Hypertension
Cases & Questions

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Disclosures

• I currently have no relationships of any kind with any company whose products or services in any way relate to the practice of medicine, medical education or research.
Q1: If the target blood pressure is not reached within one month after initiating therapy, you should...?

1. Increase the dosage of initial medication
2. Add a second medication
3. Refer to a hypertension specialist
4. Admit to the hospital for aggressive medication titration
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2. **Add a second medication**

3. Refer to a hypertension specialist

4. Admit to the hospital for aggressive medication titration
Recommendation 9

The main objective of hypertension treatment is to attain and maintain goal BP. If goal BP is not reached within a month of treatment, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB). The clinician should continue to assess BP and adjust the treatment regimen until goal BP is reached. If goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. Do not use an ACEI and an ARB together in the
Case 1

A 55 year old man repeatedly has a BP of 145/95. He reports occasional exercise (“I try to make time for it, really!”), consumes 2 beers per week and has a BMI = 31. Physical exam is normal.

Which of the following lifestyle interventions is the best strategy for management?

1. Decrease alcohol intake
2. Dietary supplementation with potassium
3. Weight loss
4. Increase exercise
5. Stress management
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<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 eating plan</td>
<td>8–14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</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>
Dietary Approach to Stop Hypertension

• Fruits, vegetables, & low-fat dairy
• Grains, poultry, fish & nuts
• Small amounts of red meat, sweets & sugary beverages
• Small amounts of total & saturated fat & cholesterol
• Large amounts of K+, Mg²⁺, Ca²⁺, dietary fiber & protein

Sacks FM et al. NEJM 2001
Case 2

• You are asked by your colleague to see a challenging hypertensive patient. 62 year old woman with long standing hypertension on multiple medications.
  – Nifedipine 90 XL qd
  – Metoprolol succinate 200 bid
  – Enalapril 20 mg bid
  – Chlorthiladone 25 mg qd
• Swears to compliance
• $K^+ = 4.2$, $Cr = 1.3$ mg/dl
Case 2

What is your next step?

1. Refer to Hypertension specialist
2. Repeat a detailed history
3. Obtain renal artery Doppler study
4. Obtain a Sleep Study
5. Add a 5th medication
Case 2

What is your next step?

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Resistant HTN

- **Definition**: BP above goal despite use of 3 meds of different classes (should include TD and at max doses)
- **Prevalence**: 9-30%

- **Must rule out Pseudo-resistant**
  - Inaccurate measurement
    - consider ambulatory BP monitoring
  - Poor adherence
  - Lifestyle/Diet
  - White Coat
    - 20-30% pts, 37-44% of “resistant HTN”
Poor Adherence

• 40% of newly diagnosed patients discontinue treatment in the first year
  – Poor communication, side-effects, cost, multiple dosing, inappropriate treatment
    (Markis et al. Int J of Hypertension 2011)

• 50-66% of pts took 75% of their prescribed BP meds
  – Main association with taking >75% was the number of pills. (Winickoff RN et al, Arch Intern Med. 1987)
Resistant HTN

• Other factors to remember:
  – Salt
  – Meds:
    • NSAIDs, diet pills, decongestants, OCPs, glucocorticoids
    • Herbals, illicit drugs (cocaine, amphetamines)
  – Extracellular Volume Expansion
  – Obstructive Sleep Apnea
  – Chronic Kidney Disease
Q2: Which food comprises greatest source of sodium in American diets?

1. Cold Cuts
2. Chips
3. Bread
4. Pickles
5. Canned Soup
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1. Cold Cuts
2. Chips
3. **Bread**
4. Pickles
5. Canned Soup
Where's the sodium? There's too much in many common foods.

About 90% of Americans eat more sodium than is recommended for a healthy diet.

For American Heart Month, the February edition of CDC Vital Signs focuses on the amount of sodium in Americans' diets and what we can do to reduce it. Too much sodium increases a person’s risk for high blood pressure. High blood pressure often leads to heart disease, stroke, and other vascular diseases.

Most of the sodium we eat comes from processed foods and foods prepared in restaurants. Sodium is already part of processed foods and cannot be removed. Learn what you can do to reduce sodium in your diet.

Highlights from the Report:

- About 90% of Americans eat more sodium than is recommended for a healthy diet.
- Reducing the sodium Americans eat by 1,200 mg per day on average could save up to $20 billion a year in medical costs.
CDC Top Sources of Dietary Sodium

1. Breads and rolls
2. Cold cuts and cured meats
3. Pizza
4. Fresh and processed poultry
5. Soups
6. Sandwiches
7. Meat mixed dishes
8. Snacks: chips, pretzels, and popcorn
Features of Salt-Sensitive Hypertension

• Epidemiologic features
  – Black race
  – Obesity
  – Advanced age
  – Diabetes
  – Renal dysfunction
  – Use of cyclosporine

• Clinical features
  – Microalbuminuria
  – Non-dipper
  – Absence of modulation of renal blood flow in response to sodium loading

Johnson RJ et al, NEJM 2002
Case 3

Patient with poor BP control & CKD stage 3. What change in BP med scheduling might reduce risk of future MI & improve BP?

