dihydropyridine CCBs

- Mechanism: Decrease calcium influx into cells of vascular smooth muscle
- Examples:
  - Amlodipine 2.5-10 mg PO daily
  - Felodipine 2.5-10 mg PO daily
  - Do not use immediate release nifedipine
- Monitor: Peripheral edema, HR (can cause reflex tachycardia)
- Good add on agent if cost is not an issue

## Vasodilators




Arteries

Dihydropyridine CCBs  
Hydralazine  
Minoxidil

- Mechanism: Direct vasodilation of arterioles via increased intracellular cAMP
- Examples:
  - Hydralazine 20-400 mg BID-QID
  - Minoxidil 2.5-40 mg PO daily-BID
- Monitor: HR (can cause reflex tachycardia), Na/Water retention
- Hydralazine is an alternative in HF if ACEI contraindicated
- Consider minoxidil in refractory patients on multi-drug regimens

## Alpha<sub>1</sub> Blockers




Arteries

Dihydropyridine CCBs  
Hydralazine  
Minoxidil  
Alpha<sub>1</sub> Blockers

- Mechanism: Inhibit peripheral post-synaptic alpha<sub>1</sub> receptors causing vasodilation
- Examples:
  - Terazosin 1 – 20 mg daily
  - Doxazosin 1 – 16 mg daily
- Cause marked orthostatic hypotension, give dose at bedtime
- Consider only as add on therapy
- Can be beneficial in patients with BPH

## ACEI & ARB's






**Arteries**

|                             |
|-----------------------------|
| Dihydropyridine             |
| CCBs                        |
| Hydralazine                 |
| Minoxidil                   |
| Alpha <sub>1</sub> Blockers |
| ACEI                        |
| ARB                         |




- Mechanism: Inhibit vasoconstriction by inhibiting synthesis or blocking action of angiotensin II; provides balanced vasdilation
- Examples:
  - Enalapril 2.5-40 mg daily –BID
  - Lisinopril 5 – 40 mg daily
  - Irbesartan 150-300 mg daily
  - Losartan 25-100 mg Daily - BID
- Monitor: SCR, K
- Compelling indications: HF, post-MI, High CAD risk, Diabetes, CKD, Stroke

## Pharmacologic Sites of Action

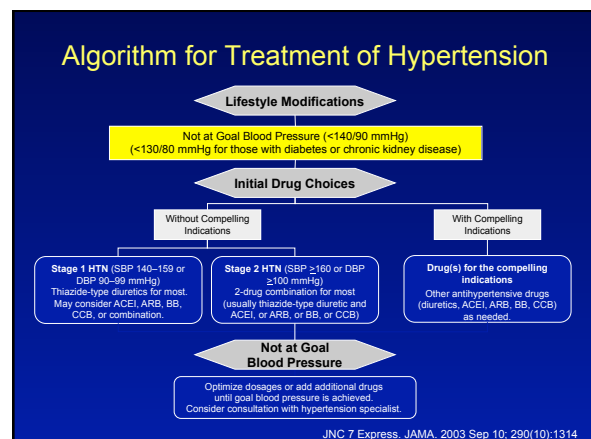
|   |   |   |
|---|---|---|
| Thiazides<br>Loops<br>Aldosterone Ant.<br>Nitrates<br><br>ACEI<br>ARB | Beta Blockers<br>Diltiazem<br>Verapamil<br><br>Via Central<br>Mechanism:<br>Clonidine | Dihydropyridine<br>CCBs<br>Hydralazine<br>Minoxidil<br>Alpha <sub>1</sub> Blockers<br>ACEI<br>ARB |
|---|---|---|

## Chinese Menu Approach

|  |  |   |
|--|--|---|
| ✓ <b>Thiazides</b><br>Loops<br>Aldosterone Ant.<br>Nitrates<br><br>ACEI<br>ARB | ✓ <b>Beta Blockers</b><br>Diltiazem<br>Verapamil<br><br>Via Central<br>Mechanism:<br>Clonidine | Dihydropyridines<br>Hydralazine<br>Minoxidil<br>Alpha <sub>1</sub> Blockers<br>✓ <b>ACEI</b><br>ARB |
|--|--|---|

✓ Choose one agent from each category



## Follow-up and Monitoring

- Patients should return for follow-up and adjustment of medications every 1-2 months until the BP goal is reached
- After BP at goal and stable, follow-up visits at 3- to 6-month intervals
  - More frequent visits for stage 2 HTN or with complicating comorbid conditions
  - Continue to encourage self BP monitoring
- Serum potassium and creatinine monitored 1-2 times per year

JNC 7 Express. JAMA. 2003 Sep 10; 290(10):1314

## Cases

### Case 1: Diagnosis

AB is a 56 yo female with no significant PMH. Her BMI is 26 kg/m<sup>2</sup> and she has a family history positive for Type 2 Diabetes. Her BP measured on two consecutive clinic visits is 132/84. What is AB's BP classification?

