JNC 8 Hypertension Guidelines
ACP Arizona Chapter Annual Meeting 2014

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Disclosure/COI

• None
The burden of disease

> 32.5% of US population (2011-2012)

Source: Health, United States, 2013, table 64
Would all of us develop hypertension?

• Individuals who are normotensive at 55 years have a 90% likelihood of developing high blood pressure during the next 25 years

Case

• 38 year old AA woman New patient coming in with cold noted BP 138/99 mmHg (untreated)
• Strong family history of hypertension (parents, 2 older sibs)
• Exam/evaluation unremarkable
Meta-analysis of one million adults aged 40 to 89 in 61 prospective observational studies.

- Changes in **SBP of 20 mm Hg** or **DBP of 10 mm Hg** associated with a **two-fold difference** in death from ischemic heart disease, stroke or other vascular reasons.

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

LANCET 2002;60:1903-13
JNC VII JAMA 2003;289:2560-72
Impact of Treating Hypertension

Which one of the following predicts CV mortality more accurately?

Systolic HTN or Diastolic HTN
Relative Importance of DBP and SBP as Predictors of CHD as a Function of Age

CHD, coronary heart disease.

*The difference between SBP and DBP proportional hazard regression coefficients, ie, $\beta(\text{SBP}) - \beta(\text{DBP})$, was estimated for each age group.

SBP, But Not DBP, Increases Throughout Life

With age,

- **SBP** increases in linear fashion
- **DBP** rises less steeply, plateaus, and declines slightly after the fifth decade

Adapted from Galarza CR et al. *Hypertension*. 1997;30:809-816.
The Risk of CHD Rises With SBP

Age-adjusted CHD death rates per 10,000 person-years by level of SBP of men screened in MRFIT

Adapted from Neaton JD et al. Arch Intern Med. 1992;152:56-64.
Systolic BP is directly correlated to risk of stroke and CHD death

Adjusted relative risks of stroke and coronary heart disease death according to baseline SBP in men screened for the Multiple Risk Factor Intervention Trial. Relative risk was adjusted for age, race, serum cholesterol, cigarettes per day, use of medication for diabetes, and income, using a multiple Cox proportional hazards model. Adapted from He, *J Hypertens*, 1999.
Case

• 38 year old AA woman New patient coming in with cold noted BP 138/99 mmHg (untreated)
• Strong family history of hypertension (parents, 2 older sibs)
• Exam/evaluation unremarkable
How to proceed

• **Three** key questions to address before starting therapy
  – Essential vs **Secondary**
  – Assessing other **CV risk factors**
  – Presence of target organ damage (TOD)
The management of hypertension is all about global cardiovascular risk management.
Treating Hypertension and Other Risk Factors


<table>
<thead>
<tr>
<th>Treatment</th>
<th>Predicted Reduction in Major CVD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipids</td>
<td>-6 to -12</td>
</tr>
<tr>
<td>BP</td>
<td>-6 to -10</td>
</tr>
<tr>
<td>Overall</td>
<td>-17 to -37</td>
</tr>
</tbody>
</table>

**Treatment thresholds**
- Top 10%
- Top 20%
- Top 30%

Case

- 38 year old AA woman New patient coming in with cold noted BP 138/99 mmHg (untreated)
- Strong family history of hypertension (parents, 2 older sibs)
- Exam/evaluation unremarkable
Treatment of Hypertension

Stage 1 Hypertension

Target organ Damage, CVD, or 10yr CVD risk ≥20%?

YES = Treat

NO = Lifestyle and review 1 yr.*

Stage 2 Hypertension

Treat

*for people aged <40ys, 10yr CVD risk assessments underestimate lifetime risk – consider referral for exclusion of secondary causes and more detailed assessment of TOD
Is it the lowering of BP or the use of specific medication that reduces CV mortality?
STOP-2
Swedish Trial in Old People with Hypertension-2

6614 people aged 70 to 84 years

ACEI  CCB  D/BB

? Difference in BP control
? CVD mortality and morbidity

VHAS/CONVINCE/INSIGHT/NORDIL/UKPDS/CAPP

ALLHAT

42,418 people

ACEI CCB DIUR

? Difference in BP control
? CVD mortality and morbidity

ALLHAT-JAMA 2002. 288
Cumulative Event Rates for the Primary Outcome (Fatal CHD or Nonfatal MI) by ALLHAT Treatment Group

