

HYPERTENSION: An Evidence-Based Approach

Robert F. Raspa, MD

Objectives: by the end of this you:

- Can state the readings considered optimal blood pressure control and classify by stage
- State initial therapy for hypertension considering risk factors
- Choose therapy based on special disease/demographic circumstances

Evidence Based Practice

- **The USPSTF strongly recommends clinicians screen for high blood pressure**
- **Treat with diuretics, ace inhibitors or beta blockers to reduce morbidity and mortality**
- **Post-myocardial infarction hypertensives should receive aspirin, beta blockers and angiotensin converting enzyme inhibitors whenever possible to prevent mortality, recurrent myocardial infarction and cardiovascular death**



American Academy
of Family Physicians



Web Revision 1/06

Faculty Documentation Form for Evidence-Based CME Clinical Content

This form must be completed to be considered for AAFP EB CME designation. Please print supporting evidence for each practice recommendation from the approved source web site. Submit only the page(s) where the evidence is cited. This page must show the specific web site address. No more than three recommendations are needed per topic. All information for each approved recommendation must be disclosed to learners in writing.

Date of Submission: **May 4, 2006**

Activity Title: **2006 AAFP Scientific Assembly, Annual Lecture Series**

Topic Title: **Hypertension: An Evidence-based Approach**

Date (if applicable): **September 27 – October 1, 2006** Author/Speaker: **Robert F. Raspa, M.D., FAAFP**

Number of EB CME credits requested: **1**

In the past year, has this topic been approved for AAFP EB CME designation? Yes No

PROVIDE KEY PRACTICE RECOMMENDATIONS AND EBM DOCUMENTATION FOR THIS TOPIC

Handwritten recommendations can not be accepted for review.

RECOMMENDATION # 1: The USPSTF strongly recommends that clinicians screen adults aged 18 and older for high blood pressure.

Name of AAFP-approved source of systematic evidence review: **U.S. Preventive Services Task Force**

Specific web site of supporting evidence from the approved source identified immediately above (not the source's home page):

www.ahrq.gov/clinic/uspstf/uspshype.htm

Strength of evidence (description and/or grade as provided by the approved source):

A recommendation

RECOMMENDATION # 2: Treat hypertensive patients with diuretics, ace inhibitors or beta blockers to reduce morbidity and mortality.

Name of AAFP-approved source of systematic evidence review: **National Guideline Clearinghouse**

Specific web site of supporting evidence from the approved source identified immediately above (not the source's home page):

http://www.guideline.gov/summary/summary.aspx?doc_id=5635&nbr=003796&string=hypertension

Strength of evidence (description and/or grade as provided by the approved source): **A**

A recommendation

RECOMMENDATION # 3: Lower blood pressure in the elderly, using diuretics and beta blockers preferentially, to reduce stroke, decrease cardiovascular morbidity and mortality and reduce overall mortality

Name of AAFP-approved source of systematic evidence review: **Cochrane Collaboration**

Specific web site of supporting evidence from the approved source identified immediately above (not the source's home page):

www.cochrane.org/reviews/en/ab000028.html

Strength of evidence (description and/or grade as provided by the approved source):

Fifteen trials including 21,908 elderly subjects were identified.

“This is simplistic—we can do this”

- BUT, We don't do this—studies show
- We think we do the right things—but we don't
- We can't be sure our patients do what we want them to do

Evidence Based Approach

- Meta-analysis
- Randomized controlled trials
- Retrospective analysis

Do I have hypertension?

- Am I normal?



Do I have hypertension?

- 140/90--simple answer
- Normal <120 and <80
- **Prehypertension: 120-139/80-89**--twice the risk to develop hypertension vs. normal
- Stage 1: 140-159/90-99
- Stage 2: 160 or greater/100 or greater

On what do you base treatment?

- Risk stratification:
- Risk Factors
- Target Organ Damage
- Clinical Cardiovascular Disease

Risk Factors

- Smoking
- Obesity--BMI equal to or greater than 30
- Physical inactivity
- Dyslipidemia
- Diabetes

Risk Factors

- Age >55 for men or over 65 for women
- Family history of heart disease--women <65/men <55
- Microalbuminuria
- GFR <60ml/min

Target Organ Damage

- Heart Disease--LVH, Angina, CAD, CHF
- Stroke or TIA
- Nephropathy
- Peripheral arterial disease
- Retinopathy

Treatment Basics

- Prehypertension--No risk factors or Target organ disease--lifestyle changes
- Stage 1 try lifestyle change but **newer approach is aggressive--one drug needed**
- **Stages 2 -- start with 2 drug therapy**
- Note--this is not evidence based and has not been systematically studied--based on existing natural history

On what do you base treatment?

