Getting to Systolic and Diastolic Blood Pressure Goals

Bryan Batson, MD
Case Study

D.C. is a 61-y/o male smoker who presents for a second opinion in regards to his hypertension. Despite 2 months of lifestyle modifications, his BP remains 162/92. Assuming his work-up is otherwise normal, you decide to initiate pharmacologic treatment. What would be your choice for initial therapy?

A. Thiazide diuretic
B. ACEI + thiazide diuretic
C. Beta blocker + thiazide diuretic
D. ACEI + CCB
E. ACEI + ARB
## Goal Blood Pressures

<table>
<thead>
<tr>
<th>Condition</th>
<th>Goal Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>&lt;140/90 mmHg</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Chronic Kidney Failure</td>
<td>&lt;130/80 mmHg</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>&lt;130/80 mmHg</td>
</tr>
</tbody>
</table>

Combined Efforts of the Provider & the Patient Using Combined Therapies are Needed to Reach Goal BP

Complimentary Fixed Combination Drug Therapy

Goal Bp

Provider /Patient Communication & Expectations

Lifestyle Changes
Combined Efforts of the Provider & the Patient Using Combined Therapies are Needed to Reach Goal BP

Complimentary Fixed Combination Drug Therapy

Provider /Patient Communication & Expectations

Lifestyle Changes
Life Style Changes to Improve Blood Pressure Control

• Dietary Approach to Stop Hypertension (DASH) Diet
• Weight Loss for the Overweight
• Reduction in Alcohol Intake to no more than 1 ounce per day
• Dietary Sodium Restriction
• Increased Daily Physical Activity

Benefit of Life Style Modifications in Pre-hypertension

- **DASH Diet**
  - Weight Loss: -5.5/3 mmHg

- **Sodium Restriction**
  - -2.9/2.2 mmHg

- **Alcohol Reduction**
  - -1.2/0.7 mmHg

Ref: Ard & Svetsky. Am Heart J 149:804, 2005
**Dietary Approaches to Stop Hypertension**

The DASH Eating Plan

**DASH Diet**
- Fruits & Vegetables
- Low Fat Dairy
- Reduce Cholesterol
- Rich in Potassium & Calcium

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Goal BP

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Lifestyle Changes
Combined Efforts of the Provider & the Patient Using Combined Therapies are Needed to Reach Goal BP

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Lifestyle Changes
JNC 7 Algorithm for the Treatment of Hypertension

Lifestyle Modifications

Not at Goal Blood Pressure (<140/90 mm Hg) (<130/80 mm Hg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Without Compelling Indications

Stage 1 HTN (SBP 140–159 or DBP 90–99 mm Hg)
Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.

Stage 2 HTN (SBP ≥160 or DBP ≥100 mm Hg)
2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)

With Compelling Indications

Drug(s) for Compelling Indications
Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

Not at Goal Blood Pressure

Optimize dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with HTN specialist.

JNC-7 First Step Antihypertensive Monotherapy for Uncomplicated Hypertension

- Angiotensin Converting Enzyme Inhibitors
- Angiotensin Receptor Blockers
- Calcium Channel Blockers
- Thiazide Diuretics
- Beta Blockers
**Life Style Changes:**

- Weight Reduction for Excessive Body Weight
- Low Salt Diet & South Beach Diet / DASH
- Reduced Alcohol Intake
- Increased Physical Activity
- Smoking Cessation

**COSEHC Global Approach to CV Disease**

<table>
<thead>
<tr>
<th>Hypertension</th>
<th>Hyperlipidemia</th>
<th>Hyperglycemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>ACE/ARB</td>
<td>Statins</td>
</tr>
<tr>
<td>Step 2</td>
<td>CCB</td>
<td>Fibrates</td>
</tr>
<tr>
<td>Step 3</td>
<td>Thiazide</td>
<td></td>
</tr>
</tbody>
</table>

Combination therapy – many African Americans will need to start on at least two medications in order to successfully lower their blood pressure.

European Society of Hypertension
Arterial Hypertension Guidelines
2009 Update

The combination of two antihypertensive drugs may offer advantages also for treatment initiation, particularly in patients at high cardiovascular risk in which early BP control may be desirable.
## Patient Benefits of Fixed-dose Combination Therapy for Hypertension

<table>
<thead>
<tr>
<th>Benefit</th>
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<tbody>
<tr>
<td>✓ Less Pills</td>
</tr>
<tr>
<td>✓ Increased Blood Pressure Control Efficacy</td>
</tr>
<tr>
<td>✓ Better Tolerability vs. Higher Dose Monotherapy (Possibly Less Side Effects)</td>
</tr>
<tr>
<td>✓ Improved Compliance</td>
</tr>
<tr>
<td>✓ Easy Titration Process</td>
</tr>
<tr>
<td>✓ Fewer Insurance Co-payments</td>
</tr>
</tbody>
</table>

