Endocrinologists as Hypertension Specialists

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CASE
62 yr old male with hypertension

HPI:
Diagnosed age 38
Rx initially atenolol
BP steadily required more meds

Home BP 155/90 mm Hg

PMHX:
Obesity: weight gain 30 pounds over 30 years
DM2 diagnosed 3 years ago, insulin requiring
OSA - CPAP not regular
Hypercholesterolemia
ANTI-HYPERTENSIVE DRUGS: 1st line

ACE Inhibitors/ Angiotensin Receptor Blockers

Beta-Blockers

Calcium Channel Blockers

Diuretics

Rule Out Endocrine Causes

- onset before age 25
- not controlled on 3 drugs, including diuretic*
- palpitations, headache, sweats (1/300)
- abdominal bruit; central obesity, striae
- adrenal nodule; hypokalemia
Evaluation for Endocrine Causes

- **Renal Vascular Hypertension**
  Clinical Suspicion

- **Pheochromocytoma**
  HISTORY

- **Cushing’s Syndrome**
  EXAM

- **Primary Aldosteronism**
  LAB

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**Renal Vascular Hypertension: Clinical Clues**

- Resistant hypertension (with hypokalemia)
- Accelerated/malignant hypertension
- Flash pulmonary edema
- Renal asymmetry (one small kidney; >1.5 cm)
- Systolic/ diastolic subcostal or flank bruit
- Worsening renal function, esp. on ACE inhibitor
- Demographics: older with vascular disease (20-50% will have RAS), smoking, hyperlipidemia. Young women: FMD
### Renal Vascular Hypertension Evaluation

**FUNCTION**

PRA, captopril-stimulated renin, renal vein renins:
- Not helpful

**IMAGING**

Doppler Ultrasound: least $, yields reliable velocities, waveforms when done well. Time consuming, requires technical expertise; difficult with obesity

*CTA: contrast risk with CRD; radiation; +/- predictive values comparable to MRA

*MRA: gadolinium risk with CRD [nephrogenic systemic fibrosis]

Angiography: gold-standard; invasive, (emboli)

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### Pheochromocytoma

#### Frequency of Symptoms

- **1** Headache ~60%
- **2** Sweating ~60%
- **3** Palpitations ~60%
- Pallor* 40%
- Nausea 30%
- Tremors 20%

* Ross EJ, Griffith DNW. Q J Med 1989
You Initiate the Workup

Plasma Metanephrines: convenient, sensitive

But ~15% false positives
24-hour fractionated metanephrines and catecholamines (highly sensitive and specific)

PHEO PEARLS

Neither suppression nor provocative testing needed

If pheo is causing dramatic spells, metanephrine levels should be clearly high – usually >4 times normal

Most are large, > 3 cm

MRI advantage: tissue characterization; no radiation
CT advantage: better spatial resolution

Plasma normetas: 15% false positives, esp with age. Given rarity, 97% with htn and increased norepi don’t have pheo.  

Young JCEM 2003
1. Provide Diagnosis

2. Non-CV therapy: psychotherapy, meditation, Resperate; anxiolytic, anti-depressant

3. Mixed alpha and beta blockade

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**Pseudopheochromocytoma**

299 out of 300?

You Continue the Workup

- Overnight Dexamethasone Test:
  - 1 mg dose at 11 pm
  - 8 am plasma cortisol

  Negative = plasma cortisol <1.8 mcg/dl

- 24-hour UFC
- Late night salivary cortisol x2
### When to Suspect Primary Aldosteronism?

- Hypokalemia (spontaneous, or new)
- Hypertension and an adrenal lesion
- Resistant hypertension
- Family h/o early onset hypertension, stroke

### Clinical Presentation

HTN. physical exam otherwise unremarkable

### Screening Test for Primary Aldosteronism

<table>
<thead>
<tr>
<th>Plasma Aldosterone / Plasma Renin Activity</th>
<th>before aldactone</th>
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<tbody>
<tr>
<td>PA (ng/dl)</td>
<td>PRA (ng Angl/ml/hr)</td>
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</table>

Most commonly adopted cutoff value: **30:1**  

*With PA ≥ 10 ng/dl: why?