- Diabetes and renal disease need more aggressive treatment
- Goal is <130 systolic and <80 diastolic.

Can I prevent getting HTN?

Can I prevent getting HTN?

- Blood pressure rise is not inevitable with age--prospective follow up study.
- Diet rich in fruits, vegetables, and low-fat dairy foods, with reduced fats lowers BP--randomized trial.
- Population wide--reduce salt in processed foods.

Hypertension 1991;18: 1-95--1-107:
N Engl J Med 1997;336:1117-24

Can I prevent getting HTN?

- Blood pressure rise is not inevitable with age--prospective follow up study.
- However, Framingham data suggest that normotensive 55 year olds have a 90% lifetime risk for developing hypertension!
- Treatment for over one year did not prevent the onset of hypertension—only delayed it.

What are the treatment goals?

- Reduce morbidity and mortality
- <140 Syst/<90 Diast.
- Lower if preserving renal function--Ra
- Lower to slow heart failure progression--
Ra

Hypertension 1997;29:641-50.
JAMA 1993;270:713-24.

What can I do besides drugs?

- Lifestyle modifications--Ra
- Lifestyle modification can reduce number of meds and dosage of meds--Ra
- May prevent hypertension
- Little cost--minimal risk

N Engl J Med 1997;336:1117-24.
JAMA 1993;270:713-24.

What are the lifestyle changes?

What are the lifestyle changes?

- Weight reduction--if BMI >25 or waist >34 in. in women, >39 for men.
- **Only 10 lbs. results in 5-20mm Hg--Ra**
- Caloric restriction
- **Increase physical activity--Meta**
- No anorectic agents--increase BP

Arch Intern Med 1997;157:657-67.

Ann Int Med 2002;136:493-503

What are the lifestyle changes?

- **Moderation of alcohol intake-Meta**
- Causes resistance to antihypertensive meds
- Men 2 drinks, women 1 drink:
- 1 ounce--24 oz beer, 10 oz wine, 3 oz 80 proof
- Women, recommend 0.5 ounce
- Lowers BP 2-4 mm Hg

What are the lifestyle changes?

- Physical activity to a moderate level of fitness reduces risk for CV disease and mortality--4-9mm Hg lower--Meta
- 40-60% max heart rate
- 30 min. brisk walk per day--most days
- Patients with cardiac disease may need exercise eval

What are the lifestyle changes?

- Sodium restriction--reduction to 2.4g Na
or 6g NaCl--may lower 2-8 mm Hg--Meta
- Reduced meds
- Reduce diuretic hypokalemia
- Reduce LVH

What are the lifestyle changes?

- High potassium and calcium intake--Ra
- DASH diet: 90 mmol per day from fresh fruits and vegetables, lower fat--Ra
- 8-14 mm Hg reduction--same as single drug therapy!
- Use K supplements with caution if ACEI or K sparing diuretics

What are the lifestyle changes?

- **Increased calcium intake has a minimal effect on BP--Meta**
- No data to support increased magnesium intake
- Caffeine has no direct effect

What are the lifestyle changes?

- Dietary fat--although a risk factor--little effect on BP
- Omega-3 fatty acids can lower but have side effects--4mm Hg--Ra,
- Relaxation and biofeedback--no effect, except one study in African Americans(Currently no recommendation)--Ra

What are the lifestyle changes?

- Smoking a cigarette raises BP
- Smoking cessation may not significantly lower BP but
- It prolongs life!
- Stop smoking
- Nicotine cessation aids don't raise BP significantly

What if lifestyle change is ineffective?

- Pharmacologic treatment works--Meta
- Reduces CV mortality, morbidity, stroke, CHF, renal disease, and all cause mortality--Meta
- Low dose
- Once a day
- Low dose of second drug--diuretic

What drug do I start with?