Combining Antihypertensive Drugs

- Diuretics
- B-Blockers
- AT1 Blockers
- Alpha-blockers
- Calcium Antagonists
- Renin Blocker
- ACE Inhibitors
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Combining Antihypertensive Drugs

- Diuretics
- B-Blockers
- AT1 Blockers
- Calcium Antagonists
- ACE Inhibitors
- Alpha-blockers
- Renin Blocker
Poor Antihypertensive Combinations

\( \beta \)-Blocker & \( \alpha_2 \)-CNS Stimulant
Not additive
Potential for paradoxical BP Rebound hypertension

\( \beta \)-Blocker & Verapamil / Diltiazem
Potential excessive bradycardia
Possible heart block
Systolic heart failure

\( \alpha_2 \)-CNS Stimulant & \( \alpha_1 \)-Blocker
Not additive

Combining Antihypertensive Drugs

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Concomitant Effectiveness of Antihypertensive Drugs

Thiazide Diuretics

- B-Blockers
- Alpha-blockers
- Renin Blocker
- Calcium Antagonists
- AT1 Blockers
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Concomitant Effectiveness of Antihypertensive Drugs

- Diuretics
- B-Blockers
- AT1 Blockers
- Calcium Antagonists
- ACE Inhibitors
- Alpha-blockers
- Renin Blocker
ACCOMPLISH Trial

- 11,506 high risk hypertensive patients randomized benazepril & amlodipine vs. benazepril & hydrochlorothiazide
- 42 month trial
- Primary end point composite cv death, non-fatal MI or stroke and hospitalization for angina, coronary artery revascularization and resuscitation sudden death were reduced to a greater and significant degree by the ACEI/CCB compared to ACEI/Thiazide (Relative risk reduction was 20% (hazard ratio, 0.80; 95% CI, 0.72 to 0.90; P<0.001).

ACCOMPLISH Trial
Effect of Treatments on Systolic & Diastolic BP Over Time

Blood Pressure (mm Hg)

ACCOMPLISH = Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension.
ACCOMPLISH Trial

Time to First Occurrence of Primary Endpoint*

*Composite of death from cardiovascular causes, nonfatal MI, nonfatal stroke, hospitalization for angina, resuscitation after sudden cardiac arrest, and coronary revascularization.


Patients With Primary Events (%)

<table>
<thead>
<tr>
<th>Months</th>
<th>Benazepril + HCTZ</th>
<th>Benazepril + amlodipine</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>12</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>18</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>24</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>30</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>36</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>42</td>
<td>16</td>
<td>16</td>
</tr>
</tbody>
</table>

HR (95% CI): 0.80 (0.72, 0.90)
Concomitant Effectiveness of Antihypertensive Drugs

Diuretics

B-Blockers

AT1 Blockers

Alpha-blockers

Calcium Antagonists

ACE Inhibitors

Renin Blocker
Concomitant Effectiveness of Antihypertensive Drugs

- Diuretics
- B-Blockers
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- Alpha-blockers
- Renin Blocker
- ACE Inhibitors
Monotherapy vs Fixed Combination of Olmesartan & Amlodipine

1940 Patients
8 weeks
Baseline Bp
164/102 mmHg
79% Stage 2

Concomitant Effectiveness of Antihypertensive Drugs
Does Blocking the Renin Angiotensin System (RAS) at Multiple Levels Lead to Complementary Effects on Bp?

Angiotensinogen

Non-renin (eg tPA)

Angiotensin I

Non-ACE (eg chymase)

Angiotensin II

ARB

AT$_1$

AT$_2$

Renin

ACE

Bradykinin

Inactive peptides

Adapted from Hypertension Online Website. http://www.hypertension-online.com
Concomitant Effectiveness of Antihypertensive Drugs

Diuretics

B-Blockers

AT1 Blockers

Alpha-blockers

Calcium Antagonists

ACE Inhibitors

Renin Blocker
ONTARGET was a randomized, double-blind trial (n=25,620) comparing single drug therapy against combination drug therapy. Patients were > 55 years (mean 66.4 years) with no evidence of heart failure but with a history of heart disease, diabetes, HTN, PAD and stroke or TIA. After randomizing into 3 groups participants were given ramipril 10 mg daily, Telmisartan 80 mg daily or a combination of the two. Primary endpoints were CV death, MI, Stroke or hospitalization for HF. Mean follow up = 56 months.

