

Hypertension: A Focus on JNC 7

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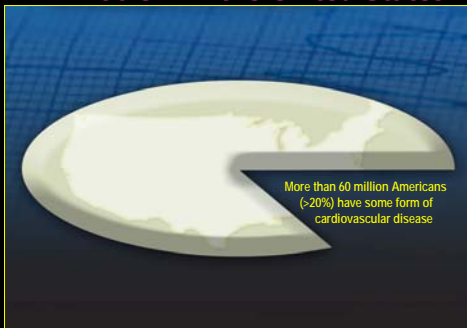
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Objectives

- Upon completion of this lecture, the participant will be able to:
 - Identify the various classifications of prehypertension, Stage I and Stage 2 hypertension
 - Discuss nonpharmacologic treatment options for the patient with hypertension
 - Discuss pharmacologic treatment options for the patient with hypertension

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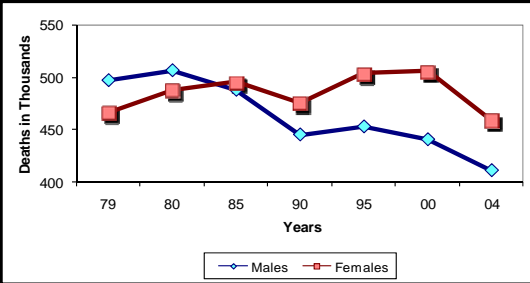
CVD Is the Most Common Health Problem in the United States



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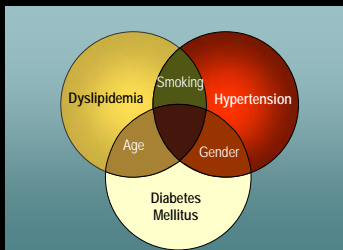
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CVD disease mortality trends for males and females



CVD disease mortality trends for males and females (United States: 1979-2004).
Source: NCHS and NHLBI.
Wright, 2009

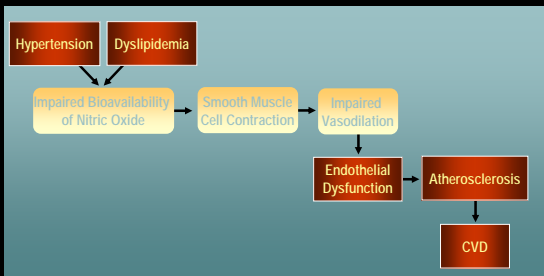
Evolution in Understanding Cardiovascular Disease: Total Risk Perspective



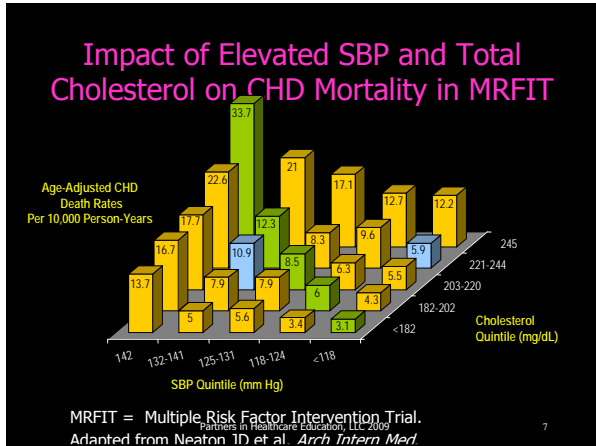
Cardiovascular Disease Is an Interplay of Risk Factors

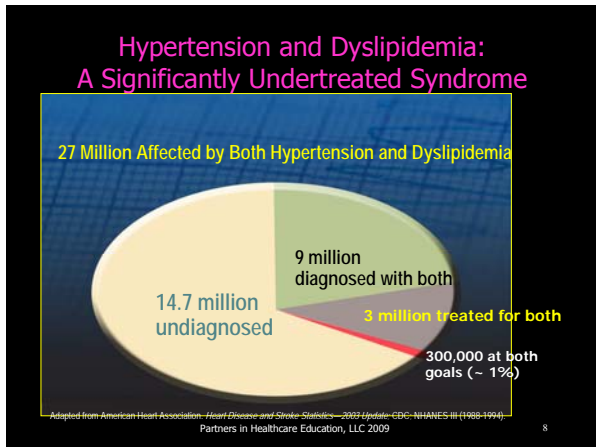
Kannel WB. *Am J Hypertens*. 2000;13(4):465-471. PMID: 10809955.