1. All prescribed BP medications in morning
2. At least 1 medication at bedtime
3. Spread evenly throughout the day
4. Does not matter
Case 3

Patient with poor BP control & CKD stage 3.

What change in BP med scheduling might reduce risk of future MI & improve BP?

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# Bedtime Dosing of Antihypertensive Medications Reduces Cardiovascular Risk in CKD

Ramón C. Hermida, Diana E. Ayala, Artemio Mojón, and José R. Fernández

Bioengineering and Chronobiology Laboratories, University of Vigo, Campus Universitario, Vigo, Spain

<table>
<thead>
<tr>
<th>Variable</th>
<th>Awakening(^b) ((n = 332))</th>
<th>Bedtime(^b) ((n = 329))</th>
<th>(P) between groups(^c)</th>
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</thead>
<tbody>
<tr>
<td><strong>Primary end points</strong></td>
<td></td>
<td></td>
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<tr>
<td>Total events</td>
<td>57.9 (48.6 to 67.1); 104</td>
<td>19.8 (13.6 to 26.0); 35</td>
<td>&lt;0.001</td>
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<td>Major events</td>
<td>14.5 (9.1 to 19.8); 26</td>
<td>5.1 (1.8 to 8.4); 9</td>
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<td><strong>Secondary end points</strong></td>
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<tr>
<td>Total death</td>
<td>7.8 (3.8 to 11.8); 14</td>
<td>4.0 (1.0 to 6.8); 7</td>
<td>0.056</td>
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<td>Cardiovascular death</td>
<td>3.9 (1.0 to 6.8); 7</td>
<td>1.1 (0.0 to 2.7); 2</td>
<td>0.059</td>
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<td>Other cause</td>
<td>3.9 (1.0 to 6.8); 7</td>
<td>2.8 (0.4 to 5.3); 5</td>
<td>0.758</td>
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<td>Cardiovascular events</td>
<td>26.1 (19.2 to 33.1); 47</td>
<td>6.2 (2.6 to 9.8); 11</td>
<td>&lt;0.001</td>
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<tr>
<td>Myocardial infarction</td>
<td>8.9 (4.7 to 13.2); 16</td>
<td>2.8 (0.4 to 5.3); 5</td>
<td>0.005</td>
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<td>Angina pectoris</td>
<td>10.0 (5.5 to 1.45); 18</td>
<td>1.7 (0.1 to 3.6); 3</td>
<td>&lt;0.001</td>
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<tr>
<td>Revascularization</td>
<td>7.2 (3.4 to 11.1); 13</td>
<td>1.7 (0.1 to 3.6); 3</td>
<td>0.004</td>
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<td>Cerebrovascular events</td>
<td>2.2 (0.3 to 4.4); 4</td>
<td>1.1 (0.0 to 2.7); 2</td>
<td>0.310</td>
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<td>Heart failure</td>
<td>15.0 (9.6 to 20.5); 27</td>
<td>4.5 (1.4 to 7.6); 8</td>
<td>&lt;0.001</td>
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<tr>
<td>Other events</td>
<td>6.7 (3.0 to 10.4); 12</td>
<td>0.0 (1.0 to 6.8); 7</td>
<td>0.119</td>
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Q3: Which factor(s) are associated with ↑ Risk of HTN in elderly men?

1. Duration of Sleep
2. Amount of sleep-disordered breathing
3. Duration of slow-wave sleep
4. Nocturnal hypoxia
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1. Duration of Sleep
2. Amount of sleep-disordered breathing
3. **Duration of slow-wave sleep**
4. Nocturnal hypoxia
Decreased Slow Wave Sleep Increases Risk of Developing Hypertension in Elderly Men

Fung MM et al. Hypertension. 2011;58:596-603
Sleep in HTN

- OSA as cause of HTN more common in age<60
- Prevalence of OSA
  - may be as high as 85% in patients with resistant HTN vs. 38% in controlled HTN
- Severity of OSA correlates with severity of HTN
- Treating with CPAP decreases sympathetic activity and decreases BP – BUT only modestly
Case 4

A 75 yo woman with long standing HTN has +1 lower extremity edema & BP = 150/95 on amlodipine 10 mg daily. She has been intolerant of diuretics. Adding which class of BP med might help her edema as well as her BP