<table>
<thead>
<tr>
<th>Bp Changes</th>
<th>Ramipril</th>
<th>Telmisartan</th>
<th>Combination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>-6.0</td>
<td>-6.9</td>
<td>-8.4</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-4.6</td>
<td>-5.2</td>
<td>-6.0</td>
</tr>
</tbody>
</table>

Results

• Ramipril and Telmisartan were equally effective at reducing primary outcomes – RR = 1.01 [ 95% CI, 1.01 (0.94 – 1.09)]

• Ramipril v combination therapy were equally effective at reducing primary outcomes – RR =0.99 [95% CI, (0.92 – 1.07)]

Conclusions

• In patients without HF but with pre-existing CVD co-morbidities the use of an ACEi in combination with an ARB does not reduce the primary outcomes compared to single drug therapy.

Concomitant Effectiveness of Antihypertensive Drugs

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Concomitant Effectiveness of Antihypertensive Drugs

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- ACE Inhibitors
Blood Pressure Effect of Aliskiren 300 mg, Valsartan 320 mg, and Both

**p < 0.0001 vs placebo; ‡p < 0.0001 vs aliskiren/valsartan combination.**

msDBP, mean sitting diastolic blood pressure; msSBP, mean sitting systolic blood pressure. 8 weeks

ALTITUDE was a randomized, double-blind trial (n=25,620) evaluating the efficacy of adding aliskiren on top of ACE-inhibitor or angiotensin receptor blocker (ARB) therapy in patients with Type 2 diabetes and renal impairment compared with placebo add-on. Primary end points were time to develop: CV death, resuscitated death, nonfatal MI, nonfatal CVA, CHF hospitalization, ESRD, renal death, doubling of serum creatinine.

• Results:
  – Trial terminated in December 2011 due to increased incidence of non-fatal stroke, renal impairment, hyperkalemia, & hypotension
  – April 2012 label change:
    – Aliskiren contraindicated in diabetic patients who are also on an ACEI or ARB
    – Warning to avoid aliskiren in combo with ACEI or ARB in patients with GFR <60
  – July 2012: Combination pill of aliskiren+valsartan no longer available

Source: www.fda.gov/drugs/drugsafety
Concomitant Effectiveness of Antihypertensive Drugs

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**Triple Therapy for Hypertension**  
*(CCB, ARB, Thiazide)*

![Graph showing blood pressure reduction with triple therapy](image)

- **Am/Hctz 10/25**
- **Am/Val 10/320**
- **Val/Hctz 320/25**
- **Am/Val/Hctz 10/320/25**

2060 Patients  
Av 53 Yrs Old  
55% Men  
8 weeks  
Mean Seated Bp  
169.9/106.5 mmHg

* * p<0.001 Compared to Am/Val/Hctz

Ref: Calhoun, Hypertension 54:32, July 2009
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- Alpha-blockers
Atenolol Meta-analyses

• Meta analysis originally published in *Lancet* in 2004
• Data was re-examined and published again in *Journal of American College of Cardiology* in August 2007
Atenolol Meta-analyses

All-Cause Mortality

Cardiovascular Mortality

MI

Stroke

Relative Risk (95% CI)

0.5

1.0

1.5

Atenolol Better

Placebo / Other Antihypertensive Better

Atenolol vs placebo or no treatment

4 studies (n=6825)

Atenolol vs other antihypertensive therapy

5 studies n=17,671

Trials included in meta-analysis vs placebo: Treatment of Hypertension in Elderly Patients in Primary Care (HEP); Dutch Transitory Ischemic Attack Trial; Tenormin After Stroke and TIA (TEST); Medical Research Council Trial of Treatment of Hypertension in Older Adults (MRC Old). Trials included in meta-analysis vs other antihypertensive agent: MRC Old; UKPDS; European Lacidipine Study of Atherosclerosis (ELSA); Heart Attack Primary Prevention in Hypertension Trial (HAPPHY); Losartan Intervention for Endpoint Reduction Study (LIFE).

Selective beta-blockers (propranolol, metoprolol, & atenolol) have not reduced the risk of heart attack when compared to other antihypertensive therapies in hypertensive patients without coronary artery disease.

Beta Blockers reduce the risk for stroke less than other antihypertensive agents.

Beta Blockers when compared to ARB or CCB therapy, have been less effective in preventing strokes and other cardiovascular events, even when combined with a diuretic.

Side effects from Beta Blockers are greater (including the risk for Type 2 diabetes mellitus) compared to ACE inhibitors, ARBs and CCBs.