<table>
<thead>
<tr>
<th>Years to CHD Event</th>
<th>Cumulative CHD Event Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>1</td>
<td>0.04</td>
</tr>
<tr>
<td>2</td>
<td>0.08</td>
</tr>
<tr>
<td>3</td>
<td>0.12</td>
</tr>
<tr>
<td>4</td>
<td>0.16</td>
</tr>
<tr>
<td>5</td>
<td>0.20</td>
</tr>
<tr>
<td>6</td>
<td>0.24</td>
</tr>
<tr>
<td>7</td>
<td>0.28</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number at Risk:</th>
<th>Chlorthalidone</th>
<th>Amlodipine</th>
<th>Lisinopril</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorthalidone</td>
<td>15,255</td>
<td>14,477</td>
<td>13,820</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>9,048</td>
<td>8,576</td>
<td>8,218</td>
</tr>
<tr>
<td>Lisinopril</td>
<td>9,054</td>
<td>8,535</td>
<td>8,123</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/C 0.98 (0.90-1.07)</td>
<td>0.65</td>
</tr>
<tr>
<td>L/C 0.99 (0.91-1.08)</td>
<td>0.81</td>
</tr>
</tbody>
</table>
• 48 year old AA man, new patient came in for URI but noted sustained BP 158/99 mmHg (untreated). Strong family history of hypertension (parents, 2 older sibs). Exam and evaluation unremarkable.

• What would you prescribe (in addition to diet and life style modification)

1. Atenolol
2. HCTZ
3. Lisinopril
4. Nifedipine
5. Terazocin
BHS Antihypertensive Drug Treatment

Aged <55yrs

Step 1
A

Step 2
A + C*

Step 3
A + C* + D

Step 4
A + C* + D + Further Diuretic*
Consider specialist Advice

Aged ≥55yrs or Black AC

A = ACEi or ARB
C = CCB
D = Thiazide-like diuretic

C* = CCB preferred but D is an alternative in people intolerant of C or at high risk of heart failure

Further Diuretic:
Consider low dose spironolactine or higher dose thiazide
Evidence Based Drugs

- ACE-inhibitors
- ARB
- CCB
- DIURETICS
Evidence is unfavorable

- $\alpha$-blockers
- $\beta$-blockers
- Do not combine an ACE inhibitor with an ARB to treat hypertension
Drugs lacking evidence

There are no randomized controlled trials of acceptable quality to determine CV benefit when starting drug therapy with:

- Loop diuretic,
- Nitroglycerin containing agents
- Combined α/β blocking agent
- Direct vasodilator
- Central α2-adrenergic agonist
- Mineralocorticoid receptor antagonist +
- Peripheral adrenergic neuron antagonist
## Lifestyle Modification

<table>
<thead>
<tr>
<th>Modification</th>
<th>Approximate SBP reduction (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>5–20 mmHg/10 kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH Diet</td>
<td>8–14 mmHg</td>
</tr>
<tr>
<td>Low Dietary sodium</td>
<td>2–8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>4–9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol consumption</td>
<td>2–4 mmHg</td>
</tr>
</tbody>
</table>
Non Antihypertensive medications

• Aspirin:
  – use 75mg daily if patient is aged $\geq 50$ years with blood pressure controlled to $<150/90$ mm Hg
  – target organ damage
  – diabetes mellitus,
  – 10 year risk of cardiovascular disease of $\geq 20$

• Statin:
  – use sufficient doses to reach targets (up to age 80 years),
  – with a 10 year risk of cardiovascular disease of $\geq 20$

Case

• 58 year old white man with history of MI two years ago. What is his BP goal?

1. <150/90
2. <140/90
3. <130/90
4. <140/80
5. <180/85
Case

- 59 year old woman with Type 2 DM. What is her BP goal?

1. <130/80
2. <150/90
3. <140/90
4. <130/90
5. <140/80
Case

• 72 year old woman with severe osteoarthritis taking 500 mg naproxen twice daily.
• BP on an ACE-inhibitor is 152/76 mmHg.
## Modifiable Factors/Conditions