- In Uncomplicated HTN--Diuretic--Ra, Meta
- ABCD--ACE I, Beta Blocker, Calcium Antagonist, Diuretic
- Diuretic first line, unsurpassed-- Ra, ALLHAT
- White males may do better with ACE I first--Ra--ANCP 2 (Australian)
- Diuretic second if not first! Still underused

100 trials 29,294 Rx vs 23,926 controls

What drug do I start with?

- Most patients need 2 or more anti-hypertensives--Ra
- Add a second drug from a different class
- If 160/100 or greater--consider starting with 2 drugs (or combo)

Are there reasons to use others?

- Diabetes (type 1) with proteinuria--ACE
- ARBs reduce progression to macroalbuminuria--Ra
- Heart failure--ACE/Beta Blocker--Ra
- Heart Failure, End Stage, Ventricular Dysfunction--ACE/Beta Blocker/
Aldosterone Blocker and Loop diuretic--Ra

Are there reasons to use others?

- Isolated systolic HTN--elderly--Diuretic then long acting dihydropyridine CA antagonist or Beta blocker--Ra
- MI (Acute Coronary Syndromes--Beta blocker (non-ISA), ACE (systolic dysfunction)--Ra
- Post MI--Beta blocker, ACE, Aldosterone blocker

Are there reasons to use others?

- Angina--Beta blocker or CA
- Atrial tachycardia and fib--Beta blocker, non--DHP CA
- Cyclosporine--CA
- Essential tremor--Beta blocker
- Heart failure--Carvedilol/Losartan
- Hyperthyroidism--Beta blocker

Are there reasons to use others?

- Migraine--Beta blocker, non DHP CA
- Osteoporosis--thiazides
- Preop Hypertension--Beta blocker
- Prostatism--Alpha blocker
- Raynaud syndrome--CA

Are there reasons not to use?

- Bronchospasm--Beta blocker
- Depression--Central alpha-agonist, reserpine
- Diabetes and dyslipidemia--high dose diuretic (beta blocker)
- Gout--thiazides
- Heart block, CHF--Beta blocker, non DHP CA

Are there reasons not to use?

- Liver disease--labetalol, methyl dopa
- Peripheral vasc disease--Beta blocker
- Pregnancy--ACE I, Angiotensin II blocker
- Angioedema--ACE I
- Renal insufficiency--K sparing agents
- Renovascular disease-- ACE I, ARB
- Drug and supplement interactions

Which combinations work?

- Low dose diuretic--6.25 HCTZ--Ra (no adverse side effects)
- ACE and nondihydropyridine CA, reduces proteinuria better
- Metolazone/loop diuretic in renal failure
- CA and ACE--less pedal edema--Ra

Arch Intern Med 1994;154:1461-8.

Am J Cardiol 1997;79:431-5.

Eplerenone

- Selective Aldosterone Receptor Antagonist
- Both raise potassium levels—worse with higher Creatinine levels (>2)
- Less gynecomastia/breast pain and impotence than spironolactone
- Watch with ACE I and NSAIDS (higher K+)
and with Lithium
- Expensive

ACE and ARBs

- Angiotensin escape is theoretical
- ARBs work lower in the cascade
- ACE I and ARBs studies show benefit with CHF
- No benefit with diabetes
- Cost effectiveness not clear

Natural Products that Raise BP

- Blue Cohosh (*Caulophyllum thalictroide*)
- Dong quai Ephedra increases BP
- Licorice (*Glycyrrhiza glabra*)
- Yohimbe (*Pausinystalia yohimbe*)
- Coltsfoot (*Tussilago farfara*)
- Ginseng (*Panax ginseng*) increases or decreases BP

Natural Products that Lower BP

- Coenzyme Q (*Ubiquinone*) lowers 2-7%
- Garlic (*Allium sativum*) may or may not
- Ginkgo (*Ginkgo biloba*) probably doesn't
- Ginseng (*Panax ginseng*) may lower—may be dependent on preparation
- Hawthorn (*Crataegus laevigata*) doesn't
- St. John's wort (*Hypericum perforatum*)
one case report

Natural Products that Lower BP

- Thunder god vine (*Tripterygium wilfordii*)
one case report
- African mistletoe (*Loranthus bengwensis*)
extract may
- Broom (Scotch) (*Sarothamnus scoparius*)
spartein contains tyramine
- Black cohosh (*Cimifuga spp.*) may

Natural Products that Lower BP

- Cat's claw (*Uncaria callophylla*) reduces when active ingredient given IV
- Ginger (*Zingiber officinale*) given IV but probably won't when eaten
- Golden seal (*Hydrastis canadensis*) extract given IV
- Mistletoe (*Viscum album*) causes bradycardia
- Nettle (*Urtica dioica*) causes bradycardia

Can I quit taking meds?