Hypertension and Dyslipidemia Contribute to Atherogenesis



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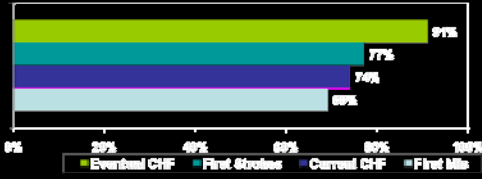
Impact of Hypertension

- 50 million individuals in the United States have hypertension¹
- 277,000 deaths annually in US due to hypertension²

<http://www.cdc.gov/nchs/hus.htm>

Hypertension Remains One of the Most Important Multipliers of CV Risk

BP >140/90 mm Hg is associated with:



BP, blood pressure; CHF, congestive heart failure; MI, myocardial infarction.

Rosamond W et al. *Circulation*. 2007;115:1-103.

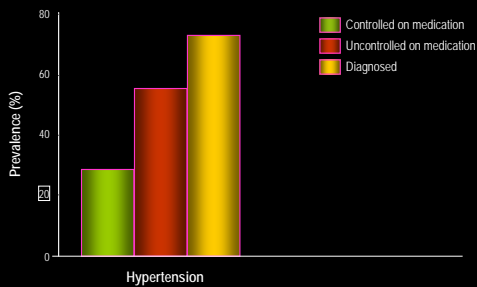
It is currently estimated that...

- 90% of normotensive 55 year olds will develop hypertension at some point in his/her lifetime

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Hypertension: Controlled or Not?



Adapted from NHANES III Morning Examination Subset: Hypertension (June 1998); Partners in Healthcare Education, LLC 2009

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Statistics of Interest

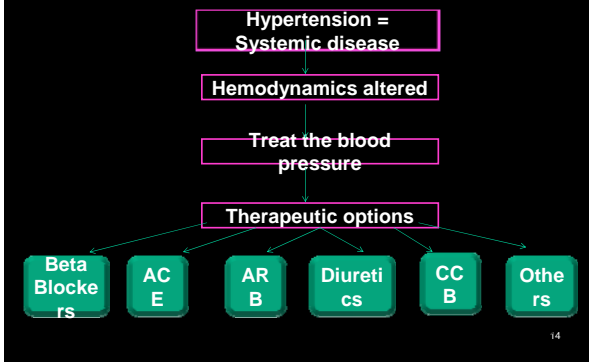
- 53% of patients with hypertension are being treated with medications
- Of those treated, 29% have their blood pressure < 140/90

Lookinland, S. and Beckstrand, R. Evidence-Based Treatment of Hypertension: JNC 7 Guidelines Provide an Updated Framework; Advance for Nurse Practitioners, Sept 2003.

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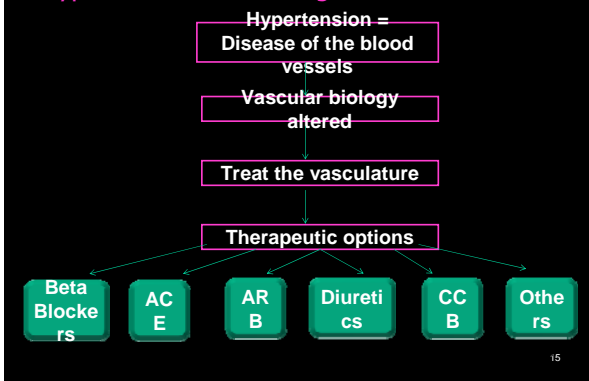
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Hypertension and Management: Old School

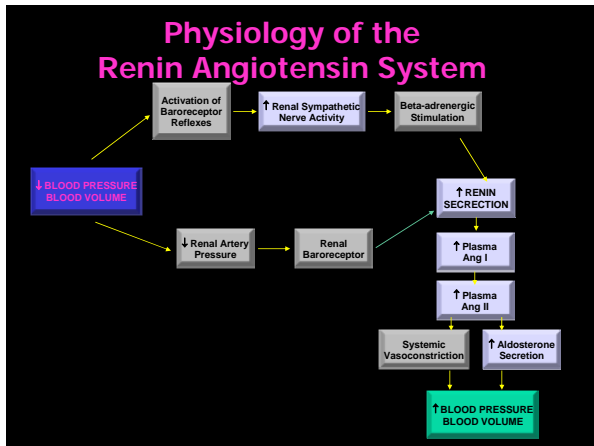


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Hypertension and Management: New School