<table>
<thead>
<tr>
<th>Left Column</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt</td>
</tr>
<tr>
<td>Smoking</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Lack of physical activity</td>
</tr>
<tr>
<td>Sleep apnea</td>
</tr>
<tr>
<td>Anxiety (GAD)/ Panic attack</td>
</tr>
<tr>
<td>Pain-acute or chronic</td>
</tr>
<tr>
<td>Vasculitis</td>
</tr>
<tr>
<td>Delirium with autonomic excess</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Right Column</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cocain</td>
</tr>
<tr>
<td>NSAIDs, including coxibs</td>
</tr>
<tr>
<td>Alcohol use &gt;12-14 g/day</td>
</tr>
<tr>
<td>Corticosteroids/anabolic steroids</td>
</tr>
<tr>
<td>Oral contraceptive /sex hormones</td>
</tr>
<tr>
<td>Sympathomimetic decongestants</td>
</tr>
<tr>
<td>Cyclosporin and tacrolimus</td>
</tr>
<tr>
<td>Erythropoietin and analogues</td>
</tr>
<tr>
<td>Antidepressants: Monoamine oxidase inhibitors (MAOIs), SNRIs, SSRIs</td>
</tr>
<tr>
<td>Midodrine</td>
</tr>
</tbody>
</table>
Case

- 55 year old white male with hypertension and LVH (by EKG).
- Currently on a diuretic, with BP of 147/90 mmHg.
Case

- 64 year old diabetic man. BP 156/78 mmHg.
- Creatinine is 1.3 mg/dL (eGFR of 44 mL/min/1.73m²).
- K+ of 5.4 mEq/l
## Comorbid Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Initial Therapy Options</th>
<th>Clinical Trial Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>THIAZ, BB, ACE, ARB, CCB</td>
<td>NKF-ADA Guideline, UKPDS, ALLHAT</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>ACEI, ARB</td>
<td>NKF Guideline, Captopril Trial, RENAAL, IDNT, REIN, AASK</td>
</tr>
</tbody>
</table>
• 59 year old man on an Lisinopril 40 mg qd, aspirin, atorvastatin come for post-hospital f/u. Had a small thrombotic stroke (weak right arm) 2 weeks ago.

• BPs are 154-162/80 (seated) without orthostasis; heart rate is 68 beats/minute. Labs are normal; EKG Left ventricular strain pattern

• **What is his BP goal?**
  1. <150/90
  2. <140/90
  3. <130/90
  4. <140/80
  5. <180/85
What would you suggest to get him to goal?

1. Metoprolol
2. Nifidipine
3. Chlorthalidone
4. Losartan
5. Increase Lisinopril to 80 mg
Recurrent stroke prevention

• Thiazide type diuretics plus ACEI

NICE and BSH guidelines 2012
JNC VIII 2003
New patient coming to you. 58 AAM with BP 166/98, creatinine of 3.2, and a K of 4.2.

What would you start?

1. Lisinopril
2. Terazocine
3. Verapamil
4. Amlodipine
5. HCTZ
Case

• Same patients. Now tells you that he had an MI and stroke 5 years ago in another city. His labs also showed that he is poorly controlled diabetic.

• What should be his goal BP?
  1. <150/90
  2. <140/90
  3. <130/90
  4. <140/80
  5. <180/85
Case

• 45 year old man (BMI is 34 kg/m²)
• BP 148/100 mmHg
• Fasting glucose 123 mg/dl
• Exam normal
In obese patients

- **Diuretics**: Highest rate of “diagnosing” new onset diabetes (NOD)
- **Beta Blocker**: Higher rate of NOD
- **CCB**: Neutral
- **ACE inhibition**: Decreased rate of NOD

**BUT**
Long term consequences of NOD in hypertensive patients???
Case

- 69 WM with HTN, NIDDM, hypercholesterolemia, CAD s/p CABG, CHF NYHA class II, DJD with occasional LBP and depression on maximum doses of Lisinopril, Metoprolol XL, Amylodipine, Imdur, Simvastatin, Glyburide, Celebrax and Aspirin.
- F/u visit today VS 88, 162/80

Is this resistant hypertension? How do you manage this patient?
RESISTANT HYPERTENSION

• Blood pressure that remains higher than 140/90 mmHg with the optimal or best tolerated doses of 3 meds (ACE inhibitor or angiotensin-II receptor blocker plus a calcium channel blocker plus a diuretic).

• Consider adding a fourth antihypertensive drug and/or increasing diuretic doses and/or seeking expert advice.
Dual RAS Inhibition?

- A systematic review and meta-analysis: 33 randomized controlled trials with 68,405 patients (mean age 61 years, 71% men) and mean duration of 52 weeks
- Dual blockade of the renin-angiotensin system was not associated with any significant benefit for all cause mortality (relative risk 0.97, 95% CI 0.89 to 1.06) and cardiovascular mortality (0.96, 0.88 to 1.05) compared with monotherapy.