Combining Antihypertensive Drugs

- Diuretics
- B-Blockers
- AT1 Blockers
- Calcium Antagonists
- Alpha-blockers
- ACE Inhibitors
- Renin Blocker
Initial Antihypertensive Therapy

Stage 1
140/90- < 160/100
- ACEi, ARB, CCB or Thiazide
- Life Style Changes

Stage 2
>=160/100
- Fixed Combination
- Life Style Changes

or

Bp> 20/10 above Goal
- Fixed Combination
- Life Style Changes
Case Study

- D.C. is a 61-y/o male smoker who presents for a second opinion in regards to his hypertension. Despite 2 months of lifestyle modifications, his BP remains 162/92. Assuming his work-up is otherwise normal, you decide to initiate pharmacologic treatment. What would be your choice for initial therapy?
  A. Thiazide diuretic
  B. ACEI + thiazide diuretic
  C. Beta blocker + thiazide diuretic
  D. ACEI + CCB
  E. ACEI + ARB
Combined Efforts of the Provider & the Patient Using Combined Therapies are Needed to Reach Goal BP

Complimentary Fixed Combination Drug Therapy

Provider / Patient Communication & Expectations

Lifestyle Changes
Combined Efforts of the Provider & the Patient Using Combined Therapies are Needed to Reach Goal BP

Provider /Patient Communication & Expectations

Complimentary Fixed Combination Drug Therapy

Goal Bp

Lifestyle Changes
Evidenced Based Expectations

**Stage 1 Hypertension**
- Bp Goal < 140/90 mmHg
- 2 classes Antihypertensives *may* be needed
- Reach Goal within 3 months
- Life Style Changes Can Reduce Number Bp Medications

**Stage 2 Hypertension**
- Bp Goal < 140/90 mmHg
- 4 classes Antihypertensive *may* be needed
- Reach Goal within 3 months
- Life Style Changes Can Reduce Number Bp Medications

Ref. Moore, MA. Clinical Hypertension 11:1 January 2009
Provider Check List to Improve BP Control

• Communicate BP goal to the patient and include patient’s Rx bottle

• Educate and Involve the patient’s family, spouse, children on the BP goals

• Emphasize the Importance of Lifestyle changes

• Enlist the patient’s involvement in their own care by having them measure and record their out-of-office BP values and fax them back to your office.

Adapted from Table II Cushman & Basile. “Getting to Goal BP: Why Aren’t We?” *J Clin Hypertens* 2006; 8:865-872
Provider Check List to Improve BP Control

- Patients should always bring medication bottles to clinic.
- Address side effects—"If there is any reason why you cannot take the medication, please call the office and I will get back with you"
- Simplify regimens using combination tablets
- Reduce cost when it’s an issue
- Regular follow-up appointments using telephone reminders 2 days before the appt.
- A missed appointment is a missed opportunity—Always call and ask why?

Adapted from Table II Cushman & Basile. “Getting to Goal BP: Why Aren’t We?” J Clin Hypertens 2006; 8:865-872
Convey the message....
Lowering Blood Pressure Saves Lives

• For every 12mm that blood pressure is decreased over 10 years:
  – 1 death is prevented out of 9 patients with diabetes
  – 1 death is prevented out of 12 patients with coronary artery disease
  – 1 death is prevented out of 20 otherwise healthy patients with no comorbidities

Bottom Line........

In the words of Dr. Guyton....

“Just get it down, stupid!”*

*except don’t use Atenolol
Extra Slides
For your consideration..  
“The Batson Approach”

- **ACEI/ARB**
  - May need higher doses in ‘low-renin’ pts
  - Don’t forget to check a K+ and creat before and 2-3 weeks after starting

- **CCB**
  - DHP preferred unless pt has h/o migraine or palps
  - Furosemide (loop) should be dosed bid if being used for HTN
  - Don’t use in combo with non-DHP CCB
  - Non-selective BB preferred due to better metabolics

- **Thiazide diuretic**
  - Chlorthalidone preferred over HCTZ due to longer half-life
  - Use sooner if clinical indication i.e. CAD
  - Use with extreme caution with frequent lab

- **Beta blocker**
  - Works well with HCTZ in patient’s with OSA
  - Minoxidil: hirsutism
  - Use with extreme caution with frequent lab

- **Aldosterone blocker**
  - Caution men about gynecomastia with spiro
  - Hydralazine: +ANA
  - Often cause orthostatic hypotension; contraindicated in pts at high risk for falls

- **Direct vasodilator**
  - Can cause reflex tachycardia, fluid retention
  - Dose at night

- **Alpha blocker**
  - Good option for men with BPH, but interact with PDE-5 inhibitors
  - Guanfacine preferred over Clonidine due to longer half-life (less rebound)

- **Sympatholytic**
  - Clonidine patch an option for pts with rapid GI transit time
  - Guanfacine preferred over Clonidine due to longer half-life (less rebound)

- **SSRI?**
  - Don’t forget to check a K+ and creat before and 2-3 weeks after starting

- **Avoid if pregnancy a possibility**
  - Use sooner if clinical indication i.e. CAD

- **Unless patient has gout or sulfa allergy**
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- **Use sooner if clinical indication i.e. CAD**
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When medications aren’t enough

- Resistant Hypertension
- Secondary Hypertension
- Pseudo-resistance
Resistant Hypertension is defined as blood pressure that remains above goal despite concurrent use of 3 agents of different classes at optimal doses, one of which must be a diuretic.
When medications aren’t enough

Resistant Hypertension

Secondary Hypertension

Pseudo-resistance

Can be due to:
- Poor BP technique
- Pseudohypertension
- Poor adherence
- Whitecoat effect
- Interfering substances
When medications aren’t enough

- Resistant Hypertension
- Secondary Hypertension
- Pseudo-resistance
Is it Secondary HTN?

