Session 1: Hypertension 2013: What To Do While We Wait For the New JNC Guidelines

Learning Objectives

1. Understand the importance of proper technique for diagnosing hypertension and monitoring treatment effectiveness.
2. Apply insights about the complexities and causes of hypertension to individualize therapy, especially for high-risk patient groups.
Session 1

Hypertension 2013: 
What to Do While We Wait for the New JNC Guidelines

Faculty

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Dr Townsend directs the hypertension program at Penn. His research interests are in vascular compliance and CKD progression and CKD complications. His clinical practice includes drug-resistant hypertension, secondary hypertension, and in particular adrenal disorders. He is an empaneled member of JNC 2013 and a co-chair of the American Heart Association’s 2013 Hypertension Summer School.

Faculty Financial Disclosure Statement
The presenting faculty reports the following:

Dr Townsend has no financial relationships to disclose.
Session 1:
7:45 AM - 9:00 AM
Hypertension 2013: What To Do While We Wait for the New JNC Guidelines
Raymond Townsend, MD

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Demographic Question

How many patients with hypertension do you see each week?
1. None
2. 1 - 5
3. 6 - 15
4. 16 - 25
5. 26 - 40
6. Over 40

Outcomes Question #1

Which of the following is TRUE?
1. Women tend to run higher home BP readings than men
2. Home and clinic BP readings tend to vary even in normotensive patients
3. Differences in home and clinic BP increase with age
4. The “white coat” effect is typically an increase in SBP of 5 -10 mmHg
5. All of the above

Outcomes Question #2

In the treatment of hypertension, which is generally TRUE?
1. HCTZ and chlorothalidone are equally effective
2. Furosemide needs to be dosed twice daily
3. Edema seen with amlodipine is due to volume expansion
4. Ethacrynic acid should not be used in patients with sulfa allergy
Outcomes Question #3

Which of the following may be suggestive of renovascular disease as the cause of hypertension?

1. Reduced serum creatinine with ACE-I or ARB
2. Elevated plasma renin
3. Slow, steady increase in blood pressure over time
4. Strong family history of hypertension
5. All of the above

Case 1

Case 1: Jerry

• 39 y/o WM who presents to your office for wellness check
  – No complaints
• Exam
  – BP 162/100 mmHg (single reading)
  – Pulse 72 RR-20
  – No evidence of target organ damage (TOD)
  – Height: 5’10” Wgt: 205 lbs (BMI-29.4)
• Family history: hypertension-father age 74
• Social history: non-smoker, occasional beers

Jerry: Next Steps?

1. Order home BP monitoring
2. Initiate treatment with HTN medication
3. Restrict salt intake to 2000 mg/day
4. Any of the above would be appropriate next steps
5. None of the above

Blood Pressure Measurement

How many errors of BP measurement do you see?

1. One
2. Two
3. Three
4. Four
5. Five
6. Six

BP Measurement

• Early 1900s BP measured by palpation
• By 1914 life insurance industry recognized that in asymptomatic men, their BP (after their age) was the best way to predict premature death and disability1
• Population-based studies of standardized BP measurement began in 1948 with Framingham  
  - Large-scale studies required training in BP measurement2

1. Fisher JAMA 1914;63:1752-1754
Question

In an observational study of BP measurement in various settings (office, hospital, skilled nursing facility, home health) what percentage of BP measurements were done according to the guidelines?

1. 60%
2. 30%
3. 10%
4. 0%

Grim et al. Can J Cardiol 1995;11 (suppl H):38H-42H.

BP Measurement: Common Errors

<table>
<thead>
<tr>
<th>Error</th>
<th>Potential Impact on BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improper cuff size (small)</td>
<td>Highly variable</td>
</tr>
<tr>
<td>Improper arm placement</td>
<td>2.5 mmHg for every inch</td>
</tr>
<tr>
<td>Improper positioning (ie, examination table)</td>
<td>5 mmHg DBP seated&gt;supine</td>
</tr>
<tr>
<td></td>
<td>5 mmHg DBP sitting without back support</td>
</tr>
<tr>
<td></td>
<td>5 mmHg SBP sitting with legs crossed</td>
</tr>
<tr>
<td>Talking</td>
<td>10 mmHg SBP talking</td>
</tr>
<tr>
<td>Non-validated device</td>
<td>5 mmHg SBP listening</td>
</tr>
</tbody>
</table>

Pickering et al Hypertension 2005;45:142-161.