1. Normal
2. Prehypertensive
3. Stage 1 Hypertension
4. Stage 2 Hypertension

### Case 1: Therapy

What therapy should be initiated for AB?

1. Enalapril 5 mg PO daily
2. Hydrochlorothiazide 25 mg PO daily
3. No therapy is indicated
4. Lifestyle modifications including weight loss and DASH eating plan should be encouraged

### Case 1: Goal of Therapy

What is the goal of lifestyle modification in AB?

1. Goal BP < 140/90, the goal is to get to goal
2. Goal BP < 130/80, the goal is to get to goal
3. Improve patients quality of life
4. Prevent onset of hypertension

### Case 1: 5 years later

AB, now 59, returns to clinic with marginal success at lifestyle changes. Her BP has repeatedly measured around 146/92.

What is AB's BP classification?

1. Normal
2. Prehypertensive
3. Stage 1 Hypertension
4. Stage 2 Hypertension

### Case 1: 5 years later

AB, now 59, returns to clinic with marginal success at lifestyle changes. Her BP has repeatedly measured around 146/92. What should be done?

1. Enalapril 5 mg PO daily
2. Hydrochlorothiazide 25 mg PO daily
3. No therapy is indicated
4. Reinforce lifestyle modifications including weight loss and the DASH eating plan.

### Case 2: Goal of Therapy

CD is a 50 yo black male with diet controlled type 2 diabetes. Consecutive BP measurements during recent clinic visits are 162/98 and 158/96. He is diagnosed with Stage 2 Hypertension. What is the goal of therapy for CD?

1. Goal BP <140/90
2. Goal BP <130/80
3. Slow the progression of diabetic renal disease by reducing BP to <125/80
4. Improve patients quality of life

## Case 2: Therapy

What therapy should be initiated for CD?

1. A 6 month trial of lifestyle changes should be initiated immediately
2. Hydrochlorothiazide 25 mg PO daily
3. Enalapril 10 mg PO daily
4. Enalapril / Hydrochlorothiazide 5/12.5 mg PO daily

## Case 2: 5 years later

CD reaches goal BP of <130/80 after titrating antihypertensive regimen to enalapril/hydrochlorothiazide 10/25 mg PO QD. At a subsequent follow up visit you learn CD was hospitalized 2 weeks ago for "chest pain". Reading the discharge summary you note he had ACS for which he was taken to the CATH lab and was found to have 90% occlusion of his LAD which was stented.

In clinic his current regimen includes:

- Aspirin 81 mg PO daily
- Clopidigrel 75 mg PO daily
- Enalapril/ hydrochlorothiazide 10/25 mg PO daily

## Case 2: 5 years later cont.

He brings you his home BP log; Daily readings over the last week are:

140/80, 128/74, 132/80, 156/88, 160/90, 130/82, 125/74.

What is the best course of action for CD?

1. Reinforce lifestyle changes
2. Add atenolol 50 mg PO daily
3. Increase hydrochlorothiazide to 50 mg PO daily
4. Add amlodipine 5 mg PO daily

## Case 3: Complicated Management

EF is a 56 year old black female with ESRD secondary to membranous glomerular nephropathy. She is compliant with dialysis three times weekly, a low sodium diet and her medication regimen including:

- Atenolol 50 mg PO daily
- Clonidine 0.2 mg PO TID
- Hydrochlorothiazide 25 mg PO daily

Her HR is in the 60's, and her BP readings before and after dialysis are consistently 150's/80's. What can be done to improve EF's BP control?

## Case 3: Complicated Management



|                     |           |                   |
|---------------------|-----------|-------------------|
| Hydrochlorothiazide | Atenolol  | <b>ACEI/ARB</b>   |
| Dialysis            | Clonidine | <b>Amlodipine</b> |

## Summary

- Lifestyle modifications are important for the prevention of hypertension
- The goal is to get to goal:
  - Initial therapy with a thiazide is indicated for most
  - Consider compelling indications
  - Initiate low dose combination therapy if BP >20/10 mmHg above goal
- Consider the physiologic site of action of agents when choosing combination therapy