1. Angiotensin Receptor Blocker (ARB)
2. Direct Renin Antagonist (Aliskerin)
3. Beta blocker (Carvedilol)
4. Clonidine
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# Effect of Renin-Angiotensin System Blockade on Calcium Channel Blocker-Associated Peripheral Edema

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CCB/RAS Blocker</th>
<th>CCB</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>1.2.1 CCB+ACEi vs CCB</td>
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<tr>
<td>Chrysant 2007</td>
<td>4</td>
<td>541</td>
<td>7</td>
<td>0.29 [0.08, 0.97]</td>
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<tr>
<td>Jamerson 2004</td>
<td>3</td>
<td>182</td>
<td>9</td>
<td>0.33 [0.09, 1.21]</td>
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<tr>
<td>Kuschnir 1996</td>
<td>1</td>
<td>77</td>
<td>4</td>
<td>0.25 [0.03, 2.19]</td>
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<tr>
<td>Miranda (ATAR) 2008</td>
<td>3</td>
<td>131</td>
<td>2</td>
<td>1.53 [0.26, 9.03]</td>
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<tr>
<td>Scholze 1999</td>
<td>4</td>
<td>255</td>
<td>1</td>
<td>1.35 [0.15, 11.91]</td>
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<tr>
<td>Steiner 1994</td>
<td>0</td>
<td>52</td>
<td>3</td>
<td>0.16 [0.01, 2.85]</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td>0.42 [0.22, 0.80]</td>
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<tr>
<td>Total events</td>
<td>15</td>
<td>1238</td>
<td>805</td>
<td>26</td>
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<tr>
<td>Heterogeneity: Chi² = 4.34, df = 5 (P = 0.50); I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 2.64 (P = 0.008)</td>
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<tr>
<td>1.2.2 CCB+ARBs vs CCB</td>
<td></td>
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<td></td>
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<tr>
<td>Philipp 2007</td>
<td>6</td>
<td>1437</td>
<td>7</td>
<td>0.27 [0.09, 0.81]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td></td>
<td>1437</td>
<td>460</td>
<td>0.27 [0.09, 0.81]</td>
</tr>
<tr>
<td>Total events</td>
<td>6</td>
<td>2675</td>
<td>1265</td>
<td>7</td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
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<td></td>
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<tr>
<td>Test for overall effect: Z = 2.34 (P = 0.02)</td>
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<tr>
<td>Total (95% CI)</td>
<td></td>
<td>21</td>
<td>33</td>
<td>0.38 [0.22, 0.66]</td>
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<tr>
<td>Heterogeneity: Chi² = 4.80, df = 6 (P = 0.57); I² = 0%</td>
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<tr>
<td>Test for overall effect: Z = 3.42 (P = 0.0006)</td>
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<tr>
<td>Test for subgroup differences: Not applicable</td>
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</tbody>
</table>

Case 5

• Remember our patient from Case 2
• 62 year old woman on multiple medications.
  – Nifedipine, Metoprolol, Enalapril, Chlorthiladone
  – $K^+ = 4.2$, $Cr = 1.3$ mg/dl
• BP still 165/95
Case 5

• Which of the following is most concerning for secondary HTN for her?

1. Her age >60
2. Long chronicity of HTN
3. Potassium >4.0
4. Need for 4 medications
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Secondary HTN

• 50% of resistant HTNives may have secondary cause

• Most common in adults:
  – **Primary aldosteronism** and **renal artery stenosis**

• Look for clinical clues
  – Rapid onset or acceleration, early or late presenting
  – Associated symptoms (pheo, thyroid, Cushing’s)
  – Hypokalemia → Primary aldo
  – Rapid rise in creatinine with ACE-I → RAS
Evaluation for Suspected Secondary Hypertension

Check accuracy of blood pressure measurements, rule out diet- and drug-related causes

History, physical examination, laboratory testing

Clinical clues

No clinical clues, but secondary hypertension remains a concern (e.g., in a child, rapid onset or acceleration of hypertension, resistant hypertension)

See Table 1

Child/adolescent

Urinalysis*
Urine culture
Renal ultrasonography

Young adult

MRI with gadolinium contrast media or CT renal artery†
TSH*

Middle-aged adult

Renin and aldosterone levels
TSH*

Older adult

MRI with gadolinium contrast media or CT renal artery†
TSH*
Urnalysis*

NOTE: Dashed arrows indicate further studies to consider if no cause is identified and secondary hypertension is still suspected.

*—If not done as part of the initial evaluation.
†—Choice of renal artery imaging modality based on availability, institutional expertise, and patient factors.
Thank You