BP Measurement Devices

Ensure that device is validated

- Manual
  - Mercury is still gold standard but disappearing
  - Aneroid- ease of calibration
  - Non-mercury manual- new device

BP Measurements Outside the Office

What do you recommend to your patients?

1. Purchase a device and take readings at home
2. Take BP at the pharmacy at least once a week
3. Ambulatory BP monitoring (ABPM)
4. Any of the above
5. None of the above

Pickering et al Hypertension 2005;45:142-161.

Back to Jerry

- Multiple BP readings were recorded
  - 145/95 mmHg average reading
- He was begun on the DASH diet and provided with resources for exercise and weight loss programs
- He was told to monitor his BP and follow-up in office in 2-3 months

DASH = Dietary Approaches to Stop Hypertension

BP Measurement Devices
Automated
- Finger devices worthless
- Wrist devices difficult to use satisfactorily
- Most have not undergone validation process
  - None that are used widely in community (drugstores)

Ambulatory blood pressure monitoring (ABPM) devices
- Placed on non-dominant arm
- Pre-set readings—typically every 15-20 min during the day and 30 min at night
- Usually oscillatory measurement

“White Coat” Effect
- The elevation of BP that occurs with a clinic visit (usually compared to daytime ABPM)
- ABPM probably better than home readings
- BUT… home BP correlate better with ABPM than clinic

<table>
<thead>
<tr>
<th>White Coat Effect</th>
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</thead>
<tbody>
<tr>
<td>HBPM 14.4/5.0 mmHg</td>
</tr>
<tr>
<td>ABPM 18.9/11.4 mmHg</td>
</tr>
</tbody>
</table>

“White Coat” Effect1
HBPM 14.4/5.0 mmHg
ABPM 18.9/11.4 mmHg


24-Hour ABPM
- Most effective method to diagnose white coat hypertension and white coat effect
- Both can be diagnosed if mean 24 hr BP is <135/85
  - White coat hypertension elevated BP in office in absence of diagnosis or treatment of BP
  - White coat effect is presence of elevated BP in office while normal outside in a patient on HTN drug therapy

Back to Jerry
Three in-office BP readings: mean 145/95 mmHg
How would you evaluate Jerry for cardiovascular risk?
1. Complete metabolic profile
2. ECG
3. Lipid profile
4. Echocardiogram
5. All of the above
6. 1, 2, and 3 only

Evaluation of Hypertension JNC-7
Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
- Assess lifestyle and identify other cardiovascular risk factors
- Reveal identifiable causes of high BP
- Assess target organ damage
- Laboratory
  - Complete blood count (CBC)
  - Blood chemistry (including creatinine, potassium, calcium and fasting blood sugar)
  - Lipids (total cholesterol, HDL)
  - Urinalysis
  - Electrocardiogram

Jerry: Laboratory Results
- CBC WNL
- CMET
  - K+ 4.5 mEq/mL
  - Creatinine 1.1 mg/dL
  - FBS 88 mg/dL
- U/A WNL
- Lipids TC -298 mg/dL; LDL 218 mg/dL; HDL 48 mg/dL; TG 175 mg/dL
- EKG NSR; Rate 74; no LVH
Jerry: Follow Up

Returns 8 months later
- Mean office BP: 156/98 mmHg  HR 88
- HBP- mean: 150/94 mmHg
- Weight is unchanged; admits difficulty with DASH diet and keeping exercise regimen
- He’s begun on treatment with lisinopril 40 mg qd
  - Considered combination treatment, but deferred

