

Practical Aspects of Hypertension: Simple Strategies to Help You and Your Patients Meet Guideline Blood Pressure Targets

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Conflict of Interest Disclosure

None

Learning Objectives

1. Understand the pharmacology of common classes of blood pressure lowering medications and how to use them more effectively
2. Recognize isolated systolic hypertension as a unique entity with specific issues in the elderly and cardiac patients and know which drugs work best/less well
3. Understand the issues surrounding resistant hypertension and recognize common causes before ordering expensive tests and procedures to rule out rare conditions

CASE: Newly Diagnosed Hypertensive

- 42 yr male is referred for BP of 150/95 mmHg
 - Positive family Hx for HTN and premature CAD
 - No clinical evidence of target organ injury
 - Routine testing is normal; A1C and LDL are also normal

Advise: HBPM measurements twice/d for 2 wks

- F/U in 2 wks, office and home measurements; BP still 150/95 in office, 145/90 at home

Advise: Start ramipril 5mg/d

- Returns 2 wks later with office BP 150/95

How long to see the full anti-hypertensive effect of monotherapy with a BP-lowering medication?

- 4-6 wks for most agents, 2 wks for combination products
DISTINCT RCT & Suppl data. Kjeldsen SE. J Hypertens 2014; 32:2488-98

- More rapidly-acting drugs for use in HE/HU

Intravenous

Nitroprusside 0.5 - 10 µg/kg/min continuous IV infusion

Labetalol 20 mg IV every 10 min to a total of 300 mg

Hydralazine 10 - 20 mg IV every 4 - 6 hours

Oral

Clonidine 0.2 mg loading, 0.1 mg bid to follow

Labetalol 100-300 mg bid

Adalat XL 60 mg

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NOTE: ACEi are on neither of these lists WHY???

Is it better to change to another anti-hypertensive drug class, increase the dose or add a second agent?

- Many anti-hypertensive agents have flat dose response curves
 - Thiazide Diuretics
 - ACEi/ARBs

Heran BS. Cochrane Database Systematic Review 2008 Oct 8;(4):CD003823.

Li EC. Cochrane Database Systematic Review 2014 Aug 22;(8):CD009096.

- Several RCTs examining doubling the dose versus adding a second agent show clear superiority for adding on another treatment

Don't Combine Agents Having the Same Mechanism of Action

RAAS Blockers

Don't combine an ARB with an ACEi

Vasodilators

Don't combine hydralazine with a CCB

Diuretics

Do combine thiazides & potassium-sparing diuretics

Anti-adrenergics

Do combine alpha & beta-blockers

Do combine central & peripherally-acting sympatholytics

Other Pearls

A diuretic should be part of every multi-drug anti-hypertensive regimen

Beta-blockers are effective renin inhibitors

In addition to 1st line, use as 3rd or 4th line instead of more expensive direct renin inhibitors (aliskiren)

Alpha-1 blockers have adverse outcome data

Nitrates do not dilate arteries and are not effective BP-lowering medication unless levels are 20x usual [nitrate] (used intra-arterially)

What is the recommended treatment target for this particular patient?

- Office < 140/90 and/or home < 135/85 mmHg
- Office <130/80 mmHg
- Office sBP < 120 mmHg

2018 Hypertension Canada Guidelines

Patient Population	BP (mmHg) Threshold to Initiate Drug Rx*	BP (mmHg) Target*
Low risk (No TOD or CVRF)	sBP \geq 160 (Grade A) dBP \geq 100 (Grade A)	sBP < 140 (Grade A) dBP < 90 (Grade A)
High-risk	sBP \geq 130 (Grade B)	sBP < 120 (Grade B)
Diabetes Mellitus	sBP \geq 130 (Grade C) dBP \geq 80 (Grade A)	sBP < 130 (Grade C) dBP < 80 (Grade A)
All others	sBP \geq 140 (Grade C) dBP \geq 90 (Grade A)	sBP < 140 (Grade A) dBP < 90 (Grade A)

* If using HBP or daytime ABPM, subtract 5 mmHg

High-risk Adult Candidates for Aggressive BP Lowering

1. Clinical or subclinical cardiovascular disease, or ...
2. CKD (non diabetic, proteinuria < 1 gm/d, GFR (MDRD) 20-59 ml/min/1.73m²), or ...
3. Estimated Framingham 10-yr global risk ≥ 15%, or ...
4. Age ≥ 75 yrs