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RAAS and Adipose Tissue

- All components of the RAAS system are expressed in adipose tissue, especially the **visceral adipose tissue**^{1,2,3}
- Visceral adipose tissue of patients with insulin resistance and Type 2 diabetes is **dysfunctional** and is a source of chronic low-grade inflammation⁴

RAAS and Endothelial Dysfunction

- Growing body of evidence
 - Promotion of endothelial dysfunction
 - Microalbuminuria^{1,2}
- RAAS Inhibition (ACE, ARB and Direct Renin Inhibitor)
 - Decreased incidence of new onset Type 2 diabetes
 - Improvement in CVD outcomes³

Today –
The Hypertensive Patient Exhibits...

- More insulin resistance
- More hyperinsulinemia
- Dyslipidemia
- Microalbuminuria
- Obesity

...as compared to nonhypertensive patients!

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Blocking the RAAS has been shown to be beneficial in...

Cardiovascular Disease
Hypertension
Diabetes

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JNC VII:
Messages to Clinicians

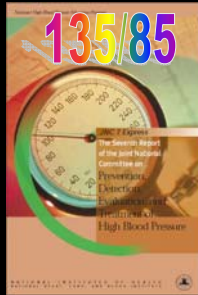


JAMA. 2003;289:2560-2577. Partners in Healthcare Education, LLC 2009

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New Messages JNC VII

- The risk of CVD, beginning at 115/75 mm Hg, **doubles** with each increment of 20/10 mm Hg.

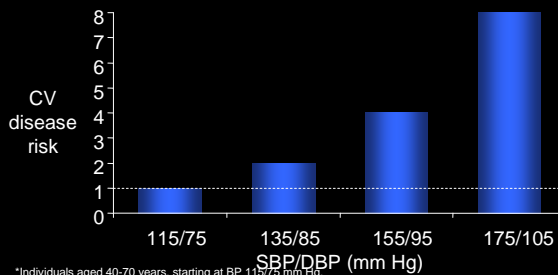


JAMA. 2003;289:2560-2577.

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CV Disease Risk Doubles with Each 20/10 mm Hg BP Increment*



*Individuals aged 40-70 years, starting at BP 115/75 mm Hg.
CV, cardiovascular; SBP, systolic blood pressure; DBP, diastolic blood pressure
1. Lewington S. Cardiovascular Issues in Ageing Pilots, et al. Lancet. 2002; 60:1903-1913

http://jama.ama-assn.org/cgi/content/full/289_19/2560v1

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Diagnosis

- 2 readings; separated apart
- Patient should not ingest caffeine or smoke for 30 minutes before readings
- Patient should sit for 5 minutes with arm at heart level before blood pressure is checked

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JNC 7: New Blood Pressure Classification

Blood Pressure Classification
SBP* DBP* (mm Hg)
Normal <120 and <80
Prehypertension 120-139 or 80-89
Stage 1 hypertension 140-159 or 90-99
Stage 2 hypertension ≥160 or ≥100

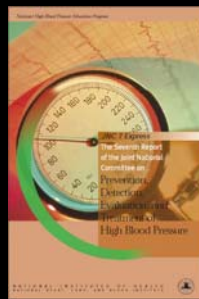
Treatment determined by highest BP category (SBP or DBP)
Adapted from Chebanian AV et al. Partners in Healthcare Education, LLC 2009 Publication No. 03-5233.

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Prehypertension

- Individuals with a systolic BP of 120-139 mm HG or a diastolic BP of 80-89 mm HG should be considered as **pre-hypertensive** and lifestyle modification initiated.

JAMA. 2003;289:2560-2577.



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Most Cases of Hypertension

- Primary hypertension
 - Also called **essential**
 - Responsible for **90-95%** of all hypertension diagnoses

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Consider Secondary Causes of HTN

- Sleep apnea
- Drug-induced or drug related
 - Including OTC medications
- Chronic kidney disease
 - Polycystic kidneys
- Renal artery stenosis
- Primary aldosteronism
- Renovascular disease
- Chronic steroid therapy and Cushing's disease
- Pheochromocytoma
- Coarctation of the Aorta
- Thyroid or parathyroid disease

JAMA. 2003;289:2560-2577.