Follow-up 3 months later
- BP still elevated (155/96) and needs additional agent

Compelling Indications for Drug Classes

<table>
<thead>
<tr>
<th>COMPelling INDICATION*</th>
<th>Recommended Drugs†</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Diuretic</td>
</tr>
<tr>
<td>Heart failure</td>
<td></td>
</tr>
<tr>
<td>Postmyocardial infarction</td>
<td></td>
</tr>
<tr>
<td>High coronary disease risk</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td></td>
</tr>
<tr>
<td>Recurrent stroke prevention</td>
<td></td>
</tr>
</tbody>
</table>

Diuretics

- Thiazide and thiazide-like: effective until GFR <35-40 mL/min/1.73m²
- Hypokalemia with usual dose may be evidence of high sodium intake and/or Conn’s syndrome (primary aldosteronism)
- Chlorthalidone: more potent (longer half-life) with similar metabolic effects of HCTZ
- Loop diuretics for hypertension: furosemide should be dosed at least BID

A HTN Treatment Tool

A: ACE/ARB
B: BB
C: CCB
D: Diuretic

Jerry: Follow Up

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**Beta Blockers**

- Selective BB lose selectivity at higher doses, even commonly used doses
- Many of the troublesome side effects are often dose dependent
- Non-duel action beta blockers (in particular tenolol) lower central aortic BP less than brachial BP

**Calcium Channel Blockers**

- Edema seen is not volume overload, but rather shift in fluid
  - Edema especially with amlodipine, felodipine, is dose dependent
  - Diuretics will not alleviate the edema in most patients
- ACE inhibitors and ARBs (in appropriate doses) when combined with CCB may improve edema
- Avoid combining verapamil with beta-blockers

**RAS Inhibitors**

**ACE Inhibitors**

- Most common and troublesome side effect is cough
  - Occasionally early effect - for most late onset
  - Usually resolves within days of discontinuation
  - May not recur with rechallenge months later
- Hyperkalemia - greater risk if comorbid diabetes, CKD
- Up to 25% increase in Scr is acceptable; look for other causes if further increase
- Use therapeutic doses
- ARBs
  - An alternative to ACE inhibitors, but more expensive
  - Angioedema is rare
  - Do not use in combination with ACE inhibitors

**Obesity and Hypertension Potential Mechanisms**

- Obese patients have higher BP levels - night and day
- Visceral obesity stimulates the RAAS system
- Fat may serve as a storage depot for aldosterone
- Increases risk of non-dipping (also in sleep apnea)
  - Esp in high sodium/low potassium intake
- High Na+ intake salt-sensitive phenotype emerges
- Afferent arteriole dilates even if BP high - further injury ensues.

**Lifestyle Modifications to Manage Hypertension**

<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approx. SBP1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (body mass index 18.5-24.9 kg/m²).</td>
<td>5-20 mmHg/10 kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat.</td>
<td>8-14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 mmol per day (2.4 g sodium or 6 g sodium chloride).</td>
<td>2-8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week).</td>
<td>4-9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol</td>
<td>Limit consumption to no more than 2 drinks (1 oz. or 30 mL ethanol; eg, 24 oz. beer, 10 oz. wine, or 3 oz. 80-proof whiskey) per day in most men and to no more than 1 drink per day in women and lighter weight persons.</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>

2. Wilson et al Hypertension 1989;24;181-86.
Case 2

Case 2: Margaret

- 42-year-old African American female presents with complaint of high blood pressure and elevated blood glucose picked up on screening at her church

- Family History
  - Parents and 4/6 siblings with history of hypertension
  - 2 older siblings have type 2 diabetes
  - Additional history of stroke in family

- Social History
  - No alcohol, no smoking, “not good with her diet”

Margaret

- Examination
  - BMI- 35.2
- VS
  - BP
    - 168/94 mmHg (mean) - left
    - 162/94 mmHg right
  - P-78
  - Fundus - AV narrowing
  - Neck- no bruit
  - Heart- PMI not displaced
  - Abdomen- no bruit, obese
  - Extremities – edema 1+ bilaterally

Racial Differences in Hypertension and Stroke Risk

- Stroke is 2-3 x more common in blacks than in whites aged 45-65
- REasons for Geographic And Racial Differences in Stroke (REGARDS) study
  - 27,748 black and white participants (normotensive, prehypertension, or stage 1 hypertension) followed 4.5 years
  - 10 mmHg difference associated with
    - 8% increased stroke risk in whites
    - 24% increased stroke risk in blacks
- These racial differences, coupled with higher prevalence, poorer control of hypertension in blacks, may account for much of the racial disparity in stroke risk


Margaret: Next Steps

How would you treat her hypertension?