CASE: Ms. Elderly Hypertensive

74 yr. old female

HTN for 10 yrs, BP labile 150-210/60-90

Many meds; ineffective or with adverse effects;
now on Bisoprolol 5 mg od

No history or symptoms of prior CV disease

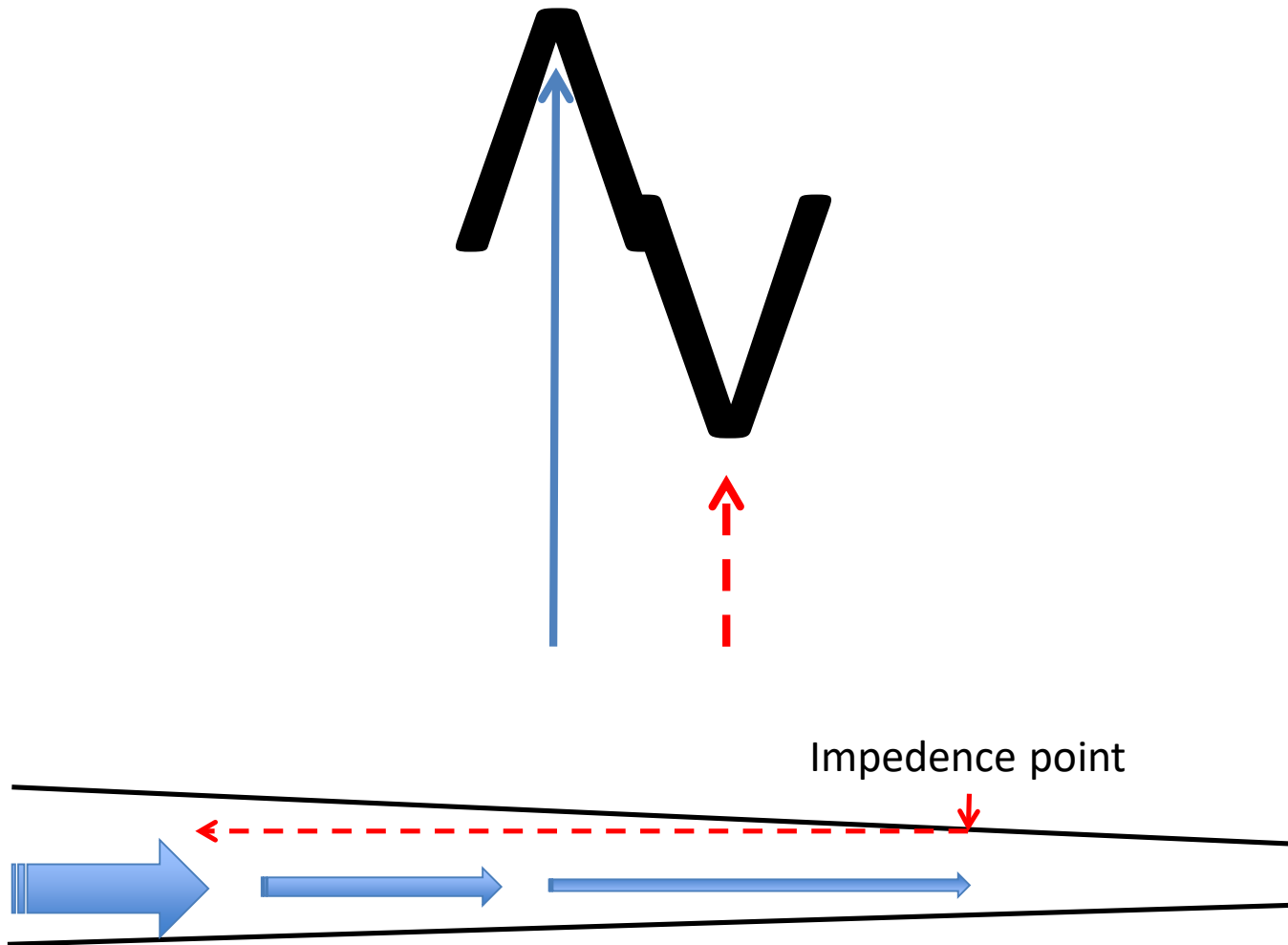
Non smoker, no EtOH

No family history of HTN or CVD

EXAMINATION

HR 50 bpm BP 160/70 supine, 100/55 upright
with orthostatic Sx

Isolated Systolic Hypertension is due to thickening and hardening of the large conduit arteries



Windkessel Effect

$$\text{MAP} = \text{CO} \times \text{TPR}$$

***Variability is the hallmark of ISH

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Stiff arteries may lead to systematic error (increases) in the measurement of BP