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What about White-Coat Hypertension?

- Patient involvement in the measurement of his/her blood pressure is recommended, particularly for those individuals whose blood pressure is normal out of the office but consistently elevated in the office
- The office blood pressure of elders is 5 mm Hg higher than their ambulatory blood pressure
- Older the individual, the greater the discrepancy between home and office blood pressures
- No longer considered a benign condition

JAMA. 2003;289:2560-2577.

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Initial Work-up

- History and review of systems
 - Medications and risk factors
- Consider home blood pressure readings with validated blood pressure cuff
- Laboratory workup: CBC, BUN, Creatinine, Glucose, Lipids, GFR, urine - protein
- EKG and/or Echocardiogram, if indicated

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Treatment of Hypertension



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How Helpful is control of BP?

In stage 1 HTN, combined with additional CVD risk factors, achieving a **sustained 12 mmHg reduction in SBP** over 10 years will prevent **1 death for every 11 patients treated.**

1 in 11 Treated!

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JAMA. 2003;289:2560-2577.

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Other Implications of Treatment

- Controlled hypertension reduces:
 - CHF by 50%
 - MI's by 25%
 - CVA's by 35%

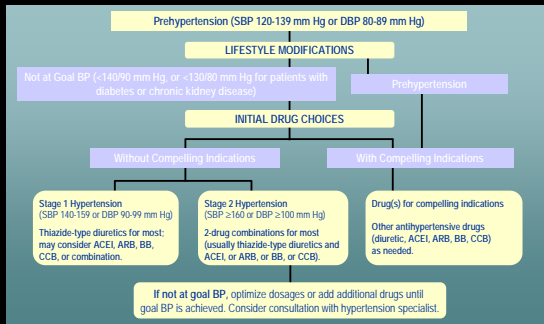
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Treatment Goals

- < 140/90 mm Hg for those with no complications
- < 130/80 mm Hg for those with diabetes or CRF (per ADA and NKF)

JNC 7: Algorithm for Treatment of Hypertension



Therapeutic Lifestyle Changes

New Messages JNC VII

- The most effective therapy prescribed by the most careful clinician will control hypertension....**only if the patient is motivated.**



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JAMA, May 21, 2003 Vol 289;No 19.

Lifestyle Modifications to Manage Hypertension

<u>Modification</u>	<u>Recommendation</u>	<u>Systolic Diastolic Chgs</u>
Weight Reduction	BMI 18.5-24.9	5-20mm/10 kg wt loss
Adopt DASH eating	Diet rich in fruits vegetables and low fat with reduced saturated and total fat	8-14 mm Hg
Dietary Sodium	2.4g Na	2-8 mm Hg
Physical Inactivity	Brisk exercise 30" day most days of week	4-9 mm Hg
Moderation of Alcohol intake	2 drinks day max 24 oz beer; 10 oz wine 2 oz 100 proof whiskey	2-4 mm Hg

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JAMA. 2003;289:2560-2577.
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Lifestyle Modifications

- Dietary sodium reduction
 - Most helpful in African Americans and patients with diabetes
 - Recommend limiting sodium to < 2000 mg/day for these individuals
 - Average individual ingests 4000 mg / day
 - ACE inhibitors and diuretics only work with a relatively low sodium diet

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How Successful Is It?

- Combination of the DASH diet and a dietary sodium reduction to 1600 mg/day is as effective as 1 medication

Alcohol Intake

- Limit alcohol intake to < 30 mL or 1 ounce of ethanol/day
 - Translation: 2 ounces of whiskey
 - 10 ounces of wine
 - 24 ounces of beer
- Excessive amounts increases treatment resistance
- Also increases risk of a CVA

** Women: ½ this amount

Electrolytes

- Diets high in potassium, calcium and magnesium are associated with a lower blood pressure
- JNC VII recommends an adequate dietary intake of these but does not recommend supplementing from an outside source to lower blood pressure

Additional Recommendations

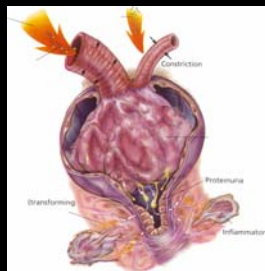
- Omega-3 fatty acids may lower blood pressure
- Caffeine may increase it but tolerance often develops
 - Most studies do not support a relationship between hypertension and caffeine
- Smoking: discontinuation is important
- Exercise: 30 minutes daily recommended

Pharmacologic Treatments

New Messages JNC VII

- Thiazide diuretics should be used in drug treatment for patients with uncomplicated hypertension.