1. Lifestyle management only
2. ACE inhibitor monotherapy
3. Beta blocker monotherapy
4. Diuretic monotherapy
5. Combination therapy that includes a diuretic

Effective Approaches in Selected Populations: The Role of RAS Blockers

- As monotherapy, ACEIs, ARBs, and conventional beta-blockers are not as effective in black patients compared with white patients
- However, ACEIs and ARBs should be used in black populations where there is compelling evidence for their effectiveness in whites

<table>
<thead>
<tr>
<th>Populations Who May Benefit From ACEIs and/or ARBs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with renal disease ✓</td>
</tr>
<tr>
<td>Patients with left ventricular hypertrophy (LVH) without diabetes ✓</td>
</tr>
<tr>
<td>Patients with LVH with diabetes ✓</td>
</tr>
<tr>
<td>Patients with diabetic nephropathy ✓</td>
</tr>
<tr>
<td>Patients with heart failure ✓</td>
</tr>
<tr>
<td>Patients with diabetes without nephropathy (based on clinical practice) ✓</td>
</tr>
</tbody>
</table>

- Additionally, the ACEI ramipril reduces the risk of fatal/nonfatal serious arrhythmic events in high-risk patients without clinical heart failure or overt left ventricular systolic dysfunction

**Hypertension in African-Americans**

**Slowing GFR Decline**

AASK (African-American Study of Kidney Disease and Hypertension)
- Amlodipine vs ramipril
  - Major benefit of RAS blockade is in pts with heavy proteinuria (regardless of race)
  - AA with non-DM CKD should have ACE inhibitor
  - <2 mmHg difference in SBP between CCB vs ACEI
- Add-on therapy included diuretic (attenuated racial difference)
- There is no evidenced-based advantage of lowering BP to less than 140/90 mmHg


**Hypertension Treatment in African Americans**

- Traditionally, CCBs and diuretics are preferred to BB, ACE-I and ARBs (RAS agents)
- Most patients will require additional therapy- especially those patients with co-existing morbidities
- Home monitoring improved control greater than usual care (MAP-dec 9.6 mmHg versus inc in 5.2 mmHg in usual care)


**Back to Jerry**

Jerry - 10 Years Later

- He is now 50 years old
- His SBP has been creeping up over the last year
  - mean HBPM: 154/78 mmHg
- Current meds
  - Lisinopril 40 mg daily
  - Chlorthalidone 25 mg daily
  - Amlodipine 10 mg daily
  - Atenolol 25 mg bid
  - Atorvastatin 40 mg daily

Jerry

- Examination 5’9” 242 pounds BMI- 35.7
- Mean office BP 166/92 mmHg P=74
  - Central obesity-circumference 45 inches
  - Neck-without carotid bruit
  - Heart-soft 1/6 systolic murmur no S3
  - Good distal pulses
- Labs
  - Creatinine 1.4 mg/dL
  - Electrolytes and other labs WNL

Question

Resistant hypertension is defined by:

1. Uncontrolled BP despite a regimen of 3 or more drugs including a diuretic
2. Controlled BP achieved on at least 4 drugs
3. Controlled BP achieved only with IV therapy
4. All of the above
5. 1 and 2 only

Resistant Hypertension

- Uncontrolled blood pressure in hypertensive patients despite treatment with optimal doses of 3 or more antihypertensive medications, of which one is a diuretic
- Also includes patients who are controlled on 4 medications
- Must exclude conditions that mimic resistant hypertension
- Prevalence: ~20% in patients with HTN (2005-2008) and increasing
  - More frequent in older, obese, male, AA, nonblack Hispanic