- Decrease after 1 year of control
- Decrease slowly
- Lifestyle modifications usually necessary

What if I don't take my medicine?

- Adherence--contributes to lack of control in 2/3 of patients!
- Ask at each visit--"many times I have trouble remembering to take medicine, how about you?"
- Have pharmacist monitor refills
- Call and ask--case management

What improves adherence?

- Involve patients in their treatment
- Maintain contact--email? Telephone?
- Inexpensive and simple
- Encourage lifestyle modifications
- Integrate into routine activities of living
- Long acting drugs

What improves adherence?

- Stop unsuccessful therapy
- Anticipate adverse effects--adjust therapy to reduce side effects
- Add effective and tolerated drugs stepwise
- Positive attitude about goals
- Good Doctor-Patient relationship--Trust

What else can cause inadequate response?

- Pseudoresistance--“white coat”, obese arm
- Volume overload--salt intake, renal damage, fluid retention, inadequate diuresis
- Drug causes--dose too low, wrong drug, wrong combo, interactions

What else can cause inadequate response?

- Smoking
- Increasing obesity
- Sleep apnea
- Insulin resistance/hyperinsulinemia
- Ethanol excess
- Anxiety, panic attacks, chronic pain
- TRUE SECONDARY CAUSE OR RESISTANCE

What is true resistance?

- Can't meet goal with 3 drugs (including diuretic)
- Maximal doses
- Suspect secondary causes, including sleep apnea, renovascular disease, other drugs, primary aldosteronism, renal disease, steroids (Cushings), pheochromocytoma, coarctation of aorta, thyroid/parathyroid

Special Situations

- African Americans
- Obesity
- Women and Pregnancy
- Elderly
- Post-MI
- Post-Stroke
- LVH and CHF
- Renal Disease and Renovascular Disease
- Dyslipidemia
- Respiratory Disease
- Gout
- Perioperative
- Cocaine and others

Summary--Questions?

What about special groups?

- American Indians--same or better control
- Hispanics--same or lower BP
- African Americans--highest in the world
 - 80% higher stroke rate
 - 50% higher heart attack rate
 - 320% higher end stage renal disease
 - Increased responsiveness to salt restriction

What about African Americans?

- Diuretics agents of first choice--Ra
- Then CA and alpha-beta-blockers--Ra
- Decreased responsiveness to Beta blockers or ACE I as monotherapy
- ACE I angioedema 2-4x more frequent
- Push for goal of $<140/ <90$

What about obesity?

- BMI >29 (waist >39 in. men, >34 in. women)
- Metabolic syndrome--3 of following:
abdominal obesity, glucose intolerance (fasting glu > 109), BP >130/85, high triglycerides, low HDL (<40 men or <50 women)
- Intensive life style modification, treat each component

What about Women?

- **No difference in response--Meta**
- Oral contraceptives--raise BP--don't use with smokers > age 35 (quit smoking)
- If need BCP's and has HTN--treat HTN
- HRT doesn't raise BP
- No ACE inhibitors if child bearing age

What about pregnant women?

- Chronic hypertension--present < 20 weeks
- Methylodopa or vasodilators
- Beta blockers after 20 weeks: may retard growth if used early in pregnancy—don't use atenolol—growth retardation
- Diuretics OK if started before pregnancy
- ACE inhibitors avoided
- **No evidence infant's outcomes improved**

What about preeclampsia?

- **No benefit with aspirin or calcium--Ra**
- Methyldopa still drug of choice
- Atenolol, metoprolol and labetalol are safe and effective in late pregnancy
- Calcium antagonists are good--with Magnesium can potentiate hypotension
- Hydralazine is parenteral drug of choice

What about the elderly?

- With the elderly, Systolic pressure is a better predictor of adverse events
- Renovascular hypertension and primary aldosteronism more common--especially with new onset
- **Salt reduction and weight loss work--Ra**
- Start drug doses lower

What about the elderly?