JAMA. 2003;289:2560-2577.



Thiazide Diuretics

- Dosing:
 - Start @ 12.5 mg of HCTZ
 - Increase to 25 mg at 6 weeks
- Benefits
 - 55% reduction in CHF
 - 37% reduction in CVA
 - 27% reduction in cardiac events
- If not adequately controlled, add additional agents

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Diuretic Precautions

- Electrolyte imbalances
- Syncope/presyncope when combined with ACE/ARB
- Hemoconcentration
- Decrease in urate excretion
- Worsening of insulin resistance at higher doses
- Fatigue

Product inserts accessed 04-20-2008

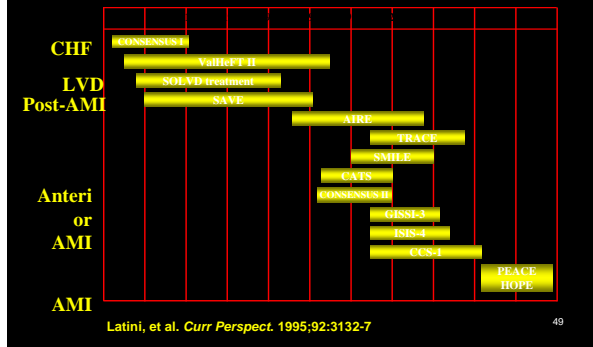
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Angiotensin Converting Enzyme (ACE) Inhibitors



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ACE Inhibitor Trials



ACE Inhibitors Precautions

- Hyperkalemia
- Increase in creatinine
- May improve insulin sensitivity
- Decrease in serum Na⁺ may result in syncope and dizziness when used with diuretics

Product inserts accessed 04-20-2008

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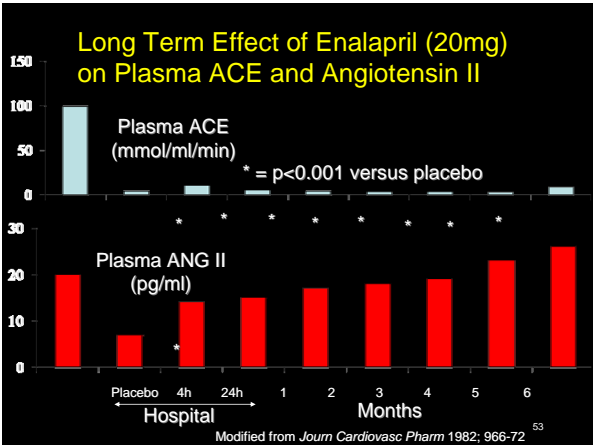
Effects on Hypoglycemia

- Several studies have shown the ability of ACE inhibition to improve glycemic control – even decrease the risk of hypoglycemia in patients using sulfonylureas.

Thamer M, Ray NF, Taylor T. Association between antihypertensive drug use and hypoglycemia: A case-control study of diabetic users of insulin or sulfonylureas. *Clin Therapeutics* 1999; 21:1387

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ACE Inhibitors
Are Highly
Effective..
But...



If you block the receptor site, you don't have to worry about the angiotension levels...

AT1

Angiotensin Receptor Blockers



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Angiotensin Receptor Blockers (ARB's)

- Utilized since April 1995
- Blocks uptake at receptor site
- Angiotensin II produced in locations other than in the lungs
- BP decreased by reducing vascular tone and enhancing Na^+ and water clearance

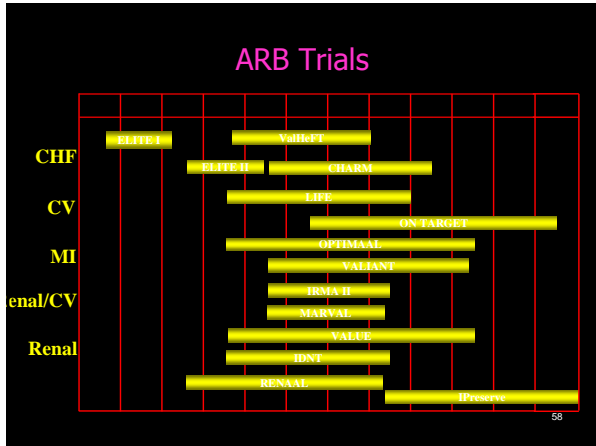
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Metabolic Effects of ARB's