BMJ 2013;346:f360
Dual RAS Inhibition?

- Compared with monotherapy, dual therapy was associated with an 18% reduction in admissions to hospital for heart failure (0.82, 0.74 to 0.92).

- However, compared with monotherapy, dual therapy was associated with
  - 55% increase in the risk of hyperkalaemia (\( P < 0.001 \))
  - 66% increase in the risk of hypotension (\( P < 0.001 \))
  - 41% increase in the risk of renal failure (\( P = 0.01 \))
  - 27% increase in the risk of withdrawal owing to adverse events (\( P < 0.001 \)).
Drugs lacking evidence

There are no randomized controlled trials of acceptable quality to determine CV benefit when starting drug therapy with:

– Loop diuretic,
– Nitroglycerin containing agents
– Combined α/β blocking agent
– Direct vasodilator
– Central α2-adrenergic agonist
– Mineralocorticoid receptor antagonist +
– Peripheral adrenergic neuron antagonist
• 50 yo male on lisinopril and aliskirin come for routine office visit. BP is well controlled, he feels well.

• Labs now showing eGFR of 55 (baseline 65) and a K of 5.1 (baseline 4.2).

• What would you do next?
  1. Add furosemide
  2. Add kayexalate
  3. Discontinue Lisinopril
  4. Discontinue Aliskirin
• The labels for the aliskiren drugs are being updated based on preliminary data from a clinical trial, “Aliskiren Trial in Type 2 Diabetes Using Cardio-Renal Endpoints (ALTITUDE).”

• The trial involved 8606 patients with type 2 diabetes and renal impairment who are at high risk of cardiovascular and renal events.

• The DSMB terminated the trial concluded that
  – patients were unlikely to benefit from treatment added on top of standard anti-hypertensives (ACEI or ARB)
  – and identified an increased incidence after 18-24 months
    • non-fatal stroke
    • renal complications
    • hyperkalemia
    • hypotension
Aliskiren - a Renin Inhibitor

- Aliskiren should not be used in combination with ACEIs and ARBs in patients with
  - diabetes
  - moderate to severe renal impairment (GFR < 60 mL/min).
Aliskiren Products

- Tekturna (aliskiren hemifumarate)
- Tekturna HCT (aliskiren hemifumarate and hydrochlorothiazide)
- Tekamlo (aliskiren hemifumarate and amlodipine besylate)
- Amturnide (aliskiren hemifumarate, amlodipine besylate, and hydrochlorothiazide)
- Valturna (aliskiren hemifumarate and valsartan). Valturna has been withdrawn from market.
A 70 man, HTN, Hyperlipidemia, CAD with MI 6 years ago presents with right knee pain for the past 6 months. X-ray - osteoarthritis.

Labs are normal

What would be the most appropriate management plan?

1. Ibuprofen
2. Acetaminophen
3. Oxycodone
4. Diclofenac
5. Celecoxib
NSAID Use in Patients with Hx of MI

- HR for Death with NSAID use
  - 1.59 at 1 year,
  - 1.63 at 5 years.

- HR for recurrent MI with NSAID use
  - 1.3 at 1 year,
  - 1.41 at 5 years.

NSAIDS and CHF

- Odds ratio for first admission for CHF if patient had heart disease and used NSAIDS - 10.5

- Odds ratio for admission for CHF for patients who have used NSAIDS - 2.1

Arch intern med 2000;160:777-784
Key Points

- The BP relationship to risk of CVD is continuous, consistent, and independent of other risk factors.

- Each increment of 20/10 mmHg doubles the risk of CVD across the entire BP range starting from 115/75 mmHg.

- Overall CVD and risk assessment is mandatory.
Life style modification is essential

Degree of blood pressure control appears to be more important than the type of antihypertensive drugs used.

Systolic hypertensions strong predictor of CVD events for persons over age 50

Establish mutual goals.
Key Points

- Monotherapy individualized-Diuretics, CCBs, ARBs, ACEIs are safe and effective.

- Most patients with hypertension will require 2 or more medications to achieve their BP goals.

- When BP is more than 20/10 mm Hg above goal, consideration should be given to initiating therapy with 2 drugs, either as separate prescriptions or in fixed-dose combinations.
Treatment Goals

• <140/90 in all hypertensives including diabetes and CRI

• <150/90 in Age 60 and older

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults: Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)  JAMA. 2014;311(5):507-520