Thyroid (hyper- or hypo-thyroidism)
Tumor (increased intracranial pressure)
Coarctation of aorta
Cushing’s Syndrome
Renal artery stenosis
Renal parenchymal disease (i.e. diabetic nephropathy)
Aldosteronism (primary or secondary)
Acromegaly
Pheochromocytoma (or pseudopheochromocytoma)
Polycythemia (primary or secondary i.e. COPD)
Sleep apnea
Substances (NSAIDs, decongestants, etc, etc.)
Patient #1

“Fast-food Frannie”

- 62y/o BF referred by OB because of consistently elevated BPs that had not improved after several medication trials
- Reports compliance with all of her medications
- Says that she “craves” salt. Typically eats fast food once or twice daily and drinks “4 or 5” cokes every day
- Has nocturia 3-4 times per night

Meds:
Amlodipine/Benazepril 5/40 qd

Physical Exam:
BP: 144/92 RA, 142/92 LA,
P: 72, Ht: 5’ 8”, Wt: 132#
Gen: WDWNBF in NAD
CV: RRR without mgr, 1+ bilateral LE edema with intact pulses

Labs/Imaging:
BMP: normal
CBC: normal
UA: normal
24 hr urinary Na: 5,630 mEq/L/day
(normal 15 – 250 mEq/L/day)
Patient #1

“Fast-food Frannie”

Diagnosis?

Essential HTN worsened by excessive sodium intake

Pearls:

1. Dietary history is very important
2. Diuretics are essential component of treatment in high-sodium diets
Patient #2

“Carotid Charlie”

- 60y/o WM referred by cardiology to help get BP down in preparation for L carotid endarterectomy
- Pt has h/o CRI, CABG at 42y/o and R CEA at 53y/o
- BP chronically elevated and has not responded to multi-drug regimen for many years
- Olmesartan added to his regimen 6 wks ago, but BP’s remain refractory

Meds:
- Olmesartan 40mg qd, HCTZ 25mg qd, Catapress TTS3 qwk, Doxazosin 1mg bid, Lopressor 50mg bid, Clopidogrel, Atorvastatin, ASA

Physical Exam:
- BP: 158/88 RA, 152/86 LA
- P: 64, Ht: 5’ 11”, Wt: 228#
- CV: RRR with SEM and B carotid bruits as well as abdominal bruit; distal pulses 1+ and =, trace edema

Labs/Imaging:
- BMP: Na 138, K 3.8, BUN 32, creat 2.44
- UA: normal
- Creatinine 4 months prior: 1.63
Patient #2  “Carotid Charlie”
Diagnosis?

Bilateral renal artery stenosis

Pearls:

1. Consider RAS is patients with h/o vascular dz
2. Check K and creat before starting and 2-3 weeks after starting and ACEI/ARB
3. HTN unresponsive to multi-drug regimen can signal secondary causes
Patient #3

“Crampy Carol”

- 75y/o BF referred for refractory HTN despite an aggressive regimen for many years
- Reports that she was diagnosed with HTN in her early 30’s and that her BP has never been consistently controlled
- Strong family history of hypertension
- Complains of muscle cramps and has been hospitalized twice due to “low potassium levels”

**Meds:**
- Olmesartan 40mg qd, Lasix 40mg bid, Metoprolol 50mg bid, Diltiazem 360mg qd, Minoxidil 2.5mg bid, Aldomet 250mg tid, Clonidine 0.1mg tid, KCl 40mEq bid

**Physical Exam:**
- **BP:** 176/90 RA, 170/92 LA
- **P:** 52, **Ht:** 5’ 5”, **Wt:** 192#
- Exam completely normal

**Labs/Imaging:**
- **BMP:** Na 136, K 3.3, Co2 30, creat 0.8
- **CBC:** normal
- **UA:** normal
- **EKG:** normal
Patient #3

“Crampy Carol”

Renin activity level = <0.15 ng/ml/hr
Aldosterone = 26.9 ng/dl

(normal 0.15 – 2.33)
(normal 1 -16)

Aldosterone:Renin ratio >179.39
Diagnosis?