Pseudohypertension

TREATING ISH

- Start with a diuretic or a long-acting dihydropyridine calcium channel blocker
- Use low dosages and increase slowly
- Avoid beta blockers, unless indicated for other reasons, as these may worsen BP control
- Other drugs can work if used in combination
- Watch for orthostatic hypotension. The mortality and morbidity from falls in the elderly may be greater than the benefit derived from BP lowering

CASE: Difficult to Control Hypertension

53 yr male admitted HTN Emergency Feb 2008

BMI 28.8, BP 214/185mmHg, grade III retina

Follows a low Na⁺ diet, minimal EtOH

No OTC meds of interest

OSA on nightly CPAP

Echo LVH, K⁺ chronically 3.1

1.3x1.2 mass (L) adrenal, 24Hr urine for metanephrine N x 2

MRA kidneys normal

Aldo 552pM/L, Renin 0.46mg/L/sec, ARR 1200 (N)

24Hr urinary cortisol & AM cortisol (N)

Stabilized on HCTZ 25/Adalat XL 30/Lisinopril 20 bid

Feb' 10 BP 132/82; is now diabetic/nephropathy. GP has started metformin 500 tid + repaglinide 2 tid

Jun'11 BP 153/93 ???

What is the issue here?

Definition:

Blood pressure that remains above goal in spite of the concurrent use of 3 antihypertensive agents of different classes. Ideally, 1 should be a diuretic and all agents should be prescribed at optimal doses.

AHA Scientific Statement. Hypertension 2008;51:1403-1419

Resistant Hypertension

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graph TD; A[Resistant Hypertension] --> B[Pseudo-Resistant HTN]; A --> C[True Resistant HTN];
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Pseudo-Resistant HTN