- **Angiotensin II Receptor Blockers**
 - Metabolically neutral
 - No impact on lipids
 - No impact on insulin
 - No impact on K^+
 - Lowers uric acid levels
 - Minimal side effect profile

Product Inserts accessed 04-20-2008

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ACE vs ARB ONTARGET Trial

	<ol style="list-style-type: none"> 1. Assess the effects of ACE VS ARB in terms of efficacy 2. Assess if the combination ACE & ARB was superior
Results:	Telmisartan was found to be "noninferior" to ramipril in patients with vascular disease or high risk diabetes
	Combination of these two agents was associated with more adverse events without an increase in benefit.

Beta Blockers

- Decreased contractility
- Decreased heart rate
- Decreased myocardial oxygen demand

<http://ama-assn.org/cgi/content/full/289.19.2560-80>

Beta Adrenergic Receptors

- 3 receptors are found in human cardiac myocytes that are coupled to a positive inotropic response and cell growth.
 - Beta₁
 - Beta₂
 - Alpha₁

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Calcium Channel Blockers



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Calcium Channel Blockers

- Effectively treat systolic hypertension
- May be superior to other antihypertensives for stroke prevention
- Effective in patients with:
 - Comorbid conditions (Raynauds, migraine)¹
- Particularly effective in
 - Elderly and African American's²

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The Calcium Blockers

Dihydropyridines

- Studies of DPH's effects on proteinuria have produced conflicting results
- NKF recommends that in patients who have diabetes and kidney disease, DPH's should only be used in combination with an ACE or ARB

Thornley-Brown D, et al for the African American Study of Kidney Disease and Hypertension Study Group. Differing effects of antihypertensive drugs on the incidence of Diabetes mellitus among patients with hypertensive kidney disease. *Arch Intern Med.* 2006;166(7):797-805.

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Nondihydropyridines

- Regression of proteinuria
- Combination of Verapamil + ACE, reduction in proteinuria can be greater than achievable with verapamil alone.
- NKF now recommends adding a NDH to treat hypertension with an ACE inhibitor or an ARB to slow the progression of kidney disease.

Alpha Blockers



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Alpha Blockers

- Block postsynaptic Alpha₁ Receptors
- Results in vasodilatation
- Relatively inexpensive
- Fair tolerability; May cause postural effects
- Additive agent for older men to decrease BPH symptomatology
- Add on agent only
- Should never be used as monotherapy due to increased risk of stroke and CHF

http://ama-assn.org/cgi/content/full/289_19_2560y1

Centrally Acting Blockers



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Centrally Acting Agents

- Stimulates central α_2 receptors which results in:
 - Inhibiting efferent sympathetic activity
- Additive agents
- Should be used 3rd or 4th line
 - Examples: Clonidine (catapres, catapres TTS); methyldopa
- Caution: sedation, orthostatic hypotension

http://ama-assn.org/cgi/content/full/289_19_2560ed

Direct Vasodilators



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Direct Vasodilators

- Direct smooth muscle vasodilatation primarily arteriolar
- Two agents
 - Apresoline (Hydralazine)
 - Minoxidil

<http://jama.ama-assn.org/cgi/content/full/289.19.2560v1>

Aldosterone Agonists



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Aldosterone Antagonists

- Spironolactone (Aldactone)
- HCTZ / spironolactone (Aldactazide)
- Eplerenone (Inspra)

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Aldosterone as a Therapeutic Target

- Aldosterone promotes:
 - Retention of sodium
 - Loss of magnesium and potassium
 - Sympathetic activation
 - Parasympathetic inhibition
 - Baroreceptor dysfunction
 - Impaired arterial compliance

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Aldosterone Antagonists

- May be recommended in the following individuals:
 - Post MI
 - NYHA Class III or IV
 - Ejection fraction of < 35%
 - Serum creatinine of < 2.5 mg/dl
 - K+ < 5.0 mmol/L