Mimics of Resistant Hypertension

- Poorly controlled hypertension
  - Inadequately treated or nonadherent
- Pseudo-resistant hypertension
  - Improper measurement technique
  - Confounding medications (NSAIDs), illicit drugs
  - Excessive alcohol consumption
  - Pain
  - White-coat effect
- Pseudo-hypertension in the elderly

Spironolactone in Resistant Hypertension

- The addition of spironolactone has been shown to be very effective in patients with resistant hypertension
- The average decrease in BP from multiple studies is 22/10 mmHg
- Adverse events include hyperkalemia, elevated creatinine and gynecomastia

Secondary Hypertension

Primary Aldosteronism

- Hypokalemia is important clue, however K+ can be normal in 40% of cases
- Plasma renin <1 ng/mL/hr and elevated plasma aldosterone makes diagnosis in most cases
- Optional confirmatory testing - salt loading with 24 hr collection of urine aldosterone (>14 ug/24 hrs) confirms
- Patients need be off aldosterone antagonists for at least 3 weeks prior to testing

Secondary Hypertension

Pheochromocytoma

- Most patients have symptoms - although extremely variable - but stereotypical:
  - Sustained or paroxysmal symptoms of forceful heart beat, pallor, tremor or diaphoresis
- However, most patients with these symptoms do not have pheochromocytoma
- Some controversy regarding single best test
  - Some institutions recommend 24-hour urine collection for metanephrines
  - Others utilize fractionated free plasma metanephrines
Secondary Hypertension

Sleep Apnea

- May be responsible for 15% of resistant hypertension
- Diagnosis with an AHI of >5 with symptoms
- Extent of clinical features may vary

<table>
<thead>
<tr>
<th>Daytime</th>
<th>Night-time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive daytime sleepiness</td>
<td>Snoring</td>
</tr>
<tr>
<td>Impaired concentration</td>
<td>Unrefreshing sleep</td>
</tr>
<tr>
<td>Irritability/personality</td>
<td>Choking episodes during sleep</td>
</tr>
<tr>
<td>Decreased libido</td>
<td>Witnessed apneas</td>
</tr>
<tr>
<td>Restless sleep</td>
<td>Nocturia</td>
</tr>
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</table>

Increased CV risk (36.7% OSAS vs 6.6% none)

Daytime Night-time

Excessive daytime sleepiness Snoring
Impaired concentration Unrefreshing sleep
Irritability/personality change Choking episodes during sleep
Decreased libido Witnessed apneas
Restless sleep Nocturia


Secondary Hypertension

Renovascular Disease

- Most common remedial cause of hypertension
- Can only be diagnosed after an intervention
- Renal artery stenosis (RAS) is NOT renovascular hypertension (RVH)
  - 32% normotensives: 56% over age 60 have advanced renal artery disease on angiogram but not RVH
  - Procedure on artery only impacted 25% of pts

Outcomes Question #1

Which of the following is TRUE?
1. Women tend to run higher home BP readings than men
2. Home and clinic BP readings tend to vary even in normotensive patients
3. Differences in home and clinic BP increase with age
4. The “white coat” effect is typically an increase in SBP of 5-10 mmHg
5. All of the above

Summary

- The diagnosis of hypertension requires proper measurement of BP and multiple readings
- Include out-of-office measurements in decision-making
- Use appropriate meds and dosing in treatment
- Recommendations for special populations are not patient specific
- Work-up resistant hypertension when appropriate
- Recognize the mimics of resistant hypertension and after excluding evaluate for resistant and secondary hypertension

Outcomes Question #2

In the treatment of hypertension, which is generally TRUE?
1. HCTZ and chlorthalidone are equally effective
2. Furosemide needs to be dosed twice daily
3. Edema seen with amlodipine is due to volume expansion
4. Ethacrynic acid should not be used in patients with sulfa allergy
Outcomes Question #3

Which of the following may be suggestive of renovascular disease as the cause of hypertension?

1. Reduced serum creatinine with ACE-I or ARB
2. Elevated plasma renin
3. Slow, steady increase in blood pressure over time
4. Strong family history of hypertension
5. All of the above