** Better than ratio: interpret both values **
Hypertension Drugs: Main Effects on Plasma Renin Activity & Plasma Aldosterone

Diuretics: raise PRA, raise aldosterone

Beta Blockers: suppress renin
Clonidine: suppresses renin

ACEI/ ARBs: raise renin, especially acutely

CCBs: neutral (minimal fall in aldosterone)

MRAs: raise PRA and aldosterone. Must be withheld ~6 wks

Causes of Secondary Hypertension

- Obesity*
- Aging*
- Improper BP measurement
- White coat phenomenon
- Noncompliance
- Sleep apnea
- Chronic kidney disease (Cr >1.5 mg/dL)
- Thyroid or parathyroid disease
- Excess sodium intake
- Drugs: NSAIDs, illicit drugs, supplements, sympathomimetics, OCs
- Excess alcohol
- Primary aldosteronism, Cushing's, pheochromocytoma
BP Measurement

Oscillometric (electronic)  
Cuff is sensor

Auscultatory  
mercury vs aneroid

http://www.dableeducational.org/sphygmomanometers.html
http://www.bhsoc.org/bp-monitors/bp-monitors/

Your advice?

Encourage weight loss;
Diet review; nutritionist referral
Review sodium guidelines
Alcohol: reduce drinking
Encourage exercise
Encourage CPAP use nightly

Monitor home BP
HOME BLOOD PRESSURE Tracker

<table>
<thead>
<tr>
<th></th>
<th>1st morning BP Before pills</th>
<th>Repeat morning BP 3 minutes later</th>
<th>1st evening BP Before pills</th>
<th>Repeat evening BP 3 minutes later</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
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<td>2</td>
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<td>7</td>
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</tbody>
</table>

Normal BP: Average <135/85 mm Hg

Lifestyle Modification

<table>
<thead>
<tr>
<th>Modification</th>
<th>~SBP reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>5-20 mmHg/10 kg</td>
</tr>
<tr>
<td>DASH diet</td>
<td>8-14 mmHg</td>
</tr>
<tr>
<td>Na+ reduction</td>
<td>2-8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>4-9 mmHg</td>
</tr>
<tr>
<td>Moderate alcohol</td>
<td>2-4 mmHg</td>
</tr>
</tbody>
</table>
LIFESTYLE MODIFICATION
Initial Therapy (Attempts)

• Exercise: ≥ 30 min 5/wk; 60 min daily?

• Sodium restriction (<2.3 gm / <1.5 gm/day*)
  *Htn, >50 years, DM, blacks, CKD
  Americans eat 3.5-4 grams sodium/day

• Moderate alcohol (1-2/day)

ANTI-HYPERTENSIVE DRUGS
1, 2 and 3: A, C, D

ACE Inhibitors/ Angiotensin Receptor Blockers
renal protection. DM. CHF. LVH. post MI
albuminuria reduction
increase insulin sensitivity

lipids

hyperkalemia. pregnancy. bilateral RAS.
cough. angioedema
**Calcium Channel Blockers**
- effective in blacks, elderly, DM
  - effective in low-renin hypertension
  - renal protection
  - angina. Raynaud’s syndrome

- insulin sensitivity
- lipids
- edema

**Diuretics**
- effective, esp in CHF, ISH, blacks, DM
  - hypokalemia
  - hyperglycemia
  - hyperlipidemia
  - hyperuricemia

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**# 4, 5**

**Beta-Blockers**
- effective in htn, coronary disease, migraine. thyrotoxicosis. essential tremor. CHF. MI. perioperative HTN
  - asthma. heart block. insulin sensitivity & glucose tolerance

  *Vasodilating BB*

**MRA**
- effective; esp post MI and CHF; resistant htn
- gynecomastia. high K+ esp with renal insufficiency
**Clonidine**
- transdermal once weekly
- fatigue, depression, xerostomia, withdrawal syndrome

**Alpha-Antagonists**
- increase insulin sensitivity and glucose tolerance
- slightly lower lipids
- prostatism

- orthostatic hypotension. CHF lacking controlled intervention trial data

**Hydralazine**
- QID dosing; tachycardia; lupus-like syndrome; unpredictable response

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### Spironolactone for Resistant Htn