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Precautions

- Must monitor electrolytes
- Must obtain baseline renal function
- Should discontinue the K⁺ supplement
- Should limit to use in severe heart failure and post MI patients

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New Classes/Agents

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Direct Renin Inhibitor



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Direct Renin Inhibition Inhibits the Entire Renin System¹⁻⁴

Class	PRA	Ang I	Ang II
ACEI	↑	↑	↓
ARB	↑	↑	↑
Direct Renin Inhibitor (DRI)	↓	↓	↓

Increased peptide levels have not been shown to overcome the blood pressure-lowering effect of these agents.
ACEI, angiotensin-converting enzyme inhibitor; Ang, angiotensin; ARB, angiotensin receptor blocker;
PRA, plasma renin activity.

1. Johnston CI. *Blood Press Suppl.* 2000;1:9(suppl 1):9-13.
2. Widdop RE et al. *Hypertension.* 2002;40:516-520.
3. Fabiani ME et al. *Angiotensin II Receptor Antagonists.* 2001:263-278.
4. Lin C et al. *Am Heart J.* 1996;131:1024-1034.

Combination Therapy



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When you put your hand in the cabinet...



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JNC 7 (2003) *Combination Therapy*

- Most hypertensive patients will require two or more antihypertensive medications to achieve goal BP (<140/90 mm Hg or <130/80 mm Hg in patients with diabetes/renal disease)
- Initiating therapy with combination therapy should be considered when BP is >20/10 mm Hg above goal.

<http://jama.ama-assn.org/cgi/content/full/289.19.2560v1>

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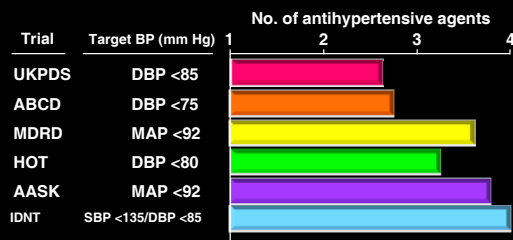
JNC 7 (2003)

Combination Therapy

- “When BP is more than 20/10 mm Hg above goal, consideration should be given to initiating therapy with two drugs, either as separate prescriptions or in fixed-dose combinations.”
- “Failure to titrate or combine medications, despite knowing the patient is not at goal BP, represents clinical inertia and must be overcome.”

<http://ama-assn.org/cgi/content/full/289.19.2560.1>

Multiple Antihypertensive Agents Are Needed to Achieve Target BP



DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure.
Bakris GL et al. *Am J Kidney Dis*. 2000;36:646-661.
Lewis EJ et al. *N Engl J Med*. 2001;345:851-860.

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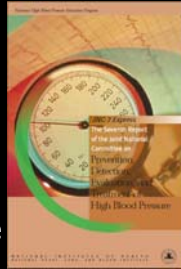
Hypertension is More than a Number!

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Target Organ Damage

- Heart
 - LVH, Angina, CHF, MI
- Brain
 - Stroke or TIA
 - Dementia
- Chronic Kidney Disease
- Peripheral Vascular Disease
- Retinopathy



JAMA. 2003;289:2560-2577.

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Pick the agent wisely

- Benefits are not the same in antihypertensive therapy at the same commensurate blood pressure control.

American Heart Association Scientific Sessions 2003; November 9-12, 2003, Orlando, Florida, USA.

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Additional Considerations for the Patient with Hypertension

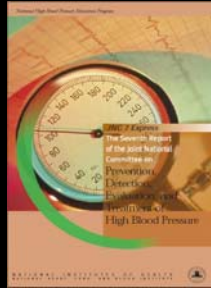
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New Messages JNC VII

- In presenting the NEW JNC VII, the committee recognizes that the responsible practitioner's **judgment** remains paramount.

JAMA. 2003;289:2560-2577.



Summary

- Hypertension is highly prevalent and is a significant risk factor for CHD
- Current guidelines recognize the importance of assessing multiple cardiovascular risk factors in patients with hypertension
- Health-promoting lifestyle modifications are an important part of prevention and treatment of hypertension
- Antihypertensive therapy reduces CHD risk
- ≥ 2 antihypertensive agents are usually required to achieve BP goals in patients with hypertension

Thank You!

I Would Be Happy To Entertain Any Questions

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