Primary Hyperaldosteronism

Pearls:

1. Hyperaldosteronism is present in up to 20% of patients with refractory hypertension

2. Consider hyperaldosteronism in patients with unprovoked hypokalemia or those with refractory hypokalemia
Patient #4

“Tired Trey”

- 9 y/o BM referred because of persistently elevated BPs that were being monitored by school nurse
- Started on HCTZ but BP’s still 140-150/80-90
- Strong family history of hypertension
- Very poor diet and no exercise
- Having severe trouble in school because he is unable to stay awake during class

**Meds:**
- HCTZ 25mg qd

**Physical Exam:**
- **BP:** 134/92 RA, 130/90 LA, 136/94 RL, 136/94 LL
- **P:** 96, **Ht:** 4’ 5”, **Wt:** 136#
- **Gen:** obese BM in NAD
- **HEENT:** large tonsils
- **CV:** RRR without mgr, no edema

**Labs/Imaging:**
- **BMP:** normal
- **CBC:** Hct 58
- **UA and tox screen:** normal
- EKG, renal u/s and echo normal
Patient #4  “Tired Trey”
Diagnosis?

Obstructive Sleep Apnea

Pearls:

1. Take a sleep history in all hypertensive patients regardless of age
2. Sleep apnea (both central and obstructive) usually causes diastolic hypertension
3. Occasionally will see polycythemia on lab with sleep apnea
Patient #5

“Stony Sally”

- 57y/o WF with h/o nephrolithiasis referred by Urology due to elevated BPs
- Has never had regular checkups but has been told by OB over last 2 years that BPs are slightly elevated
- Both parents have hypertension
- Fair dietary and exercise habits

**Meds:**
Paroxetine 30mg qd

**Physical Exam:**
- BP: 160/98 RA, 162/98 LA
- P: 92, Ht: 5’ 5”, Wt: 188#
- Remainder of exam normal

**Labs/Imaging:**
- BMP: Na 147, K 4.6, BUN 17, creat 1.0
- Ca 12.1 (normal 8.5 – 10.5)
- TSH: normal
- UA: normal
- Phos 2.0 (normal 2.7 – 4.5)
- PTH 139.3 (normal 11 – 80)
Patient #5  “Stony Sally”
Patient #5

“Stony Sally”

Diagnosis?

Secondary HTN from Hyperparathyroidism

Pearls:

1. Both thyroid and parathyroid abnormalities can lead to secondary hypertension
Patient #6

“Jogger Jim”

Meds:
- Amlodipine 10mg qd
- OlmesartanHCT 40/25 qd

Physical Exam:
- BP: 138/92 RA, 136/96 LA
- P: 60, Ht: 5’11”, Wt: 158#
- Gen: WDWN fit WM in NAD
  - Completely normal exam

Labs/Imaging:
- BMP: Na 141, K 4.4, BUN 9, creat 1.1
- TSH: normal
- UA: trace blood, no protein, no WBC
- EKG: normal
- Echo: mild LVH and mild MVP

• 27y/o WM referred because patient wanted further explanation as to why he needed antihypertensive therapy at his age
• Jogs 4-6 miles daily and limits his sodium aggressively
• No family h/o HTN
• Denies any drug use, caffeine, NSAIDs, steroids, or supplements
• Noticed two episodes of blood in his urine after half-marathons
Patient #6

“Jogger Jim”
Diagnosis?

Renal cell carcinoma

Pearls:

1. Even though HTN is extremely common, consider secondary causes in young, healthy patients with no family history

2. Urine studies need to be included in standard workup of hypertension
Patient #7

• 60y/o WM with COPD re-referred 3/2012 for abrupt worsening of BP over previous 2 months
• Initially seen in 2005, and pt responded nicely to tx
• Last seen in 12/07 with BP 122/70 on lisinopril 20mg qd and HCTZ 25mg qd
• In 2/12, began having severe HA’s and SBPs >200; PCP added amlodipine 5mg qd
• 4 days later wife stopped the Amlodipine because it was causing pt to be very “confused”

Meds:
Lisinopril 20mg qd, HCTZ 25mg qd

Physical Exam:
BP: 182/94 RA, 182/90 LA
P: 94, Ht: 6’ 0”, Wt: 260”
CV: RRR with SEM, no carotid bruits
Resp: coarse BS throughout
MS: A & O x4 with fair memory

Labs/Imaging:
BMP: normal
CBC: normal
UA: normal
EKG: old Q waves, NS ST-T changes
Patient #7  “Confused Carl”
Diagnosis?