- Diuretics are drug of choice--Meta
- Beta blocker with diuretic--Meta
- Long acting dihydropyridine CA--Ra
- Postural hypotension--adrenergic blockers, alpha-blockers, viagra, diuretics
- Cognitive dysfunction--can slow progression if HTN controlled--Ra

What about after a MI?

- Use non-selective beta blocker if at all possible-META.
- Use ACE I or ARB if LVH or Left Ventricular Dysfunction-Ra.
- Remember the ASA-META.
- Lipid lowering good but controversial-Ra.

What about stroke patients?

- Reduce blood pressure gradually
- Treat syst >180, diastolic >105 with IV agents
- Goal acutely 160/100
- Prevent recurrence with ACE I and diuretic combo--Ra
- No aspirin until BP controlled--Meta

What about LVH?

- Salt reduction, weight loss, aggressive BP treatment work
- All classes of antihypertensives cause regression except direct vasodilators--Ra
- Find LVH on EKG

What about CHF--cardiac failure?

- After MI, ACE I prevents heart failure--Ra
- ACE inhibitors and Beta Blockers--reduce morbidity and mortality--Ra
- Hydralazine and Isosorbide--Ra
- Symptomatic dysfunction/end stage--ACE I, Beta blocker, ARB, spironolactone, loop--Ra
- Only amlodipine or felodipine CA in CHF--Ra

N Engl J Med 1992;327:669-77.

JAMA 1995;273:1450-6.

CHF - Eplerenone

- Works as well as spironolactone but with fewer anti-androgen side effects—breast tenderness, etc.
- So, it can't be used as a hirsutism treatment.
- Much more expensive.

ACE and ARBs.

- Work together—theoretic basis of Angiotensin receptor increase.
- Work with CHF together.
- Doesn't work as well with diabetes.
- Not sure benefit outweighs the cost.

What about renal disease?

- Creat 1.5 (GFR 60), or albuminuria > 300mg
- Lower BP goal--130/80
- All classes of antihypertensives work
- **ACE/ARB with type 1 diabetics--Ra**
- **ACE/ARB with non-diabetic renal disease--Ra**

N Engl J Med 1993;329:1456-62.

Arch Int Med 2002;162:1636-43.

What about renal disease?

- Reduce salt--100mmol, reduce K and Phos
- Creatinine can increase 35% above baseline with ACE I and ARB OK, unless increased K develops
- **With advanced renal disease, creat 2.5 (GFR <30), add a loop diuretic to ACE as well--Ra, Meta**

What about renal disease?

- If creatinine increases 1mg/dL and K up-- suspect renal artery stenosis
- Thiazides not effective if Creatinine greater than 2.5mg/dL
- Can add metolazone to furosemide
- Avoid K sparing agents

Clues to renovascular disease?

- Onset before age 30
- Onset of significant HTN after age 55
- Abdominal bruit--esp. lateralized
- Resistant HTN
- Recurrent pulmonary edema
- Renal failure with normal urinary sediment
- Diffuse atherosclerosis--smokers

What about dyslipidemia?

- Lifestyle modifications first
- Low dose thiazides, no metabolic effects--
Ra
- Beta--blockers reduce HDL but reduce
death, MI--Meta
- Alpha-blockers--lower cholesterol and
increase HDL

JAMA 1996;275:1549-56. Prog
Cardiovasc Dis 1985;27:335-71.

What about respiratory disease?

- Sleep apnea can reduce HTN control
- Beta blockers and alpha-beta-blockers can exacerbate asthma
- ACE I--safe with asthma--if cough, try ARB
- Avoid sympathomimetic decongestants
- Cromolyn, atrovent, inhaled steroids OK

What about gout?

- Hyperuricemia is common finding--
?decreased renal blood flow
- Diuretics can increase uric acid--don't treat
- Rarely cause acute gout
- If gout, avoid diuretic

What about perioperative HTN?

- BP >180/110 increases risk for perioperative ischemic events
- **Cardioselective beta-blocker before and after surgery--Ra**
- Parenteral drugs--diuretics, vasodilators, ACE I or transdermal clonidine
- CA may increase surgical bleeding

Treatments for other causes?

- Cocaine and Amphetamines--treat with benzodiazepines, nitroglycerine, alpha-beta blockers
- **Propranolol avoided due to unblocked alpha-receptors--Ra**
- Immunosuppressants--CA
- Erythropoietin, steroids, MAOI, lead, cadmium, bromocriptine

Summary--Questions?