Error in BP Measurement

- Improper cuff size

- Improper measurement technique

Whitecoat Hypertension

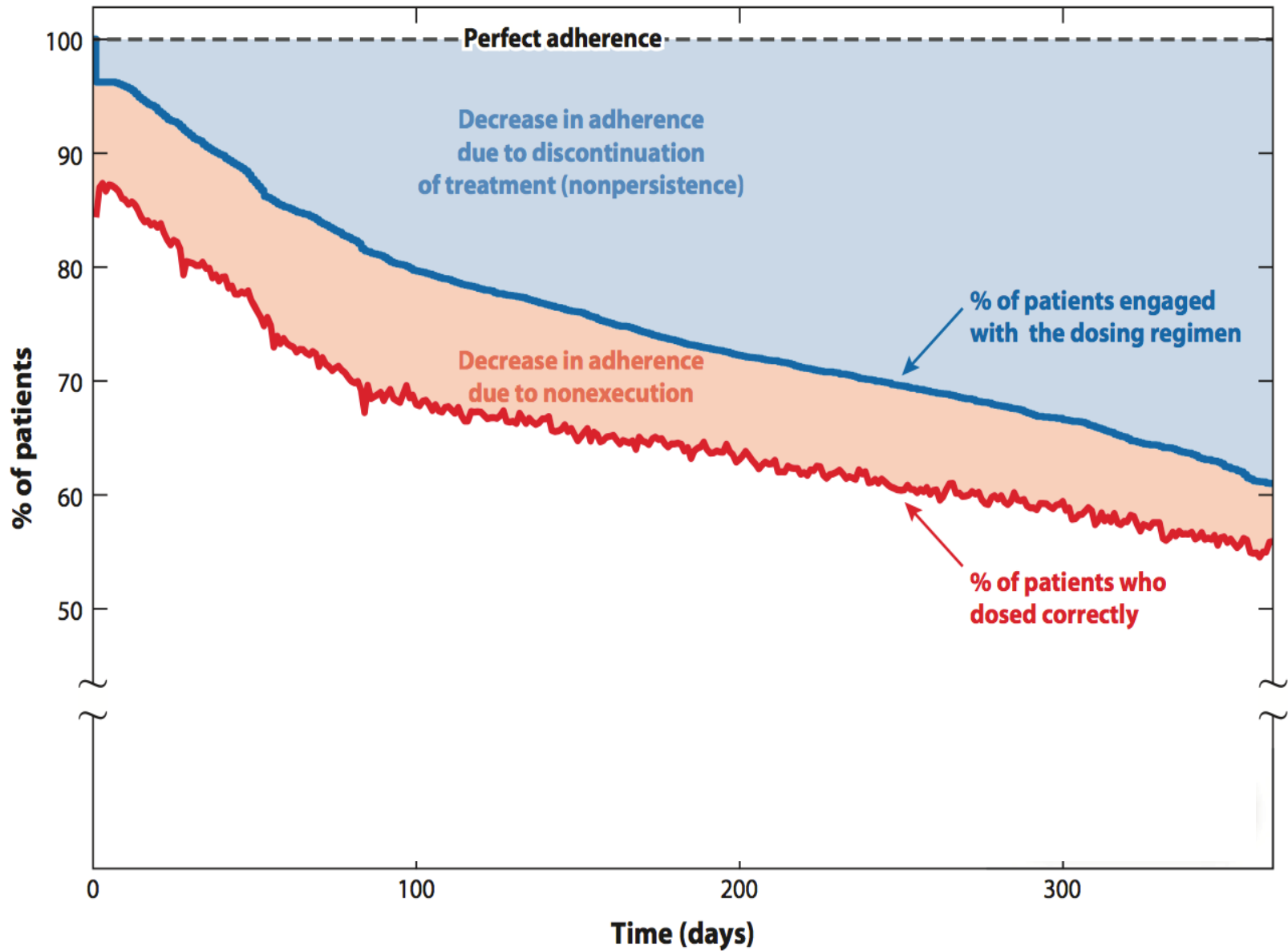
Non Adherence / Non Compliance

- Patient factors

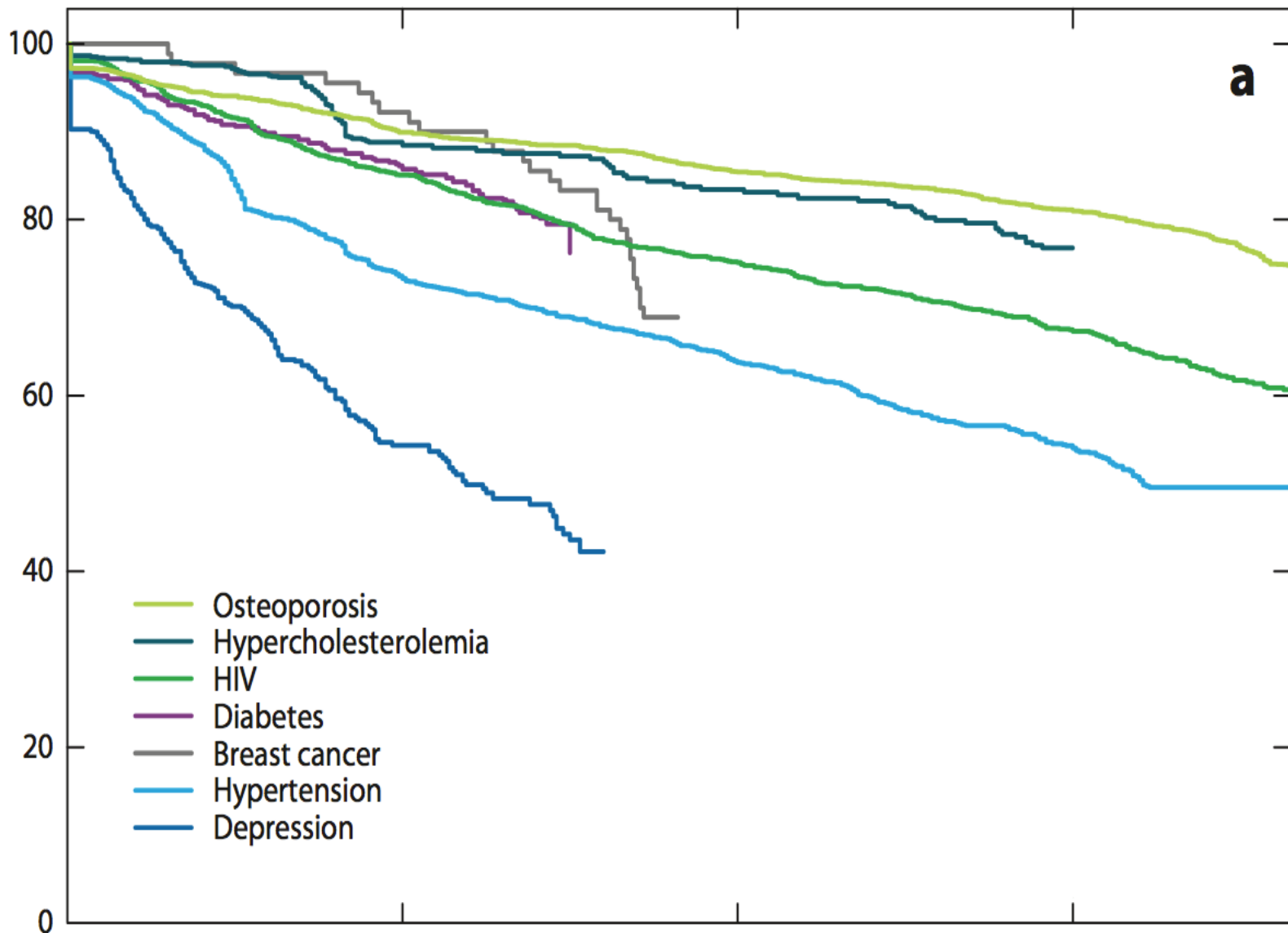
- Physician factors

Drugs that ↑ BP or interfere with
BP-lowering medication

True Resistant HTN



Blaschke. Ann Rev Pharmacol Tox 2012; 52:275-301



True Resistant Hypertension

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graph TD; A[True Resistant Hypertension] --> B[Secondary HTN]; A --> C[Rare endocrine disease  
Other uncommon causes];
```

Secondary HTN

OSA

Renal vascular or
parenchymal disease

Metabolic Syndrome

Hypo/Hyperthyroidism

Primary Aldosteronism

Rare endocrine disease
Other uncommon causes

Start with Lifestyle Interventions

Limit Sodium intake to < 2000 mg/d (5 gm salt)

Exercise 40 min/d 5 days out of 7

Weight control

Smoking cessation (2 yrs to risk of a non smoker)

Limit EtOH consumption

Optimize Diuretic Treatment by Switching to a Long-acting Thiazide

Chlorthalidone PK properties:

longer $t_{1/2}$, 3-fold greater potency/duration of action

Clinical trials:

HDFP, ALLHAT, SHEP all used chlorthalidone; multiple studies of HCTZ, but only in combination products

Head-to-head comparison of chlorthalidone vs HCTZ:

ABPM greater 24 hour BP lowering effect at night

No comparison of cardiovascular outcomes in the literature

Ernst ME et al. Hypertension 2006;47:352-8

Spironolactone

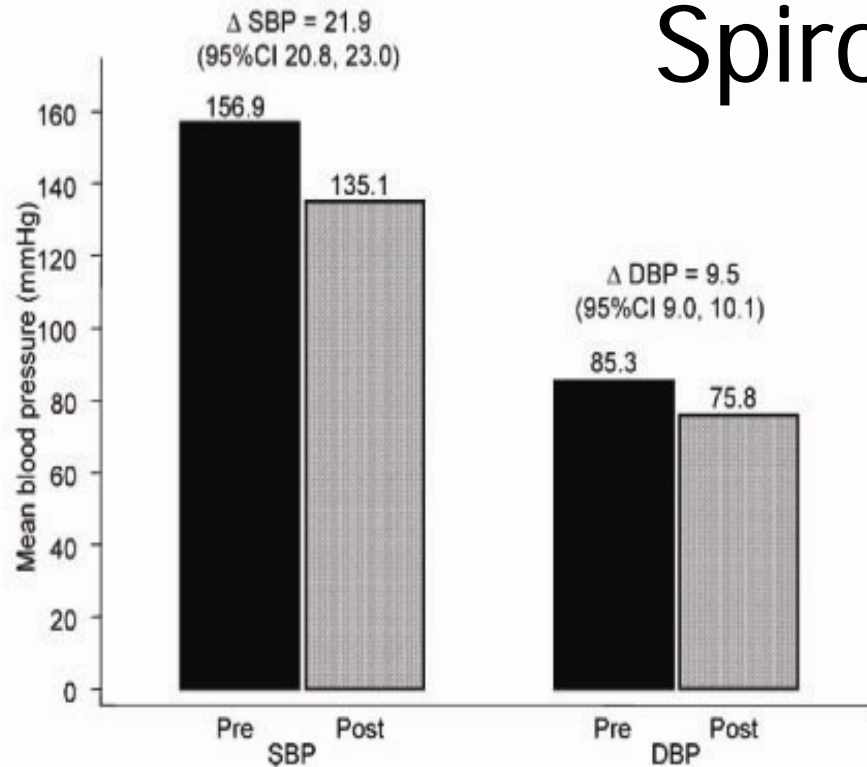


Figure 2. Mean BP before and during spironolactone treatment. Effect in 1411 ASCOT participants who received spironolactone for treatment of high BP with available BP measurements before (pre-), and during (post-), spironolactone treatment.

2012 Cochrane Review:

Chapman N et al. Hypertension 2007; 49: 839-845

- *five crossover RCTs*
- *mean BP decreases of 20/7 mmHg*
- *no DRAE at Spironolactone doses below 100 mg/day*
- *no data on clinical outcomes*

Spirolonolactone

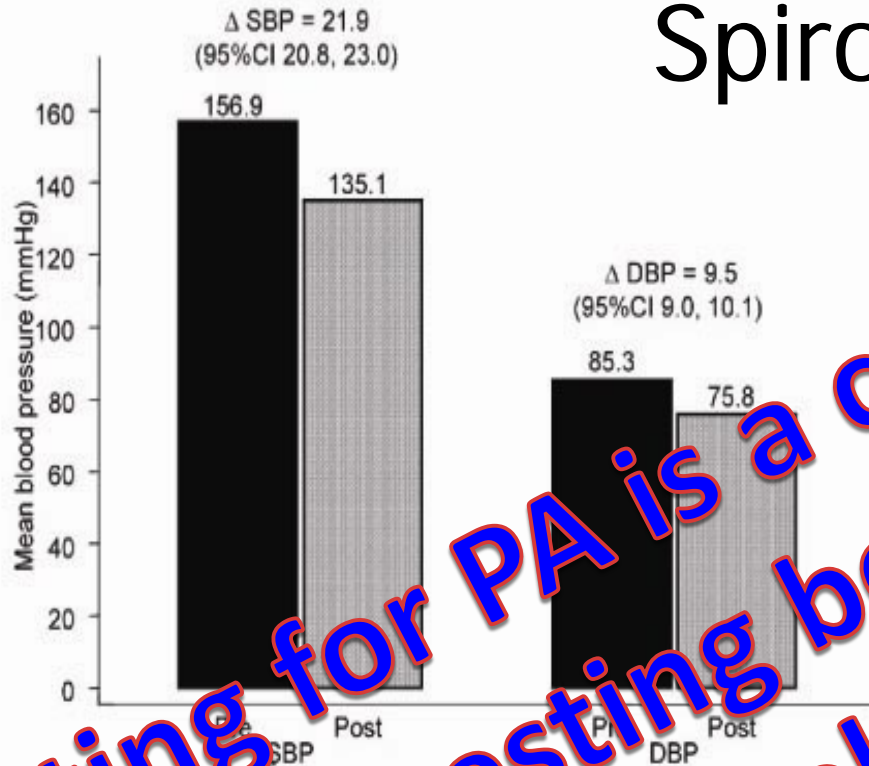


Figure 1. Mean BP before and during spironolactone treatment. Effect in 1411 (95% CI) participants who received spironolactone as treatment of high BP with available BP measurements before (pre-), and during (post-), spironolactone treatment.

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If testing for PA is a consideration, do your testing before starting Spironolactone