Secondary HTN from brain metastases

Pearls:

1. Hypertension usually does not cause headaches
2. Amlodipine usually does not cause confusion
3. Abrupt worsening of previously well-controlled BP can signal secondary causes
Patient #8

“Student Sammy”

- 16y/o BM referred because BPs unresponsive to ARB therapy
- Mother reports that patient was started on Valsartan by school nurse approx. 6 years prior but BP has remained consistently elevated
- Has a 22 y/o sister who is on dialysis; both parents with HTN
- No records of any previous labwork

Meds:
- Amlodipine 10mg qd,
  ValsartanHCT 320/25 qd

Physical Exam:
- BP: 172/120 RA, 182/120 LA,
  180/118 RL, 176/122 LL
- P: 88, Ht: 5’ 9”, Wt: 290#
- Gen: WDWN obese BM
- CV: RRR without mgr, no abd bruit; no edema, and distal pulses strong

Labs/Imaging:
- BMP: Na 142, K 3.9, BUN 29, creat 2.9
- TSH: normal
- UA: 100 protein, no RBC or casts
- Echo: normal with no LVH
Renal u/s: “...small dense right kidney with no visualization of the left kidney...”
Diagnosis?

Unilateral renal artery stenosis with congenital absence of contralateral kidney

Pearls:

1. Family history is important, especially in pediatric HTN
2. Check K and creat before starting and 2-3 weeks after starting and ACEI/ARB
3. Even when essential HTN seems the likely cause, children with HTN need extensive workup including renal and cardiac imaging as well as labwork
Patient #9

“AVM Annie”

- 51y/o WF referred in 12/2011 for severe HTN over the previous 2 months
- On 8/28/11, pt underwent embolization of a large renal AVM by IR/Urology for severe hematuria
- In 11/11, began having HA’s and SBPs >200
- Subsequently tried on multiple agents, yet BP remained refractory

**Meds:**
Nifedipine 90mg qd, KCl 20mEq tid

**Physical Exam:**
- BP: 148/100 RA, 150/102 LA
- P: 80, Ht: 5’ 6”, Wt: 184#

**Labs/Imaging:**
- BMP: normal
- UA: normal
- Images from outside show an AVM occupying nearly ½ of her R kidney

- Plasma renin activity 40.13 ng/ml/hr
  (normal 0.15 – 2.33)
- Aldosterone 43.8 ng/dl (normal 1 -16)
Diagnosis?

HTN due to hyper-reninism with secondary hyperaldosteronism from partial renal hypoperfusion

Pearl:

1. Renovascular hypertension can be present in many forms, not just renal artery stenosis

2. Dr. Guyton was a pretty smart guy
Patient #10

“Biker Billy”

- 11y/o WM referred by pediatrician because of BP’s consistently 95th-99th%ile over last two months
- BP’s initially found to be elevated during 6/2011 hospitalization for femur fracture (from a motorcross accident) and were thought to be elevated due to pain
- Very active with no hypertension in either parent
- No stimulant meds or drugs

**Meds:**
- none

**Physical Exam:**
- **BP:** 134/88 RA, 138/84 LA, 120/76 RL, 120/74 LL
- **Gen:** WDWNWM in NAD
- **CV:** RRR without mgr, no abd bruit; distal pulses intact with no edema

**Labs/Imaging:**
- **BMP:** normal
- **CBC:** normal
- **TSH:** normal
- **UA and tox screen:** normal
- **EKG and Renal U/S:** normal
Patient #10  “Biker Billy”

Echo:
1. Bicuspid aortic valve without stenosis
2. Myxomatous mitral valve
3. Moderate concentric LVH
Diagnosis?

Coarctation of the Aorta

Pearls:

1. Always get 4-extremity BPs in children
2. Always get an echo in children with elevated BPs
3. High incidence of bicuspid aortic valve with coarct
Patient #11

“Thyroid Tom”

- 36y/o WM referred by PCP in 5/2012 because of recent BP spikes and refractory hypokalemia
- History of medullary thyroid ca in 2007, now s/p total thyroidectomy
- Significant increase in LE edema recently but no SOB, PND, or orthopnea
- No episodes of flushing, palpitations, or severe diaphoresis
- Recent hospitalization at MD Anderson where K was found to be 1.4 with normal sodium

**Meds:**
Lisinopril 40mg bid, Furosemide 40mg bid, KCL 80mEq bid, Amlodipine 10mg qd, Metoprolol 100mg qd, Levothyroxine 175mcg qd

**Physical Exam:**
- BP: 180/104 RA, 184/106 LA
- Gen: thin WM in mod discomfort
- CV: RRR without mgr, no abd bruit; distal pulses intact with 2+ edema throughout
- Skin: very thin, friable, pink striae on abd

**Labs/Imaging from PCP:**
- BMP: K 2.8, Na 141, creat 0.7, Mg 1.8, Ca 7.6
- TSH: normal
**Patient #11**  

“**Thyroid Tom**”

### Differential Dx:
- Hyperaldo
- Liddle’s
- Recurrent thyroid ca
- MEN?

### Additional Labs:
- "Thyroid Tom"
  - Renin: normal
  - Aldo: normal
  - Plasma free mets: normal
  - 24 hr free cortisol: 8611 ug/24hr (0-50)
  - ACTH: 110 pg/mg (7-63)