**ACD+**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Diastolic</th>
<th>Systolic</th>
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</thead>
<tbody>
<tr>
<td>Baseline (n=314)</td>
<td>77 ± 10</td>
<td>143 ± 15</td>
</tr>
<tr>
<td>Placebo (n=274)</td>
<td>78 ± 10</td>
<td>143 ± 15</td>
</tr>
<tr>
<td>Spironolactone 25-50 mg (n=285)</td>
<td>80 ± 10</td>
<td>141 ± 15</td>
</tr>
<tr>
<td>Doxazosin 4-8 mg (n=282)</td>
<td>82 ± 10</td>
<td>139 ± 15</td>
</tr>
<tr>
<td>Bisoprolol 5-10 mg (n=285)</td>
<td>83 ± 10</td>
<td>138 ± 15</td>
</tr>
</tbody>
</table>

*p<0.001 c/w placebo*

**HOME BP**

**12 wks Crossover**

n=285

*Bryan Williams et al Lancet 2015*
Primary Aldosteronism:
Endocrine Society Clinical Guidelines
2016

Patients with Hypertension that are at Increased Risk for PA
PA Unlikely
- ARR to Detect Cases (1)
+ Confirmatory Testing (1)
PA Unlikely
- Confirmatory Testing (1)
+ Adrenal CT (1)
If Surgery Desired
- If Surgery Not Desired
AWS (1)
Bilateral
- Unilateral
Treat with MR Antagonist (1)
Marked PA, Young Age, and + CT (2)
Treat with MR Antagonist (2)

+ K+ < min
+ PAC > 20 ng/dL
Patient Unwilling/ Unable to Proceed

Where Are We?
JNC7 Blood Pressure Classification
2003

<table>
<thead>
<tr>
<th>Category</th>
<th>SBP</th>
<th>and/</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td></td>
<td>&lt;80</td>
</tr>
<tr>
<td>Prehypertension</td>
<td>120–139</td>
<td>or</td>
<td>80–89</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140–159</td>
<td>or</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥160</td>
<td>or/</td>
<td>≥100</td>
</tr>
</tbody>
</table>

JNC 8 Recommendations
2014

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Target SBP (mm Hg)</th>
<th>Target DBP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60 years</td>
<td>&lt;150</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&lt; 60 years</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&gt; 18 years with CKD</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>&gt; 18 years with diabetes</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>

CKD = chronic kidney disease; DBP = diastolic blood pressure; SBP = systolic blood pressure

**SPRINT**

Systolic Blood Pressure Intervention Trial

**Background:** Optimal target for SBP lowering uncertain

Randomized 9300: SBP 120 vs 140 mm Hg

Stopped at 3.3 years; planned average 5 year f/u

“Landmark NIH study… Milestone…. Major Advance… SPRINT shows intensive blood pressure management may save lives”

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**Systolic Blood Pressure over Course of the Trial**

**Average SBP during follow-up:**

- **Standard:** 134.6 mm Hg
- **Intensive:** 121.5 mm Hg

**MDs chose drugs**
SPRINT: MAIN RESULTS

Primary Outcome

Death from any Cause

25% MI, ACS, Stroke, CHF, CV death

27% ANY DEATH

243 vs 319 NNT 61

155 vs 210 NNT 90

DIABETES GOALS?

“More uncertainty about appropriate BP targets in diabetic patients” Feb 2016
2003
JNC7  <130/80 mm

2013
ADA raised target to
<140/90 mm Hg

2016…
Goal may revert to
<130/80 mm Hg

SUMMARY

MANY CAUSES of resistant hypertension
Obesity      Salt
White Coat   Sleep Apnea   Alcohol
Renovascular disease

Primary aldosteronism
Cushing’s
pheochromocytoma

THOROUGH EVALUATION crucial,
including history, habits, exam and labs
LOWERING BP reduces risk, prevents death: assess risk and BP

CHANGING GOALS
140/90 still. 135/85, 130/80
Individualized; ranges

LIFESTYLE, COMBINED REGIMENS crucial