Lower on the List, in Combination Rx

Increase the dose of the CEB

Clonidine

Low dose, 0.1 mg bid

Beta-blockers

These are renin blockers

Labetalol has added α_1 -blockade

Alpha blockade

Doxazosin: Caveat - withdrawn from ALLHAT because
of adverse outcomes

Adapted from Resistant Hypertension, presented by K. Zarnky
Rocky Mountain/ACP Internal Medicine Meeting 2011

Summary: Investigation & Treatment RHTN

1. Confirm the BP measurement
2. Evaluate non-adherence
3. Identify interfering meds/other agents causing HTN
4. Screen for secondary causes (esp CKD, Metabolic Syndrome, HoThy, OSA, PA)
5. Address lifestyle issues
6. Optimize antihypertensive therapy
 - Add or switch to chlorthalidone 12.5 mg/d
 - Add spironolactone 12.5-25 mg/d
7. Follow, follow & follow up, again ... consider **Testing**

Our Patient with resistant HTN, continued ...

- Jun'11 BP 153/93; Creat 129; started spironolactone 25 → 12.5 mg b/o breast effects
- Oct'12 BP 145/90; switch HCTZ → chlorthalidone 12.5 mg/d
- Jan' 13 BP 122/84; Creat 218
- Jan' 18 gets an itchy red rash?

My Last Pearl ...

Ethacrinic acid is loop diuretic that is not a sulphonamide-derivative

Discussion and Questions