### Additional Labs – Part 2:

<table>
<thead>
<tr>
<th>Feature</th>
<th>MEN 1</th>
<th>MEN 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Eponym: Wermer syndrome</td>
<td>Sipple syndrome</td>
</tr>
<tr>
<td></td>
<td>OMIM: 131100</td>
<td>171400</td>
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<tr>
<td>Pancreatic tumors</td>
<td>gastrinoma (50%(^7)), insulinoma (20%(^7)), vipoma, glucagonoma, PPoma</td>
<td>-</td>
</tr>
<tr>
<td>Pituitary adenoma</td>
<td>66%(^7)</td>
<td>-</td>
</tr>
<tr>
<td>Angiofibroma</td>
<td>64%(^8)</td>
<td>-</td>
</tr>
<tr>
<td>Lipoma</td>
<td>17%(^8)</td>
<td>-</td>
</tr>
<tr>
<td>Parathyroid hyperplasia</td>
<td>90%(^7)</td>
<td>50%(^7)</td>
</tr>
<tr>
<td>Medullary thyroid carcinoma</td>
<td>-</td>
<td>100%(^7)</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>-</td>
<td>&gt;33%(^7)</td>
</tr>
<tr>
<td>Marfanoid body habitus</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Mucosal neuroma</td>
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</tr>
</tbody>
</table>
Diagnosis?

Recurrent medullary thyroid carcinoma causing Cushing’s Syndrome from ectopic ACTH

Pearls:

1. Unprovoked severe hypokalemia in the face of severe hypertension is usually a sign of an endocrine abnormality

2. Plasma free metanephrines are best screening test for pheochromocytoma

3. Don’t throw away your Harrison’s text book
Patient #12

“British Betty”

Meds:
Lisinopril 40mg qd, HCTZ 12.5mg qd,
Clonidine 0.2mg bid, Nifedipine 60mg qd

Physical Exam:
BP: 176/80 RA, 174/84 LA
P: 68, Ht: 5’ 9”, Wt: 148#
Gen: WDWNWF in NAD
Normal physical exam

Labs/Imaging:
BMP: normal
CBC: normal
UA: normal
TSH: normal
Renin and aldo: normal

- 54 y/o WF referred by USM employee health due to severe HTN
- Pt originally from England, and moved to U.S. 2 years ago
- Reports her HTN was severe when living in London but improved significantly after moving to U.S. and was able to get to monotherapy
- Says she has been very homesick lately
Patient #12  “British Betty”
Diagnosis?

11β-Hydroxysteroid Dehydrogenase Type 2 Inhibition from Glycyrrhetinic Acid

Pearls:

1. Dietary history is very important
2. When in Europe, stay away from the licorice
When medications aren’t enough

Resistant Hypertension

Secondary Hypertension

Pseudo-resistance
Objectives

• Briefly review JNC-7 guidelines
• Review clinical trial data published after JNC-7
• Evaluate hypertension guidelines from organizations other than JNC
• Examine an approach to resistant hypertension
• Learn about emerging options for hypertension treatment
Emerging non-pharmacologic treatments for hypertension:

- Gene-based therapy
  - Antisense cDNA against ACE and AT1 receptor
  - Virus-based delivery system
- Vaccination against Ang1 & Ang2
  - Mixed results in animal models
- Device-based interventions
  - Carotid baroreceptor activation
When medications aren’t enough

Rheos® by CVRx)
When medications aren’t enough

Device Based Therapy of Hypertension (DEBuT-HT)

Baseline 3 mo 1 yr 2 yrs

SBP

DBP

Pulse
Emerging non-pharmacologic treatments for hypertension:

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  - Device-guided breathing
When medications aren’t enough
When medications aren’t enough

Schein MH et al. J Hum Hypertens 2008
Emerging non-pharmacologic treatments for hypertension:
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- Vaccination against Ang1 & Ang2
  - Mixed results in animal models
- Device-based interventions
  - Carotid baroreceptor activation
  - Device-guided breathing
  - Renal artery sympatheticotomy
Afferent Renal Sympathetics

The kidney is a source of central sympathetic drive in hypertension, heart failure, chronic kidney disease, and ESRD

Efferent Sympathetic Activation

Patients cannot develop and/or maintain elevated BP without renal involvement

- ↑ Vasoconstriction
- ↓ RBF/GFR
- ↑ Renin
- ↑ Na⁺/Volume
- ↑ HR
- ↑ Contractility
When medications aren’t enough
When medications aren’t enough
To date, over 2,000 patients in Europe and Australia have been treated with this procedure. Over 275 patients treated in HTN-1 and HTN-2 trials, and HTN-3 trial is currently active in U.S.
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Questions?